25. HRVATSKI SKUP KEMIČARA I KEMIJSKIH INŽENJERA
s međunarodnim sudjelovanjem
3. simpozij „VLADIMIR PRELOG“
19.-22. travnja 2017.
Poreč, Hrvatska

25
Poreč, 2017.
HSKIKI

25th CROATIAN MEETING OF CHEMISTS AND CHEMICAL ENGINEERS
with international participation
3rd symposium “VLADIMIR PRELOG”
19-22 April 2017
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Knjiga sažetaka
Book of abstracts

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Dobro došli

U ime Znanstveno-organizacijskog odbora iznimna mi je čast i zadovoljstvo pozdraviti Vas u Poreču povodom održavanja jubilarnog 25. hrvatskog skupa kemičara i kemijskih inženjera (25HSKIKI) s međunarodnim sudjelovanjem koji se održava od 19. do 22. travnja 2017. godine. Skup donosi ukupno 15 poludnevnih sesija s predavanjima iz svih područja kemije, kemijskog inženjerstva i edukacije, 7 plenarnih predavanja eminentnih svjetskih znanstvenika, 27 pozvanih predavanja, 40 usmenih i gotovo 180 posterskih priopćenja. Uz to, tijekom Skupa održava se i niz podnevnih događanja te bogat društveni program. Sve to omogućit će brojne prilike za susrete, povezivanje i buduće suradnje. Posebna značajka ovogodišnjeg Skupa je pružanje prilike za snažnije povezivanje znanosti s industrijom te naglasak na edukaciju novih generacija znanstvenika. Upravo s tim razlogom održat će se i dvije nove sekcije *Ja to mogu – znanost i tržište* te *Kako uspjeti u znanosti*.

Vjerujemo da će 25HSKIKI stoga biti uzbudljivo i intenzivno četverodnevno znanstveno događanje s mnogo mogućnosti za razmjenu ideja i ostvarivanje novih kontakata koji će rezultirati budućim suradnjama. Ponosni smo da na Skupu sudjeluje više od 400 sudionika iz 21 države.

Zahvaljujemo pokroviteljima našeg skupa, kao i brojnim sponzorima, podupirateljima i izlagačima. Posebnu zahvalu upućujemo IUPAC-u za financiranje sudjelovanja mladih znanstvenika. I, konačno, hvala svima Vama koji ste svojim sudjelovanjem omogućili uspjeh našeg skupa!

Marijana Đaković
Predsjednica Znanstveno-organizacijskog odbora

Welcome

On behalf of the Scientific and Organizing Committee, it is a great honour and real pleasure to welcome you to Poreč on the occasion of the 25th Croatian Meeting of Chemists and Chemical Engineers (25HSKIKI) with international participation, held from 19-22 April 2017. The meeting offers a total of 15 half-day sessions on all aspects of chemistry, chemical engineering and chemical education, 7 plenary talks on cutting-edge topics by internationally renowned leaders in their fields, followed by 27 invited talks, 40 oral contributions, and almost 180 poster presentations to stimulate interdisciplinary discussions. In addition, there are several lunchtime events and a social programme with many opportunities to meet, connect and exchange ideas. In this 25th edition of the main and most important biennial gathering of chemists and chemical engineers in Croatia, special attention is paid to strengthening the relationship between academia and industry and to nurturing a new generation of scientists, for which reason two new sessions are introduced, I can do it – science and business and How to succeed in science.

We hope that 25HSKIKI will thus be a vibrant and intensive three-day scientific meeting with many learning opportunities in every current aspect of chemistry and related fields. We believe, it will provide for all of us, more than 400 participants from 21 countries, an exciting forum for exchanging ideas and making new contacts to initiate future collaborations.

We are also grateful to more than 35 sponsors, donors and exhibitors for their support, and to IUPAC for supporting the attendance of young scientists. And, to all of you for your participation, making this meeting a success!

Marijana Đaković
Chair of the Scientific and Organizing Committee

Sadržaj

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PLENARNA PREDAVANJA

PLENARY LECTURES

Development of peptide and peptidomimetic therapeutic agents from a New Zealand perspective

Razvoj peptidnih i peptidomimetskih terapeutika iz novozelandske perspektive

Margaret Brimble
School of Chemical Sciences and School of Biological Sciences, The University of Auckland,
Maurice Wilkins Centre for Molecular Biodiscovery
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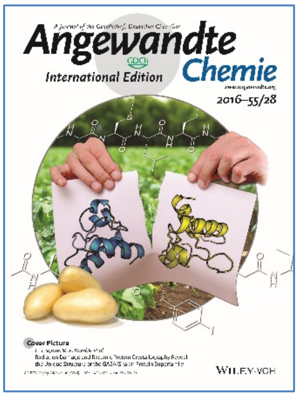
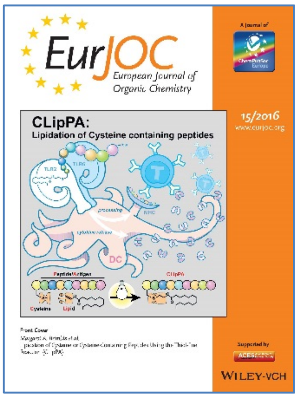
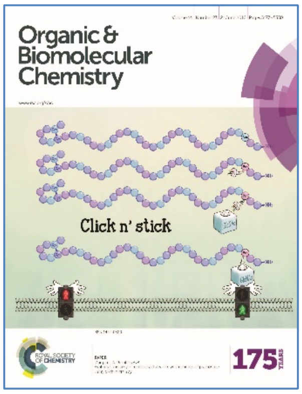
Prof Brimble’s lecture will showcase how pursuing an academic career focused on the intricate science of “making molecules” can result in innovation leading to commercialization of molecules that not only reap economic rewards but also transform lives. The lecture will describe her lab’s research on the synthesis of bioactive natural products and the synthesis of peptides, glycopeptides, and peptide mimetics as a platform for the discovery and development of new therapeutic agents. She discovered the drug candidate NNZ2566 for Neuren Pharmaceuticals that was successful in phase 2 clinical trials for Rett Syndrome and Fragile X Syndrome. NNZ2566 has recently been named trofinetide by the WHO and has received orphan drug status and fast-track designation by the FDA as the first drug to treat these two indications. Trofinetide is also currently in phase 2 clinical trials for traumatic brain injury (INTREPID2566) and concussion funded by Neuren Pharmaceuticals (ASX) in partnership with the US Army. Professor Brimble’s laboratory has also been licensed by Medsafe NZ to manufacture clinical grade peptides as APIs under cGMP and successfully delivered 5 clinical grade peptide vaccines for a melanoma vaccine clinical trial (MELVAC).







