THE **CROATIAN CHEMICAL SOCIETY**
PROUDLY PRESENTS

THE COMPILATION OF THIS YEAR'S NEW

SOLUTIONS IN CHEMISTRY

8–11 November 2022 • Sveti Martin na Muri, Croatia

INTERNATIONAL CONFERENCE RECOGNISED BY THE **EUROPEAN CHEMICAL SOCIETY** (EuChemS)

BOOK OF ABSTRACTS

SOLUTIONS IN CHEMISTRY 2022
8–11 November 2022

Hotel Terme Sveti Martin☆☆☆☆
Sveti Martin na Muri, Croatia

BOOK OF ABSTRACTS

IMPRESSUM

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UNDER THE AUSPICES OF

Zoran Milanović, President of the Republic of Croatia

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Ministry of Science and Education of the Republic of Croatia

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Welcome from the Chairmen of the Organising Committee

On behalf of the Organising Committee, it is our great pleasure to welcome you to the Solutions in Chemistry 2022 conference taking place in Sveti Martin na Muri from 8 to 11 November 2022. The focus of the Conference organised by the Croatian Chemical Society can be deduced from the two meanings of the word "Solutions" in its title. The first one refers to the solution as a phase and comprises the experimental and computational studies of the processes occurring in liquid media. The second one is concerned with general solutions to chemical problems which are met in academia and various branches of industry. Thus, the Conference aims to gather the scientists dealing with different fields of chemistry and to deepen and strengthen the collaboration of the experts from universities, research institutes, schools, and industrial companies.

A number of plenary, invited, and section lectures will be delivered by top-tier scientists, and various sponsor presentations and workshops will be held as well. These will provide a new insight into the current problems in chemical science and industry, and an opportunity to learn and obtain new skills from prominent chemists and entrepreneurs. In addition, the Conference participants will have a chance to find out more about the newest instruments and consumables available from our numerous sponsors, exhibitors, and donors to whom we are grateful for their support. The poster session will give everyone the opportunity to present their work: from undergraduate students to experienced scientists in diverse fields of chemistry and chemical engineering. The education section will be held in parallel, focusing on finding new solutions in teaching new generations of chemists.

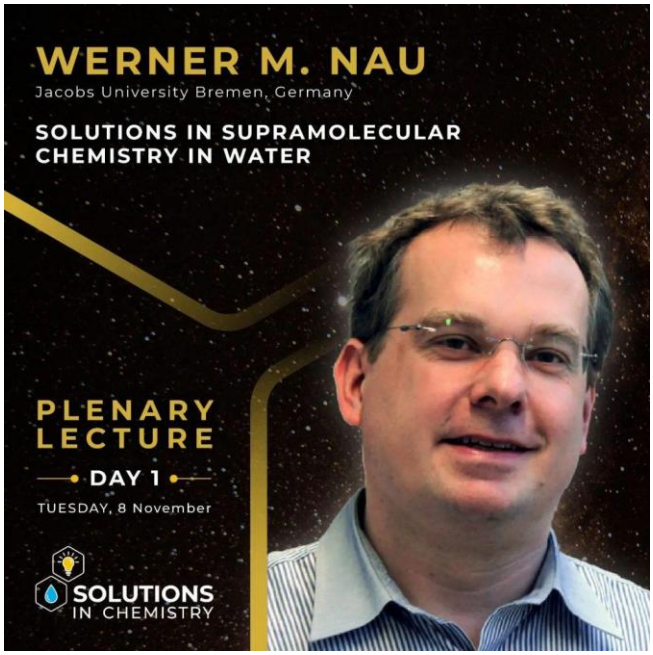
A significant emphasis will also be put on an irreplaceable part of every great conference: social activities. Thus, we plan to organize various social events and encourage the participants to interact in a non-formal manner as well as to take the opportunity to discover the beauty of the picturesque Međimurje County and taste the local delicacies.

LET'S FIND THE NEW SOLUTIONS IN CHEMISTRY!

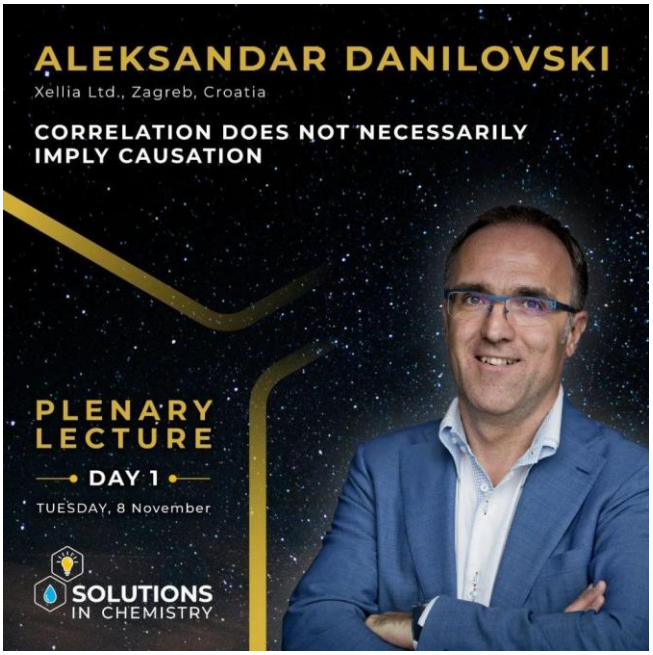
Ernest Meštrović & Vladislav Tomišić

PLENARY LECTURERS

(IN CHRONOLOGICAL ORDER)



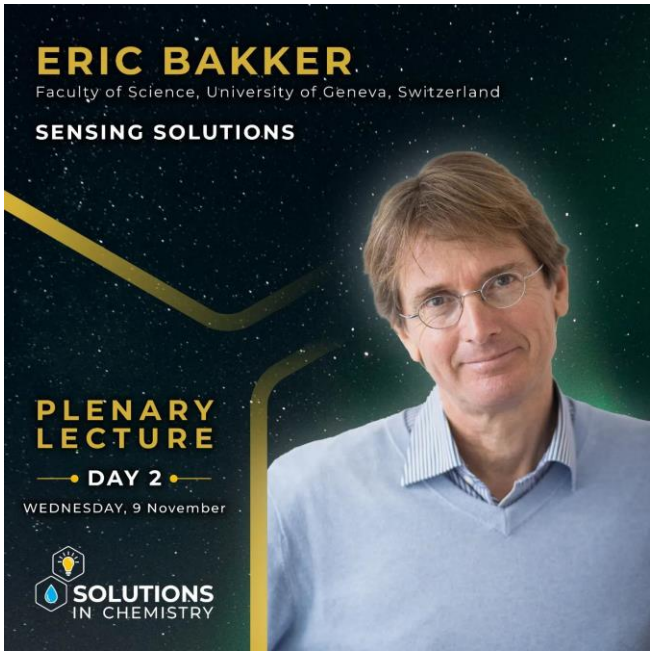
Professor **Werner M. Nau** obtained his MSc in 1991 at St. Francis Xavier University, Canada, and his PhD in 1994, at the University of Würzburg, Germany. He was a postdoctoral researcher at the University of Ottawa, Canada, and became an Assistant Professor at the University of Basel, Switzerland. Since 2002, he is a Professor of Chemistry at Jacobs University Bremen (Germany), and, since 2011, Dean of the faculty. Prof. Nau has held visiting professorships at the University of Wisconsin-Madison (USA), the University of Cambridge (UK), the University of Huelva (Spain), and the Institute of Chemical Research of Catalonia (Spain). His research combines principles of organic photochemistry with spectroscopy and supramolecular chemistry and is directed towards applications in bioanalytical chemistry, peptide folding, drug delivery, drug discovery, catalysis, chiral recognition, fluorescent dye design, chemosensing, as well as enzyme and membrane assays. His research is published in ca. 300 research publications, 6 book chapters, and 4 patents. Prof. Nau received several scientific awards; the Grammaticakis–Neumann Prize of the European Photochemistry Association (2000), the ADUC-Jahrespreis für Habilitanden (2000), the Werner Prize 2002 of the Swiss Chemical Society, and the EPA-PPS Prize 2010. He has served, among others, as President (2012-2014) of the European Photochemistry Association (EPA) and Vice Chairman (2010–2013) of the Photochemistry Section of the German Chemical Society.



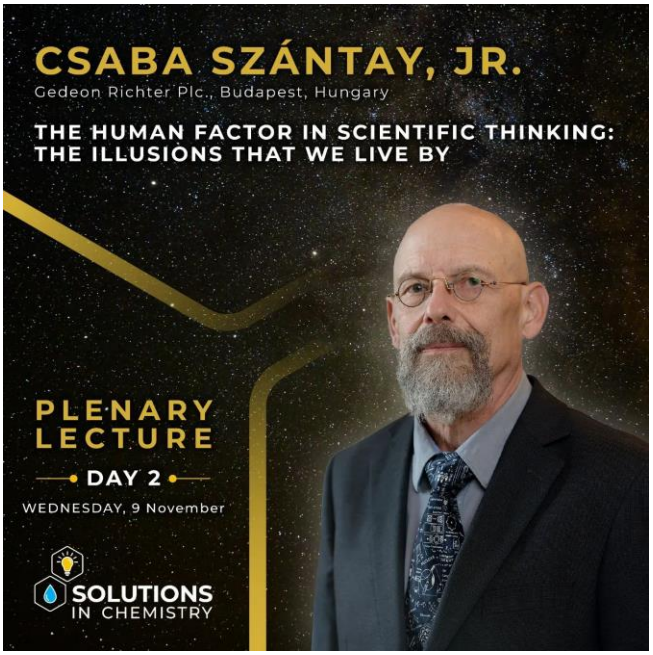
Dr **Aleksandar Danilovski** obtained his MSc in chemistry in 1997 at the Faculty of Science, University of Zagreb, and his PhD in 2001 at the same faculty. He started his career in the industry at the PLIVA Research Institute, where he was a member of the Management Board for 20 years. In 2009 he held the position of Senior Vice President of the Management Board XELLIA Pharmaceuticals (Denmark), and the position of Chief Scientific Officer (CSO), which he still holds today. In 2011, he founded the research company XELLIA Ltd. (Croatia) where he is the Managing Director. Dr Danilovski is one of the co-founders of a biotechnology start-up company (Pharmaero, Denmark). He is a member of the Board of Directors in Pharmaero (Denmark), of the Scientific Selection Board in Novo Holdings, REPAIR Impact Fund (Denmark), of the Board of Directors in Active Biotech (Sweden), and of the Scientific Advisory Board in Bugworks (USA/India). In 2017, he was elected as a member of the Committee for Chemistry of the Croatian Academy of Sciences and Arts, and since 2018 he is a member of the Croatian Academy of Engineering. Dr Danilovski led the research and development, registration and launch on the global market (US and EU) of more than 100 different active substances and over 200 different finished pharmaceutical products of which several innovative and patent-protected medicines with added value.

PLENARY LECTURERS

(IN CHRONOLOGICAL ORDER)



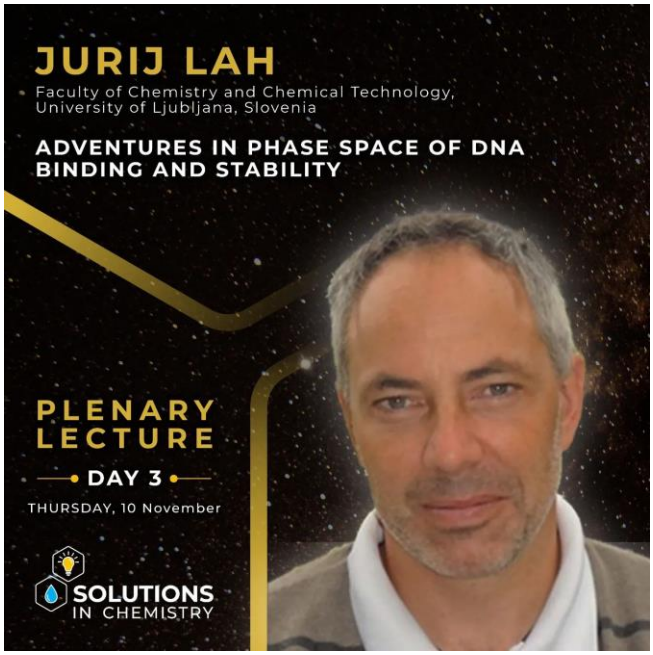
Professor **Eric Bakker** was educated at the Swiss Federal Institute of Technology (ETH) in Zurich, Switzerland and earned his PhD in 1993. He spent many years in the United States and Australia before moving to the University of Geneva in Switzerland where he is a professor of analytical chemistry. His research interests are in the area of chemical sensors for environmental (aquatic) and biomedical applications. The main emphasis is the development and understanding of electrochemical and optical sensing principles, often using membrane transport, complexation, and extraction phenomena. New principles and materials are developed, prototype instrumentation is engineered, and their use is tested in the final sample environment of interest, making this research quite broad in scope. His research group has published nearly 400 highly cited research papers. Prof. Bakker also serves as the Executive Editor of the journal ACS Sensors.



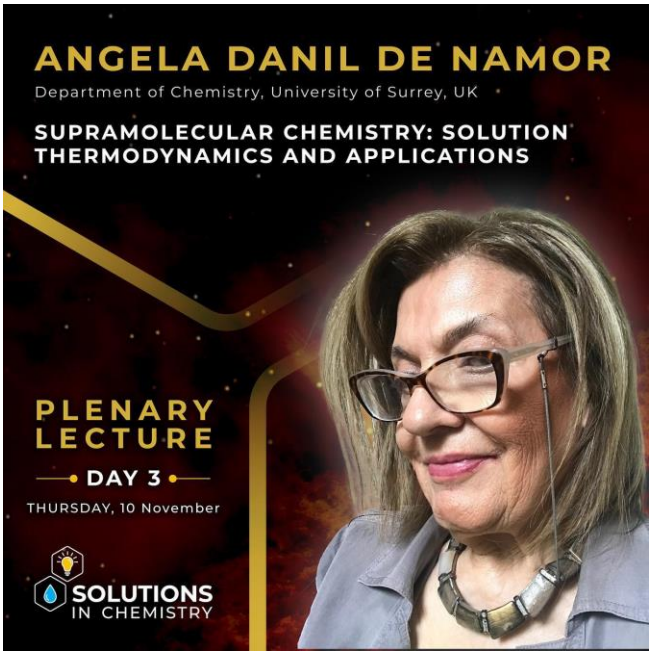
Professor **Csaba Szántay, Jr.** received his MSc in chemical engineering at the Technical University of Budapest in 1982, where he obtained his PhD in 1986. He was a postdoctoral fellow at Leeds University (UK) in 1988, and after he continued his work as an NMR spectroscopist in the Spectroscopic Research Department of Gedeon Richter Plc., Hungary's largest pharmaceutical company. Since 1994 he has been the Head of this department. He and his team are committed to maintaining strong ties with academia in terms of education as well as research collaborations. Prof. Szántay habilitated at the TUB in 2002, and in 2003 elected to be a Private Professor at the same university. His main fields of research are the physical and mathematical theory of NMR spectroscopy and the application of high-resolution NMR in the structure determination of organic molecules. He obtained from the Hungarian Academy of Sciences a Candidature in 1991 and a Doctor of Sciences title in 2000. One major project of his that transpired from blending philosophy, psychology, physics, mathematics, and applied NMR and MS, was published worldwide as a book (Anthropic Awareness: The Human Aspects of Scientific Thinking in NMR Spectroscopy and Mass Spectrometry. New York: Elsevier, 2015.). He has published around 190 original scientific papers, including three books. He also holds numerous high-ranking positions in various scientific committees and institutions, as well as in several foundations aimed at supporting the teaching of natural sciences in elementary and secondary schools.

PLENARY LECTURERS

(IN CHRONOLOGICAL ORDER)



Professor **Jurij Lah** obtained his PhD in Chemistry in 2000 at the Faculty of Chemistry and Chemical Technology, University of Ljubljana (UL FCCT), Slovenia. He was a postdoctoral researcher at the Vrije Universiteit Brussel (VUB), Belgium. Since 2013, he is a full professor in charge of courses Physical Chemistry, Biophysical Chemistry, Chemical Thermodynamics and Biomolecular Thermodynamics at the Faculty of Chemistry and Chemical Technology, University of Ljubljana, Slovenia. Prof. Lah is a distinguished lecturer, awarded four times (in 2004, 2011, 2018, and 2020) for the best lecturer at the UL FCCT. He is very active in the popularisation of science through interviews, lectures, and cover pages. He is currently principal investigator in several basic research projects and projects with the pharmaceutical industry. His main research areas include different topics related to thermodynamic stability, interactions, and structural features of biologically important molecules in relation to their function, and his recent research is focused on describing the behaviour of non-canonical nucleic acids and intrinsically disordered proteins. Prof. Lah publishes research results in reputable journals (*PNAS*, *Angew. Chem*., *JACS*, *Nucleic Acids Res*., etc.). He was awarded in 2014 for outstanding research achievements in chemistry and related sciences, and in 2019 he received Zois Award for Outstanding Achievements in Physical Biochemistry.



Professor **Angela Danil de Namor** is the first female professor of chemistry at the University of Surrey, UK. She graduated in biochemistry at the National University of the South, Bahia Blanca, Argentina and in 1973 obtained a PhD in chemistry at the University of Surrey, UK. After postdoctoral research sponsored by Unilever Research Laboratories, she joined the Department of Chemistry in 1977 where she is now an emeritus professor of physical chemistry. Her research interest is in the area of solution thermodynamics involving mostly supramolecular systems; solution thermodynamics of electrolytes, cyclodextrins and calix-based receptors, their interaction with ionic and neutral species and their broad applications. She published more than 170 papers in prestigious chemical journals and supervised over 50 PhD students. She has coordinated several EU contracts involving Partners from Europe, Latin America, Africa, and Middle East Countries. Prof. Danil de Namor has received numerous awards and recognitions; the Doctor Honoris Causa from three Universities in South America for contributions given to the development of chemistry in Latin America, fellow of the Royal Society of Chemistry and fellow of the International Union of Pure & Applied Chemistry (IUPAC), emeritus fellowship from the Leverhulme Trust (2014). She was the first foreign woman elected member of the National Academy of Sciences of Argentina and in 2021 Prof. Danil de Namor was awarded the Doctor of Science degree by the University of Surrey for proven evidence of the international impact of her research to advances in the discipline, following the thesis entitled “Supramolecular Chemistry: Personal Contributions to the Discipline”.

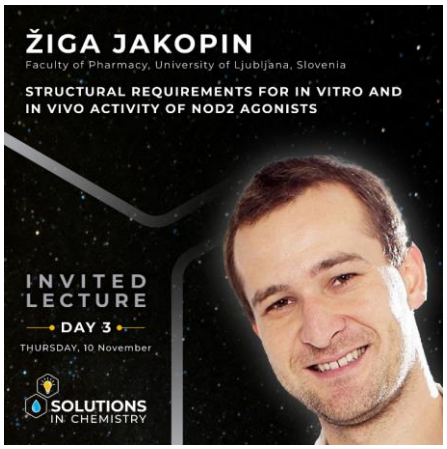
PLENARY LECTURERS

(IN CHRONOLOGICAL ORDER)

Dr **Nicoletta Ravasio** graduated in chemistry at the University of Milano (Italy) in 1982, and in 1987 obtained PhD in chemical sciences at the University of Bari, Italy. She is currently the research director at the "Giulio Natta" Institute of Chemical Sciences and Technologies (SCITEC) of the National Research Council (CNR), Italy. Her main scientific interests are sustainable organic synthesis and renewable raw materials. In the field of vegetable oils, she developed a selective hydrogenation process, a process for the esterification and transesterification and a process for the synthesis of bio-lubricants. Recently she has been devoted to the valorization of agri-food waste with different added value, from building materials to cosmetics, performing even better than the fossil-based ones. Dr Ravasio is principal investigator in several national and international research projects and contracts, and the author of highly cited 164 papers and 6 patents. As a recognized expert she evaluated EU Horizon 2020-Waste 7 and Horizon2020-Bio Based Industries projects. Since 2015 she is chair of Oleochemistry, Molecule and Polymer Science division of European Federation on Lipid Science, and since 2018 a member of Technical-Scientific Committee Italian Cluster of Green Chemistry (SPRING), and a member of Team of Experts to support the High Level Roundtable on the implementation of the Chemicals Strategy for Sustainability (EuChemS). In 2021 she was awarded with the Piero Pino medal of the Italian Chemical Society "For studies of scientific, innovative and applicative relevance in the field of heterogeneous catalysis with particular attention to the substitution of noble metals in fine chemicals synthesis and to selective transformation of renewable raw materials".

INVITED LECTURES

(IN CHRONOLOGICAL ORDER)



NAGRADA Leopold Ružička

Winner of the
Leopold Ružička Award
given by the
Croatian Chemical Society

CONFERENCE PROGRAMME

DAY 1 • TUESDAY, 8 November

9:00 – 14:00	**REGISTRATION** **EARLY CHECK IN** from 12 h for guests of Hotel Terme Sveti Martin	Technobis CRYSTALLIZATION SYSTEMS **PRE–CONFERENCE WORKSHOP** (Mura III)

9:30 – 10:30	**Solubility Crystallization with Small Scale Parallel Crystallizers**
10:30 – 10:45	BREAK
10:45 – 11:45	**API Improvements through Co-Crystallization**
11:45 – 12:00	BREAK
12:00 – 12:30	**Nucleation and Induction Time Measurements**

14:00 – 14:40	**OPENING CEREMONY** (Mura Halls)	
	SECTION I (Mura Halls) (Chair: Vladislav Tomišić)	
14:40 – 15:25	**PLENARY**	**Werner M. Nau**: SOLUTIONS IN SUPRAMOLECULAR CHEMISTRY IN WATER
15:25 – 15:55	**INVITED**	**Predrag Čudić**: POTENTIAL SOLUTION FOR PEPTIDE-BASED DRUG DELIVERY TO THE BRAIN: DESIGN AND ACTIVITY OF MULTIFUNCTIONAL CYCLIC PEPTIDE–BASED ANALGESICS
15:55 – 16:15	**SECTION**	**Gordan Horvat**: Cyclopeptides as Versatile Anion Sensors in Solution
16:15 – 16:35		**Gracjan Kurpik**: Metallosupramolecular Assemblies – From Simple Complexes to Functional Nanostructures
16:35 – 17:15	**COFFEE BREAK** (in front of Mura Halls)	
	SECTION II (Mura Halls) (Chair: Ernest Meštrović)	
17:15 – 18:00	**PLENARY**	**Aleksandar Danilovski**: CORRELATION DOES NOT NECESSARILY IMPLY CAUSATION
18:00 – 18:30	**INVITED**	**Tomislav Biljan**: NMR SPECTROSCOPY AND GENERIC PHARMA R&D: PAST, PRESENT AND THE FUTURE
18:30 – 19:00	**INVITED**	**Luna Maslov Bandić**: MOLECULES BEHIND WINE TASTING
19:00 – 20:15	**DINNER BREAK**	
20:15 – 21:15	**WINE TASTING** by Štampar Winery (Restaurant Falat)	
21:15 – 22:45	**WELCOME PARTY** (Restaurant Falat)	

DAY 2 • WEDNESDAY, 9 November

8:30 – 9:45	**REGISTRATION FOR TEACHERS** (1 DAY)

	SECTION III – PART ONE (Mura Halls) (Chair: Petar Kassal)	
9:00 – 9:45	**PLENARY**	**Eric Bakker**: SENSING SOLUTIONS

	EDUCATION SECTION – PART ONE (Chair: Vladimir Stilinović)	
9:45 – 10:30	**PLENARY**	**Csaba Szántay, Jr.**: THE HUMAN FACTOR IN SCIENTIFIC THINKING: THE ILLUSIONS THAT WE LIVE BY

10:30 – 11:00	**COFFEE BREAK** (Ion Bar)

MORNING SECTIONS:

	SECTION III – PART TWO (Mura I + II) (Chair: Petar Kassal)	
11:00 – 11:20	**SECTION**	**Ivo Piantanida**: Triarylboranes: Novel Type of Dye for Biomacromolecules
11:20 – 11:40		**Miroslava Čonková**: From Single Molecule to Responsive Aggregate: Multiresponsive Photoswitch in Nonpolar Solvents
11:40 – 12:00		**Nikola Sakač**: Solutions for Pollutants Sensing – Surfactants, Estrogen and Glyphosate Sensors
12:00 – 12:30	**SPONSORS**	**Selvita**
12:30 – 12:40		**CAS**
12:40 – 12:50		**Labtim**
12:50 – 13:00		**Shimadzu**

	EDUCATION SECTION – PART TWO (Mura III) (Chairs: Jurica Bauer, Vladimir Stilinović)	
11:00 – 11:30	**INVITED**	**Ewald Edink**: SUPPORTING STUDENTS IN SOLVING QUANTITATIVE CHEMICAL PROBLEMS USING AN ADAPTIVE DIGITAL PLATFORM
11:30 – 12:00	**INVITED**	**Krešimir Molčanov**: CHEMISTRY IN THREE DIMENSIONS: CHIRALITY, SYMMETRY, ISOMERISM
12:00 – 12:20	**SECTION**	**Mirta Malčić**, **Suzana Lovrić**: From Old to New Towards Sustainable Development
12:20 – 12:40		**Daria Stejskal**: Innovative Approaches in Teaching Chemistry
12:40 – 13:00		**Nikola Bedeković**: Carbonated Water: Acid, Buffer or Both?

13:00 – 14:30	**LUNCH BREAK**

AFTERNOON SECTIONS:

14:30 – 15:30	**SiC × AlphaChrom PUB QUIZ** – details at the registration desk!
15:30 – 15:50	**SHORT BREAK**

	SECTION IV (Mura I + II) (Chair: Ines Topalović Piteša)	
15:50 – 16:20	**INVITED**	**Iva Rezić**: SOLVING COMPLEX PROBLEMS IN SOLUTION CHEMISTRY BY DESIGN OF EXPERIMENT
16:20 – 16:50	**INVITED**	**Nikolina Letić**: FUNDING OPPORTUNITIES IN INNOVATIVE PROJECTS FOR THE 2021–2027 PERIOD
16:50 – 17:30	**POSTER SETUP**	

	EDUCATION SECTION – PART THREE (Mura III) (Chair: Vladimir Stilinović)	
14:30 – 14:50	**SECTION**	**Marijana Bastić**: How to Facilitate the Evaluation of Student Achievements by Using Written Papers in Chemistry?
14:50 – 15:10		**Monika Pavić**, **Maja Jurić-Babaja**: Challenges in Chemistry Classes Using ICT Technology
15:10 – 15:30		**Jurica Bauer**: Fostering Transdisciplinary Learning in Science and Technology
15:30 – 15:50		**Olgica Martinis**: The Current Challenges of Improving Chemistry Learning
15:50 – 17:00	**ROUND TABLE**	***What Our Education Gave Us?*** (*"Što je nama naša nastava dala"*) – Mementos, comments, and critiques by former Croatian students (Filip Topić, Ilija Čorić, Jana Volarić, Vedran Vuković, Petra Vizjak, Anđela Šarić)
17:00 – 17:30	**EVALUATION**	

17:30 – 20:00	**POSTER SESSION** (Mura I + II) **BEER BREAK** by local craft brewery "Lepi Dečki"

20:00 – 21:00	🍽 **DINNER BREAK** 🍽

	SECTION H_2O (Pub Potkova) (Chair: Nikola Bregović)	
21:00 – 21:30	**INVITED**	**Vladimir Stilinović**: DISCOVERIES, CONTROVERSIES AND BEHEADINGS – HOW WATER STOPPED BEING AN ELEMENT
21:30 – … 😊	**#MoreThanWater CONFERENCE PARTY** with DJ Bregi	

DAY 3 • THURSDAY, 10 NOVEMBER

	SECTION V – PART ONE (Mura I + II) (Chair: Rosana Ribić)	
9:00 – 9:45	**PLENARY**	**Jurij Lah**: ADVENTURES IN PHASE SPACE OF DNA BINDING AND STABILITY
9:45 – 10:15	**INVITED**	**Žiga Jakopin**: STRUCTURAL REQUIREMENTS FOR IN VITRO AND IN VIVO ACTIVITY OF NOD2 AGONISTS
10:15 – 10:25	**SPONSORS**	**IMROH (IMI)**
10:25 – 10:35		**Jasika**
10:35 – 11:10	☕ **COFFEE BREAK** (in front of Mura Halls) ☕	
	SECTION V – PART TWO (Mura I + II) (Chair: Rosana Ribić)	
11:10 – 11:30	**SECTION**	**Maša Safundžić Kučuk**: JGL's Experience in Demonstrating Extended Pharmaceutical Equivalence in Drug Product Solutions
11:30 – 11:50		**Želimir Kurtanjek**: Causal Analysis of Molecular Descriptors of Eutectic Solutions of Choline Chloride Systems Applicable in Pharma Technologies
11:50 – 12:10		**Riya Sailani**: Spectrophotometric Kinetic and Thermodynamic Investigation for the Oxidation of Anilines by Hexachloroiridate(IV) in Solution Media: A Combined Experimental and Computational Study
12:10 – 13:45	🍽 **LUNCH BREAK** 🍽	
	SECTION VI (Mura I + II) (Chair: Josip Požar)	
13:45 – 14:30	**PLENARY**	**Angela Danil de Namor**: SUPRAMOLECULAR CHEMISTRY: SOLUTION THERMODYNAMICS AND APPLICATIONS
14:30 – 15:00	**INVITED**	**Giuseppe Cappelletti**: TAILORING THE LIQUID/LIQUID INTERFACE BY TRADITIONAL AND PICKERING GREEN EMULSIONS
15:00 – 15:20	**SECTION**	**Aleks Logožar**: ML_2 Metal Complexes with bpa and imda Ligands – In Solution and Solid-State
15:20 – 15:40		**Marin Liović**: Halogenide Anions as Hydrogen and Halogen Bond Acceptors in Simple Cocrystals with a Neutral Halogen Bond Donor

	CONFERENCE EXCURSION	
16:15 – 17:00	**ORGANISED BUS TRANSIT**: Terme Sveti Martin → Čakovec + a surprise visit … **The buses** (GROUP 1 and GROUP 2) **leave at 16:15** from the **main entrance to Hotel Terme Sveti Martin**. PLEASE **BE THERE AT 16:00. Thank you!**	
17:00 – 18:15	**GROUP 1** Treasury of Međimurje	**GROUP 2** Local food tasting by Slađana Herman
18:15 – 18:30	**GROUP SWITCH**	
18:30 – 19:45	**GROUP 1** Local food tasting by Slađana Herman	**GROUP 2** Treasury of Međimurje
19:45 – 20:15	**ORGANISED BUS TRANSIT**: Čakovec → Terme Sveti Martin	
21:00 – … 😋	**CONFERENCE DINNER** (Mura Halls) Classical serving, local food paired with local wines, live music	

DAY 4 • FRIDAY, 11 NOVEMBER

9:00 – 9:30	**WAKE UP LECTURE**	Surprise, surprise … A positive one!

	SECTION VII (Mura I + II) (Chair: Giovanna Speranza)	
9:30 – 10:15	**PLENARY**	**Nicoletta Ravasio**: CHEMICAL SOLUTIONS FOR AGRI–FOOD WASTE UPCYCLING
10:15 – 10:35	**SECTION**	**Davor Kovačević**: Applications of Polyelectrolyte Multilayers for the Reduction of Bacterial Adhesion
10:35 – 10:55		**Ina Erceg**: Comparison of Albumin and Chitosan Effects on Calcium Phosphate Formation on Titanate Nanomaterials
10:55 – 11:15		**Gloria Zlatić**: Protective Ability of *Artemisia Annua* L. Against Microbiologically Influenced Corrosion of Aluminium Alloy 5083 Caused by *Pseudomonas Aeruginosa* in Artificial Seawater

	SECTION VIII (Mura I + II) (Chair: Marina Šekutor)		
11:15 – 11:45	**INVITED** Winner of the **Leopold Ružička Award** given by CCS	**Igor Živković**: ALL BUT ONE: HOW NEGATIVE CATALYSIS SHAPED EVOLUTION OF THE ISOLEUCYL–tRNA SYNTHETASE'S EDITING DOMAIN	NAGRADA Leopold Ružička
11:45 – 12:00	**BEST POSTER PRESENTATION** Winner of the **Tomislav Cvitaš Award** given by CCS	Presenting author to be announced after the Poster session …	TOMISLAV CVITAŠ AWARD 1943

12:00 – 12:30	**CLOSING CEREMONY** SEE YOU IN 2024!

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PLENARY LECTURES

SOLUTIONS IN SUPRAMOLECULAR CHEMISTRY IN WATER

Werner M. Nau

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Supramolecular chemists have explored and developed a large portfolio of noncovalent driving forces to understand and ultimately control assembly formation. The formation of discrete host-guest complexes in aqueous solution has proven particularly instructive in this respect, also due to its implications for biological and environmental recognition events. Besides electrostatic interactions between host and guest, the driving force portfolio in water has been limited to two attractive interactions. These include the hydrophobic effect and dispersion interactions, which are additionally difficult to dissect. Here we present results which – conceptually – expand the portfolio of noncovalent driving forces in aqueous host-guest chemistry. First, besides the classical, entropically driven hydrophobic effect related to guest desolvation, a nonclassical, enthalpically driven counterpart related to the desolvation of intermediary sized host cavities needs to be considered, which can be traced back to the removal of high-energy cavity water as the driving force.[1] Second, the hydrophobic effect can be further dissected into two separate components, one related to differential cavitation energies, the other one related to differential dispersion interactions.[2] In supramolecular design, both need to be optimized separately, with the result that very small, non-solvated cavities contribute an extra driving force in the binding of very small guests such as gases; this can be exploited, for example, for gas-storage materials. Finally, through recent studies in the binding of large, so-called superchaotropic, anions to hydrophobic cavities, the chaotropic effect has emerged as a thermodynamically orthogonal driving force to the hydrophobic effect.[3] The two effects derive from a different aqueous solvation pattern of hydrophobic and chaotropic guest molecules, which ultimately drives their desolvation and binding to hydrophobic cavities either entropically (hydrophobic) or enthalpically (chaotropic), see Fig. 1. Most recently, the first biological application of the chaotropic effect has been introduced, which related to the use of superchaotropic ions for transmembrane transport of amino acids, peptides, and drugs.[4]

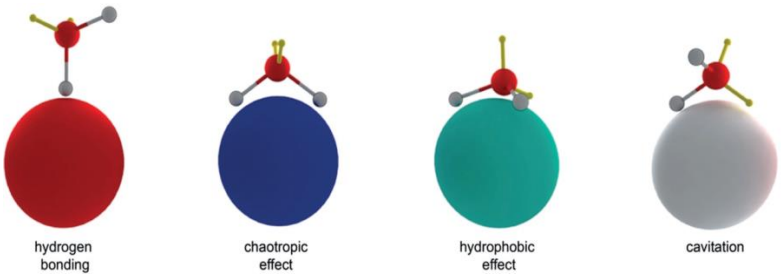

Figure 1. Continuum of aqueous solvation patterns and associated driving forces.

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SENSING SOLUTIONS WITH POTENTIOMETRIC PROBES

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Throughout the history of potentiometric sensors, the concept of symmetry has been central for assuring optimal signal stability. With pH electrodes, for example, the internal Ag/AgCl element at the indicator electrode side is accompanied with a similar Ag/AgCl electrode at the reference electrode side. The overall cell potential no longer depends on the specific redox couple because the two are compensated. Commercial pH probes of high E^0 potential reproducibility and stability are designed for the two redox elements to be similarly configured and placed within the sensor body so that temperature fluctuations affect both elements at very similar rates. This concept of symmetry was also used by Simon for the realization of a calibration-free potentiometric sensor where the observed value of the cell potential gives direct information about sample ion activity.[1]

This symmetry is broken when the internal Ag/AgCl element of an indicator electrode is replaced with a solid contact transducing material because the reference element is now formed by a different redox couple. This is unfortunate because a major research effort of recent years has been the aim to realize highly stable all-solid-contact potentiometric probes, which is not helped by the asymmetric nature of the cell.

This talk will underline the importance of symmetry in such electrochemical sensors and show examples on how it can be restored with modern all-solid-state potentiometric probes. Examples will include a recently published example for the detection of the nutrient nitrate[2] where nitrate is added to the bridge electrolyte of the reference element so that a second nitrate electrode of the same design, rather than an Ag/AgCl can be used. This study will then be extended to solid contact pH probes that may behave in complete analogy to commercial pH probes, with a zero potential value at pH 7. Symmetry may also help to avoid the lengthy conditioning periods often required for best stability. Moreover, it is shown that when the reference element is matrix matched to the sample, the sensor can be made to directly output concentrations, rather than ion activities. The concept of symmetry is then applied to the design of submersible aquatic sensing probes, which are deployed successfully in freshwater systems in Switzerland.

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THE HUMAN FACTOR IN SCIENTIFIC THINKING: THE ILLUSIONS THAT WE LIVE BY

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The talk is based on a book published in 2015, and takes a candid look at science from an unusual perspective, attempting to offer some insights into how psychological factors secretly infiltrate its fabric.[1] The common notion that science is the world of objective rationality based on methodological rigor, stringent logic, irrefutable experimental proofs, and unbiased peer reviewing and testing, is an idealistic myth which all too often dissents from what "scientific truth" is in reality, and from how scientists truly „function" in practice. Actually, our scientific thinking is influenced by deep-rooted human ("anthropic") factors of which we are not normally aware of. Some of these lead to what we call mental traps, i.e., the hidden sources of mistaken or misleading inferences, a phenomenon we refer to as the illusion of understanding, and mass misconceptions about apparently well-established "scientific truths". By their very nature, mental traps affect even the smartest, most knowledgeable, and most attentive scientists. However, by understanding the essence of the traps one can develop the enlightening faculty of detecting and avoiding them both in one's own and in others' thoughts. It is this mental aptitude/attitude of being keenly conscious about our human nature during scientific thinking which is captured in the phrase "anthropic awareness" in the title of the aforementioned book. The talk will address the concept of "anthropic awareness" as a kind of philosophy, will outline the reasons behind the mental traps, and will discuss some of the traps, including a few real-life examples. I will attempt to show that "anthropic awareness" has a general relevance throughout all of natural sciences, and is useful not only in our everyday professional lives as researchers, but also in our nonprofessional everyday lives.

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ADVENTURES IN PHASE SPACE OF DNA BINDING AND STABILITY

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In 1953, Watson and Crick presented their iconic structure of double-stranded DNA, which has become firmly imprinted in the cultural memory of mankind. However, DNA is capable of adopting other structures that occur in the context of regulating common and disease-related cellular processes, leading to complex DNA stability landscapes. Here we show how thermodynamics can be used to estimate the mechanism of DNA folding and structural transformation processes, determining their driving forces, and for predicting DNA transcription regulation properties. This will be demonstrated using two model systems:

(i) Guanine-rich DNA can form G-quadruplex structures in key regions of the genome, including promoter regions, oncogenes, and telomeres. We will address one of the key questions in G-quadruplex formation, namely why a single guanine-rich sequence can fold into and switch between different G-quadruplex structures depending on temperature and the presence of co-solvents, co-solutes and ligands.[1–4]

(ii) The bacterial stress response through genetic systems called toxin-antitoxin modules (TA) could be a major cause of chronic infections. TA modules encode a stable toxin (T) and an unstable antitoxin (A) responsible for the formation of the transcription repressor complexes with DNA. We will explain the molecular mechanism of transcriptional regulation of the TA module.[5]

The thermodynamic characterization of these systems is based on the global analysis of a variety of calorimetry (DSC, ITC) and spectroscopy (CD, fluorescence) data [1-3]. We will show how the obtained thermodynamic parameters can be related to structural properties and used to predict DNA behavior under different conditions.

ACKNOWLEDGEMENTS The financial support of the Slovenian Research Agency projects P1-0201 and J1-1706 is gratefully acknowledged.

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THE BIGGEST CROATIAN PHARMACEUTICAL COMPANY JOINS FORCES WITH TOP SCIENTISTS IN R&D

JGL Establishes Scientific Advisory Board to Advance the Development of Innovative and Complex Products

This is a big step forward for us, and for Croatia as a whole, because we are developing science-based, advanced products tailored to the needs of patients and consumers, says JGL

The JGL Scientific Advisory Board was established in September 2021 with the aim of positioning JGL as an innovator in the development of advanced, differentiated products in three strategic therapeutic areas – flu and cold, ophthalmology and dermatology. This independent body comprises top domestic and foreign experts and raises the science profile of the company's R&D projects. The company now operates in 60 markets around the world, either directly or through partners, and its portfolio consists of 150 brands, 300 products and 650 variations tailored to the needs of specific markets.

- The establishment of the Scientific Advisory Board is another step forward in the development of innovative products around which we build our science and innovation ecosystem. The goal of this body is to cooperate with the JGL team and steer existing and develop new ideas for the company's manufacturing and technology portfolio, all of it based on sound science, says Mislav Vučić, CEO of JGL. He also adds that he is very proud of the combination of cutting-edge science and talent, especially during their annual in-person meetings, where they network and share relevant, science-based knowledge and ideas through synergy and lay the groundwork for increasing the company's competitiveness.

Second SAB meeting was organized in September 2022. The Advisory Board consists of nine experts, internationally recognised in their respective fields, same being of high relevance for JGL projects. They include Prof. Henning H. Blume, PhD, Prof. Ralph Mösges, PhD, Prof. Stipan Jonjić, PhD, Jag Ahluwalia, PhD, Prof. Özgen Özer, PhD, Prof. Vladimir Trkulja, PhD, Chief Physician Sonja Jandroković, PhD, Andreas Bilstein, PhD, and Prof. Jasmina Lovrić, PhD. The team is coordinated by Zdravka Knežević, PhD, Director of Scientific Operations at JGL, who participated in a number of similar initiatives and projects and has over 30 years of experience in R&D, drug registration, and clinical development.

> - I am delighted that I get to share my knowledge and experience from international companies at JGL, as well as cooperate with a great team of experts from the EU, UK, Turkey and other global markets on the Board. I believe that this represents great progress for JGL and our teams, as well as for Croatia as a whole, because we will be able to develop new products for the benefit of our patients and the treatment needs of modern society, with clear scientific rationale, emphasises Knežević.

In cooperation with SAB Memebres, relevant JGL teams conducted a series of innovative formulation, preclinical, clinical, and analytical studies in 2021 and 2022, all with the aim of creating a network of relevant knowledge and identifying new projects for the company's therapeutic areas and technology portfolio.

The JGL Scientific Advisory Board, with Zdravka Knežević, PhD, Director of Scientific Operations

A Major European Manufacturer of Sterile Forms

For more than 30 years, JGL has been growing and developing its business globally. Thanks to continued investments in R&D, production facilities and technology, it currently ranks among the leading manufacturers of sterile pharmaceutical forms in the EU. The business, research and manufacturing complex JGL Pharma Valley in Rijeka combines best practices in production process management, state-of-the-art technology in pharmaceutical production and high environmental standards.

JGL is currently implementing a new investment project, Integra 2020, worth HRK 375m, which will integrate the company's development, production, and storage capacities and encompass three units – R&D, commercial production and logistics centre.

Nearly 85 Per Cent of Revenue Comes From Exports

The JGL Group ended 2021 with total revenue of HRK 1.1 billion and a profit before tax of more than HRK 100 million. Nearly 85 per cent of the company's core earnings is generated outside of Croatia, and JGL Group employs just over a thousand people.

The company's leading export brand is Aqua Maris, launched in 1999, which consists of 100% natural products based on seawater from the Adriatic, used for the prevention and treatment of upper respiratory tract diseases. Other key brands include Vizol S, Meralys, Aknekutan and Dramina.

Prof. Ralph Mösges, PhD, a world-renowned expert in allergology, pulmonology and clinical immunology

Prof. Henning H. Blume, PhD, who specialises in biopharmaceutical and pharmacokinetic research, with a particular focus on characterising the bioavailability and bioequivalence of drugs

SUPRAMOLECULAR CHEMISTRY: SOLUTION THERMODYNAMICS AND ITS APPLICATIONS

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Following a brief introduction on the strategy adopted in our research on the thermodynamics of Supramolecular Chemistry involving neutral and ionic species and their applications, the lecture will address some aspects related to the thermodynamics of common salts in low permittivity media and their use in several processes. Given the scope of Supramolecular Chemistry for the availability of new salts in which one of the components is a complexed anion or cation resulting from the ion- receptor interaction, advances so far made by our Group on their behaviour in solution will be based on research carried out with a wide range of macrocycles such as crown ethers, cryptands[1] and calix [4] based macrocyclic receptors.[2–4] Evidence supporting the solvation changes observed in the reactants and the product resulting from their transfer from one solvent to another will be given. Their contribution in assessing the main factors controlling the selective, non-selective or non-interactive behaviour of the receptor towards the guest in solution processes as well as the relevance of solution thermodynamics in the design of new materials for various purposes will be illustrated with representative examples.[5]

ACKNOWLEDGEMENTS A F D de N thanks the European Commission for the financial support given under various Framework Programmes, the Science & Engineering Research Council (UK) and the Leverhulme Trust Foundation for financial support.

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CHEMICAL SOLUTIONS FOR AGRI-FOOD WASTE UPCYCLING

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The food supply chain generates enormous amount of waste: veggies residues left over in the fields, side stream of food production, post-consumer waste. Most of them are used as feed or in bioenergy production, some are disposed of as waste.

However, a green chemistry approach can allow one, once the different chemical classes present in the waste are identified, to design specific valorization pathways for each of them also outside the food value chain. Two examples will be reported and discussed: the valorization of rice waste carried out in the frame of RiceRes project and the upcycling of silverskin, a waste of coffee roasting, in the CirCo project.

The multivalorization of rice waste led to green building materials, innovative polymer matrix composites, sterolesters for nutraceutical use and high added value protein hydrolysates.[1] Both chemical and enzymatic processes were used for the upgrade of the cellulose, the lignin, the oil and the protein fraction of straw, husk and bran.

Extraction of silverskin with supercritical CO_2 led to a fat of unusual composition that was found to be suitable for the formulation of makeup products.[2] The subsequent extraction of a powerful antioxidant and its esterification by heterogeneous catalysis led to a product with increased antioxidant properties. Finally, the residue was used as a replacement of virgin cellulose in the production of graphic paper. A detailed LCA analysis allowed to state that substitution of 15 % virgin cellulose with silverskin derived cellulose can reduce the environmental impact of paper production by 10 % and greenhouse gas (GHG) emissions by 13 % compared to conventional production.[3]

The hydrogenation of lactose, the main component of cheese whey, to sorbitol and dulcitol will also be discussed[4].

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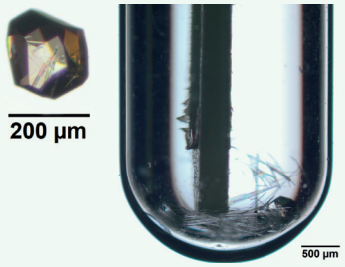

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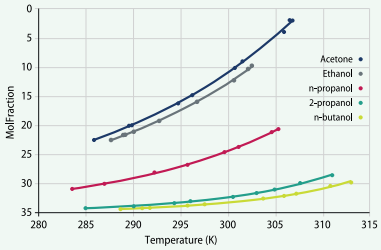

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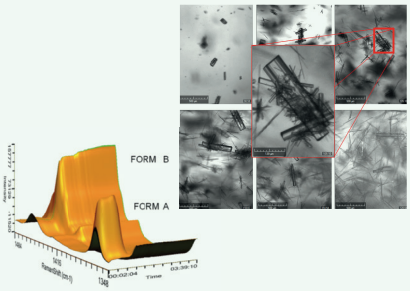

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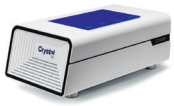

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INVITED LECTURES

POTENTIAL SOLUTION FOR PEPTIDE-BASED DRUG DELIVERY TO THE BRAIN: DESIGN AND ACTIVITY OF MULTIFUNCTIONAL CYCLIC PEPTIDE-BASED ANALGESICS

Predrag Cudic,[a,*] Shahayra Majumder,[b] Heather Stacy[b], Thomas Cirino,[b] Brandon Williams,[a] Jay P. McLaughlin[b]

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Chronic pain is the leading cause of disability worldwide, accounting for significant hospitalization, prolonged care and economic cost. Most clinically-used opioid drugs are μ-opioid receptor (MOR) agonists with liabilities of tolerance, high potential for addiction and respiratory depression mediated by this receptor.[1] In contrast, κ-Opioid receptor (KOR) agonists are effective pain suppressors and unlike MOR agonists do not cause respiratory failure or addiction[1]. However, KOR agonists developed to date exhibit undesirable dysphoria and aversion attributed to KOR suppression of dopamine and serotonin. Given the severity of the problem, there is an undeniable and urgent need for new pain medication without the unwanted side-effects of existing opioid drugs. Among the chemical entities utilized in drug discovery, peptides emerge as particularly attractive lead compounds for the discovery and development of new central nervous system (CNS) drugs due to their roles as potent regulators of normal CNS function. However, conventional drug delivery methods (oral and intravenous) are inefficient in delivering hydrophilic and high molecular weight drugs, such as peptides and proteins to the brain. Both the blood-brain barrier (BBB) and blood-cerebrospinal fluid barrier (BCB) restrict the transport of these therapeutic agents from systemic circulation into the CNS. Alternatively, intranasal (i.n.) administration may enable these therapeutic agents to directly enter the brain by bypassing the BBB and BCB, avoiding systemic circulation of the drug and reducing the risk of systemic side effects as well as hepatic/renal clearing and toxicity. To address the need for novel therapeutics to treat chronic pain, we designed new cyclic peptide-based analgesics suitable for i.n. delivery that combine selective KOR agonist and antidepressant pain reliving mechanisms. This is achieved by grafting bioactive analgesic sequences into a carrier cyclic peptide scaffold exhibiting bioadhesive properties.[2,3] Combining KOR agonist activity with simultaneous delivery of serotonin may improve chronic pain management when more than one physiological mechanism or system is implicated and may potentially minimize side effects associated with the KOR activation.

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NMR SPECTROSCOPY AND GENERIC PHARMA R&D: PAST, PRESENT AND THE FUTURE

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Past, present and future use of NMR spectroscopy in generic pharma industry is presented. Special emphasis is given to the following aspects relevant for generic pharma industry: organic synthesis, kinetics, impurities, catalysts, quantitative NMR, beyond proton and carbon, solid state NMR, polymorphs, excipients, drug products, quality and regulatory aspects. These aspects are highlighted by the use of real life examples.