Bio-inspired designer materials

Bioinspirirani dizajn materijala

Jasper van der Gucht
Laboratory of Physical Chemistry and Soft Matter, Wageningen University
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In our group, we have developed various strategies to design soft materials with carefully tuned properties. In particular, we use block copolymers with carefully chosen self-assembly domains, often inspired by motifs occurring in natural proteins, such as silk, elastin, or collagen. In this lecture, I will highlight some of these strategies and show how polymers with well-chosen self-assembly motifs can be used to design materials with tailored mechanical properties.

From molecules to materials

Od molekula do materijala

Christer B. Aakeröy
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As molecules get closer and closer they will, at a certain point, exert some influence on one other. They can readily affect each other's shape, spatial orientation, reactivity, and stability. In other words, they communicate, exchange information, and respond to each other. When molecules transition into the condensed phase, their behavior and properties are to a large extent governed by intermolecular interactions. Despite the fact that such chemical bonds are relatively weak and reversible they are critically important to solubility, thermal and mechanical stability, optical properties, and many other key performance parameters of modern materials. Consequently, if we want to acquire the ability to design and construct new materials through a bottom-up approach that is both robust and versatile, we need a better understanding of the structural consequences, and balance between, intermolecular forces. In addition, we also need to establish more reliable and tangible connections between molecular structure and materials properties.

In this presentation we will examine how several fundamental physical properties of a substance can be modified and 'dialed-in' through the use of co-crystallization technologies that are firmly anchored in a fundamental understanding of intermolecular forces [1-7].

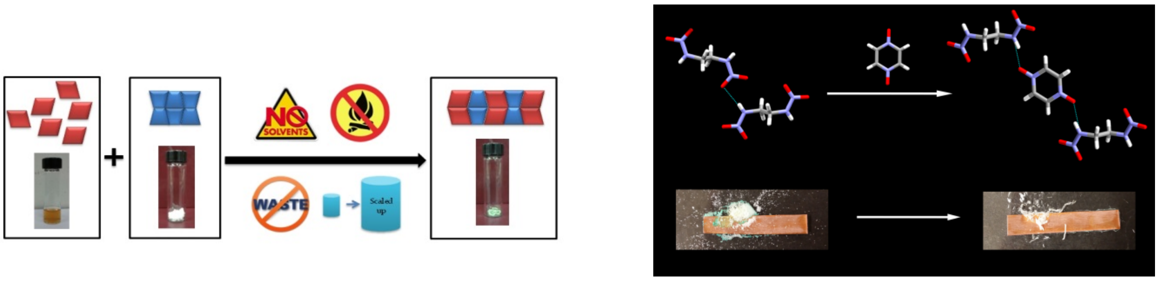

Figure 1: Stabilizing volatile materials (left). Improving energetic materials (right).

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Product design form and function needs process design

Dizajn produkta: oblik i funkcija trebaju dizajn procesa

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Product design, especially, in industrial crystallization needs a proper process design in order to come up with the wanted physical properties with respect to form and function of the product [1, 2].
What are the most important properties of industrially crystalline products – purity shape, size distribution, modification (polymorph or solvate) -.
Influencing parameters are:

- nucleation,
- driving force (program),
- retention time,
- additives.

These influencing parameters determine also the tools:

- seeding procedures (time, amount and kind of seeds) [3]
- position of the process in phase diagram, respectively in the metastable zone [4]
- the use of additives [5].

What are the tools and the process parameters which can be used to design a process to achieve those desired product properties?
Answers to the a.m. questions will be given.

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Dynamics, flexibility, cooperativity and the evolution of enzyme function

Dinamika, fleksibilnost, kooperativnost i evolucija enzimske funkcije

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Recent years have seen an explosion of interest in both experimental and computational studies of the evolution of enzyme function [1,2]. In particular, it has been argued that conformational selection plays a major role in allowing old enzymes to acquire new activities [3]. My group and I have performed detailed computational studies of a broad range of catalytically promiscuous enzymes, in order to probe the molecular origins of both their multifunctionality and its implications for their functional evolution [4-7]. These include alkaline phosphatases [4], organophosphate hydrolases [5,6], aldolases [7] and Kemp eliminases [8], to name a few examples. Based on this work, we present a molecular model for enzyme evolution, highlighting the critical importance of a fine-tuned interplay between enzyme dynamics, electrostatic cooperativity and conformational selection in allowing for the acquisition of new activities, as well as the ability to select more than one possible reaction from a pool of given substrates.

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Pharmaceutical product design and development

Dizajn i razvoj farmaceutskih proizvoda

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Chemical Product Design has been recognized as a new concept and also research challenge in area of chemical engineering as nowadays it is necessary to focus on much broader elements in addition to process design, its efficacy and yields. Product design is based on systematic and integrated approach towards imaginary „product pyramid“. It is multivariable and multifunctional relationship between product composition, its structure and its use. It is therefore mandatory to have appropriate knowledge about starting materials, about process which will change them and about product use properties that must be fulfilled [1]. Pharmaceutical industry is still in its significant part- chemical process industry- therefore such concept and approach is very critical for bringing innovative products to the market, to patient and to fulfill medical need.

In pharmaceutical industry we work on Quality by Design (QbD) approach, since it is believed that quality should be designed or 'built' into a product. In a pharmaceutical QbD approach to product development, Developer identifies characteristics that are critical to quality from the patient's perspective, translates them into the drug product critical quality attributes (CQAs), and establishes the relationship between formulation/manufacturing variables and CQAs to consistently deliver a drug product with such CQAs to the patient [2].

The key elements of pharmaceutical QbD can include the targeted product profile, product design and understanding, process design and understanding, scale up, control strategy and continual improvement. Prior knowledge, risk assessment, design of experiments, and process analytical technologies are tools to facilitate QbD implementation [3].

Application of product design in pharmaceutical product development will be presented with case studies [4].

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Supramolecular electronic circular dichroism: Characterization of aggregated phases of conjugated functional polymers

Supramolekulski elektronski cirkularni dikroizam: karakterizacija agregiranih faza konjugiranih funkcionalnih polimera

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Electronic Circular Dichroism (ECD) is mostly renowned for the assignment of absolute configurations of single molecules, or for the characterization of protein secondary structures. However, it also lends itself as a powerful tool to detect and study supramolecular aggregates of chiral species [1], including conjugated polymers (CP). CP are the starting materials for optoelectronic devices including light emitting diodes (LED), solar cells and field-effect transistors (FET). The fundamental properties of these materials, such as light absorption and emission, charge and exciton transport, and the performances of the derived devices, depend strongly on the supramolecular organization at various levels of hierarchy. Introducing chirality in CP represents one possible way to control polymer aggregation, and allows the use of ECD for characterizing aggregate structures and pathways [2].

We have synthesized in years a number of chiral poly phenylene vinylenes (PPVs) and poly phenylene ethynylenes (PPEs) with pendants selected from the chiral pool, and studied their aggregation phenomena in solution and as thin films, using primarily ECD [3]. The aggregate phases of these materials often manifest polymorphism, and thin films are composed of heterogeneous domains (Figure 1). Recently, we carried out the first spatially-resolved ECD analysis of thin films of a chiral PPE using synchrotron light source (Diamond, Oxford, UK). The lecture will introduce ECD, its application to supramolecular systems, and provide examples in the field of chiral CP.

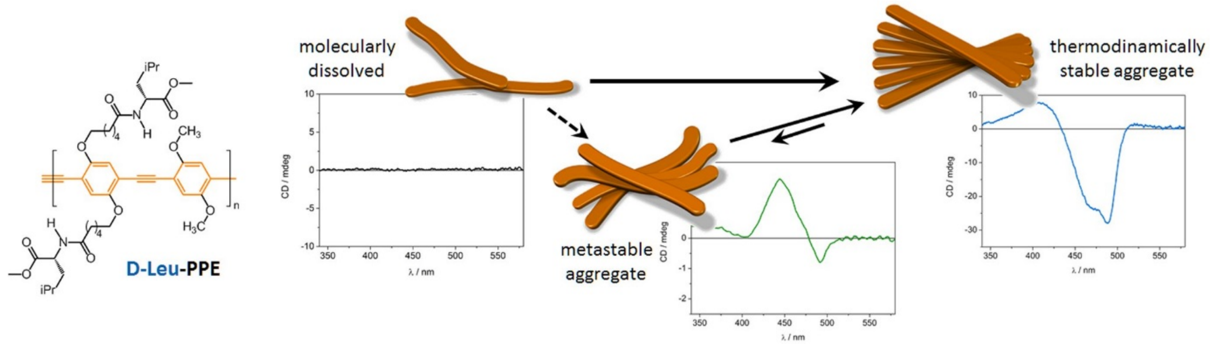

Figure 1: ECD-detected aggregation pathways of a chiral PPE.

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Teaching and learning in role of science literacy development

Učenje i poučavanje u funkciji razvijanja prirodoslovne pismenosti

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Prirodoslovna pismenost, kako ju definira Program za međunarodnu procjenu učenika PISA (Programme for International Student Assessment) [1] obuhvaća tri temeljne kompetencije: znanstveno objašnjavanje pojava, vrednovanje i osmišljavanje znanstvenih istraživanja te interpretiranje znanstvenih podataka i dokaza. Osnovna razina prirodoslovne pismenosti podrazumijeva temeljno poznavanje prirodoslovnih sadržaja na razini konceptualnog razumijevanja i primjene, u kombinaciji s proceduralnim i epistemološkim znanjima.[2]

Hrvatski su učenici 2015. godine u PISA prirodoslovnoj pismenosti postigli slabiji rezultat u odnosu na ukupni prosjek zemalja sudionica i slabiji u odnosu na ciklus 2006. godine. Na primjerima zadataka iz PISA istraživanja 2015. prikazat će se način provjeravanja prirodoslovnih kompetencija te promišljati o uzrocima nezadovoljavajuće uspješnosti. Mogućnosti unapređivanja prirodoslovne pismenosti ponajprije treba tražiti u načinu poučavanja, u kojem bi trebalo dominirati aktivno učenje.[3] Također je neophodno sustavno uvoditi istraživačko učenje [4] u redovitu nastavu predmeta prirodoslovnog područja.

Reference

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POZVANA PREDAVANJA

INVITED LECTURES

Batch and flow synthesis of nucleosides by enzymatic transglycosylation

Protočna i klasična sinteza nukleozida enzimskom transglikozilacijom

Giovanna Speranza,[1] Enrica Calleri,[2] Giulia Cattaneo,[2] Gabriella Massolini,[2] Carlo F. Morelli,[1] Marco Rabuffetti,[1,2] Daniela Ubiali[2]
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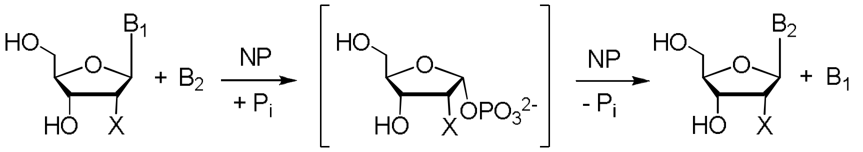
Enzymatic methods for the preparation of high-value products have clearly shown their potential in many areas, including nucleic acid chemistry. Enzymes of nucleic acid metabolism such as nucleoside phosphorylases (NPs, EC 2.4.2) can be conveniently used as biocatalysts in the synthesis of nucleoside analogues. These enzymes catalyze the reversible cleavage of the glycosidic bond of (deoxy)ribonucleosides in the presence of inorganic phosphate (P_i) to generate the nucleobase and α-D-(deoxy)ribose-1-phosphate (phosphorolysis). If a second nucleobase is added to the reaction medium, the formation of a new nucleoside can result (transglycosylation).