Xellia Pharmaceuticals is a specialty pharmaceutical company focused on providing important anti-infective treatments against serious and often life-threatening infections. Our anti-infective treatments are generics that combat serious bacterial and antibiotic resistant infections as well as certain fungal diseases. We are a world leader in the development, manufacturing and supply of fermented anti-infectives sold as active pharmaceutical ingredients and finished dosage forms to key pharmaceutical industry companies. Headquartered in Copenhagen, Denmark and owned by Novo Holdings A/S, Xellia Pharmaceuticals has more than 1500 employees globally. From state-of-the-art manufacturing sites in the U.S., China, Denmark and Hungary to R&D sites in Norway and Croatia; Xellia Pharmaceuticals excels within innovative product development to deliver high quality products to its customers.

Our product portfolio of anti-bacterial and anti-fungal products used for the treatment of severe infections, including infections caused by multi-resistant bacteria and fungi, is the foundation for our growth strategy within the antibiotics sector. Xellia is the leading supplier of important anti-infectives Vancomycin and Colistimethate Sodium (CMS). Our success and strong market position is built on more than 100 years experience in the pharmaceutical industry. Xellia Pharmaceuticals' focus its R&D investments within inhalable and injectable product technologies as we are committed to researching solutions, which not only improve patients' quality of life, but will also save lives. Based on our long-term expertise, we bring value for our stakeholders and signify a patient-centric mindset through an embedded corporate motivation of integrating science and innovation to save lives.

MOLECULES BEHIND WINE TASTING

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Wine has played and continues to play a role in a variety of religious, cultural, and social activities. Despite its almost seven millennia as a part of the human experience, our comprehension of this beverage and all of its facts remains woefully lacking, especially in light of modern science's capabilities. Wine is a fascinating chemical mixture. Each bottle contains thousands, if not tens of thousands, of different molecules ranging from acids and sugars to phenolic compounds and vanishingly low concentration aroma compounds. Although wine is sometimes offered with an impression of ancient heritage, industry uses modern techniques and analysis. There is an increasing number of examples where flavor molecules have been found and winemakers have used this information to improve their product. The most common methoxypyrazine found in wine, 2-isobutyl-3-methoxypyrazine (IBMP), provides a distinctive green bell pepper scent to particular wine grape varietals (i.e. Sauvignon blanc, Cabernet Sauvignon, etc.) with a sensory threshold ranging from 8 to 15 ng L^{-1} depending on the wine matrix[1]. Methoxypyrazines are of special importance in the wine business; while some varieties of wine are recognized for high methoxypyrazine levels (e.g., New Zealand style Sauvignon blanc), consumers may reject wines even when methoxypyrazine concentrations are in the low ng L^{-1} range. One of the most challenging aspects of methoxypyrazine analysis in wine is achieving the required analytical sensitivity. Rotundone, a sesquiterpene, was discovered as the main contributor to the aroma of black pepper in wine in 2008. This powerful flavor component has now been discovered in other grape types. Rotundone is generally well received by consumers. One of the most remarkable facts about this chemical is that it is anosmic to 20 % to 25% of the general population. According to a research of Italian *V. vinifera* varieties, furaneol is important to the aroma of Refosco and Primitivo (also known as Zinfandel in the United States and Crljenak kaštelanski or Tribidrag in Croatia). Furaneol and homofuraneol both have low odor thresholds, 5 and 125 µg/L, and have an additive and/or synergistic role in expressing the fruity and caramel flavor of rosé wines[2]. It is clear that wine's aroma depends not on a single compound but rather on the composition and interactions of the many odor-active compounds present. The potential aroma of wine is also dependent on the release of aroma compounds from their odorless precursors during wine maturation and the modification of volatiles due to chemical changes. Future discoveries will continue to be driven by development of improved and high-throughput analytical methods that will allow monitoring of a large number of volatiles, including those present at low concentrations.

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SOLVING COMPLEX PROBLEMS IN SOLUTION CHEMISTRY BY DESIGN OF EXPERIMENT

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In process and product development, *e.g.* formulation of new products, the solvent system is under control of many stochastic parameters so it cannot be fully described or optimized without the sophisticated statistical models and tools.

This presentation will therefore give an overview of several examples, from laboratory to industrial scale, in which the complex systems were optimized by using the statistical methodology *Design of Experiment (DoE).* The examples will cover:

i) the formulation of new products (detergents) [1],
ii) the development of new method (chromatographic separation of amino-acids and ultrasonic extraction) [2,3] and
iii) the optimization of the industrial process for achieving the best product performance (maximal hydrophobic coating) [4].

The results of the investigations showed that the DoE is an effective tool that significantly enabled reducing time and money required for the formulation of a new product, or optimization and manipulation with the new processes (technological, industrial and scientific). Moreover, the estimation of the influence and interactions between all factors influencing the systems was enabled. The biggest advantage of a DOE analysis was that it provided solutions that can lead to faster time to market, lower development costs, lower operating costs, and lower cost of poor product quality. Thus, DoE is an effective and unavoidable tool for chemists dealing with complex solvent systems.

ACKNOWLEDGEMENTS This research was partially funded by the Croatian Science Foundation grant number IP-2019-04-1381 (project under the title 'Antibacterial coating for biodegradable medicine materials ABBAMEDICA'). Any opinions, findings, conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the Croatian Science Foundation.

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THE PATH TOWARDS ENLIGHTENMENT? SUPPORTING STUDENTS IN SOLVING COMPLEX CHEMICAL CALCULATIONS USING AN ADAPTIVE DIGITAL PLATFORM

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A large number of our undergraduate students at the Inholland University department of Life Sciences & Chemistry encounter difficulties and frustrations when learning to solve (complex) chemical quantitative problems. This is problematic since solving chemical calculations is considered a crucial skill for the profession for which we train our students, i.e. B.Sc. level laboratory analysts. In order to identify the most common reasons why students have difficulties with learning this important skill, a literature survey has been performed. This survey resulted in identification of a large set of articles and studies adressing this specific topic, exemplifying that this is a widespread issue in secondary and higher educational settings.[1-4]

A possible solution is provided by Enlight-Ed's online digital adaptive platform[5] that enables simulation of the conversation between learner and teacher in a classroom when the learner is having difficulties solving assignments. Using a chatbot functionality, students are exposed to adaptive assignments that resemble the 1-to-1 learning experience and optimise student engagement. The platform is also capable of collecting learning data providing the teacher an overview on the level of students and common misconceptions allowing to make informed decisions.

Using the editing functionality of the Enlight-Ed platform and the obtained insights from the aforementioned literature survey, adaptive assignments were specifically created for our first-year Life Sciences & Chemistry students. These digital interactive assignments assist students in following the step-wise approach that is needed to solve such complex assignments. When needed, the students is provided with additional instructions when needed. An evaulation poll amongst particpants of this pilot-study showed high appreciation of this learning methodolgy. 77% of respondents agreed that the adaptive assignments using the Enlight Ed platform helped them in understanding how to solve such complex chemical calculations.[6]

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CHEMISTRY IN THREE DIMENSIONS: CHIRALITY, SYMMETRY, ISOMERISM

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Poor understanding of fundamental concepts of stereochemistry, such as enantiomerism or stereoisomerism, is unfortunately rather common among Croatian chemists and chemistry teachers. The reason for this is an awkward approach to education, which is based on erroneous foundations. The basic stereochemical concepts in Croatia are introduced through definition of constitutional isomerism and stereoisomerism, and definition of the "asymmetric" carbon atom. Such an approach yields questionable results: according to the author's experience with students of chemistry, graduated chemists, chemistry teachers and even some researchers, the majority of Croatian chemists actually don't understand what symmetry and chirality are.

It is well known that atoms and molecules are 3D objects, and their representation in two dimensions (on a blackboard, paper or screen) is merely projection. Therefore, for understanding basic chemical concepts which involve three dimensions - chirality, isomerism and symmetry - 3D models are indispensable. Fortunately, dedicated molecular model kits (which are expensive) are not needed. Many objects of every-day use can find a new use as models for teaching stereochemical concepts, such as symmetry (flowers, building blocks, etc.) or chirality (screws, shoes, corkscrews, snails). Toy building blocks can be used to demonstrate concepts of constitutional isomerism and stereoisomerism and also to assemble simple chiral objects.

A chiral object can be converted into its mirror image simply by watching it in a mirror. By observation of common things around us we can understand the phenomena of chirality and enantiomerism; then we make a mathematical abstraction - i.e. how to define a helix or a left or a right coordinate system, etc. Molecular chirality then becomes an easily understood phenomenon.

Thus, in teaching chemistry we can dispense with "chirality centres" and *R* and *S* configurations; they are not just needless, but superfluous. Tetrahedral carbon atom of van't Hoff and Le Bel is of a great historical importance, but it is just a special case of a common phenomenon of molecular chirality: "chirality centre" is not necessarily a tetrahedral carbon atom, it can be any atom with 4 or more atoms bound to it; there are also chiral molecules lacking "chiral centres", and they may possess quite a high symmetry. Instead of insisting on conventions and bookkeeping devices (such as *R* and *S* configurations and similar IUPAC rules), we should first focus on the basic concepts and introduce them through every-day objects. After that we can move to a more abstract, "mathematical" definition; conventions should only come at the end.

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FUNDING OPPORTUNITIES IN INNOVATIVE PROJECTS FOR THE 2021–2027 PERIOD

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Over the past couple of decades, the financing of research and development has been subject to significant changes. Public funding is not sufficient, traditional bank loans are generally difficult to obtain and yet there are EU funds that offer variety of possibilities for faculties and companies dealing with research and development to fund their innovative ideas at different level of development.

Croatian institutions and companies have access to variety of funding opportunities that can boost their research and improve their capacities in order to help them develop new processes, products or services, test innovative ideas and collaborate with other organizations. Funds that are allocated to Croatian institutions by the EU budget through *Multiannual Financial Framework 2021-2027* and through *Next Generation EU* are significant and are planned to be used to increase research and development activities in Croatian research institutions. Furthermore, research institutions and companies are entitled to apply for funding from *Horizon Europe* which is the EU's key funding programme for research and innovation for 2021 -2027 with a budget of €95.5 billion.

While average gross domestic spending on R&D in EU exceeded 2,32% in 2020, it is still rather low in Croatia - 1,25% in 2020. Thus, Croatian public institutions should build their capacities in order to use available funding opportunities.

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DISCOVERIES, CONTROVERSIES AND BEHEADINGS – HOW WATER STOPPED BEING AN ELEMENT

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On November 12th 1783, at a public session of the French Royal Academy of Sciences, Antoine Laurent Lavoisier read out his memoir "*on the nature of water and on experiments which appear to prove that this substance is not strictly speaking an element but that it is susceptible of decomposition and recomposition*".[1] In it he presented his discovery that water is in fact a chemical compound, comprising oxygen and hydrogen, and thus ended over two millennia of undisputed belief that water was an element. At least, that is the short story as usually told…

The exact nature of water was one of the central problems in the final decades of the phlogiston theory, and was tackled, with variable success, by many chemists of the day. The development of pneumatic chemistry during the 18th century has led many to observe connections between water (still considered an element in the light of the phlogiston theory) and the newly discovered (or at least identified and described) gases – mainly the dephlogisticated air (oxygen) and the inflammable air (hydrogen). This has led to several competing claimants to the priority of the discovery, and many of the controversies which have started in those days are still present amongst the historians of chemistry: has Lavoisier really made a profound discovery, or just changed the wording of Henry Cavendish; how much did Cavendish avail himself of the conclusions of James Watt; did Watt have any clearer idea then Joseph Priestly…[2]

Regardless of the questions of priority, the description of the composition of water by Lavoisier in terms of his *antiphlogistic* theory was to remove the greatest obstacle which stood in the path of its acceptance – the origin of the *inflammable air from metals* (hydrogen), described in detail by Cavendish in 1766, believed by many to be pure phlogiston – and allowed him to present a well-rounded alternative theory, virtually ending the phlogiston era. In this talk we shall attempt to reconstruct the unfolding of the events which have marked these, possibly the most dynamic, but certainly the most dramatic, decades in the history of chemistry.

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STRUCTURAL REQUIREMENTS FOR *IN VITRO* AND *IN VIVO* ACTIVITY OF NOD2 AGONISTS

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The innate immune receptor NOD2 represents an important target for the development of structurally defined small molecule immunomodulators. Here, we present the investigation of the structure–activity relationships of several series of novel synthetic desmuramylpeptide NOD2 agonists. Extensive exploration of chemical space culminated in the discovery of NOD2 agonists with improved *in vitro* as well as *in vivo* adjuvant properties. Of note, an adamantane-moiety-featuring compound emerged as the most potent NOD2 agonist in its structural class to date. Further, pivotal structural elements that confer *in vivo* adjuvant activity in conjunction with a liposomal delivery system have also been identified. Our findings thus provide deeper insights into the structural requirements of desmuramylpeptides for NOD2-activation and highlight the potential use of NOD2 agonists as vaccine adjuvants or general immunostimulatory agents.

ACKNOWLEDGMENTS This work was supported by the Slovenian Research Agency grants (P1-0208, J3-9256 and P1-0420) and the Croatian Science Foundation (HrZZ) (Project No. 7387).

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TAILORING THE LIQUID/LIQUID INTERFACE OF TRADITIONAL AND PICKERING GREEN EMULSIONS

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Emulsions are commonly employed in many different fields including pharmaceutics, drug delivery, cosmetics, food industry, and so on, especially after the advancement of methods for preparing various kinds of emulsions.

Surfactants (or surface-active agents) are amphiphilic compounds widely used in almost every industrial field because of their ability to reduce surface and interfacial tensions, thus stabilizing dispersed systems. In recent years, due to their high worldwide consumption volumes, surfactant residues are becoming an environmental risk because they are continuously discharged into treated and untreated wastewaters, thus entering in several environmental compartments, i.e., surface and marine waters, sediments and sludge-amended soils etc.[1] Environmental concerns about effects of conventional tensides, mainly derived from petroleum precursors, have increased the market demand for more benign compounds. Particularly, sugar fatty acid esters (SFAEs)[2] belong to the non-ionic surfactant family, extensively adopted as emulsifiers in many market sectors, i.e. cosmetic, food and pharmaceutical industry, being low toxic and easy biodegradable. Thus, innovative syntheses of some glycoside esters will be proposed, and their surface properties/emulsifying capabilities will be studied in details.

Over the last decades, Pickering emulsions have attracted increasing attention due to their advantages compared to conventional surfactant-stabilized emulsions. Particularly, Pickering emulsions are characterized by long-term stability to coalescence, good mechanical properties, low toxicity and recyclable stabilizers[3]. In this context, Pickering emulsions represent promising platforms for applications in numerous fields, such as medicine, pharmaceutics, cosmetics, food industry, and cultural heritage protection. In this work, highly stable and environmentally-friendly Pickering emulsion systems were prepared using food-grade vegetable oil and stabilized by the sole addition of pristine ZnO particles. The versatility of this approach was also proved changing the type of vegetable oil, the oxide content and morphology.

ACKNOWLEDGEMENTS This work was financially supported by Cariplo Foundation (Italy) (call: “Circular Economy for a sustainable future 2020”, project BioSurf, ID 2020-1094).

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ALL BUT ONE: HOW NEGATIVE CATALYSIS SHAPED EVOLUTION OF THE ISOLEUCYL-TRNA SYNTHETASE'S EDITING DOMAIN

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Aminoacyl-tRNA synthetases (AARS) activate amino acids and transfer them to cognate tRNAs. Some AARS cannot achieve the required specificity in the initial amino acid recognition at the synthetic site. Those AARS can incorrectly activate non-cognate amino acids and transfer them to tRNA. To correct the mistake and ensure faithful protein biosynthesis, these AARSs evolved a separate editing domain aimed to hydrolyze erroneously aminoacylated tRNAs (post-transfer editing). To understand what shaped the selectivity of the editing site and how it is related to the initial amino acid selectivity at the synthetic site, we used *Escherichia coli* isoleucyl-tRNA synthetase (IleRS) as a model enzyme.[1-3] We investigated the synthetic and editing reactions of IleRS using a wide range of amino acids, including non-proteinogenic and synthetic: Val, Nva, Leu, Thr, Met, Ser, Ala, Abu, Nle, F_2Abu and F_3Abu. Among these, only Val and Nva were poorly discriminated at the synthetic site (i.e. well activated and transferred to the tRNA) and thus can be considered as threat to the fidelity of translation. To our surprise, tRNAs misaminoacylated with all tested amino acids were rapidly hydrolyzed at the editing domain. Thus, it appears that amino acid's physicochemical features and how well it is rejected at the synthetic site does not pose a significant difference. Only the hydrolysis of cognate Ile-tRNA^{Ile} (misediting) was slow, suggesting that the need to keep the cognate product out of editing strongly shaped the specificity of the editing domain. Detailed kinetic analysis revealed that IleRS employs Thr246 and His333 for specific destabilization of Ile-tRNA^{Ile} hydrolysis – strategy also known as negative catalysis. Such design enabled IleRS to have broad substrate acceptance at the editing site whilst maintaining a high specificity towards preventing the futile post-transfer editing cycles. This was the first time such broad substrate specificity, paired with negative catalysis, was observed for an AARS, and as such, it marks a new moment in the understanding these vital and ancient enzymes.

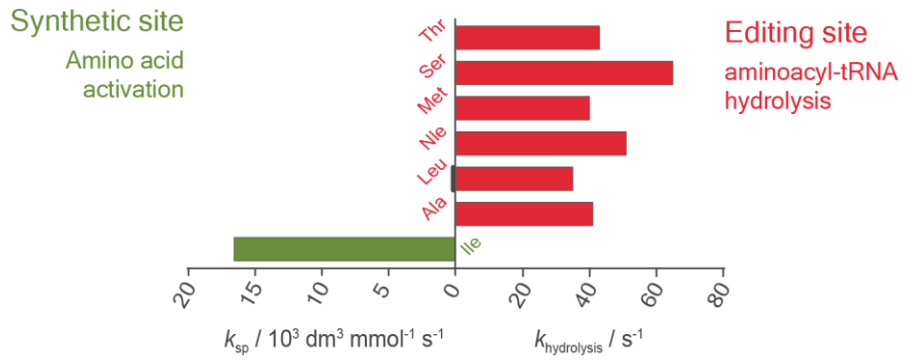

Figure 1. Specificity and activity towards different substrates in the synthetic and editing sites of IleRS.

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SECTION LECTURES

CYCLOPEPTIDES AS VERSATILE ANION SENSORS IN SOLUTION

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The design and synthesis of anion receptors is an ongoing hot topic in supramolecular chemistry. One especially interesting class of anion receptors are cyclopeptides. Their exceptional complexation properties are related to the proton-donating peptide groups, the flexibility of macrocyclic ring and to the variability of the macrocycle subunits. For these reasons, cyclopeptides stand as versatile receptors for halide and oxoanions in solution.

In this talk I will present our recent contributions to this field.[1-3] The aim of our research was to obtain as detailed as possible insight into the thermodynamic and structural characteristics of cyclopentapeptide complexes with halide and oxoanions in solution and to rationalize the relation between structure and reactivity of the investigated cyclopeptides. For the characterization of receptor-anion complexes we used various experimental methods, as well as molecular dynamics simulations. The solvent effect on equilibria of studied reactions was addressed as well.

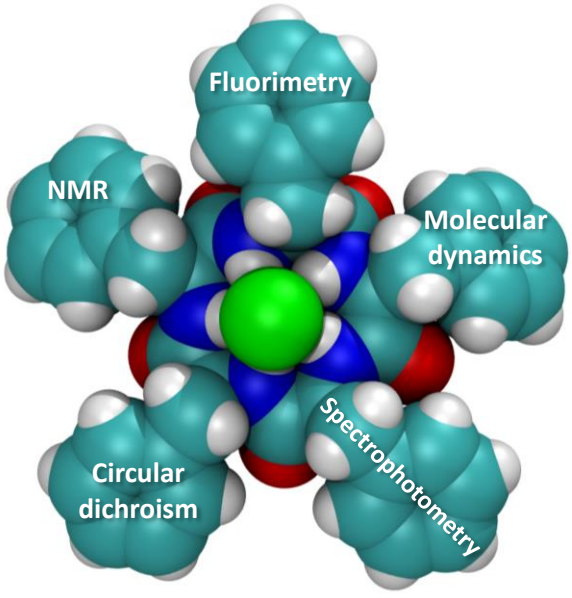

Figure 1. Cyclopentaphenylalanine in complex with the chloride anion.

ACKNOWLEDGEMENTS This work was supported by the Croatian Science Foundation under project IP-2019-04-9560 (Macrosol) and European Regional Development Fund (project CluK, KK.01.1.1.02.0016).

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METALLOSUPRAMOLECULAR ASSEMBLIES – FROM SIMPLE COMPLEXES TO FUNCTIONAL NANOSTRUCTURES

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Metal-ligand interactions are seen as one of the primary driving forces in the generation of simple coordination compounds, as well of metallosupramolecular architectures with a high degree of complexity and a precisely defined structure.[1] Taking into account the character of coordinate bond, i.e., high energy, but dynamic nature, coordination-driven self-assembly processes are characterized by the high controllability at the molecular level with respect to directionality, reversibility and then post-synthesized switchability.[2] In the presented research, a bifunctional ligand 4,4-dimethyl-1-(pyridin-4-yl)pentane-1,3-dione (H**L**) containing two distinct coordination sites, i.e., anionic β-diketonate and neutral pyridine has been used in the synthesis of Ag(I), Pd(II) and Pt(II) complexes that then have been applied as metalloligands for the construction of new heterometallic polymeric materials. The ambidentate nature of H**L** enables switching between different modes of coordination within mononuclear complexes or their conversion into polymeric species in a fully controllable way. The coordination-driven processes can be triggered by various stimuli, i.e., a metal salt addition or acid-base equilibria, and presents an efficient strategy for the generation of metallosupramolecular materials. As a consequence of self-assembly, new heterometallic coordination aggregates have been synthesized and fully characterized via different analytical techniques in solution as well as in the solid state.

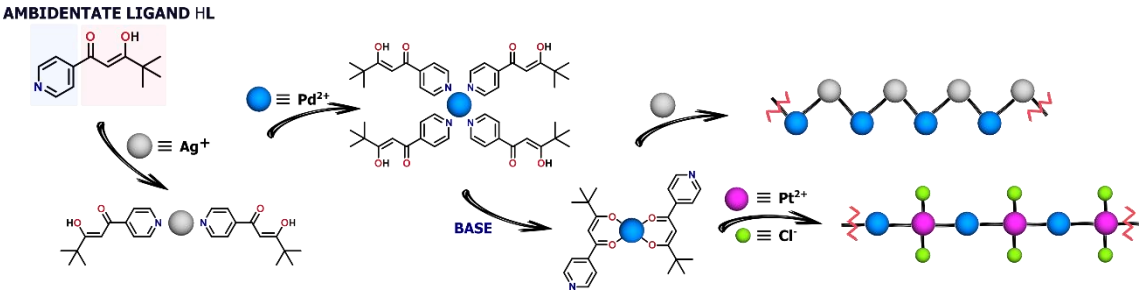

Figure 1. The supramolecular transformations within coordination-driven assemblies based on Ag(I), Pd(II) and Pt(II) ions and the pyridyl-β-diketonate ligand H**L**.

ACKNOWLEDGEMENTS The financial support was provided by the National Science Centre (ARS, grant SONATA BIS 2018/30/E/ST5/00032).

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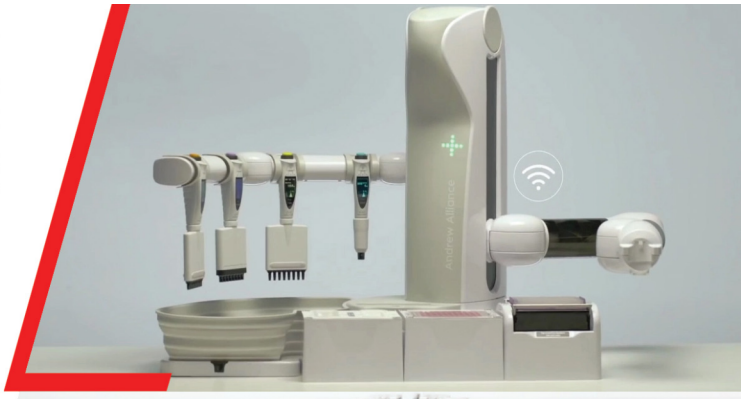

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FROM SINGLE MOLECULE TO RESPONSIVE AGGREGATE: MULTIRESPONSIVE PHOTOSWITCH IN NONPOLAR SOLVENTS

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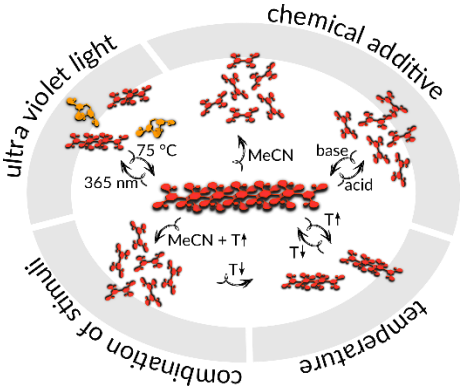
Multi-responsive, also known as smart, materials are currently one of the most appealing part of materials science.[1] Smart polymers are able to change macroscopically their structure, but also these transitions are reversible and the system return to the original state after the stimulus is removed. Since the 1990s when smart materials first appeared in the literature,[2] different reversible transformations were observed. Our unique design combines the simplicity of a monomer (low molecular weight with well-defined primary structure) with the complex properties of self-assembled architecture. The special focus is on the synergism of several different responses of the architecture, which are encoded in different moieties of the monomer. Herein we present simple yet robust tetra substituted azobenzene molecule, bearing C_4 symmetry. When dissolved in a polar solvent, the molecule behaves as a monomer and is fully molecularly dissolved. On the other hand, when in a nonpolar solvent, supramolecular aggregation occurs, forming large aggregates via hydrogen bonds and π-π stacking. After heat or light are employed we are able to control the size of the aggregate, however, when a different type of stimulus is present (acid, acetonitrile or combination of heat and solvent) even full disassembly of the aggregate is achieved. The aggregate and its behavior after applied stimuli was monitored in solution by several spectroscopic methods and on the surface by AFM.