Because of its broad substrate specificity [1,2], a purine nucleoside phosphorylase from *Aeromonas hydrophila* (*Ah*PNP) was exploited to catalyze the "one-pot, one-enzyme" transglycosylation of 7-methylguanosine iodide with a series of 6-substituted purines, resulting in a moderate to high conversion (18-65%) of the bases into a 22-compound library of 6-substituted purine ribonucleosides [2]. Successively, *Ah*PNP was covalently immobilized [3,4] in a pre-packed column containing aminopropyl silica particles. The resulting *Ah*PNP-IMER (Immobilized Enzyme Reactor) was coupled on-line to a HPLC apparatus containing a semi-preparative chromatographic column. In such a system, "one-enzyme" transglycosylation and product purification were run in a single platform, affording a set of 6-modified purine ribonucleosides at a mg scale [4]. Using this "flow-based" approach, the synthesis of adenine nucleosides through a "two-enzyme" transglycosylation was carried out by connecting the *Ah*PNP-IMER to uridine phosphorylase from *Clostridium perfringens*, immobilized on a silica monolithic column (*Cp*UP-IMER).



X = H, OH
P_i = inorganic phosphate
B_1, B_2 = purine or pyrimidine

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Minimal artificial enzymes: Application of "backdoor induction" in asymmetric catalysis

Minimalni umjetni enzimi: Primjena posredne indukcije u asimetričnoj katalizi

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The development of new small-molecule transition metal catalysts for asymmetric reactions is often fuelled by imitating metalloenzyme active sites. Nevertheless, small-molecule transition metal catalysts are still easily outperformed by metalloenzymes in terms of both selectivity and reaction rates. It is obvious that mimicking the active site alone is not sufficient to replicate metalloenzyme activity. Therefore we design artificial metalloenzymes that contain not only an enzyme active site mimic but also a minimal functional outer-coordination sphere. A major feature of these **minimal artificial enzymes** is "backdoor induction" of chirality *via* hydrogen bonding and other non-covalent interactions between distant chiral amide substituents, e. g. amino acids, diamines or dicarboxylic acids. Additional favorable properties are cheap synthesis by standard chemical methods as well as possible application to a broad range of substrates.

In this presentation, several selected approaches for the development of new catalytic systems will be discussed [1]. Particular emphasis will be focused on supramolecular systems comprising well defined artificial secondary structures [2], with the potential to transmit chiral information from the outer-coordination sphere to the prochiral catalytically active metal centre.

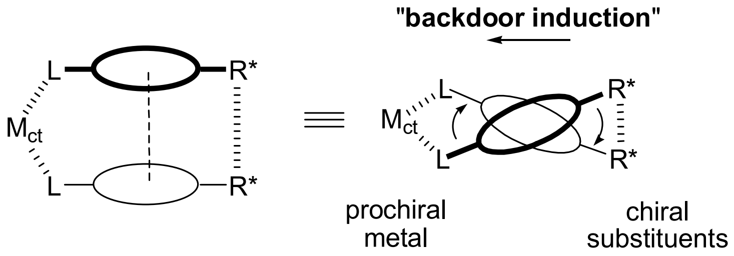

Figure 1: Side view and top view of a supramolecular transition metal catalyst (minimal artificial enzyme). The arrows indicate the sign of the helical chirality.

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Studying ion transport in electrolytes by NMR methods

Istraživanje ionskog transporta u elektrolitima NMR metodama

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For application of electrolyte materials in energy storage devices their transport properties are essential. Commonly determined transport coefficients are conductivity, viscosity and diffusion coefficients, where the latter are ion-specific quantities, available by multinuclear Pulsed-Field-Gradient (PFG)-NMR diffusion.

This lecture presents ion transport studies in advanced electrolytes for Li ion batteries, i.e. (i) ionic liquid (IL)- based liquid electrolytes and (ii) ternary polymer gel electrolytes consisting of ionic liquid, polymer and Li salt, which are suitable materials to yield a compromise between sufficient conductivity and mechanical stability [1–3]. Here, multinuclear PFG-NMR of ^{7}Li, ^{19}F (anions) and ^{1}H (cations) serves to analyze the transport processes as influenced by complex mutual interactions of the constituents. For example, in systems based on the poly(ionic liquid) PDADMATFSI a detailed comparison of relative diffusivities of anions and Li showed that charged chains are superior polymeric constituents in ternary gels in terms of their ability to enhance Li^+ conduction [2]. Transport numbers calculated from PFG-NMR diffusion coefficients thus serve to optimize materials for transport of specific ion species.

Furthermore, to identify the conductivity contribution of a specific ion species remains a challenge, since from diffusion coefficients transference numbers can only be obtained under the assumption of completely uncorrelated ion motion. In order to determine true transference numbers, the electrophoretic mobility μ has to be known. Here, electrophoretic NMR (eNMR) allows to directly measure the electrophoretic mobility μ of NMR-active ions [4]. Again, multinuclear studies (e.g. ^{1}H, ^{7}Li, ^{19}F) yield a full characterization of all ionic species of typical liquid electrolytes. Various examples such as pure ionic liquid [4], IL/Li salt mixtures, and glyme-based solvate ionic liquids are demonstrated, providing unique information on the mobility of any single ion species and thus allowing conclusions on correlated motion of different ion species.

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Advantageous disadvantages and disadvantageous advantages

Prednosti nedostataka i nedostatci prednosti

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All of us globally, currently more than 7 billion people, are essential and active participants in this new millennium in which one of the key enablers are education and innovation-based science and technology driven societies. We all live in the word of direct relationship between the quality of life and the application of numerous scientific discoveries in our everyday life.

On the other hand all of us locally, a little more than 4 million people, are only a small corner of this global village, but a small corner that has its own science, culture, language, art, music, mentality, customs, food, etc., and has its own intellectual capital. Regardless of our economic strength and size, the abundance or lack of financing options for scientific projects, and other possible “local” shortcomings the “global” arena of scientific advancements has inevitably positively influenced even our “local” lives, whether we admit it or not.

We all know that size is relative, subjective and highly restrictive category, while knowledge, skills, competences and experience are widely available to all and are unlimited resources that can and will have a positive and everlasting impact on any society. Intellectual capital and innovation capacity are completely free and are infinite assets that cannot be restricted by any predefined patterns, dogmas and potential disadvantages (like geography, economy size, financial power, education and the size of the scientific community, etc.) and we should boldly take onboard all our "so-called" disadvantages and convert them into our advantages.

Today’s world is full of such examples, and we can do it!