ACKNOWLEDGEMENTS The project was funded by the National Science Centre of Poland grants SONATA BIS 2018/30/E/ST5/00032. The conference attendance was funded by grant "Środowiskowe interdyscyplinarne studia doktoranckie w zakresie nanotechnologii" No. POWR.03.02.00-00-I032/16.

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SOLUTIONS FOR POLLUTANTS SENSING – SURFACTANTS, ESTROGEN AND GLYPHOSATE SENSORS

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Chemical sensors and biosensors are analytical devices that perform a specific or selective recognition (recognition element) of target analyte with transducer that converts the recognition into a readable signal. They have a wide range of usage, from environmental, industrial and biomedical, up to military. Global chemical sensor market in 2020 was USD 21.39 billion with estimated growth 7.51% from 2020 to 2026[1], and USD 24.9 billion in 2021 for biosensor market with estimated growth 8% from 2022 to 2030[2]. The main focus in development of chemical (bio)sensors is to be low-cost, easy to use, sensitive and selective/specific, robust, small and portable. The lecture will cover the research results of the development and application of electrochemical potentiometric anionic and cationic surfactant sensors based on the PVC-liquid membrane type membranes[3,4], and nanoparticle based localized surface plasmon resonance (LSPR) optical sensors for estrogen hormone 17β-estradiol[5] and LSPR optical immunosenor with magnetic micromixing extraction for highly sensitive detection of a broad-spectrum systemic herbicide glyphosate[6]. The research was recently conducted at the Laboratory for environmental engineering at the Faculty of geotechnical engineering, University of Zagreb (Croatia) in cooperation with partners from home and international research institutions and industry.

Keywords: Surfactant, glyphosate, estradiol, chemical sensor, biosensor

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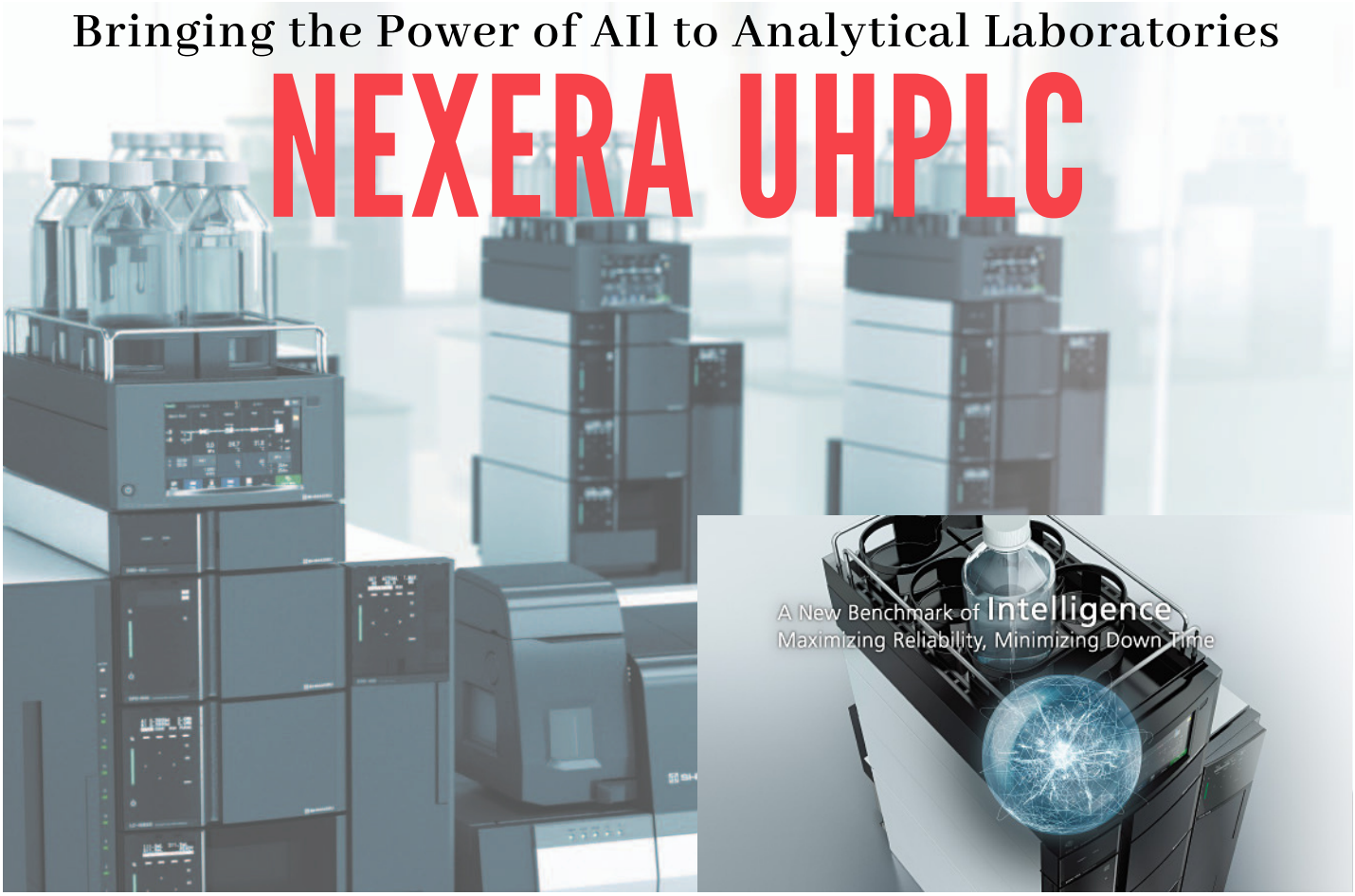

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TRIARYLBORANES: NOVEL TYPE OF DYE FOR BIOMACROMOLECULES

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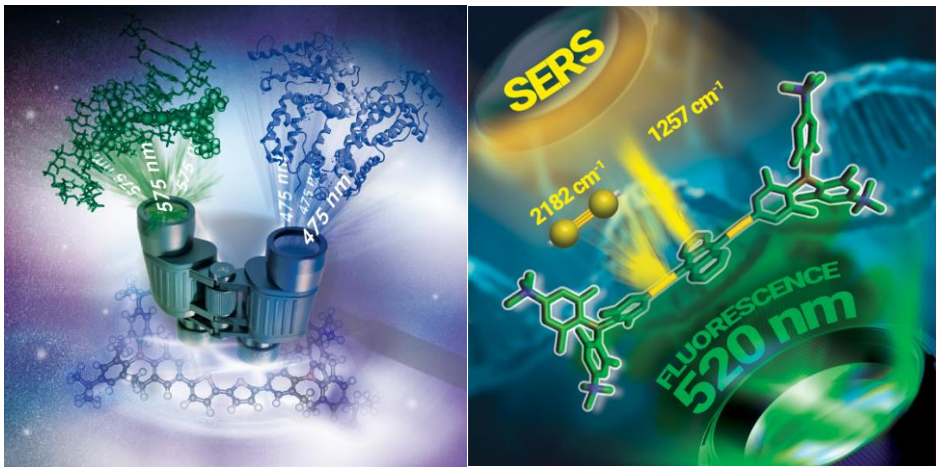
Low molecular weight fluorescent probes are frequently used tools in most molecular biology or biochemistry experiments today.[1] Due to problems related to covalent attachment of dye to biomolecule, non-covalently binding molecular probes that readily recognize and distinguish between different types of biomolecules are of huge interest.[2] However, the small size of a molecule presents a significant challenge in the design of selective probes, particularly in well-explored fluorophore families. Thus, development of a novel structural motif represents a valuable contribution. Here we report the development of a novel family of dyes based on the triarylborane system (Scheme 1.), which showed remarkable features in the interaction with biomacromolecules (DNA, RNA, proteins).



Scheme 1. Some applications of triarylborane dyes: LEFT: fluorescent response differing between DNA and protein,[3] or RIGHT: dual sensing of DNA or protein by fluorescence and SERS.[4]

Namely systematic structural variation (mostly linkers between two triarylborane units) revealed high tunability of a system in respect to emission response and Raman (SERS) response, promising photo-bioactivity or intriguing enzyme-staining propeties.

ACKNOWLEDGEMENTS The financial support of the Croatian Science Foundation project IP-2018-01-5475, the DAAD, and the Julius-Maximilians-Universität Würzburg are gratefully acknowledged.

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JGL'S EXPERIENCE IN DEMONSTRATIONG EXTENDED PHARMACEUTICAL EQUIVALENCE IN DRUG PRODUCT SOLUTIONS

Maša Safundžić Kučuk,[a,*] Leo Štefan,[a] Zdravka Knežević[b]

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During development of a pharmaceutical generic product, demonstration of its qualitative (Q1), quantitative (Q2), and microstructural (Q3) equivalence to the reference medicinal product (RMP) is the cornerstone of the R&D activities. Apart from the legal requirement to demonstrate quality, safety, and efficacy similarity with the RMP, generic companies invest considerable effort to demonstrate Q1/Q2/Q3 equivalence in order to be exempted from the costly and lengthy clinical trials, or to limit their extent.[1] First step in the demonstration of the equivalence, is to fully characterize the RMP. Full composition of the RMP is rarely fully known, and as guidelines allow up to ± 5 % difference in composition for a generic product from the RMP,[2] to consider a Q1 and Q2 equivalence demonstrated (some exceptions are allowed). To achieve this, a developer must combine extensive literature research and diverse reverse engineering activities to determine exact composition of the RMP. If a company decides to develop a product that deviates from the Q1/Q2 equivalence – for example, by excluding preservatives, or to bypass a valid patent, status of a generic product still can be achieved with demonstration of the Q3 equivalence.[3] In demonstration of the latter, various techniques are used for the purpose of characterization of the critical quality attributes (CQA) and their similarity with RMP. For each project, a case-by-case basis approach is needed, and to obtain reliable results and conclusions, in-depth knowledge of the pharmaceutical technology, analytical, physical, and organic chemistry is essential. For the purpose of accessing the specialized knowledge, or to accelerate development process, Companies often outsource their development studies. In some cases, Academia seems like an ideal partner, but some requirements need to be met.

ACKNOWLEDGEMENTS Vesna Saršon, Silvia Kamhi Saršon

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Široka paleta proizvoda koje nudimo, u kombinaciji s našim znanjem i iskustvom stečenim radom u laboratoriju, omogućuje nam da ponudimo najbolje rješenje za sve vaše analize.

Jedno od naših temeljnih načela jest etikom vođeno poslovanje, jer se tako zadovoljavaju ključne vrijednosti: vjerodostojnost, pouzdanost, kompetentnost i čestitost.

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CAUSAL ANALYSIS OF MOLECULAR DESCRIPTORS OF EUTECTIC SOLUTIONS OF CHOLINE CHLORIDE SYSTEMS APPLICABLE IN PHARMA TECHNOLOGIES

Želimir Kurtanjek

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Applied is the structural causality model (SCM) analysis of molecular descriptors and fingerprints for predicting the eutectic temperature of choline chloride systems aimed for application in pharmaceutical technologies. The SCM model predictions are compared to predictions by the ideal mixture model and COSMO-RS (Conductor like Screening Model for Realistic Solvents). The model is developed by use of a dataset of 34 molecules including common pharmaceutical compounds (ibrufen, ketoprofen, and paracetamol). The molecular descriptors and fingerprints generated by PaDEL software currently calculate 1875 descriptors (1444 1D, 2D descriptors, and 431 3D descriptors) and 12 types of fingerprints (a total of 16092 bits). The descriptors and fingerprints are calculated using The Chemistry Development Kit with additional descriptors and fingerprints such as atom-type electron topological state descriptors.[1-4] The large data sets are analyzed by the suit of numerical and statistical packages available in R software.[5] The model of the directed acyclic graph (DAG) inferred is by Hamilton-Schmidt independence criteria (HSIC) The causal functionalities between eutectic temperature and molecular descriptors are determined by deconfounding by the d-separation criteria.[6] The accuracy of SCM-DM is compared with COSMO-RS and is presented in Fig. 1. Mean absolute errors are 7.5 ^{0}C and 9.57 ^{0}C for SCM-DM and COSMO-RS respectively.[7] The causal SCM model has important advantages for application in the scan evaluation of large molecule datasets in the development of new green sustainable technologies.

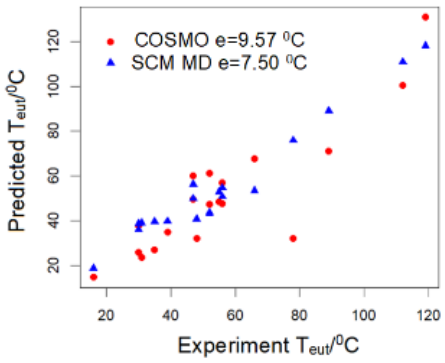

Figure 1. Comparison of eutectic temperature predictions by the causal structural SCM-MD and CSMO-RS real solution models.

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SPECTROPHOTOMETRIC KINETIC AND THERMODYNAMIC INVESTIGATION FOR THE OXIDATION OF ANILINES BY HEXACHLOROIRIDATE(IV) IN SOLUTION MEDIA: A COMBINED EXPERIMENTAL AND COMPUTATIONAL STUDY

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The oxidation kinetics of ortho and para substituted anilines with hexachloroiridate (IV) in aqueous perchloric acid have been performed. The reaction is indicated first order dependence with respect to both reactants. Reaction rates accelerated with the introduction of electron-releasing groups and retarded with electron- withdrawing groups which are elucidated by Hammett's theory of linear free energy relationship. Hammett's reaction constant (ρ) has negative (ρ < 0) value. Furtherance, an increase in temperature increased the reaction constant (ρ). Various thermodynamic parameters have been reported and discussed the validity of isokinetic relationship. Isokinetic temperature (β) from Vonthoff's plot (317 K), Compensation plot (317.4 K) and Arrhenius plot (317 K), is observed. Observed β value from Exner's plot (439.32 K) is above the experimental temperature range (303-323 K), indicating that the enthalpy factors are probably more important in controlling the reaction. The oxidation product is corresponding 2-keto azoxy benzenes. Based on the kinetic results, a suitable mechanism has been proposed.

To further support our proposed mechanism, density functional theory (DFT) computations were done at M06/6-311*G showing that activation energy barriers predict the same reactivity trend as shown by the kinetics experiments.

ACKNOWLEDGEMENTS This work was supported in part by the University Grant Commission, New Delhi, India through start-up grant (BSR) for financial support. Acknowledgment is also made to Head of Department of Chemistry, UOR, Jaipur, Rajasthan, India. Author wants to dedicate this work to (late) Prof. P. D. Sharma, ex-Head of Department of Chemistry, UOR, Jaipur, Rajasthan, India.

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ML_2 METAL COMPLEXES WITH BPA AND IMDA LIGANDS – IN SOLUTION AND SOLID-STATE

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Bis-tridentate metal complexes of flexible ligands with $[M(A\text{-}X\text{-}A)_2]$ structure can form three different geometric isomers: *mer*, *trans-fac* and *cis-fac*.[1] Many factors influence the stability of a certain isomer. Important factors to consider are electronic and steric properties of the coordinating ligand, type of central metal ion and counter-ion present, possibilities of forming non-covalent interactions and others. Understanding of the isomer preferences in hereby described systems would give us a head start in the development of new coordination compounds with desired form and properties.[2,3]

Derivatives of tridentate ligands bis(pyridine-2-ylmethyl)amine (bpa) and 2,2'-iminodiacetamide (imda) were prepared in this work, as well as their corresponding complexes with different Zn(II), Cu(II), Ni(II) and Co(II) salts (Figure 1). Oxygen and sulfur, as well as -NH-, -NPh-, -PH- and -PPh- functional groups were chosen to occupy a central position in the ligand structure. The stoichiometry and the stereochemistry of these complexes, together with possible conformations of their substituents, were studied using the DTF computational approach to determine their relative stability in solution. The systems in solution were studied by NMR and UV-Vis spectroscopy, while the solid-state structures of prepared complexes, characterized by single-crystal X-ray diffraction, gave us an insight of the isomerism in the solid-state. Experimental and computational results were discussed and preferences of some central donor atoms to form certain isomers of ML_2 complexes were shown. One of our goals was to determine which factors lead to formation of *cis-fac* isomers, which could, in the case of nitrogen or phosphorous as central atoms, be used in the development of new type of selective catalysts.

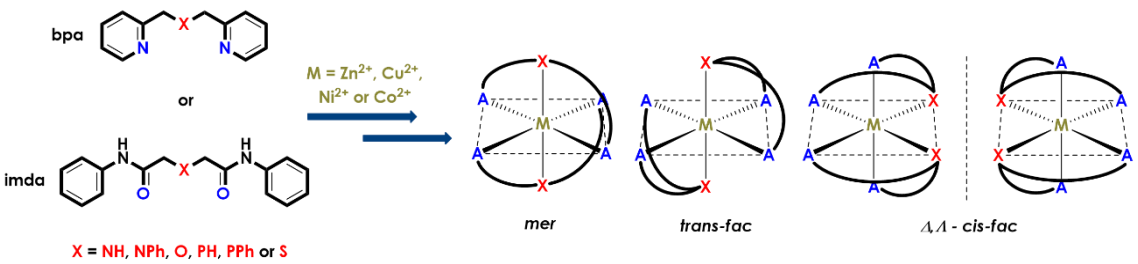

Figure 1. ML_2 complexes of flexible tridentate bpa and imda ligands.

ACKNOWLEDGEMENTS This project was partially supported by CAT Pharma (KK.01.1.1.04.0013).

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HALOGENIDE ANIONS AS HYDROGEN AND HALOGEN BOND ACCEPTORS IN SIMPLE COCRYSTALS WITH A NEUTRAL HALOGEN BOND DONOR

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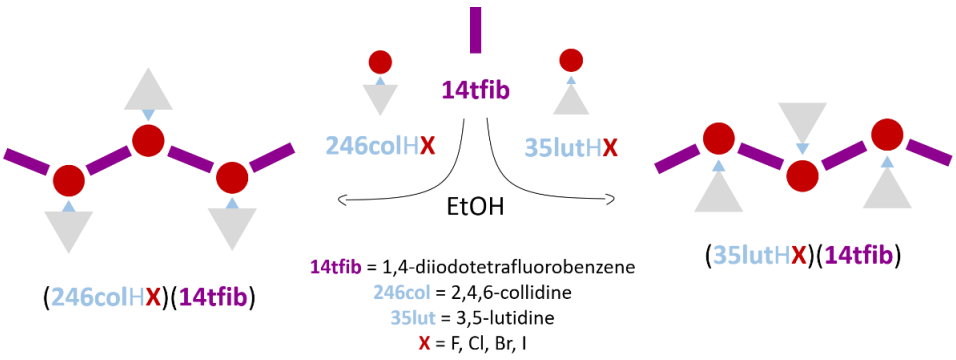
In comparisson to the other Lewis bases, halogenide anions stand out with having no covalently bound atoms which would hinder the approach of one or multiple Lewis acids. That being said, halogenides have been investigated in solid state as acceptors of either hydrogen or halogen bonds,[1,2] but scarcely researched as simultaneous acceptors of both interactions. One of the simplest systems used for such an investigation are halogenopyridinium halogenides,[3] as well as their cocrystals with neutral halogen bond donors.[4] In order to examine halogenides in that role, we prepared cocrystals of 3,5-lutidinium and 2,4,6-collidinium halogenides (X = F, Cl, Br, I) with 1,4-diiodotetrafluorobenzene (**14tfib**) *via* solution synthesis. The molecular and crystal structures of seven cocrystals were determined from the data obtained by single crystal X-ray diffraction experiments. In all the prepared solids, along with N–H···X$^-$ hydrogen bonds formed between cations and halogenides, every halogenide and **14tfib** alternate forming 1D chains *via* C–I···X$^-$ halogen bonds. Comparing interaction lengths relative to the sum of van der Waals and ionic radii of the interacting atoms within both cation series, hydrogen bonds are relatively shorter for smaller halogenides while halogen bonds vary slightly in relative length and do not follow any trend. Despite the differences in cations and halogenides, halogen bonded motifs are preserved in all the cocrystals.



Schematic representation of cocrystal synthesis and the resulting motifs.

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APPLICATIONS OF POLYELECTROLYTE MULTILAYERS FOR THE REDUCTION OF BACTERIAL ADHESION

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Polyelectrolyte multilayers (PEMs) are very well known surface coatings which could be prepared by alternating deposition of positively and negatively charged polyelectrolytes (polycations and polyanions) on a solid surface. PEM build-up strongly depends on applied experimental conditions such as ionic strength, supporting electrolyte type, pH and concentration. In recent years we have developed new PEM strategies which could be valuable for designing soft nano materials whose properties can be finely tuned according to the requirements of specific applications, especially in the field of biomedicine. The emphasis in our studies was in the application of PEMs for the prevention of bacterial adhesion to various surfaces. We investigated the influence of polyelectrolyte multilayer properties on bacterial adhesion capacity,[1] as well as the bacterial adhesion capacity of protein-terminating polyelectrolyte multilayers.[2] We also applied this PEM strategy to study bacterial adhesion capacity of uropathogenic *Escherichia coli* to polyelectrolyte multilayer coated urinary catheter surface.[3] In this case it was shown that on non-treated PVC surfaces, biofilm was formed which was not the case for polyelectrolyte multilayer coated surfaces.

ACKNOWLEDGEMENTS This research was supported by the Croatian Science Foundation under the bilateral Slovenian-Croatian APPLPEMS project (IPS-2020-01-6126).

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COMPARISON OF ALBUMIN AND CHITOSAN EFFECTS ON CALCIUM PHOSPHATE FORMATION ON TITANATE NANOMATERIALS

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The constant need for advanced materials for bone regeneration motivates the development of calcium phosphate (CaPs) composites with different types of materials.[1] The most frequently used materials are biomacromolecules for enhancing biological response and nanomaterials for improving mechanical properties. A possible method for preparing such composites is precipitation at low temperatures,[2,3] a simple and inexpensive method that allows successful incorporation of components with low stability. Recently, the composites of CaPs, biomacromolecules and nanoparticles have emerged as promising new materials for bone regeneration. To successfully prepare such multicomponent materials by precipitation, a study of the influence of individual components on CaPs formation is required.

In this study, the effects of bovine serum albumin (BSA) and chitosan (Chi) on the precipitation of CaPs on titanate nanomaterials (TiNMs) of different morphologies (nanoparticles, nanoplates, nanotubes, and nanowires) were compared. Both biomacromolecules inhibited the transformation of amorphous to the crystalline phase, regardless of the presence of TiNMs which promote the transformation. Neither biomacromolecule influenced the composition of the formed CaP, as calcium deficient hydroxyapatite (CaDHA) was formed in all cases. However, in the presence of both BSA and Chi, the crystalline size and CaDHA morphology were influenced. As well, they inhibited the formation of CaDHA on the surface of the nanowires.

The obtained results may contribute to the development of precipitation methods for the preparation of multicomponent composites.

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PROTECTIVE ABILITY OF *ARTEMISIA ANNUA* L. AGAINST MICROBIOLOGICALLY INFLUENCED CORROSION OF ALUMINIUM ALLOY 5083 CAUSED BY *PSEUDOMONAS AERUGINOSA* IN ARTIFICIAL SEAWATER

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Aluminium-magnesium alloys, 5000 series, are used in many marine applications because of their versatile benefits of strength, weldability, and high corrosion resistance. The mechanisms of corrosion processes in marine environments are quite complex and largely dependent on pH, concentration of dissolved gases, temperature, salinity and the presence of microorganisms. Certain microorganisms are able to colonize the metal surface and indirectly inhibit or accelerate corrosion processes. Microbiologically influenced corrosion (MIC) of aluminium alloy 5083 (ALA) caused by the bacterium *Pseudomonas aeruginosa* (PA) in artificial seawater (ASW) was investigated by electrochemical, surface and spectroscopic techniques without and with the addition of *Artemisia annua* L. extract (AAE). Electrochemical tests proved good corrosion resistance of ALA in ASW, where corrosion current densities, j_{corr} determined from Tafel plots decreased with the increasing immersion time, which was confirmed by electrochemical impedance spectra (EIS) recorded at open circuit potential (OCP) where an increase in the resistance of the film was observed. In a medium inoculated with PA, OCP of ALA shifted to more negative values, while obtained j_{corr} values increased with the increasing immersion time which indicated that PA accelerated corrosion of ALA in ASW. Further obtained results showed that the plant extract prevents the MIC of ALA in ASW by reducing both anodic and cathodic current densities with an inhibition efficiency of 80 %. After 14 days of incubation, the addition of plant extract to inoculated medium at a concentration of 1.0 g L^{-1}, led to an increase in resistance of the surface film, which confirmed inhibitory effect of AAE on MIC of ALA. 3D profiles of treated ALA surface, obtained by Optical Profilometer (OP) revealed that pitting of ALA occurred during 21 days incubation in ASW inoculated with PA, while the addition of AAE led to a decrease in film thickness and roughness. The concentration of aluminium ions in the solution, measured by inductively coupled plasma - optical emission spectrometry (ICP-OES) after short immersion tests of treated coupons, was also in accordance with the electrochemical results, whereby the measured concentration in the inoculated samples was 77.6 µg L^{-1} cm^{-2}, while after the addition of AAE, the concentration was 43.5 µg L^{-1} cm^{-2}.

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INNOVATIVE APPROACHES IN TEACHING CHEMISTRY

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The physiology of learning and memory of today's children is different. A higher level of activity, speed, and stimulus is needed. There is an ever-widening gap between students' needs and established teaching methods, which causes dissatisfaction on both sides. Students are unmotivated, they do not see the point of learning, and they give up further schooling, especially in the field of science. On the other hand, regardless of major advances achieved in the approach to teaching and in the light of new insights in the field of neuroscience and neurodidactics, teachers ought to adapt to new generations and change learning strategies by combining formal and informal methods. According to findings from neuroscience, learning should be meaningful, connected with actual situations (contextual), directed towards learning by solving problems, research, cooperative learning, and play-based learning. The student is thus placed at the centre of learning, while the teacher acts as a moderator who directs and encourages the process itself.[1] Using the stated learning strategies, we do not separate emotions from cognition, which neuroscientists find to be decisive in the learning process.

Information „coloured" by emotion has a greater meaning, i.e. according to the broaden-and-build theory, positive emotions build and broaden the repertoires of thoughts and actions. In that context, students learn by creating and constructing their own insights (knowledge) based on interaction with the environment (physical and social) and by imparting their own meaning, understanding, and interpretation to the environment. Active learning strategies; practical work, research, and games affect the plasticity of the brain by forming new neural connections.[2]

Taking into account the mentioned findings and needs, both of students and teachers, at Fran Galović Primary School we have been using games in chemistry classes for years as an integral part of teaching. By using directed activities in games, students learn in a fun and creative way the concepts and processes that were previously distant, imaginary, and uninteresting to them, e.g.: the structure of the atom, electron configuration of atoms of various elements, formation of ions, conversion between units of measurement, change of the state of matter, etc. Evaluating the project, we have come to the conclusion that we are on the right track. By introducing games in chemistry classes, we have achieved much better results than in the previous years, all in a fun and motivating way.

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FROM OLD TO NEW TOWARDS SUSTAINABLE DEVELOPMENT

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Recycling is a procedure important for the economy development of every country, for the preservation of the living environment and the sustainability of energy sources. That is why it is crucial to start educating children from a young age, so that as they grow, their awareness of ecology and the importance of recycling will grow as well. Children easily learn and acquire new and useful knowledge on how to live healthier and in harmony with nature. Through the education of the youngest, we achieve a common goal, which is to make environmental protection a priority in the lives of all members of the community.

Waste oils are one of the biggest polluters of our nature, especially water. Most of the waste oil ends up in nature, which poses a danger to the environment: it can make the soil unsuitable for plant growth, and it can have a fatal effect on the animal life in the waters.

The goal of the workshop is to recycle waste oil from fryers by making scented candles. The candles are colored with natural colors (cocoa powder and turmeric) and orange essential oil is added to them. Students prepared for practical work using the teaching method of the flipped classroom.[1,2]

Flipped classroom is a form of combined learning in which students learn course content online, watching video content at home. After that, they check the adoption of the content with some of the digital tools (Forms)[3] and send the output to the teacher who, based on the received answers, plans the lesson at school. At school they discuss and ask the teacher questions about what they watched at home. The teacher intervenes when the students cannot come up with a solution on their own, explaining the problem to them. The goal of the flipped classroom is for students to learn through practical work and by asking questions.

After the finished practical work, the scent of candles enriched with orange essential oil spreads through the classroom.

The adoption of the content and the realization of the outcome are checked with the digital tools *Plickers*[4] and *Socrative*.[5]

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CARBONATED WATER: ACID, BUFFER OR BOTH?

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When presenting teaching lessons related to buffer solutions, teachers mostly resort to explaining standard examples of acetate or ammonia buffers.[1,2] Of course, such an approach is not necessarily wrong or bad, but certainly an additional link of the teaching content with everyday substances or phenomena would help the students to learn the material better.

By dissolving pressurized carbon dioxide in water, a chemical reaction occurs between the dissolved gas and water resulting in carbonic acid, commonly known as "carbonated water". Such a solution is acidic with an average pH value of 3.3-4, and could be used as a refreshing drink, or as a base for the production of carbonated juices. It is also frequently used in combination with certain types of wine in noble drink called *gemišt*. In this lecture, the composition of mineral water will be explained on a microscopic level, and its potential as a buffer solution will be determined experimentally.

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CHALLENGES IN CHEMISTRY CLASSES USING ICT TECHNOLOGY

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Technology is present in the lives of all of us, including our students. Survey of the population of 7th and 8th grade students shows that students spend four hours online on average. The idea of the activity was to bring chemistry closer to them in an interesting way and so enter their lives.

By correlating chemistry and informatics, students learned to create a website, upload chemistry content to it and organize materials (videos, recordings of experiments, etc.). In this way, children learn and acquire new and useful knowledge more easily, use the Internet, apply learned material and in the end information spreads quickly and is available to everyone at the same time. Students are encouraged to work together, collaborate and work on joint documents for repetition. The goal of this work is to prepare students for life and in this way show them how chemistry and technology go together and complement each other.

We organized the work through joint preparation and cooperation of chemistry and informatics teachers, and through work in chemistry classes (dealing with introductory topics of the 7th grade of elementary school[1]). The topics that we put on the website are as follows: Chemistry is a natural science, Trial or experiment, Chemical utensils and accessories, Precautions and protection when performing experiments.[2]

In the computer science class, students created a website using the Webnode[3] online tool. The students were divided into pairs and each pair was given their own section of the website to edit according to the content they received from chemistry. All students worked on one website and were added as page editors. The computer science teacher was the administrator of the website. In the informatics class, the students were introduced to the used tool and its possibilities.

The joint presentation of the work was made through the evaluation of the work according to the given evaluation criteria. We communicated with students via Yammer and checked the adoption of the content and the achievement of the results through Socrativa[4] i Testmoza.[5]

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HOW TO FACILITATE THE EVALUATION OF STUDENT ACHIEVEMENTS BY USING WRITTEN PAPERS IN CHEMISTRY?

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Monitoring and evaluating student achievements is an important part of the curriculum teaching cycle that needs to be carefully planned. In student-oriented teaching for the purpose of adopting educational outcomes, it is possible to achieve it by implementing individual and collaborative project tasks.[1] At the same time, it is necessary to highlight what is expected of the students (goals), how they will work and why (which competencies they will acquire). These competencies are, for example, learning how to learn, learning to search and select information, acquiring communication skills, acquiring skills in the use of ICT and/or laboratory equipment, modeling, creating in some material, etc.

The teacher's autonomy in the development of educational outcomes and evaluation planning enables to achieve certain outcomes in the framework of different thematic units during repetition and practice of the teaching content, some parallel and interdisciplinary, and some through vertical connection.[2]

Circumstances caused by the Covid-19 pandemic resulted in special conditions for teaching, learning and evaluation, which became predominantly individual in elementary school. Teachers needed to show flexibility both in teaching methods and methods of evaluation. For this purpose, the students' written papers in the form of project tasks that had a given structure proved to be a good choice. The students were introduced in advance to the rubric for evaluating the work, which consisted of the written part and the creation of a model. In addition to the analytical rubric for evaluation, the students were also given a table for self-assessment of the performance of the project task with a rating scale from 2 to 5. At Rudeš Elementary School, seventh-grade students created a brochure about the selected non-metal chemical element at the end of learning about the structure of matter and the periodic table of elements, and eighth graders about the DNA molecule. In addition to their written work, they created a corresponding atom/molecule model. Analysis of the student marks showed that they differ very little from the self-assessment of the quality of the student's work. This method of evaluation contributes to the satisfaction of the students[3] through the process of checking knowledge and the final evaluation, and makes it easier for the teacher to assess the quality of the students' knowledge.

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FOSTERING TRANSDISCIPLINARY LEARNING IN SCIENCE AND TECHNOLOGY

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The presented work will highlight two education initiatives from Dutch universities at the undergraduate level. These examples reflect and illustrate the recent trends in science and technology, as well as in the corresponding education programs and processes, to work and study not only at the interface of various disciplines but also across disciplines in order to achieve creative solutions to ongoing societal challenges.

The first initiative concerns an innovative approach to teaching nanotechnology as part of the undergraduate Chemistry curriculum at the Inholland University of Applied Sciences in Amsterdam[1]. Students work in pairs to review a relevant and contemporary multidisciplinary topic in nanotechnology and to propose and develop an original research idea. This is presented and defended in the form of an oral presentation before an audience of peers and is written using an article template. The aim of the described approach is to not only help students learn about nanotechnology in a fun and active manner but also to stimulate critical scientific thinking in students as well as to foster the development of their academic, professional, and soft skills. In line with this, the assessment of students relies on the assessment of the oral presentation, engagement in discussion, and the written research proposal.

The second initiative comes from the Maastricht University where a multidisciplinary Bachelor program with the focus on Regenerative Medicine & Technology is being set up. Regenerative Medicine is a relatively new field found at the intersection of science, engineering and medicine. Applying the principles of problem- and research-based learning the new program intends to offer a solid science and engineering foundation strongly integrated with the relevant aspects of medicine and entrepreneurship. As such, the program aims to educate a new generation of researchers that will be able to swiftly adapt to any area of regenerative medicine, and contribute to the design and development of medical therapies, products and devices for research and clinical use. The desired competencies and final qualifications have been defined and translated into a concept curriculum. The education is now being developed in further detail keeping the principles of constructive alignment and the CCCS (Constructive, Contextual, Collaborative, Self-Directed) learning principles in mind. The program is undergoing the initial accreditation process at the moment and is intended to start in September 2023 pending a positive decision by the accreditation committee.

ACKNOWLEDGEMENTS The Department of Life Sciences and Chemistry at the Inholland University of Applied Sciences, including their Chemistry student population, is acknowledged for the support and freedom to design the Nanotechnology course in its described form. The Faculty of Health, Medicine and Life Sciences at the Maastricht University and especially the MERLN Technology-Inspired Institute for Regenerative Medicine are acknowledged for the opportunity to lead the design and development of the new Bachelor program Regenerative Medicine & Technology as well as all the support during this project.

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THE CURRENT CHALLENGES OF IMPROVING CHEMISTRY LEARNING

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We face numerous and different challenges in day-to-day life. New challenges in teaching the chemistry have caused the changes in the existing way of teaching it.[1] In order to discuss successfully possible solutions for improving the teaching of chemistry, it is necessary to understand the current encounters. One of the current challenges of teaching chemistry are changes in teaching strategies in certain periods. Participants will learn about the dominant teaching strategies during chemistry classes at the beginning of the 20th century. Therefore, we will talk about the behaviorist theory of teaching and the application of the cognitivist theory that applied in most of Europe, as well as the increasingly widespread use of the constructivist theory.[2] By applying this theory, the student is placed in the center of the teaching process, and thus the teaching performance is different. Student's activities are planned and based on their own experience during chemistry classes, especially when guided teaching is applied. Furthermore, the strategy of independent teaching can be applied to the activities for gifted students. The need for an appropriate choice and elaboration of a teaching strategy depending on the predictions and needs of the students and on the teaching situation is evident.[3] Since teaching strategies are part of the curriculum circle, the participants will be able to conclude about the need to change each component of the curriculum circle, if there is a change in only one of them. Application of experiential teaching is desirable and possible in the conditions of face-to-face and online teaching. It is essential to plan the activities of students who will have their own experience, regardless of the way of teaching (face-to-face or online) and the form of work (individual, in pairs or groups).[4] One of the competencies of a successful teacher refers to a teacher who knows how to recognize successfully conducted lessons and what and at what point has to be changed in order to make chemistry lessons more successful.[5]

Successful chemistry teaching is the result of the synergy of the work of students and teachers, who understand the professional content, apply a pedagogical approach and regularly evaluate their work, regardless of current challenges regarding the application of teaching strategies and other factors that affect the quality of chemistry teaching.

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POSTER PRESENTATIONS

SELECTIVE GUEST BINDING AND RELEASE: TUNING THE PROPERTIES OF OCTAMERIC NANOCAPSULES

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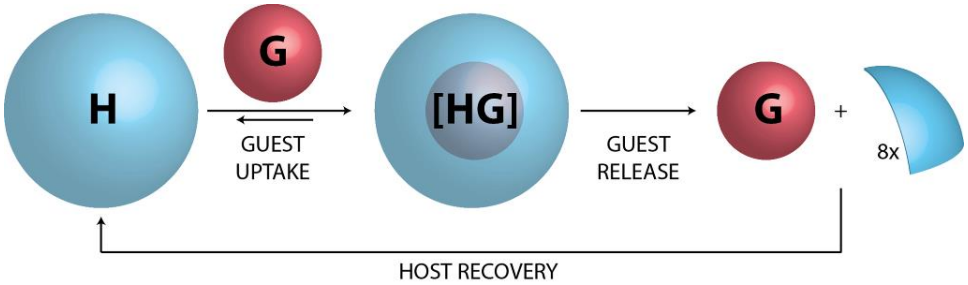
Supramolecular chemistry is built on non-covalent interactions including hydrogen bonds, π-π interactions, and van der Waals forces. By controlling molecular self-assembly and recognition processes through the application of these weak intermolecular forces, it is feasible to produce complex supra-structures from synthetically simple molecules that have adjustable functions and features. Many other self-assembled supramolecular structures, such as capsules, have been discovered throughout the years.[1] These structures are of great interest to many scientists because of their singular capacity to attach the guest molecules inside clearly defined internal spaces.

Our team presented the first hydrogen-bonded octameric capsule based on the benzene-1,3,5-tricarboxylic acid (BTA) core a few years ago.[2] The capsule is held together by 48 cooperative hydrogen bonds. Thanks to a large internal cavity of 1719 Å^3, this assembly is an excellent receptor for C70 and C60 fullerenes, with encapsulation of C70 being highly favored. In our recent research, we outline a synthetic approach to finely tune and target the solubility of the octameric capsules for preparative guest separation in addition to the encapsulation of the catalytically-active species.



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STRUCTURAL AND THERMODYNAMIC FEATURES OF DIAMONDOID AMMONIUM SALT INCLUSION COMPLEXES WITH CYCLODEXTRINS

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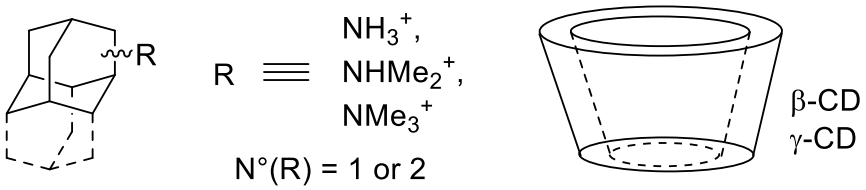
Functionalized diamondoid ammonium salts are an intriguing class of compounds capable of forming ultra-stable complexes with cucurbituril hosts (CB[n]) in aqueous environment with binding constants up to 10^{15} mol^{-1} dm^3.[1] Inspired by these properties, we decided to broaden the research scope of inclusion complexes stabilized by hydrophobic interactions between various cage ammonium salt guests and cyclodextrin (CD) as a different macrocycle host molecule.[2]

Herein we present the synthesis of a continued series of diamondoid ammonium salts and a detailed thermodynamic study of their complexation with β- and γ-CDs. The complex stability constants were determined by ITC and ^{1}H NMR titrations in aqueous solutions. Additional NMR spectroscopic techniques (^{1}H-^{1}H NOESY, ^{1}H DOSY) along with computational methods were employed to provide a deeper insight into the thermodynamics of hydrophobically driven complexations and structural features of the formed supramolecules.

The binding strength was assessed as a function of diamondoid salt size, functional group position and cyclodextrin cavity size and by varying these parameters, a structure-selectivity relationship can be determined in order to facilitate the design of next generation of suitable guests.



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SUSTAINABLE SOLUTION FOR SYNTHESIS OF DIAMONDOID ETHERS

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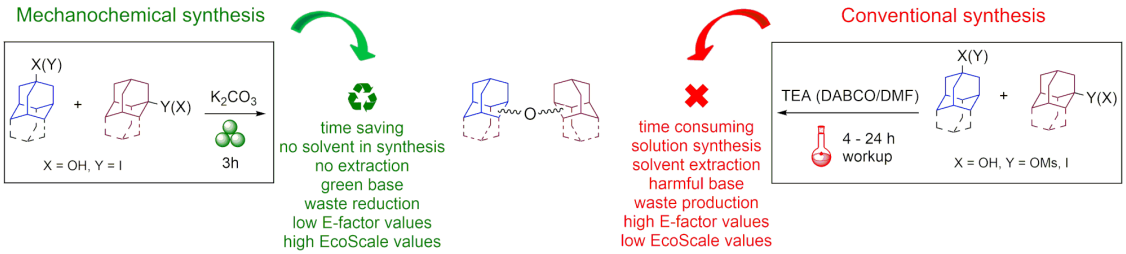
Diamondoids are diamond-like hydrocarbon cage molecules that have emerged as promising candidates in a wide range of applications.[1, 2] Their inherent properties and availability for selective functionalization allows for a development of variously applicable scaffolds. However, the tendency of smaller diamondoid derivatives to sublimate at even slightly elevated temperatures coupled with solubility issues of larger derivatives offers a challenge for their preparation. Here, we present the first mechanochemical synthesis of several diamondoid ethers differing in the size and number of their cage subunits. Efficient mechanochemical preparation of such ethers is enabled solely by high-temperature ball milling conditions[3] and does not proceed under ambient conditions. When compared to the conventional synthesis[4] of the same ether derivatives, the calculated green chemistry metrics showed significant sustainability benefits of the mechanochemical approach. Thus, mechanochemical procedures are faster, allow for the use of an inorganic green base, result in comparable or superior reaction yields, and are overall more sustainable and eco-friendlier. Furthermore, application of mechanochemistry in the preparation of large diamondoid composites opens up a sustainable approach to the synthesis of next-generation materials consisting of diamondoid subunits, unhampered with solubility capabilities of the reactants.



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COMPLEXATION THERMODYNAMICS OF BENZENE DERIVATIVES WITH MACROCYCLIC RECEPTORS

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Cucurbit[7]uril (**CB7**) and β-cyclodextrin (**β-CD**) are well-known macrocyclic receptors for hydrophobic compounds in aqueous solutions.[1,2] Since the host and guest engage in relatively weak van der Waals interactions, the stability of formed complexes is predominantly ascribed to the thermodynamically favourable dehydration of the host cavity[3] and the guest.[4] In contrast with **β-CD**, the inclusion of simple benzene derivatives within **CB7** was not systematically explored. A variety of mono- and 1,4-disubstituted benzene derivatives with different electron-donor (-acceptor) properties were hence chosen as potential guests for heptameric glycouril receptor. The corresponding complexation reactions were explored by means of isothermal titration microcalorimetry and ROESY NMR spectroscopy in a wide temperature range. Guests functionalized with electron-donor groups formed more stable complexes with **CB7** due to more favourable complexation energetics. The stability of **β-CD** complexes was always lower than that of the corresponding **CB7** complexes because of the less favourable enthalpic contribution to $\Delta_r G°$. Significant temperature dependence of $\Delta_r H°$ and $\Delta_r S°$ resulted in an almost complete enthalpy-entropy compensation. These results suggest that the guests behave as structure makers at lower temperatures (classic iceberg hydration model) and as structure breakers at higher explored temperatures.[4]

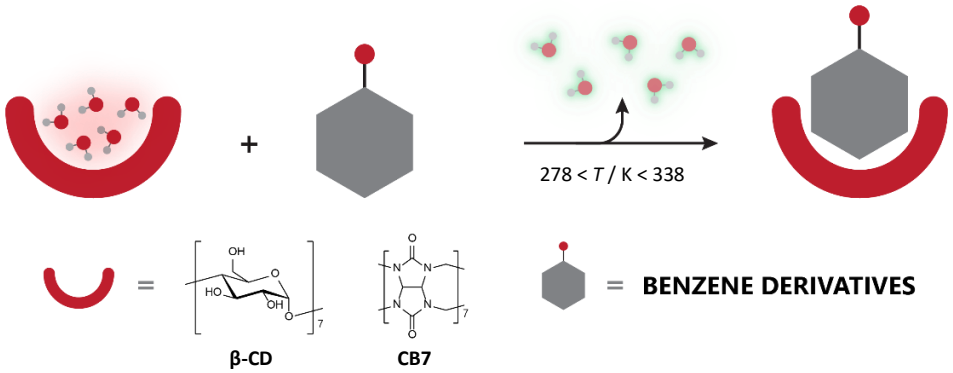

Figure 1. Schematic representation of the complexation process.

ACKNOWLEDGEMENTS This research was fully supported by the Croatian Science Foundation (project MacroSol, IP-2019-04-9560) and European Regional Development Fund (project CIuK, KK.01.1.1.02.0016).

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STOICHIOMETRIC DIVERSITY OF HALOGEN BONDED COCRYSTALS DERIVED FROM *o*-DIIODOTETRAFLUOROBENZENE AND MONOTOPIC ACCEPTORS

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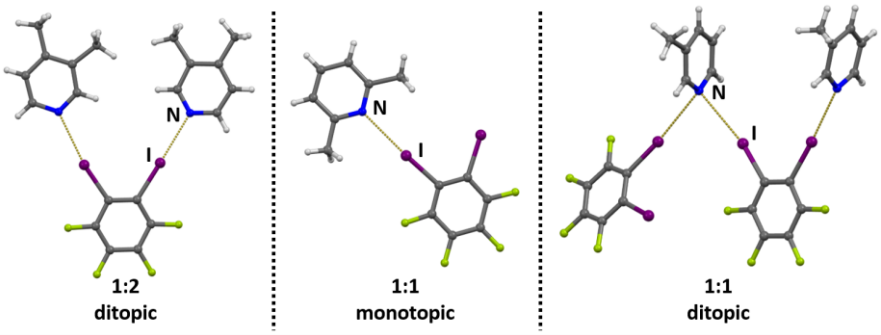
Perfluorinated halogenobenzenes are a group of halogen bond donors that include a wide range of compounds with different number of donor atoms (i.e. different topicities), what ultimately allows to synthesize halogen bonded cocrystals with various stoichiometries and crystal packing motifs.[1,2] The structural and the statistical study of the compounds including 1,3- and 1,4-diiodotetrafluorobenzene and simple monotopic acceptors have pointed out significant differences in their topicities in corresponding crystal structures: **14ditfb** has been found to be mostly ditopic, while **13ditfb** is generally monotopic halogen bond donor.[3] The third isomer – **12tfib** – consists of two donor atoms located at an angle of 60° one to another, which can be a limiting factor for the formation of two halogen bonds simultaneously, due to unfavourable steric influences between the acceptor molecules. To test this hypothesis, we have prepared and structurally characterized six binary cocrystals of **12tfib** and six simple monotopic pyridines (3-picoline, 2,6-lutidine, 3,4-lutidine, 3,5-lutidine, 2,4,6-collidine and isoquinoline). Four obtained cocrystals are of 1:1, and two are of 1:2 stoichiometric ratio, while **12tfib** has served as a ditopic donor in total four structures (two with 1:1 and two with 1:2 stoichiometry). In 1:1 cocrystals with 3-picoline and isoquinoline acceptor molecules participate in bifurcated halogen bonds, while enabling ditopicity of the **12tfib** molecule in those compounds. Halogen bonded complexes in 1:2 cocrystals are not planar, but were found in bent conformations due to the unfavourable steric repulsions of two halogen-bonded acceptor molecules.



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MOLECULAR MODELLING OF MntR TRANSCRIPTION FACTOR FROM *BACILLUS SUBTILUS*

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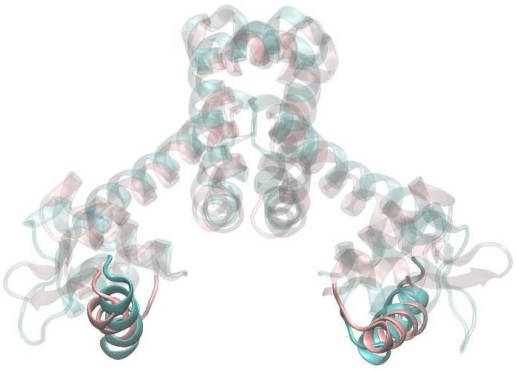
Manganese homeostasis is a highly sensitive process in bacteria. On the one hand, manganese ions are essential for the survival of a bacterium since they are necessary for basic cellular processes, such as DNA replication and resistance to oxidative stress. At the same time, manganese ions are toxic for the cell if present in high concentrations. Therefore, a bacterium must have a sensitive cellular mechanisms for regulation of manganese homeostasis.[1] In case of the bacterium *Bacillus subtilis* this mechanism relies on the MntR protein which is a transcriptional repressor that is activated for DNA binding by manganese ions (Mn^{2+}).[1] Although extensive experimental data on *B. subtilis* MntR is available, the molecular mechanism through which *B. subtilis* MntR is activated for interaction with DNA upon Mn^{2+} binding is still a puzzle.