Ignorance management as a prerequisite for innovation

Upravljanje ignorancijom kao preduvjet inovacija

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Principal driver of organic growth today is innovation – regardless if we talk about companies, states, or regions. Three most important traits of the innovative organizations are (1) right infrastructure and culture to foster and support innovation, (2) strong visionary business leadership, and (3) willingness to take risks and challenge organizational norms. In recent decade-or-so, Croatia has managed to significantly improve the infrastructure and support systems for innovative projects with commercial potential. Excellent examples are the BIOCenter, the incubation center for biotechnology, the Institute Ruđer Bošković Multidisciplinary Science Incubator, or the Science-technological park of the University of Rijeka. However, we are constantly ignoring the future, which brings fast technological changes as well as business model changes. Consequently, we "stick with what we have" and remain in a slow and incremental innovation mode of development. In order to pass the Rubicon toward radical innovations, we need to improve the ignorance management and stop ignoring the opportunities that we encounter. We will be only able to do this if we start challenging the present culture and organizational norms and step out of complacency of our comfort zones.

Example of spin off entrepreneurship: Comprehensive Water Technology

Primjer spin off poduzetništva: Comprehensive Water Technology

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Spinning off companies raised more than few discussions among Croatian opinion makes in recent years commenting need for a change of universities towards commercialization combined with governmental and/or institutional support. Some opinions define spinning off process as a second academic revolution addressing successful incorporation of research into the core of enterprise as the first one. Stanford University as initiator and later on in particular Massachusetts Institute of Technology proved that spin off companies are valid measure of knowledge and technology transfer potential taking under consideration facts that they are complex and multistage projects aimed at transforming existing knowledge into an innovative product to meet the needs of the market. Form social responsibility point of view spin off company creates new economy, new sectors and knowledge pool bridging the gap between local business and universities.

The aim of this lecture is to initiate discussion how spin off company can influence societies and economic grow and prosper. For that purpose the example of good practice will be presented: Comprehensive Water Technology as the first spin off company founded by University of Zagreb (20% University of Zagreb; 80% Faculty of Chemical Engineering and Technology).

The use of nanomaterials in fabrication of surfactant potentiometric sensors

Primjena nanomaterijala u izradi tenzidnih potenciometrijskih senzora

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Among the electrochemical sensors, potentiometric sensors belong to one of the most important category, which measure the potential of the sensor that is correlated with the activity of analyte species. They have been widely used for direct determination of of many organic and inorganic ions in industrial, medicinal and environmental analysis.

Due to large-scale and increasing consumption of surfactants in many branches, their monitoring in different products and in environment is of great interest.

Although surfactant sensors represent a great progress in surfactant analysis [1], they suffer from many disadvantages: leaching of the membrane components, extraction of lipophilic molecules into the polymeric membrane, limited life time, use of internal solution, poor mechanical properties, low resistance to organic solvents, slow response at some types of sensors.

Nanomaterials (NMs) have been widely used for fabrication of various chemical sensors and biosensors, due to their unique physical and chemical properties, such as large surface area/volume ratio, good conductivity, excellent electrocatalytic activity and high mechanical strength.

By development of potentiometric sensors, NMs can be investigated as conducting substrates, as substrates for electroactive material immobilization and as a potential sensing materials after their functionalization.

The application of NMs has been demonstrated by the development and application of a few surfactant potentiometric sensors, by using graphene and carbon nanotubes for immobilization of the sensing material in the membrane, preventing the leaching of the electroactive material from the membrane as well as reducing its electrical resistance and signal noise [2,3]. The new nanomaterial-based sensors were employed for the determination of anionic surfactants in commercial products and effluents, and the results were compared with those obtained with conventional surfactant potentiometric sensors and standard methods.

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The potential of computed crystal energy landscapes to aid solid-form development

Potencijal izračunatih ploha potencijalnih energija u kristalu u razvoju istraživanja u čvrstoj fazi

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A key first step in developing a solid oral dosage form is to identify crystalline forms of the drug molecule, generally through some form of crystallization screening. Crystallization provides a means to purify and recover the drug substance coming out of the final step of the synthesis and to isolate the drug in a crystalline form that is suitable for downstream processing. It is also used to define the material properties (e.g., stability or solubility) of the drug substance that will ensure consistency in the safety and efficacy profile of the drug product throughout its shelf life. The ability of molecules to crystallize in many different forms (including salts and co-crystals) creates opportunities to design properties into the drug substance, but at the same time introduces challenges in deciding which form to develop, selectively crystallizing the preferred form on a large scale, and establishing control strategies around crystal form in the drug product. An ever-expanding range of techniques has been shown capable of producing novel solid forms, yet it is possible that practically important forms might not be found in the short timescales currently allowed for solid-form screening. Here, we report on the state-of-the-art use of computed crystal energy landscapes to complement pharmaceutical solid-form screening [1–2]. We illustrate how crystal energy landscapes can help establish molecular-level understanding of the crystallization behavior of APIs.

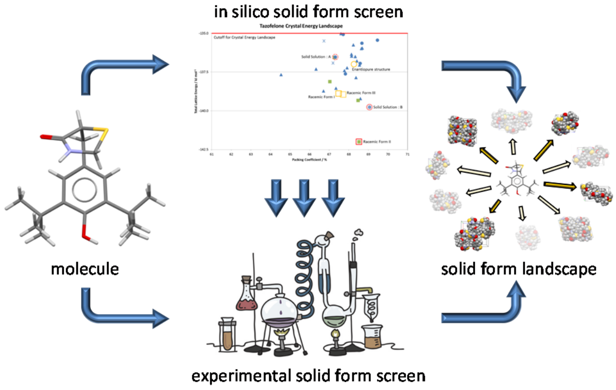

Figure 1: Crystal structure prediction improves the effectiveness of experimental solid form screening.

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Quantitative in situ monitoring as tools to study mechanisms of mechanochemical milling reactions

Kvantitativne tehnike in situ u otkrivanju mehanizama mehanokemijskih reakcija mljevenjem

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We will here describe the development of mechanistic understanding from the first *in situ* monitoring by synchrotron powder X-ray diffraction [1,2], followed by laboratory Raman *in situ* monitoring [3,4] and finally focus on the most recent quantitative evaluation from tandem *in situ* monitoring combining the two techniques in a high-throughput approach enabling quantitative assessment and kinetic analysis even in systems involving novel and short-lived phases of unknown crystal structures. These recent results provide the necessary infrastructure for a thorough mechanistic description of mechanochemical milling reactions which was thus far hindered mainly by the inability of their quantitative evaluation. We will address also the issue of the temperature of the reaction mixture and its influence of reaction kinetics and mechanisms. Tandem in situ monitoring via PXRD and Raman spectroscopy, applied to cocrystallisation of nicotinamide and benzoic acid, revealed a rich polymorphic system with multiple phase transformations and a variety of reaction pathways that can be altered and controlled by the type of the liquid additive as well as by its amount. For the first time, we observe a decelerating effect of the liquid additive on LAG reaction kinetics. Quantitative assessment from tandem in situ monitoring, performed in seconds-time resolution, establishes by extension quantitative in situ Raman monitoring as a quantitative technique that is readily implemented in a conventional laboratory.