Starting from available crystal structures of different forms of this protein, systems with and without Mn^{2+} bound in the binding sites were prepared for molecular dynamics (MD) simulations. Special attention was put on protein protonation and different approaches for adding polar hydrogen atoms were applied since hydrogen bond networks might have an important role in the protein's molecular mechanisms. The results of analyses of all-atom MD simulations point to the changes in the protein's dynamics as the most pronounced change due to Mn^{2+} binding. It seems that Mn^{2+} binding reduces the conformational space of the protein and "locks" the DNA binding helices in the conformation appropriate for DNA binding. In order to validate this hypothesis, mutations that should induce activity of *B. subtilis* MntR even in the absence of Mn^{2+} ions were constructed *in silico* and computationally studied.



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BIOLOGICAL ACTIVITY OF 3-AMINOQUINUCLIDINE QUARTERNARY SALT

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Quaternary ammonium compounds (QACs) are amphiphilic compounds with exceptional properties and a wide range of applications. They display very good biological activities. Due to the development of bacterial resistance to QACs, the current aim is to synthesize new QACs which are biodegradable, but still efficient.[1] Quaternization of heterocyclic quinuclidine and its derivatives has proven to be a good solution since its quaternary salts have great antibacterial and antifungal properties. For this research, the antibacterial activity of synthesized 3-aminoquinuclidine quaternary salt with an alkyl chain of 16 carbon atoms has been investigated by microdilution method on seven bacterial strains: *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Enterococcus faecalis, Salmonella enteritidis, Listeria monocytogenes* and *Bacillus cereus*. The best MIC value obtained was 9 nM against two Gram-positive bacteria: *L. monocytogenes* ATCC 7644 and *S. aureus* ATCC 25923. The second-best MIC was against Gram-positive *E. faecalis* ATCC 29212 at 36 nM. Obtained values are considered the potential for future investigations of that quaternary ammonium salt.

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PREPARATION AND MASS SPECTRAL CHARACTERIZATION OF DIAMONDOID DERIVATIVES

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Diamondoids are hydrocarbons with characteristic cage structures[1] and in nature these molecules are predominately found in mature oils as final products of fossil decomposition, indicating their high thermodynamical stability.[2] They were named after diamond, but unlike diamond diamondoids can be selectively functionalized since they possess terminal hydrogen atoms with different reactivity. Diamondoid derivatives have already found application in many fields,[2] with preparation of new molecules constantly in progress. However, derivatization of diamondoid cages can often lead to formation of several products and many of them are constitutional isomers. Such isomers can show different fragmentation pathways in mass spectrometry, making gas chromatography with mass spectrometric detection (GC-MS) an ideal tool for monitoring the reactions, analyzing the reaction mixtures and characterizing the isolated products.[3] For example, a common route in diamantane cage functionalization is its direct oxidation,[4] a reaction that benefits from usage of the GC-MS analytics since slight variations in the reaction conditions result in the formation of different products in different ratios (Figure 1). Here we will showcase the application of combined chromatographic and mass spectral characterization for fast reaction screening.

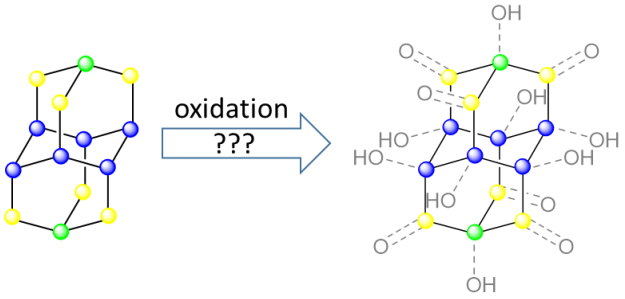

Figure 1. Oxidation of diamantane leads to different products.

ACKNOWLEDGEMENTS

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THERMODYNAMICS OF SEVERAL ION-PAIRINGS IN ACETONITRILE

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In the field of supramolecular chemistry, ditopic receptors capable of binding ion-pairs play a significant role.[1] The binding of cation on a ditopic receptor often allosterically affects the binding of an anion (or *vice versa*) enhancing the stability of the resulting complexes. In order to fully understand and exploit such cooperativity it is necessary to characterize the underlying structural and thermodynamic aspects.[2]

Recently we synthesized amide-ureido-calix[4]arene derivative and investigated its ability as ion-pair receptor in acetonitrile. During this investigation a need for the values of equilibrium constants for ion-pairing in this solvent emerged. Namely, organic solvents are generally better media for the complexation of ions with organic receptors because ions are poorly solvated in them in comparison to water. However, the latter fact also results with the increase of significance of ion-pairing in organic solvents. As the literature lacks the constants of ion-pairings in acetonitrile, we investigated the thermodynamics of ion-pairing for several lithium and sodium salts using conductometric and microcalorimetric titrations. The obtained results were correlated with the basicities of the examined anions in acetonitrile,[3,4] and compared with standard Gibbs energies of transfer of the appropriate ions from water to acetonitrile.[5]

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RHEOLOGICAL CHARACTERIZATION – IMPORTANT TOOL IN REVERSE ENGINEERING OF OPHTHALMIC SOLUTIONS

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Eye drops are the prevalent ophthalmic drug delivery system with certain limitations in terms of delivery to ocular tissues. To improve delivery, polymers are often added in formulations due to their unique properties such as prolonged release and improved drug solubility.[1] Development of the topical generic ophthalmic drug products revolves around demonstration of the equivalence to the reference medicinal product (RMP). If RMPs contain polymers, reverse engineering studies are conducted to determine grade and concentration of added polymer, to ensure required similarity. Due to complexity of the polymers, and their non-Newtonian behavior, several analytical techniques are applied during this process, however rheological characterization is essential for the final confirmation of equivalence with RMP[2] because it can be used to compare the behavior of the products on the eye. Tests that are required are: shear rate sweep test (viscosity curve), amplitude sweep and frequency sweep. These tests gather information about visco-elastic properties of added polymer in formulation. For more complex ophthalmic topical systems (e.g., in situ gels), gelation time of polymer with tear fluid provides information about gel characteristics of the final product, and its behavior during application. Presented work provides overview of different rheological tests and points out their importance during development of ophthalmic solutions.

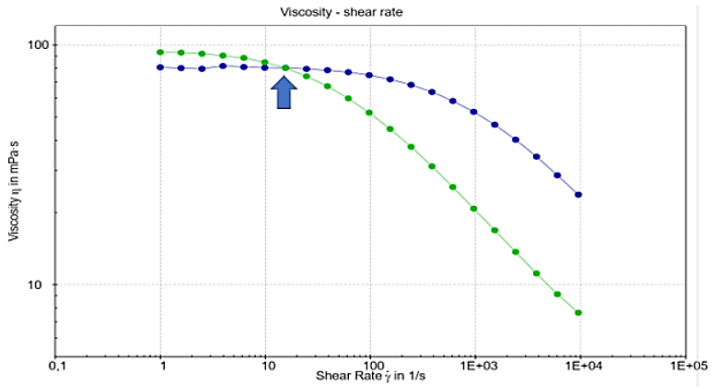

Figure 1. Viscosity curves obtained for JGL formulation (blue) and RMP (green) containing the same type of thickener, but different grade based on molecular weight (MW). Although the same at one point (arrow), during applied shear rate range, viscosity profile is different.

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CALCIUM PHOSPHATE/TITANATE NANOMATERIAL COMPOSITES FOR BIOMEDICAL APPLICATIONS

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In recent years, calcium phosphates (CaPs) composites with TiO_2 nanomaterials (TiNMs) have emerged as a promising solution to the poor mechanical properties of CaPs based bone regeneration materials.[1] Using TiNMs of different morphologies opens up an opportunity to fine-tune the properties of composites. Among different TiNMs, the formation of CaPs has been investigated most frequently on nanotube arrays, while the studies on other TiNMs are scarce. To fill this gap, in this study CaPs composites with TiNMs of different structures, compositions, and morphologies were prepared by precipitation at room temperature.[2,3] Four different TiNMs were used: anatase nanoparticles and nanoplates, titanate nanotubes and TiO_2 (B) / hydrogen titanate nanowires. In all cases, calcium-deficient apatite (CaDHA) was formed after one hour of aging. Although the morphology and size of the crystalline domains of CaDHA obtained on the TiNMs were different, no significant difference in their local structure was observed. To test the potential of the composites for biomedical applications, their effect on hemostasis, cell viability of Jurkat T-cells and cytokine expression in Jurkat T-cells were investigated. The largest effect on hemostasis and cytokine expression, as well as a significant reduction of Jurkat cell viability after 24 hours was observed for composites with nanotubes and nanowires.

The obtained results indicate a rapid and versatile method for the preparation of CaP/TiNMs composites and confirm the potential of such composites for biomedical applications.

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CAN HALOGEN BOND PAY THE ENTHROPY PENALTY?

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Halogen bond is an attractive, strong and directional noncovalent interaction in which a halogen atom acts as a Lewis acid.[1] Most commonly used acceptors of halogen bonds are anions[2] and neutral molecules containing nitrogen or oxygen atoms[3] – i.e., species capable of acting as Lewis bases. Typical halogen bond donors are perfluorinated iodobenzenes,[4,5] whereas the donor properties of perflourinated iodoalkanes, such as 1, 4-diiodooctafluorobutane (**ofib**) remained almost completely unexplored.

This type of bonding has attracted considerable attention in the solid state chemistry, where it is widely used for the synthesis of halogen bonded cocrystals. According to the most recent definition, cocrystals are solids that are crystalline materials composed of two or more molecules/coformers in the same crystal lattice.[6] Cocrystals are commonly composed of two conformers, which as separate substances are solids at room temperature. Less commonly one conformer will be a liquid (unless it was also the crystallisation solvent and therefore present in huge excess), while cases where two liquids at room temperature produce a solid cocrystal are extremely rare, as formation of a solid from two liquids is extremely entropically unfavourable.[7]

This study reports the structures of five new cocrystals of the aliphatic ditopic **ofib** and monotopic nitrogen-based aromatic halogen bond acceptors which were obtained by reaction of liquid halogen bond donor (**ofib**) and liquid acceptor in 1:2 molar ratio. Single crystal X-ray diffraction analysis of obtained crystal products revealed that the cocrystals are comprised of discrete C–I···N halogen bonded complexes of 1:2 stoichiometry. The $\Delta_r H$ values for the reaction of **ofib** and investigated acceptors were determined calorimetrically at 25 °C. As expected, the cocrystal formation was strongly exothermic in all cases. The particularly favourable halogen bonding realized within the products can thus overcome the entropy penalty arising from association of two liquid reactants into a solid at room temperature.

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LC-MS/MS AS A SOLUTION IN PRECISE, SELECTIVE, CONFIRMATORY AND COST EFFECTIVE FOOD MULTI-CONTAMINANT ANALYSIS

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The LC-MS/MS has over the last decade matured into the leading technique for detection of organic contaminants in Food and Feed. The sensitivity, selectivity and robustness of LC-MS/MS instruments has continuously improved, positioning them in legislation as confirmatory instruments. Although initially it was not possible to obtain accurate results down to the ppb range (as required in legislation) without any matrix removal and analyte enrichment, the latest generation of instruments can use dilute & shoot approach. This is one of the pre-requisites for multi-contaminant analysis due to widely different physico-chemical properties of all organic contaminants that are legally regulated.

The scheduled MRM (multiple reaction monitoring) mode has enabled acquisition of large analyte lists, e.g., multimycotoxins, bacterial metabolites, veterinary drug residues, pesticide residues, where methods covering more than 500 compounds have become fairly routine.[1]

We have applied a LC-MS/MS multicontaminant analysis method covering more than 500 fungal metabolites and dilute & shoot approach for analysis of multiple legally regulated mycotoxins with indicative levels and unregulated mycotoxins in cereals and feed samples from Croatia.

The results showed that multiple contaminants are predominantly present in analyzed cereals and feed, usually grouping within one fungal genera metabolites. The 100 % co-occurrence of mycotoxins with some bacterial and yeast metabolites was confirmed and the usage of such dilute & shoot with LC-MS/MS multi-contaminant method was justified.

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STRUCTURE COMPARISON AND STRUCTURAL ALIGNMENTS OF OLIGOMERIC PURINE NUCLEOSIDE PHOSPHORYLASES

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It is known that enzymes can be composed of one or more, same or different, subunits. If some protein is composed of more than one subunit, it is called an oligomeric protein,[1] and one example of such proteins are purine nucleoside phosphorylases (PNPs). There are two main classes of this enzyme: trimeric PNP or "low molecular mass" protein which can mostly be found in eukaryotic organisms, and hexameric PNP or "high molecular mass" protein which can mostly be found in prokaryotic organisms (Figure 1).[2] These two types of enzymes share only 20 - 30 % sequence identity, but the overall fold of the single monomer is similar, and yet this similar monomeric building block makes a different quaternary structure. A large number of 3D structures of PNPs have been determined so far. We can base our understanding of the mechanism by which monomeric subunits communicate in these enzymes on this structural data, and take into account the oligomeric arrangement of subunits in enzymes from different organisms.

As part of the ALOKOMP project (alokomp.irb.hr) which tries to understand the allosteric communication between these monomeric subunits, the relational database of PNPs is constructed. As a special subset of this database, an all-to-all overlap of these structures is also made, where we can cluster this data as well as compare some of the structures according to their assembly symmetry and their crystallographic symmetry.

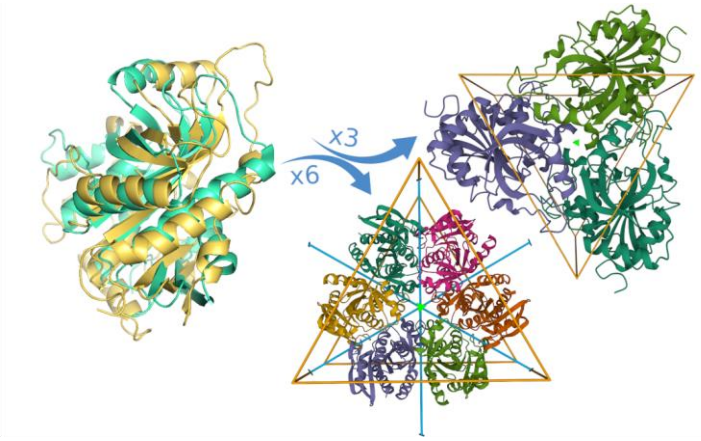

Figure 1. Monomeric units from trimeric PNP and hexameric PNP show similar overall fold but form different quaternary structures.

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A COMPUTATIONAL STUDY OF CALIXARENE-CYCLOPEPTIDE ANION RECEPTORS

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Calixarenes are macrocyclic oligomers consisting of phenolic subunits linked by methylene bridges in the *ortho*-position. Unsubstituted calixarenes show only moderate affinity for the binding of smaller molecules and ions. A particularly interesting group of calixarene derivatives with proton donating groups on their substituents are secondary amide derivatives.[1,2]

Cyclopeptides are macrocyclic compounds that contain amide groups within their backbone, and sometimes on their sidechains. Due to this, they are sometimes used as anion receptors.[3,4] Their good complexation properties are a result of the proton-donor properties of peptide groups and the flexibility of the macrocyclic ring.

By combining the calixarene part, which determines the rigid conformation of the molecule and the cyclopeptide part, which carries the proton donor groups essential for the anion coordination, we created receptors that could have high affinity, and possibly selectivity, towards anions in the solution (Figure 1). Here we present the results of molecular dynamics simulations of several calixarene-cyclopeptide derivatives complexed with halogen and oxoanions in solution. We observed stable complexes in which the anions were coordinated by amide protons of calixarene and cyclopeptide ring.

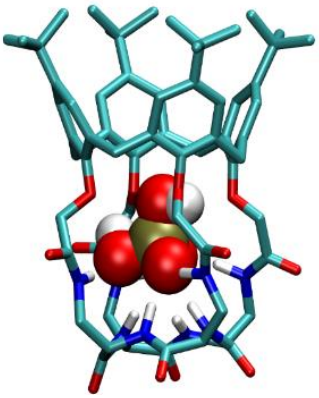

Figure 1. Calixare-cyclopeptide receptor in complex with dihydrogen phosphate.

ACKNOWLEDGEMENTS This work was supported by the Croatian Science Foundation under project IP-2019-04-9560 (MacroSol). Scientific resources of Center of Excellence in Chemistry were used in this research.

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INFLUENCE OF DIFFERENTLY STABILIZED SILVER NANOPARTICLES ON CALCIUM PHOSPHATE FORMATION AND TRANSFORMATION

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Calcium phosphate (CaP) composites with antimicrobial metal/metal oxide nanoparticles are emerging as a promising replacement for antibiotic therapy in implant-related infections. Silver nanoparticles (AgNPs) are attracting special attention due to their nonselective antibacterial activity.[1] A promising method of preparing CaP composites with AgNPs is precipitation.

The effect of differently stabilized silver nanoparticles on the formation and transformation of calcium phosphates was investigated. Polyvinylpyrrolidone (PVP), citrate (Cit) and sodium bis(2-ethylhexyl) sulfosuccinate (AOT) were used as stabilizers. Different effects on the rate of amorphous calcium phosphate (ACP) transformation to crystalline phase, as well as properties of formed amorphous and crystalline solid phases were observed depending on the type of AgNPs. After 60 min ageing time, in the control system ACP was transformed into mixture of calcium deficient hydroxyapatite (CaDHA) and small amount of octacalcium phosphate (OCP), as confirmed by PXRD, TEM, and SEM analysis of the formed precipitate. AOTAgNPs inhibited ACP transformation and OCP formation, at concentrations of 10 and 25 ppm. Furthermore, CitAgNPs at a concentration of 5 ppm promoted ACP transformation, but the effect on the composition of the obtained solid phase was not evidenced. No effect of PVPAgNPs on rate of transformation and precipitate composition was detected. The behaviour in the local environment was monitored by electron paramagnetic spectroscopy. SEM micrographs revealed that the best incorporation into CaPs was achieved for AOTAgNPs.

The obtained results provide new insights important for understanding CaPs formation on different nanomaterials.

ACKNOWLEDGEMENTS Financial support from the Croatian Science Foundation, Grant HRZZ- IP-2018-01-1493 is greatly acknowledged.

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GLASS SURFACE MODIFICATION WITH INKJET PRINTABLE AMPHIPHILIC SILVER NANOPARTICLES

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Additive manufacturing is one of the most rapidly adopted technologies today because it provides an efficient process for manufacturing devices. The ability to inkjet print thin films onto glass substrates is attractive for the application in electronics (i.e., printing active layers in sensors and memory devices), or in architecture and interior design to produce decorative glass surfaces.[1,2] Inkjet printing is able to produce sophisticated and complex designs, as the process is fully digitally controlled and involves effective control at the micro-scale.

In this work, formulation and characterization of an ink containing amphiphilic silver nanoparticles (AgNPs) for the modification of glass surfaces by inkjet printing is presented. The AgNPs were prepared by modifying the primary particle stabilizer[3] with functional amine (3-morpholinopropylamine) via an amidation reaction. The amphiphilic particle coating balances the hydrophilic-hydrophobic equilibrium and improves the dispersibility in less polar solvents, as well as adhesion of the printed features to clean glass surfaces in the fabrication of high-resolution metal patterns. Highly stable nanoink was prepared by redispersing 10 wt % AgNPs in a ternary solvent mixture of water, ethanol and ethylene glycol. The main characteristics of the formed ink, such as particle size and size distribution, stability over time and rheological properties were studied in detail. Multiple layers were printed on microscope slides, and post-printing treated both thermally and with intense pulsed light (IPL). In addition, electrical properties were evaluated using a four-point probe. Thus, new fabrication technologies (inkjet printing) and post-processing treatments (photonic annealing) combined with innovative materials (AgNPs as inorganic pigments) enabled the modification of glass surfaces with a thin metallic film that can be used in printed electronics or as customized decorative products.

ACKNOWLEDGEMENTS This work is funded by the European Regional and Development Fund for the Industrial Research and Innovation (IRI) Project "*Research and development of innovative glass processing techniques*" (KK.01.2.1.02.0059)

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UTILIZATION OF A KINETIC ISOTOPE EFFECT TO DECREASE DECOMPOSITION OF CEFTRIAXONE IN A MIXTURE OF D_2O/H_2O

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The labile β-lactam ring of penicillins and other β-lactam antibiotics is characterized by its pronounced susceptibility to various nucleophiles, acid-base reagents, oxidizing agents or even solvents like water and alcohol. However, the major pathways of β-lactams degradation are similar, leading to various breakdown products. The discovery of cephalosporin and demonstration of its improved stability in aqueous solution, as well as its enhanced *in vitro* activity against penicillin-resistant organisms, were major breakthroughs in the development of β-lactam antibiotics. Although cephalosporins are more stable with respect to hydrolytic degradation than penicillins, they still experience a variety of chemical and enzymatic transformations.

The present study was designed to gain insight into the kinetics of cephalosporin degradation, more specifically, ceftriaxone degradation at its therapeutic concentration. As ceftriaxone is one of the most frequently used parenteral antibiotics in treating specific infections, understanding of its degradation mechanisms at the concentration administered parenterally is essential for development of formulations containing this API.

Therefore, our study was focused on obtaining information on the rates and mechanisms of ceftriaxone degradation in aqueous environment at the therapeutic concentration of 20 mg/mL. The study was directed towards obtaining kinetic information on the rates and mechanisms of ceftriaxone degradation in water, a mixture of water and deuterium oxide, and deuterium oxide itself at the neutral pH (range of 6.7 to 7.6). Specific ceftriaxone degradation products were observed in aged samples prepared in the examined solvents using HPLC and MS. By comparing the degradation rates in H_2O and D_2O, the observation of a kinetic isotope effect (KIE) provided some valuable insight as to the nature of the initial ceftriaxone degradation. This result, in combination with an investigation of the reaction order for the degradation using the method of initial rates, highlighted the important contribution of the formation of a previously unreported dimer-type species. Computational analysis was utilized to get a molecular insight into chemical processes governing the ceftriaxone degradation and to rationalize the stabilizing effect of replacing H_2O with D_2O. For that purpose, molecular dynamics simulations in both explicit solvents were carried out, together with a range of mechanistic DFT calculations to obtain the underlying kinetic and thermodynamic parameters of the most prevailing reactions in solution. In doing so, focus was on two dominant processes, (i) the opening of the β-lactam ring following the hydrolytic cleavage of its C–N amide bond, and (ii) the breaking of the C–S bond linking the triazine moiety with the rest of the structure.

ACKNOWLEDGEMENTS: The results presented here are co-financed by the European Union from the European Regional Development Fund (Liquid antibiotics and active substances with antibiotic-like stabilization mechanisms for intravenous and intramuscular application, KK.01.2.1.02.0175).

GLUTEN IN DIETARY SUPPLEMENTS USED IN THE TREATMENT OF INFLAMMATORY BOWEL DISEASES

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Gluten is naturally found in food, especially in certain grains such as wheat, rye, and barley. The consumption of gluten causes damage to the lining of the small intestine, preventing the absorption of nutrients and causing deficiencies that can lead to severe conditions and diseases. Inflammatory bowel diseases, Crohn's disease and ulcerative colitis, are chronic relapsing diseases affecting millions worldwide and disrupting their daily lives and requiring prescribing of drugs and dietary supplements. In addition to the active substance, orally formulated drugs contain a whole range of ingredients, such as excipients. Excipients can be synthetic or from natural sources originating from plants. One common excipient is starch. Corn, potatoes, and wheat are the most common starch types. Therefore, oral drugs and dietary supplements in the form of tablets and capsules are potential sources of gluten contamination. Plants and dietary supplements are important sources of biologically active components that have a positive effect on human health. In addition, the use of dietary supplements is constantly increasing. On the other hand, health professionals do not recognize the potential sources of gluten in orally formulated drugs. For all the listed reasons, this work aimed to evaluate gluten content in dietary supplements.

Forty-five samples were collected from local pharmacies, food health stores and purchased from the Internet (products online-only available in Croatia). All dietary supplements were classified as botanical monopreparations and multipreparation, as they contained one or more of the investigated herbal extracts: Indian frankincense, Green chiretta and Turmeric. Enzyme-linked immunosorbent assay (ELISA) was used to detect and quantitate gluten in investigated samples. All samples were analyzed in duplicate prior to stated expiry date.

Based on the obtained results, the gluten content was above the LOQ value (0.15 ng/mL) in 12 samples, while in one dietary supplement was over 20 ppm (28 µg/mL). Therefore, there are currently no labeling requirements for gluten found in orally formulated drugs and dietary supplements, while all foods labeled "gluten-free" must contain less than 20 ppm gluten.

To sum up, all analyzed dietary supplements except one sample contained gluten less than the FDA criteria.

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OPTIMIZATION OF LC-QqQ-MS/MS METHOD FOR QUANTIFICATION OF ANDROGRAPHOLIDES IN HUMAN PLASMA

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Andrographolides are diterpenoids found in the plant *Andrographis paniculata* and are widely used in traditional medicine, exhibiting anti-inflammatory properties.[1] In this research we developed and validated high-performance liquid chromatography coupled with electrospray ionization triple-quadrupole tandem mass spectrometry (LC-QqQ-MS/MS) method for quantification of andrographolides in human plasma. The chromatographic analysis of pharmacological active andrographolide (AND), neoandrographolide (NAND) and 14-deoxy-11,12-didehydroandrographolide (DAND) was performed on a 15 cm HSS Cyano column with a gradient mobile phase of ultra-pure water and acetonitrile with the addition of formic acid (0.1%) as a modifier at a flow rate of 0.8 mL/min in 21 min.