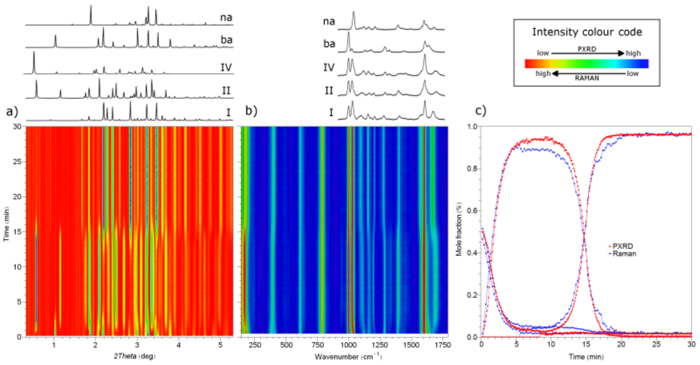

Figure 1: (a) PXRD and (b) Raman in situ monitoring and (c) their comparison

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A different view – DOK-ING saving lives

Iz drugog ugla – DOK-ING spašava živote

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DOK-ING is a privately owned Croatian company established in 1991 registered for the production of robotized and special purposes systems and equipment. Headquarters, production facilities and service elements are located in the capital, Zagreb. Secondary production facilities are located in Slunj some 50 km southwest of Zagreb. Branch offices are also located in the USA and a subsidiary in South Africa (DOK-ING Africa), which supports programs for South African mines. DOK-ING employs more than 150 employees, 100 located in Zagreb, 30 in Slunj and 20 in South Africa. DOK-ING specializes in capturing the needs of the user and then producing effective solutions drawing on the skills and expertise of its partners around the globe.

The company motto is “Don't send a man to do a machine's job” and this is exemplified by their supply of world class remote controlled ground vehicles (UGVs), most notably in the Humanitarian Demining, Military Route Clearance and Counter IED, then in Mining and Mineral Extraction, Catastrophe Intervention and Firefighting, Search and Rescue roles. Over two hundred remotely controlled systems are currently deployed in some thirty countries around the World, mostly on Humanitarian Demining projects, but also in a number of potentially dangerous situations providing a high level of protection and security for all involved.

Trying to see the everyday life problems from a different perspective, the solutions are following the same direction. The innovative approach is realized through the constant and comprehensive protection of human life in all possible situations. DOK-ING is not waiting for a problem to arise, we are envisioning solutions for individual situations and problems. Communicating worldwide, our people are introduced to a various ways of dealing with efficiency and protection in humanitarian demining, in simplicity and adaptability in combat engineering missions, in performance of mining. The first concern always being the security of operations, and moreover the safety of operators and all people involved.

As a number references confirmed, DOK-ING is recognized for its innovative approach to intractable problems. The engineering solutions are practical, concise and based on world class engineering and innovation. DOK-ING is actively engaged in research and development projects with various international and domestic research organizations, working on improvements of products and launching new innovations that are continuously diversifying our unique production program. The company has been ISO 9001:2000 certified and capable of providing tailor-made solutions for customers around the world.

Science FOR Business: What are the risks and opportunities?

Znanost u funkciji biznisa: Koji su rizici i poslovne prilike?

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The interaction between science and business very often is not straightforward. The differences in philosophy and culture between two fields often result in misunderstanding or a difference in expectations on either side. However, despite all obstacles in today's, and especially tomorrow's world that is based on the innovation-driven economy, science and business are more than ever encouraged to establish productive partnership.

The lecture will review the process of translating scientific discoveries in biomedicine into marketable product, the obstacles that arise at interface points between science and business, as well as recommendations how to avoid them.

In addition, current trends and future opportunities for engagement of science in global and local economy will be discussed.

Mentoring is a people building business
«Who are you...as a scientist?»

Mentoriranje je posao izgradnje ljudi
«Tko si ti...kao znanstvenik?»

Fran Mikuličić

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A mentor's vision is simple: to provide support and to help young people in their professional careers. The purpose of mentoring is to identify, organize and transfer knowledge, skills and experiences to mentees and to enable them to make better decisions. The mentors' values are, among others, human growth and development, selfless giving, the inner satisfaction of helping and modesty without a compelling need for external confirmation and recognition. Who is a mentor then? A mentor is a person who shares the vision, purpose and values and possesses valuable elements of knowledge, skills and experience. A person with intrinsic motivation to help others, ready to donate his or her time and energy. A person who understands that his or her personal development is connected with the teaching others, and that his or her life's prints are as shiny as how much he or she gave to others.

When mentors in their building and development activities of future responsible leaders, limit their impact on the explicit knowledge and technical skills, they reject the opportunity to truly transform young people, to lead the growth of the complete human beings, and to encourage the growth of future generations of mentors. Observation and correction of behavior, and providing access to and transfer of knowledge and technical skills through education and training are important tasks that, unfortunately, mainly focus on the behaviorist theory of learning and consequences. To create lasting change, it is necessary to go three steps backward and harmonize all levels of growth and development of young people on their life paths.

The first level is identity. The question we asked ourselves in the title. Who are they as scientists? As students? As human beings? The greatest gift a mentor can give is to lead mentees through the creation of new experiences so they can realize different ways to become the best versions of them. The second level is values. What is important to them in their lives? What is it that pushes them forward and what is it that will enable them to jump over, get around or knock down every obstacle in their life's journey? The third level is beliefs. Their personal truths. What do they think it is possible for them or not; they are allowed or not; they deserve or not? How do they perceive the world around them and themselves in it? How many empowering thoughts and emotions they have about themselves and how much do they believe in their willingness, ability and determination to follow their visions?

The most profound changes, long lasting results and the most fulfilling people are achieved through a systematic and simultaneous access to all three levels described above, as well as through the development of knowledge and skills, and behavior. Very often, this approach is neither easy nor quick, nor painless. But if we ask ourselves: "Who am I as a mentor?” we would realize that it is the only right way.

The molecular mechanism of splicing: an evolutionary computational journey from ribozymes to the spliceosome

Molekularni mehanizam prekrajanja: evolucijsko računalno putovanje od ribozima do kompleksa za prekrajanje

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The spliceosome biology is currently undergoing a revolutionary phase due to increasing number of the cryo-EM structures at near-atomistic resolution recently solved. The presence of non-coding sequences (introns) in nascent RNA transcripts is a hallmark of the genomes of all organisms. Understanding the mechanism of splicing (i.e. introns removal before protein translation) is of utmost biotechnological and pharmacological importance since aberrant splicing is associated to numerous complex diseases (cancer and neurodegeneration).

The spliceosome carries out splicing in eukaryotes in two subsequent reactions, mediated by Mg^{2+} ions, undergoing a series of compositional and conformational changes. In this talk I will initially elucidate how splicing occurs in group II introns, Mg^{2+}-dependent ribozymes considered to be the evolutionary ancestors of the eukaryotic spliceosome. By employing hybrid quantum–classical QM(Car–Parrinello)/MM molecular dynamics (MD) simulations we elucidated the molecular mechanism of the first and rate-determining step of the splicing process catalyzed by these ribozymes [1]. Remarkably, our results show a new RNA-specific dissociative mechanism in which the bulk water accepts the nucleophile’s proton during its attack on the scissile phosphate [1]. We suggest that this novel reaction path might be an evolutionary ancestor of the more efficient two-metal-ion mechanism found in enzymes.

This mechanism is then integrated in the more complex biological context of the spliceosome from Schizosaccharomyces Pombe, for which we reconstructed the central core (16 proteins and 3 RNA filaments) from the near atomistic EM map. Multiple microseconds long MD simulations of this system in explicit water have revealed how conformational plasticity modulates the properties of the RNA catalytic core, affects molecular recognition of the splicing site and how carcinogenic mutations interfere with these processes. Besides contributing to the fundamental understanding of the spliceosome structural and functional biology, our study provides valuable information to harness splicing for revolutionary gene modulation tools and novel therapeutic approaches.

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Microscopic insights of the molecular associations in liquid systems

Molekularna dinamika asocijacija molekula u tekućim sustavima

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Classical molecular dynamic simulations offer an insight into the microscopic evolution of the structural organisation, which is not easily accessible by experiments. The critical issue is the choice of the effective potentials or force field models, as well as the choice of the system size and the time scale of the simulations. We address these questions in analyzing the associations in several liquid systems by means of statistical mechanics. In this presentation, we show two distinct examples: the domain formation in the molecular liquid mixtures [1] and the association of the antimicrobial peptide with the membrane [2].

In the former case, the aim is to describe changes in molecular associations, which depend on the molar ratio of the components. We use the microscopic view obtained from the simulation data and connect this with the experimental, mostly thermodynamic results. The evolution of the structure is described by static properties such as pair correlation functions and atom-atom structure factors. The heterogeneity in the structural organisation is then connected with the behaviour of excess properties, Kirkwood-Buff integrals, and diffusion coefficients.

In the latter case, we seek to elucidate the behavior of antimicrobial peptides. These peptides are part of the innate immune system in all organisms, which act against pathogens by disrupting the integrity of their membrane. We show the simulation results for peptides in different solutions and within the membrane. By combining the numerical results with the biological and biophysical measurement of the peptide structure and activity we aim to understand their mechanism of action.

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Supercritical CO_2 - Research topics and industrial applications

Superkritični CO_2 – Istraživanja i industrijska primjena

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There is a strong demand applying supercritical fluids, especially supercritical CO_2 ($SCCO_2$), instead of organic solvents for different processes (extraction, impregnation, particle design, reactions). The number of installed lab scale equipment and plants is increasing, but very often with limited facilities. For an efficient scale-up to industrial size (extractor volumes of 100 liters up to several m^3) it is essential to verify the results and models based on the data of lab scale plants within a pilot plant (5-10 liters up to 100 liters). Several aspects have to be taken into account for the set-up of an economically process.

Supercritical fluid extraction of solid and liquid raw materials is still the dominating application. The main advantage is that completely solvent free products but also residues are produced without additional down-stream processes. One main drawback is still the limitation that only non-polar substances have good solubilities in $SCCO_2$ and can be extracted. But it has to be taken into account that within the residues still all polar compounds are present, which might be extracted by a subsequent liquid extraction process.

The layout of industrial scale plants is based on the know-how of already existing plants in operation and on new ideas of design, optimization and engineering. For industrial scale plants no standardized layout is available because each new plant has to be engineered according to the special purposes of the raw materials and to the needs of the operator.

Extraction parameters like pressure and temperature (influencing solubility and phase equilibria), like particle size and distribution (influencing mass transfer and hydrodynamic), like bulk density (essential for an economic process and the design of the extractors), like separation method and closed solvent cycle (essential for product quality and optimal investment and operation costs) have to be optimized.
The design of different industrial applied $SCCO_2$ extraction plants will be presented.

The unique distribution of substances within solid carriers becomes more and more important. For this purpose $SCCO_2$ offers perfect transport properties and thus big advantages in comparison with conventional processes. Impregnation of wood or dyeing of synthetic fibers are already industrial applied processes. Further applications like tanning of leather or impregnation of polymers for different applications will be presented.

Improvement of transport phenomena in nanofluids

Poboljšanje prijenosnih svojstava u nanofluidima

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The ideas and concepts behind nanoscience and nanotechnology started with a talk entitled *There's Plenty of Room at the Bottom* by physicist Richard Feynman at an American Physical Society meeting at the California Institute of Technology on December 29, 1959, long before the term nanotechnology was used [1].

Since the end of the 20th century, nanoscience and nanotechnology comprise a whole range of disciplines that study and exploit the potential of the nanosize substance. A slightly different nuance is given by the deliberate and controlled manipulation, precision placement, measurement, modeling and production of matter at the nanoscale in order to create materials, devices, and system with fundamentally new properties and functions [2].