The validation results showed acceptable linearity of the method (r>0.999) for all analytes within the calibration range 0.7–10 µg/mL. The acceptable accuracy of the method was indicated by recovery of 90–107 %. The limit of quantification was found to be between 2 and 70 ng/mL while the limit of detection was found between 0.6 and 20 ng/mL. Multiple reaction monitoring (MRM) mode was optimized to quantify data under monitoring precursor-product ion transitions of m/z 351.1 → 105.0, 351.5 → 91.0, 351.1 → 79.0 and 351.1 → 77.0 for AND, m/z 481.6 → 319.0, 481.6 → 301.2, 481.6 → 289.2, 481.6 → 95.1 for NAND and m/z 333.1 → 314.9, 333.1 → 297.2, 333.1 → 257.3, 333.1 → 91.0 for DAND (Figure 1). This advanced method is simple, selective, accurate and cost-effective. As a result, this assay can be easily transferred in clinical settings for pharmacokinetic studies and therapeutic drug monitoring programs.

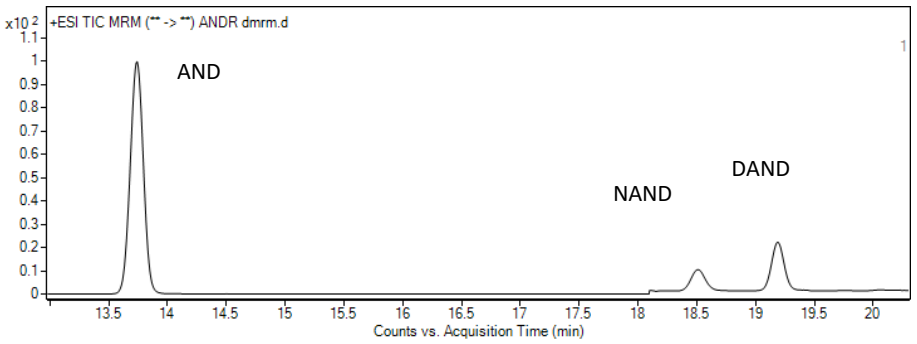

Figure 1. Total ion scan (TIC) of AND, NAND and DAND collected in dynamic MRM mode.

ACKNOWLEDGEMENTS This work has been supported in part by the Croatian Science Foundation under the project numbers [UIP-2017-05-3949, DOK-2021-02-7922] and project FarmInova (KK.01.1.1.02.0021) funded by the European Regional Development Fund.

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ALL-SOLID-STATE FLEXIBLE AMMONIUM-SELECTIVE ELECTRODE BASED ON INKJET PRINTED GRAPHENE SOLID CONTACT

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Continuous chemical monitoring presents an imperative for environmental and healthcare-related analysis, often inaccessible to classical analytical techniques, such as HPLC and UV/Vis spectroscopy. Within the scope of this work, miniaturized planar electrochemical sensor platforms set up in an all-solid-state manner have been developed by inkjet printing. We developed, characterized and optimized the printing process of a planar all-solid-state ammonium ion-selective electrode (NH_4-ASS-ISE) (Figure 1). Silver connection pads were made by inkjet printing commercial Ag-ink on flexible polymeric substrates. For the solid contacts, we have previously formulated an inkjet printable water-ethanol-ethylene glycol graphene suspension.[1] The number of graphene overprints and the volume of the drop-cast ammonium-selective membrane were optimized with the aid of electrochemical impedance analysis, cyclic voltammetry and potentiometry. NH_4-ASS-ISE prepared by 50 graphene ink overprints and drop-cast with 120 µL of the ammonium-selective membrane demonstrated the best properties, in terms of sensitivity (64.3 mV/dec in the linear range from 10^{-4} M to 10^{-1} M NH_4Cl), potential stability, reproducibility of measurements (n = 3), reversibility, and linearity (R^2 = 0.9980).

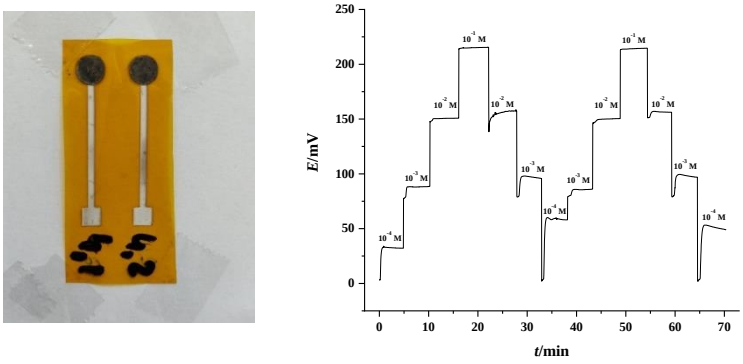

Figure 1. Photograph and reversibility measurements of the inkjet printed electrode with 50 overprints of graphene solid contact and 120 µL of the ammonium-selective membrane.

ACKNOWLEDGEMENTS This work was funded by the Croatian Science Foundation under grant UIP-2020-02-9139.

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DETERMINATION OF THE OPTIMAL CONDITIONS FOR THE BIODEGRADATION OF POLYVINLY CHLORIDE BY THE YEAST *CANDIDA PARAPSILOSIS* USING A FULL FACTORIAL PLAN

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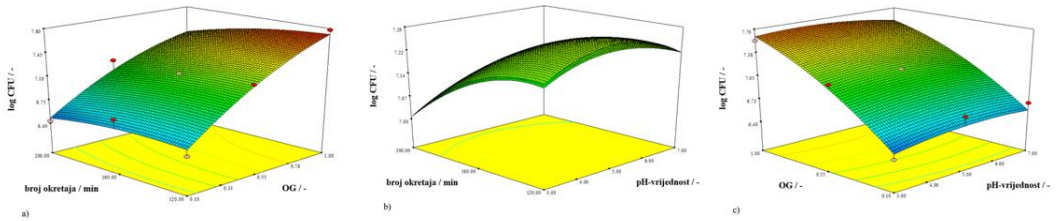
The introduction of plastic waste into the components of the environment is increasing. We find plastic particles smaller than 5 mm in the environment, which we call microplastics (MP). MP has been attracting increasing attention for years and is considered a new pollutant in the environment. During the production of plastic products, various additives are added to improve their chemical and physical properties.[1] As a new pollutant, MP needs to be removed from the environment, so recently research has been conducted to find possible solutions for its removal. A combination of physical, chemical and biological processes can enhance the removal of MP from the environment. Microorganisms have a good potential for MP biodegradation which is an environmentally acceptable process.[2] In this research, the optimal conditions for biodegradation were investigated according to the design of a full-factorial plan. For this purpose, the study was conducted at three different optical densities (OD) (0.1, 0.5 and 1.0), pH values (3, 5 and 7) and revolutions per minute (120, 160 and 200). During the 30 days of the biodegradation experiment, changes in OD, pH values and the total number of grown yeast colonies (CFU) were monitored. For a better insight into the biodegradation process, TOC analysis, HPLC/MS analysis of filtrate, and FTIR-ATR analysis of MP were carried out. The toxicity of the filtrate was determined using the bacterium *Vibrio fischeri*. The experimental results were processed by statistical analysis of variance (ANOVA) using a full factorial experimental design. This study showed that the optimal conditions for PVC biodegradation are the rpm, at low values (120 rpm), at a higher OD (1.0) and an intermediate pH (5).



ACKNOWLEDGEMENTS This work was done as part of the project "Application of advanced water treatment technologies for the removal of microplastics" (IP-2019-04-9661) funded by the Croatian Science Foundation.

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POTENTIOMETRIC SENSORS AND WATER SOLUTIONS – SOLUTION FOR SURFACTANT ANALYSIS

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Green analytical methods[1] for anionic, cationic and non-ionic surfactants determination are presented. In all determination home-made liquid membrane potentiometric sensors as indicator electrodes and potentiometric titrator of high sensitivity and precision were used. Potentiometric titration were performed in an aqueous sample solution[2,3] (e.g., detergents, washing and cleaning agents, etc.) or directly (wastewater samples[4]) without any pretreatment.

Due to the flexibility of this analytical technique, it provides the possibility of adjusting the determination conditions (e.g., adjusting the pH value of the analytical solution) with the aim of removing the influence of interferents (e.g., polycarboxylates, betaines, amine-oxides, soaps, etc.) on the accuracy of the determination. Furthermore, these methods have a whole series of other properties that make them interesting for expanding the field of their application. Besides the fact that these methods belong to green methods, and enable the quantitative determination of surfactants, they also provide monitoring of their behavior in complex matrices that are very common in reality.

Generally, these electroanalytical methods are green methods for determination of anionic, cationic and non-ionic surfactants in real samples[3] and waste waters,[4] and alternative for standard methods used. Despite the fact that standard methods[5,6] use harmful organic solvents (e.g., chloroform) and are environmentally unacceptable as a green method, they are still the most prevalent in practice today.

ACKNOWLEDGEMENTS Investigations were conducted in Saponia (Osijek, Croatia), in cooperation with partners from research institutions.

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SYNTHESIS AND SOLVATOCHROMISM OF THREE NOVEL BROOKER'S MEROCYANINE ANALOGUES

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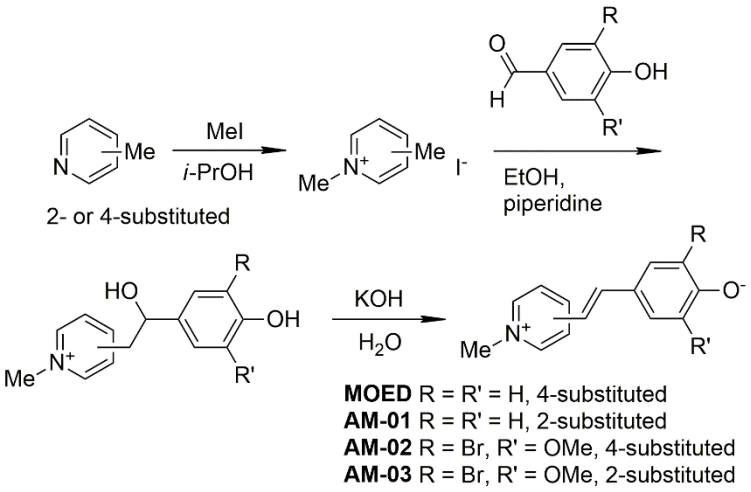
Merocyanine dyes are well known for its solvatochromism. In early 20th century the suggestion was given that merocyanine dyes can be used as solvent property indicators. A typical merocyanine, known as Brooker's merocyanine or systematically 1-methyl-4-[oxocyclohexadienylidene)ethylidene]-1,4-dihydropyridine (**MOED**), exhibits pronounced color changes with changes of solvent polarity: it goes from yellow, through red and violet, to blue in water, ethanol, acetone, and chloroform, respectively.[1] In this work we synthesized a few novel analogues of **MOED** by making slight changes in molecular structure. Three novel merocyanine dyes were synthesized by introducing structural changes on both aromatic rings of **MOED** molecule. All of synthesized compounds shows solvatochromic properties with great differences in color (Figure 1). By dissolving equal amount of four merocyanines, **MOED** and three novel ones, different color shifts occur, **MOED** and **AM-02** are showing hipsochromic (blue) shift and **AM-01** and **AM-03** bathochromic (red) shift. Synthesis of few additional **MOED** analogues, as well as their structural and spectroscopic studies are in progress.

Figure 1. Brooker's merocyanine in different solvents.



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TEMPERATURE EFFECT ON COORDINATIVE, HALOGEN AND TETREL BONDS IN CRYSTAL STRUCTURE OBTAINED FROM LEAD TIOCYANATE AND 3-IODOPYRIDINE

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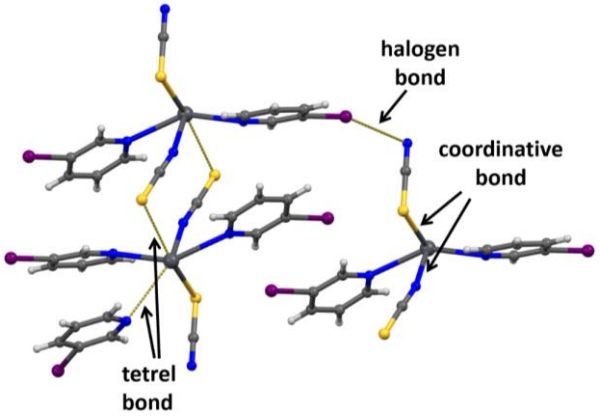
The tetrel bond is a non-covalent interaction between Lewis base and a group 14 element acting as Lewis acid. As the halogen bond, interaction is formed between the σ-hole (electron-deficient region of the donor atom) and the electron rich functional group which is a part of the same or the other molecular entity. Crystal structures in which the same types of halogen, tetrel and coordinative bonds are simultaneously present are extremely rare, which has so far reduced the possibility of direct comparison of those interactions. In this work, we have prepared single crystals of $\{[Pb_2(SCN)_4(\mathbf{3Ipy})_4](\mathbf{3Ipy})_2\}\cdot\{[Pb(SCN)_2(\mathbf{3Ipy})_2](\mathbf{3Ipy})\}\cdot[Pb_2(SCN)_4(\mathbf{3Ipy})_6]$ by slow cooling of lead thiocyanate and 3-iodopyridine solution in ethanol-water mixture. Asymmetric unit of the determined crystal structure consist of three different complexes in which lead atoms are hemi-coordinated with the corresponding coordination numbers of 4, 5 and 6. Regardless of the coordination number, lead atoms serve as tetrel bond donors toward either thiocyanate S or N atoms, as well as to the pyridine nitrogen of **3Ipy** fragment. Furthermore, iodine atoms (as good and proven halogen bond donors) participate in several types of halogen bonds with thiocyanate groups. Given the fact that coordination, halogen and tetrel bonding patterns have found in the same crystal structure, this compound has served as an excellent model system for studying the effect of temperature on the lengths and geometries of those types of interactions. Crystal structures of the model compound were determined at 14 different temperatures in the range between 170 and 300 K and it was found to be stable at any temperature of interest (no decomposition or polymorphic transition has noticed during the experimental procedure). Furthermore, by changing the temperature, various interaction length and geometry shifts were observed, which were mutually correlated and discussed.[1]



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IMPURITIES IN LATANOPROST EYE DROPS: ANALYTICAL PROCEDURE LIFECYCLE MANAGEMENT AND QbD APPROACH IN THAT PROCESS

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Latanoprost (isopropyl (*Z*)-7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(3R)3-hydroxy-5-phenylpentyl]-cyclopentyl]hept-5-enoate) is a drug molecule used to treat ocular hypertension and open angle glaucoma. It possesses a carbon-carbon double bond. Due to possible different orientations of atoms around that bond, latanoprost can be present in two isomeric forms: mainly, it is present as a *cis*-isomer, which is the active form; but under some circumstances, *trans*-isomer can also be present. This *trans*-isomer (isopropyl (5*E*)-7-{(1R,2R,3R,5S)-3,5-dihydroxy-2-[(3R)-3-hydroxy-5-phenylpentyl]cyclopentyl}-5-heptenoate), also known as Impurity F listed in European Pharmacopea (Ph. Eur.), is considered one of the latanoprost impurities that arise from the synthesis pathway.[1] Main degradation product of latanoprost is latanoprost acid ((*Z*)-7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(3R)-3-hydroxy-5-phenylpentyl] cyclopentyl]hept-5-enoic acid), also known as Ph. Eur. Impurity H. This impurity is formed in solutions, but is actually a biologically active form of latanoprost.[2] To control the amount of impurities F and H present in the final drug product, a robust and stability indicating analytical method had to be developed.

Method development is the first phase in analytical method lifecycle, followed by method validation (phase 2), routine analysis (phase 3) and change management (phase 4). All four phases constitute a cyclic process, so any phase can be re-evaluated at any time if necessary.

For phase 1, the goal was to develop one method for analysis of both impurities (F and H), having in mind p*K*a and logD of analytes. The method was successfully developed and validated and has been used in JGL for routine quality testing. In other words, phases 1, 2 and 3 were successfully completed.

As part of the continuous analytical procedure lifecycle management, phase 1 was challenged once again by using a QbD (Quality by design) approach and testing the robustness of the method. Method robustness was already tested and confirmed during validation, but a traditional approach was used: changing one parameter at a time. By using a QbD approach, robustness was tested once again by changing multiple parameters simultaneously. After QbD driven experiments, a MODR (Method Operable Design Region) was defined, which provided a better knowledge on method performance and confirmed that the method is still suitable for its intended use.

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DIVALENT CATION EFFECTS ON POLY(DIALLYDIMETHYLAMMONIUM CHLORIDE)/POLY(SODIUM 4-STYRENSULFONATE) NANOFILM DEPOSITION

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Polyelectrolytes are macromolecules that consist of a repeating sequence of subunits that bear an electrolyte group. According to the charge they are divided into polycations, polyanions and polyampholytes, while according to the degree of dissociation in solution, they are divided into strong and weak. Polyelectrolyte multilayers are films that are formed by alternating adsorption of polycations and polyanions on a surface, most often using layer-by-layer method.[1] The properties of the deposited film depend on the experimental parameters such as used polyelectrolytes, type of substrate, ionic strength, and type of background salt.[2,3] In this study, we investigated how the type of divalent cation affects the multilayer prepared from poly(diallyldimethylammonium chloride) and poly(sodium 4-styrenesulfonate). The examined cations were Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Ni^{2+}, Zn^{2+} and Cu^{2+}. Ellipsometry was used for monitoring the growth of the films up to ten layers, while atomic force microscopy was used to determine morphology and surface roughness. The change in surface wettability during polyelectrolyte adsorption was monitored by tensiometry.

While for alkaline earth metal cations ion-specific effect was observed, for transition metal cations this was not the case. The thickness, roughness, and wettability of films prepared in the presence of transition metal cations were not significantly different. In contrast, these properties differed for multilayers prepared in the presence of alkaline earth metal cations.

ACKNOWLEDGEMENTS This research was supported by the Croatian Science Foundation under the bilateral Slovenian-Croatian APPLPEMS project (IPS-2020-01-6126).

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CHARGE DENSITY OF TETRACYANOETHYLENE (TCNE) RADICAL ANION

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π-Stacking interactions of organic radicals and charge-transfer compounds are responsible for their unique properties and have recently been employed in design of optoelectronics, magnetic, and conductive molecular materials. Stacking of planar organic radicals involves some of the closest interplanar and intermolecular C–C contacts, of *ca.* 2.9 Å.[1] Recent quantum mechanical models proposed that unusually short and strong interactions between planar radicals have a partial covalent character, and this type of weak multicentre covalent bonding has been dubbed '*pancake bonding*'. The strongest interaction of this type is found in pancake bonded dimers of radicals, and its energy can exceed 15 kcal mol^{-1}.[2]

The simplest and also one of the most thoroughly studied case of pancake bonding is two-electron four-centre covalent bond between tetracyanoethylene ($TCNE^-$) radicals.[3] The π-bonded tetracyanoethylene dimer has been investigated for the first time by the experimental X-ray charge density and this study will thus serve as a standard for comparison with other types of multicentre bonding. A detailed X-ray charge density study of TCNE radicals with a short separation distance of 2.81 Å revealed two symmetry-independent bonding critical points (3, −1) between the $TCNE^-$ radical rings with maximum electron density of 0.17 e $Å^{-3}$, and one ring critical point (3, +1) (Figure 1).

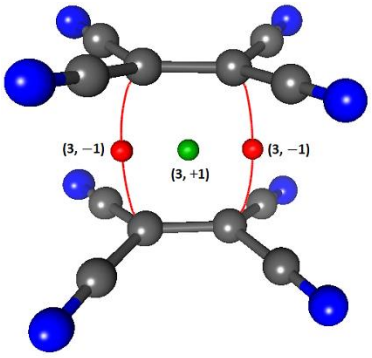

Figure 1. Critical points in a stack of $TCNE^-$ radical anions. Bond paths are shown as red lines, bond (3, −1) critical points are shown as red spheres, and ring (3, +1) critical points are green.

ACKNOWLEDGEMENTS

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THERMODYNAMICS OF ANION BINDING BY PENTAPHENYLALANINE IN ACETONITRILE

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Cyclic peptides represent a large and underexploited class of drug discovery candidates. Their improved metabolic stability and binding affinity, in comparison with linear analogues, result in greater resistance to enzymatic hydrolysis, increased bioavailability, and bioactivity.[1] In the synthesis of cyclic peptides, the main factor that affects the yield of a ring-closure reaction is the conformational preorganization, i.e., the ability of a linear precursor to adopt quasi-cyclic conformation in which the N– and C– termini are in a close proximity. One approach to achieve that is to use templating agents, such as anions, that can bind to linear precursors as well as cyclic peptides.[2,3] In the scope of this work, we studied the binding of inorganic anions to pentaphenylalanine methyl ester (Figure 1) in acetonitrile by means of ^{1}H NMR, fluorimetric, and CD titrations. In addition, we carried out the MD simulations to get insight into the structural changes which occur upon anion binding to pentapeptide.

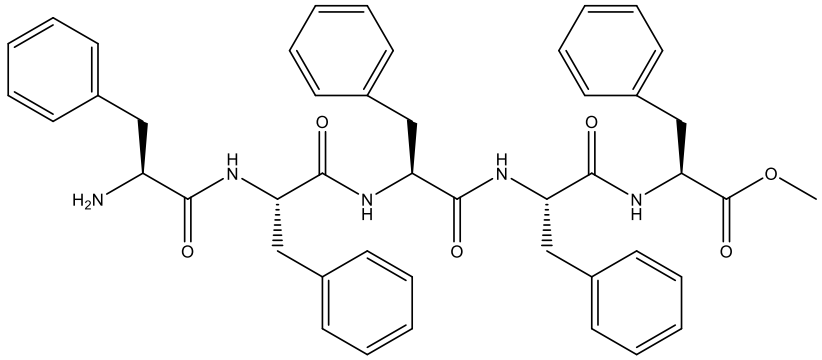

Figure 1. Structure of linear pentaphenylalanine methyl ester.

ACKNOWLEDGEMENTS This work was supported by the Croatian Science Foundation under project IP-2019-04-9560 (Macrosol) and European Regional Development Fund (project CIuK, KK.01.1.1.02.0016).

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DIMERIC CAPSULE *VS*. COLUMNAR POLYMER: STRUCTURAL FACTORS DETERMINING THE SOLUTION AND SOLID-STATE AGGREGATION BEHAVIOR OF AMINO ACID FUNCTIONALIZED BTA DERIVATIVES

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Building blocks based on benzene-1,3,5-tricarboxamide (BTA) have been widely investigated, due to their simple synthesis and countless possibilities of modification. Very well-studied and extremely important group of BTAs is amino ester decorated molecules.[1] The amino acid moiety as a structural motif has major impact on the supramolecular structure, due to encoded H-bonding pattern, which generally leads to helical structures.[2]

Herein we present the non-covalent assembly of four benzene-1,3,5-tricarboxamide (BTA) derivatives formed from glycine or L-valine esters (-Me, -iPr), in the solid state and in chloroform solution by means of several analytical methods (NMR, FT-IR, CD, single crystal and powder XRD, TGA). Two types of self-assembled structures were characterized: dimeric capsule formed by NH···O=C- (ester) and columnar assembly with characteristic -NH···O=C- (amide) bond alongside with monomers.

In-depth solid state study revealed the crucial role of C-terminus protecting group structure to supramolecular aggregation in solid state, which has not been thoroughly investigated yet. The isopropyl ester group prevents the molecule from assembly into columnar structure, instead dimeric assembly is observed. On the other hand, it has no effect in chloroform solutions, where amino acid chain determines the self-assembly. Our study points out the essential influence of substituent in both – the alpha atom of the amino ester and the ester protecting group.

ACKNOWLEDGEMENTS We thank the National Science Centre (SONATA BIS 2018/30/E/ST5/00032) for financial support.

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A NEW SOLID-STATE PROMETHAZINE HYDROCHLORIDE-SELECTIVE SENSOR BASED ON FUNCTIONALIZED MWCNT

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Promethazine hydrochloride (PM) is a phenothiazine derivative widely used as antihistaminic, antiemetic, analgesic and anticholinergic drug.[1] Also, it has an anesthetic and sedative effect, and can be used as a therapeutic agent for treating various mental disorders.[2] Regardless of its benefits, it has adverse effects, such as endocrinal, cardiac and reproductive alterations.[3] Considering that, its determination in pharmaceutical formulations and biological samples is important. Different analytical methods can be used for PM determination but they commonly have drawbacks such as expensive instrumentation, time consuming and complicated procedures, and use of toxic solvents. Due to their simplicity, ion-selective electrodes (ISEs) could be a good alternative. In order to develop ISEs with better properties, ISE membrane can be modified with multi-walled carbon nanotubes (MWCNT) considering their unique properties.[4]

The new solid-state PM-selective sensor, with liquid type of membrane, was developed using MWCNT functionalized with a sulfate group and PM ion as a sensor material. The new sensor was characterized using direct potentiometry. Response characteristics, dynamic response, influence of pH and selectivity were determined.

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CHARACTERIZATION OF SULFONYLUREAS' ADME PROPERTIES USING BIOMIMETIC CHROMATOGRAPHY AND COMPUTATIONAL PROCEDURES

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Sulfonylureas are the oldest class of oral antidiabetic medication used to treat type 2 diabetes. There are two generations of sulfonylureas, and both are equally effective in lowering glucose concentration in the blood. Still, they differ in pharmacological properties such as absorption, metabolism, elimination, and dosing. Therefore, modern and advanced methods are being researched daily to determine the pharmacological properties of the new potential drugs. One of the latest methods is biomimetic chromatography which uses columns that mimic biological conditions and computer (*in silico*) methods that predict various ADME (*Adsorption, Distribution, Metabolism, Excretion)* and QSPR (*Quantitative Structure-Property Relationship*) parameters.

The present study was designed to gain insight into the ADME parameters such as lipophilicity, solubility, phospholipophilicity, protein plasma binding, oral bioavailability, distribution coefficient, gastrointestinal absorption, and compliance with Lipinski's "rule of five" of three sulfonylureas (*N*-methylcarbamoyl)-4-methylbenzenesulfoamide, (*N*-benzylcarbamoyl)-4-methylbenzenesulfonamide, and 1,1'-trimethylenebis[3-(*p*-tolylsulfonyl)-urea] by using HPLC biomimetic chromatography and various computer programs for prediction of stated properties.

More precisely, our study focused on determining the lipophilicity and phospholipopilicity of three sulfonylureas using C18 (octadecylsilane) chromatographic and Immobilized Artificial Membrane (IAM) columns. Chromatographic columns with human serum albumin (HSA) and α-1-acid glycoprotein (AGP) were used to characterize plasma proteins binding. Various free and commercially available programs were used to predict the ADME properties of stated compounds. For the parameters for which it was possible, the experimentally obtained values were correlated with the calculated ones.

The experimental results showed that all three sulfonylureas are lipophilic, interact with phospholipids, and bind to HSA and AGP plasma proteins. Furthermore, a high coefficient of determination ($R^2 > 0.9$) was obtained for most of the calculated parameters with experimentally determined parameters. Therefore, obtained calculated and experimental results would benefit further research of the analyzed sulfonylureas as potential drugs.

RUTHENIUM(III) CATALYZED OXIDATIVE DEGRADATION OF PARACETAMOL BY HEXACYANOFERRATE(III) IN SOLUTION MEDIA – A COMPUTATIONAL SCREENING AND MECHANISTIC PATHWAY

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The ruthenium (III) catalyzed oxidation of paracetamol (PCM) by hexacyanoferrate (III) has been studied in an acidic aqueous medium. The order in paracetamol is fractional but first-order with oxidant concentration. The reaction exhibits first order kinetics to ruthenium (III) and is catalysed by hydrogen ions in the form of $k_{obs} = a + b[H^+]$. The ionic strength does not affect the rate of reaction but is maintained in the reaction. The various activation parameters have been evaluated by employing Arrhenius and Eyring equation. Quinone oxime as the oxidation product of paracetamol has been confirmed spectrally. The oxidation reaction of paracetamol has been studied in eight different solvents and the rate data correlate satisfactorily with Kamlet-Taft's solvatochromic parameters (α, β, π*) suggest that the specific solute-solvent interactions play a major role in governing the reactivity and the observed solvent effects have been explained on the basis of solute-solvent complexation. Based on the kinetic results, a suitable mechanism has been proposed.

To further support our proposed mechanism, density functional theory (DFT) computations at B3LYP/6-311*G(d,p) and LANL2MB show that activation energy barriers predict the same reactivity trend as shown by the kinetics experiments.

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CYCLIC CARBAMATE FORMATION THROUGH PALLADIUM-CATALYSED CO_2 ABSORPTION BY PROPARGYLIC AMINES

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The rise of atmospheric CO_2 presents the biggest long-term challenge for the global climate and great efforts are being made to develop efficient and cost-effective CO_2 capture and storage technologies. In organic synthesis, this has led to an increased interest in using CO_2 as a cheap and readily available C1 synthon. Building on previously published work in this area,[1] we have synthesized several propargylic amine substrates and tested their ability to form carbamates through CO_2 absorption. The carbamate forming reaction was coupled to C-C bond formation using a palladium catalyst and several allyl-, aryl- and vinyl- substrates. The thermodynamics of the CO_2-absorbing reactions have been modelled using the Gaussian 16 software to find the most favorable substrates. We have optimized the reaction conditions to produce allylated carbamates in intermediate yields, finding that copper (I) co-catalysts can significantly improve the reaction yield. We have also synthesized several substrates for an intramolecular version of this reaction which will be explored at a later date. The mechanism of this reaction has also been modelled *in silico*, with preliminary NMR studies indicating that an unstable intermediate is formed by a reaction between the propargylic alcohol and a palladium(II) catalyst.

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SELECTION OF THE DELIVERY SYSTEM FOR THE PRESERVATIVE FREE OPHTHALMIC PRODUCT

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There are specific challenges within the development of the primary packaging system in ophthalmic product without preservatives. In these products, the delivery system takes over the microbiological protection of the drug product instead of preservatives in the formulation. This brings a certain complexity that needs to be addressed.

In preservative free (PF) packaging, during the use, the product passes through dropper's chambers consisting of several different materials, prompting potential interactions, specifically in this case adsorption of the active substance.

It is known from literature data[1] that prostagladins tend to adsorb to silicone material. Within this study, the adsorption of the prostagladin was evaluated by measurement of assay in collected drops applied through the delivery system. Two prototypes were evaluated: Prototype 1 containing silicone parts and Prototype 2 without silicone parts.

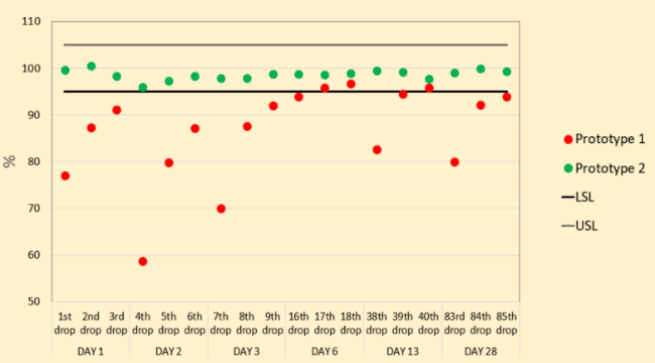

Figure 1. Results of API assay measurements during in use period

The goal of this study was to determine the level of adsorption of the API on the delivery system, by measuring the assay of API in consecutive drops when simulating daily use and selection of the appropriate delivery device. Considerable adsorption of API in Prototype 1 was observed during in use period, with clearly visible increase of API assay from the 1st to the 3rd drop in each respective day (Figure 1). Prototype 2 did not present any major signs of API adsorption and results were in line with the assay specification limits (95 – 105 %).

Based on the results of the study, it was concluded that the prototype containing silicone parts is not a suitable delivery device for the product in development containing prostaglandine, due to the unsatisfactory level of adsorption of API, as described in literature data. This was not the case for the prototype without silicone parts which was selected as a better option for further studies.

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DESIGN, SYNTHESIS AND CHARACTERIZATION OF LINEAR AND CYCLIC PEPTIDES

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Enzymes are proteins that help speed up chemical reactions by creating favorable environments for the conversion of substrates into products. The complexity of amino acid interactions and the large combinatorial space of proteins suggests that the earliest enzymes were short peptides. The peptides could have built the amyloid structures that provided the frameworks to sustain their catalytic activities. Inspired by a catalytically active peptide from Rufo et al.,[1] Ac-IHIHIQI-Am (Ac = acetyl *N*-terminal group, Am = amide *C*-terminal group), we have synthesized and characterized two linear and two cyclic peptides. The peptides were synthesized using the standard Fmoc solid phase peptide synthesis (SPPS). These peptides were tested for their supramolecular structure forming abilities in the presence of Zn^{2+}. The linear peptides, Ac-IHIHINI-Am and Ac-IHINIHI-Am were synthesized to test the effect of changing the glutamine (Q) to asparagine (N) and the changing of position of asparagine within the sequence on the self-assembly and catalytic properties of the peptide. The cyclic variations of the linear peptides, cyclo-(IHIHINIE-Am) and cyclo-(IHINIHIE-Am) were prepared through the *N*-terminal to glutamic acid side chain cyclization. The glutamic acid with the protecting group O-2-PhiPr was selectively deprotected on resin, after which the deprotected carboxyl group was coupled with the free *N*-terminus. By using cyclization to form intra-connected peptides, we expect that the increased rigidity introduced by cyclization will improve the catalytic efficiency of short peptides. The synthesized peptides were analyzed with liquid chromatography and mass spectrometry techniques. The data proved that the octapeptide on-resin cyclization was successful. Hydrogen bonding patters were analyzed using infrared spectroscopy. The linear peptides showed an amide I parallel β-sheet-like structure in the infrared spectrum in the presence of Zn^{2+}. Computational simulation was performed with the linear peptides to visualize the histidine coordination of Zn^{2+}. The catalytic activity of the peptides will be assessed in future work.

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THE BIOSURF PROJECT: A SUSTAINABLE PRODUCTION OF BIO-BASED SURFACTANTS FROM RENEWABLE RESOURCES

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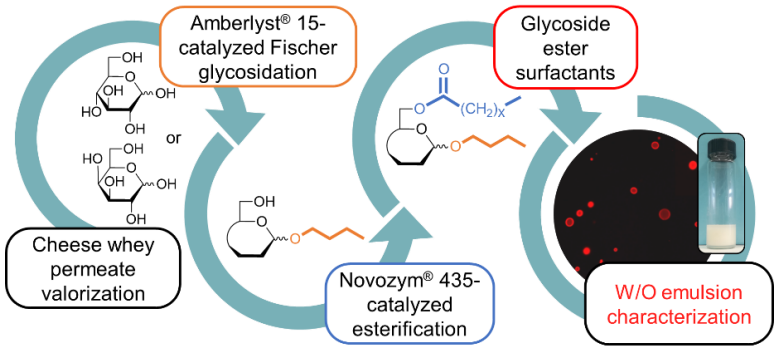
The project BioSurf aims at developing a self-sustainable productive chain of bio-based surfactants (sugar fatty acid esters, SFAEs) by fully upgrading the main waste stream of dairy industry, namely cheese whey permeate. Sugar fatty acid esters (SFAEs) are non-ionic surfactants that are characterized by excellent surface and interfacial tension reduction capability, low toxicity, and biodegradability. These features make SFAEs extremely promising for industrial applications as emulsifiers in the cosmetic and food sectors.[1] Interestingly, SFAEs can be obtained from renewable resources by enzymatic and/or chemoenzymatic approaches, thus answering the need for evermore sustainable and circular chemistry.[2]

6-*O*-Palmitoyl-1-*O*-butyl glucosides and galactosides were enzymatically synthesized by reacting *n*-butyl glucosides and galactosides, respectively, with molten palmitic acid in an easily scalable solvent-free system. Conversion of glucose and galactose into alkyl glycosides before the esterification reaction played a key role to circumvent the striking different solubility of sugars and fatty acids. In addition, 6-*O*-palmitoyl-1-*O*-β-D-butyl galactopyranoside was obtained by a two-step fully enzymatic approach, i.e., a transglycosylation reaction catalyzed by covalently immobilized β-galactosidase from *Aspergillus oryzae*, followed by Novozym® 435-catalyzed esterification. The physico-chemical properties of these tensides, such as interfacial tension features, W/O emulsification capability and W/O stability over time were deeply investigated.[3,4]



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STACKING PATTERNS OF ORGANIC RADICALS IN TETRACYANOQUINODIMETHANE SALTS

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Crystals of planar organic radicals are interesting because of pronounced π-stacking interactions. π-stacking of aromatic rings is usually weak interaction, however, interactions between planar radicals are much stronger. [1] Recent studies in crystal engineering show that energy of some π-contacts may be comparable to stronger intermolecular interactions such as hydrogen and halogen bonding. Close contact of two planar radicals usually involves spin coupling so the energy of such contacts may be as high as −20 kcal mol^{-1}. [2] Furthermore, a long infinite stack of equidistant radicals contributes to special properties of such crystals like semiconductivity and antiferromagnetism.[2] Therefore, these compounds have an important role in crystal engineering of functional materials such as optoelectronics, magnetic, and conductive molecular materials.[1,3]

Here we report a study on π-stacking and multicentre bonding in salts of 7,7,8,8-tetracyanoquinodimethane (TCNQ) radical anions with different organic cations: tetrazolium **(1)**, 1,4-dimethyl-DABCO cation **(2)**, *N,N*-dipyridylmethanium **(3)**, *N*,*N*-dimethyl-4,4-bipyridinium **(4)**, benzyl-*N*-methyl-4-pyridyl quinone **(5)** and *N*,*N*,*N*,*N*′,*N*′,*N*′-hexamethyl ethylenediamine **(6)** cations. Prepared crystals were studied by means of X-ray crystallography. In studied compounds stacking interactions are predominant with interplanar separations between rings of 3,0 – 3,2 Å. TCNQ moieties form dimers, stacks of dimers, trimers or tetramers with alternating shorter and longer separation between TCNQ rings or stacks in columns with equidistant separations (Fig 1). Besides that, in some salts N–H···N and C–H···N hydrogen bonds are present.

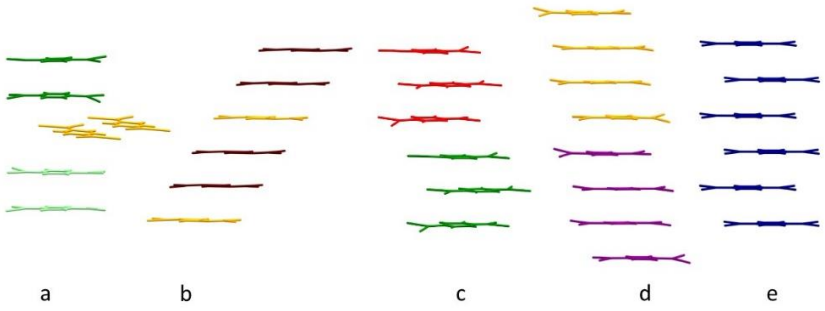

Figure 1. Different types of stacking of TCNQ moieties in prepared salts: a) and b) dimers, c) trimers, d) tetramers and e) equidistant stack.

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OPTIMIZATION STUDIES OF SOLID PHASE EXTRACTION AND LC-MS ANALYSIS OF CDK4/6 INHIBITORS IN BREAST CANCER COMBINATION THERAPY IN PLASMA SAMPLES

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Palbociclib, ribociclib and abemaciclib are novel anticancer agents used for HR+, HER2- breast cancer treatment in combination with anastrozole, letrozole or fulvestrant. They are prone to inter-individual variabilities and concentration-dependent adverse events, therefore better treatment outcomes might be achievable with therapeutic drug monitoring (TDM). One of the main prerequisites to TDM is the existence of a reliable and, preferably, fast, simple, and ecologically acceptable bioanalytical method. Few bioanalytical methods have been published so far for the determination of all these six drugs in plasma,[1,2] however using only protein precipitation for sample clean-up. In this work, a solid-phase extraction (SPE) procedure was optimized for the simultaneous extraction of all six drugs of interest from plasma. Several SPE phases were tested: octylsilyl (C8, 200 mg/3 mL, 500 mg/3 mL), octadecylsilyl (C18, 200 mg/3 mL), hydrophilic-lipophilic balance (HLB, 60 mg/3 mL), mixed-mode cation exchange (MCX, 30 mg/1 mL), and mixed-mode weak cation exchange (WCX, 60 mg/3 mL). Analytes were eluted with methanol, acetonitrile, 2 % formic acid in methanol or 5 % ammonia in methanol. The samples were analyzed with Agilent 1290 Infinity II ultra-high performance liquid chromatograph coupled to Agilent 6470 triple quadrupole mass spectrometer. Waters XBridge Phenyl column (150 × 4.6 mm, 2.5 µm) was used as the stationary phase at 35 °C. The mobile phase consisted of water and methanol with 0.1 % formic acid in gradient elution at a 0.6 mL/min flow rate. The optimal solution was found to be the C8 phase (200 mg/3 mL), eluted with 1500 µL of methanol, which yielded extraction recoveries above 90 % for all analytes. This method was validated in terms of intra and inter-day precision and accuracy, linearity and calibration in the clinically relevant ranges, selectivity, carry-over, and matrix effects. The validated method was then successfully applied for the analysis of samples from patients taking different combinations of the drugs of interest. The proposed method is simple, fast, sensitive, providing good sample clean-up and high extraction yields for all six analytes of interest. Its application on real patient plasma samples supports its suitability for the purposes of further TDM testing.

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NOVEL TECHNIQUES FOR SECONDARY STRUCTURE DETERMINATION OF PEPTIDES IN DRUG DEVELOPMENT

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Knowledge of the peptide secondary structure is essential for determining its properties. The importance of secondary structure determination is also in peptide classification, function and structural change prediction and it is an important information for the tertiary structure. In general, secondary structure is a term that refers to local folded structures that form within a peptide due to interactions between atoms of the backbone. The two most common types of secondary structure are the α-helix and the β pleated sheet.[1]

Today, regulatory agencies require detailed determination of peptide secondary structure. This is the reason why it is important to examine the secondary structure in detail when developing a new drug product in the pharmaceutical industry. It is necessary to determine the similarity of the new product and the reference drug product (RDP) in case of generic drug product development. Some of analytical techniques used in pharmaceutical industry for secondary structure determination are Raman spectroscopy, FTIR analysis, Circular Dichroism (CD) spectroscopy and Nuclear magnetic resonance (NMR).[2] Raman spectroscopy and FTIR analysis are techniques that determine the secondary structure based on the obtained spectrum in the area of amide I and amide II groups (characteristic area of secondary structure). CD spectroscopy measures the difference in absorbance of right- and left-circularly polarized light. Based on far UV spectra and mathematical calculations it is feasible to determine exact secondary structure.

This paper presents the results of secondary structure determination during drug product development using peptide active pharmaceutical ingredient (API). The secondary structure was tested on three lots of the new drug and on three lots of reference drug product. Methods were developed and samples were analyzed by Raman spectroscopy, FTIR analysis and CD spectroscopy. Analysis of RDP samples revealed the clear dominance of α-helix structure. Additionally, the percentage of α-helix structure in the range 50 – 57 % was determined. From the results obtained from the analysis of a new drug samples, the dominance and the percentage of the α-helix structure in range 50 – 57 % were also determined. Overall, the same secondary structure of all analyzed samples can be concluded, as well as the comparability of the results of all three analyses.

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DEEP EUTECTIC SOLVENT SYSTEM BASED ON AMINO ACIDS DERIVATIVES

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The focus of work presented here was to study and describe the following:

(1) The effect of proline series molecules (L-Proline, *N*-acetyl-L-proline, L-prolinamide, *N*-acetyl-L-prolinamide) on the stability of piperacillin and tazobactam considering experimental results and molecular modelling data. This is a very interesting family of molecules, since all of them are based on L-proline, yet significantly different when it comes to their overall charges and protonation states. L-Proline is neutral, but zwitterionic, *N*-acetyl-L-proline is anionic, L-prolinamide is cationic, and *N*-acetyl-L-prolinamide is neutral without any charged fragments.

(2) Utilization of deep eutectic solvent systems (DES) for stabilization of piperacillin and tazobactam, where one of the components is *N*-acetyl-L-prolinamide.

Furthermore, preparation and stability testing of formulations in the form of a deep eutectic solvent that comprise piperacillin and/or tazobactam and at least one *N*-acetyl amino acid amide was conducted. Some of the evaluated excipients were *N*-acetyl-D-alaninamide, and as mentioned above, *N*-acetyl-L-prolinamide.

It was discovered that the stability of the formulation is more enhanced in the specific DES systems. More precisely, DES compositions provided improved stability over time (evaluated through specific impurities increase and purity drop) when stored refrigerated (2-8 °C), and at room temperature (25 °C) in comparison to liquid (aqueous) formulations that only contain piperacillin and/or tazobactam. Computational analysis utilized a combination of quantum-chemical calculations and molecular dynamics simulations to characterize relevant interactions in solutions in relation with the studied degradation mechanisms, and to help in interpreting the observed experimental trends.

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NUCLEATION KINETICS OF ASCORBIC ACID IN WATER AND WATER-ETHANOL SOLVENT

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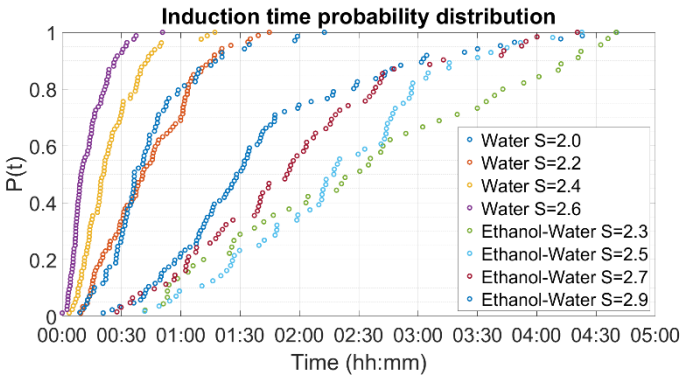
L-Ascorbic acid, commonly known as vitamin C, is an essential compound with a wide range of applications in pharmaceutical and health care industry, such as multivitamins, drug combination, nutritional supplement, and antioxidants in personal care products. Crystallization is an essential separation and purification step for the production of ascorbic acid. Furthermore, the solvent employed for crystallization plays a fundamental role in determining the crystal size and shape.[1] Nucleation is the first step of crystallization which shapes the crystal appropriately, and hence, it becomes crucial to understand the nucleation kinetics to control and optimise the crystallization process.

The present work determines the nucleation kinetics of ascorbic acid in water and water-ethanol binary solvent mixture (composition of 0.4:0.6 mole fraction), by isothermal method (induction time). Induction time is measured more than 80 times at four different supersaturations (*S*) using *Technobis Crystallization Systems' Crystal16 V3* instrument.[2,3] The experimentally measured induction time data points determine the probability to form nucleus in that timeframe. Nucleation kinetics is defined by classical nucleation theory, which relates the probability of nucleation with the supersaturation, represented by the equation



$$J = AS\ exp\left(\frac{-B}{ln^2 S}\right)$$

where *A* and *B* are kinetic and thermodynamic factors, respectively. Addition of ethanol in water solvent reduces the nucleation kinetics, indicating slower nucleation rate in the water-ethanol binary system. Ethanol reduces the polarity of the binary solvent mixture and increases the energy barrier to nucleate.

Solvent	A [$m^{-3}\ s^{-1}$]	B
Water	2868.25	1.587
0.6 Ethanol+0.4 Water	450.47	1.506

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PHOTOREDUCTION IN SOLUTIONS BY INTENSE PULSED LIGHT

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Intense Pulsed Light (IPL) is a short pulsed flash (down to 100 µs) of a xenon lamp emitting mostly visible light (190 nm to 1100 nm), which is caused by the formation of an electric arc between high-voltage tungsten electrodes (1000 V – 3000 V). Compared to other reduction methods, IPL photoreduction does not require using reducing agents; it is energy and time-efficient,[1] thereby meeting the requirements of sustainable development. In this study, IPL photoreduction was evaluated in two different systems (Figure 1). The first system was the dispersion of graphene oxide (GO) in water, buffer (pH= 10), ethanol, and ethanol with poly(vinyl butyral) (PVB). The purpose of the experiment was to determine the influence of the dispersing agent on photoreduction and to define the optimal parameters of the IPL system that provide a high-quality product. Additionally, the dispersion stability of the product was evaluated. The degree of reduction was verified by UV/Vis spectrophotometry; the largest degree of reduction and most stable dispersion was found in the buffer (pH= 10).

The second system was a methanol solution of AgCl and NaCl in the PVB polymer matrix. IPL partial photoreduction was performed at mild IPL parameters. Silver nanoparticles were formed, as evidenced by the peak at 420 nm in the UV/Vis spectra; with the excess of AgCl and NaCl still present in the PVB matrix. The obtained polymer-inorganic salts hybrid was used as a reference membrane (RM) in a proof-of-concept experiment for the development of a planar all-solid-state reference electrode. The RM has shown a great capability of ensuring potential stability in Cl^- and NO_3^- containing solutions, as well as in a broad pH range.

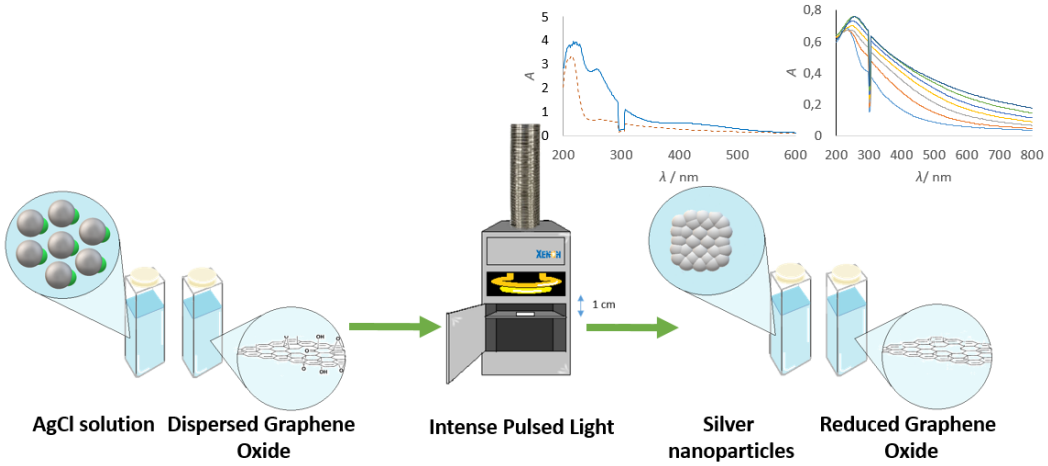

Figure 1. Scheme of the reduction of silver chloride and graphene oxide by intense pulsed light.

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AUTHORS

PARTICIPANTS

The up-to-date list of participants will be available after the Conference.

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