One of nanotechnology challenges is the preparation of stable nanosuspensions and their applications for separation processes aiming to improve the values of transport coefficient and ensure high process efficiency. Since the low thermal conductivity of conventional heat transfer fluids is a serious limitation on improving the performance and compactness of engineering equipment, recent studies in the field were connected with the improvement of thermal conductivity of nanofluids [3]. From the beginning of the researches till today it is possible to notice great improvements in heat transfer by applying nanofluids, regardless of the applied nanoparticles. However, many seemingly contradictory studies, especially about the mechanism of increasing thermal conductivity, need clarity and validation. In the future, it will be necessary to establish unique models in order to connect numerous process parameters with the thermal properties of the prepared nanofluids. Successful application of nanofluids in heat transfer raises the consequent questions whether it is possible to enhance mass transfer of multicomponent mixtures by introducing nanoparticles. According to a relatively small number of studies about mass transfer in nanofluids, the answer is positive since convective heat and mass transfer processes are analogous in nature [4]. The improvement of transport properties of nanofluids opens many opportunities for their application of separation processes (apsorption, extraction or leaching).

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How thermodynamics links biomolecular structure and function?

Kako termodinamika povezuje strukturu i funkciju biomolekula?

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A core of our research concept in biophysical chemistry is based on thermodynamics - a general physical theory that enables quantitative description of energetic changes in a system. Here we will show how to use thermodynamics for estimating the mechanism of biomolecular processes, determining their driving forces and predicting the behavior of the biomolecular system at various conditions [1].

This will be demonstrated mainly using ubiquitous bacterial stress response genetic systems called toxin-antitoxin (TA) modules responsible for persister cell formation [2]. TA modules encode two proteins, a stable toxin and an unstable antitoxin that contains an intrinsically disordered domain responsible for neutralizing the toxin by complex formation [3]. Transcription of TA genes depends on toxin/antitoxin ratio via formation of the repressor complex on the operator DNA (Figure 1). Understanding the thermodynamics of interactions between the toxin, antitoxin and DNA is crucial for connecting structural features of the toxin and antitoxin to their functional behavior. We performed detailed thermodynamic analysis of protein-protein and protein-DNA interactions for several TA modules using calorimetric and spectroscopic techniques [4,5]. We will demonstrate how thermodynamic parameters can be connected to structural properties and how we can use them to simulate the regulation of TA module functioning at different conditions.

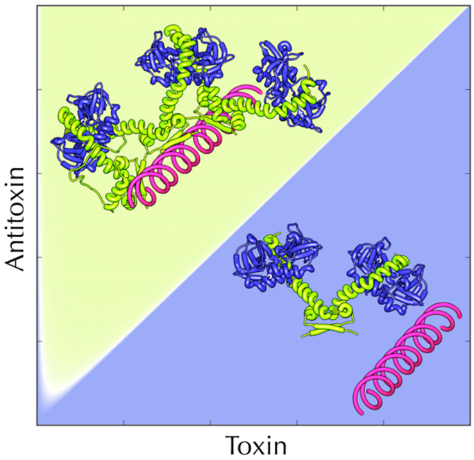

Figure 1: Phase diagram showing regions of antitoxin and toxin concentrations at which the operator DNA is repressed (bright color) or free (dark color) together with the corresponding molecular species.

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Maintaining the canonical amino acid alphabet: a story about aminoacyl-tRNA synthetases

Očuvanje kanonske aminokiselinske abecede: priča o aminoacil-tRNA-sintetazama

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Natural evolution has selected a set of 20 canonical genetically encoded amino acids to build a plethora of proteins that provide the biochemical foundations for life. To participate in protein synthesis amino acids require attachment to transfer RNA molecules (tRNAs). This reaction is accomplished by aminoacyl-tRNA synthetases (AARSs), enzymes that use ATP to activate the matching amino acid and transfer it to the cognate tRNA, which, in turn, harbors the corresponding anticodon triplet of the amino acid code. Some AARSs are not able to discriminate against highly similar near-cognate amino acids in the synthetic reaction alone, and so have evolved hydrolytic editing to clear mistakenly activated or aminoacylated amino acids.

Preventing the incorporation of protein-building amino acids at the wrong positions is not the only task of AARS quality control. Recent findings have indicated that editing may also operate to block the infiltration of natural amino acids that are not coded for protein synthesis. Using genetic, biochemical and mass spectrometry approaches we demonstrated that in the case of leucyl-tRNA synthetase the main physiological role of editing is to preclude toxic misincorporation of the non-canonical amino acid norvaline at protein positions coded for leucine [1,2]. Norvaline accumulates under oxygen limiting conditions arguing for a critical role for editing in cellular adaptation to the various conditions of growth.

Given the lack of evolutionary pressure against unnatural compounds, it had been assumed that editing would not be an obstacle for the use of artificial amino acids as protein building blocks. Yet, we have recently demonstrated that participation of trifluorethylglycine in protein translation takes place only after silencing of weak editing by isoleucyl-tRNA synthetase [3]. Thus, the advanced rational design that relies on misincorporation of artificial amino acids to create proteins with novel features relies on our ability to reengineer the AARS synthetic and editing pathways that act as powerful gatekeepers of the canonical amino acid alphabet.

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Increasing hydrophobicity of polymer blend surfaces by ICP etching

Povećanje hidrofobnosti polimernih mješavina tehnikom jetkanja ICP-om

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The concept of superhydrophobic surfaces (water contact angles higher than 150°) is inspired by the surface of lotus leaf [1]. It gained a lot of significance in the last years because the hydrophobicity of a surface depends on its chemical composition and surface roughness. The specific surface roughness is essential for the superhydrophobicity, self-cleaning (lotus effect) and it can have great influence on fluid flow inside microchannels.

In this work a method for designing hydrophobicity of polymer blends by creating specific surface topography is described. Polymers used for polymer blend preparation are: polylactide (PLA), low-density polyethylene (PE-LD), polyurethane (PUR), polyamide 12 (PA12), vinyl acetate homopolymer (PVAC) and acrylonitrile butadiene styrene (ABS). Fused deposition modeling (FDM) 3D printing technology uses polymer filaments produced from PLA and ABS. In order to increase hydrophobicity by changing the topography of two-phase polymer blend surface, blends are etched by using inductively coupled plasma (ICP) before the fluorocarbon-based coating treatment done in the second step [2]. During the surface treatment process of PLA/PE-LD polymer blends PLA is etched significantly more than PE-LD and specific "island-like" surface morphology with 10 - 20° higher contact angle is created.

This work has been supported by Croatian Science Foundation under the project entitled "Development of materials for 3D printing of microreactors" (UIP-2014-09-3154).

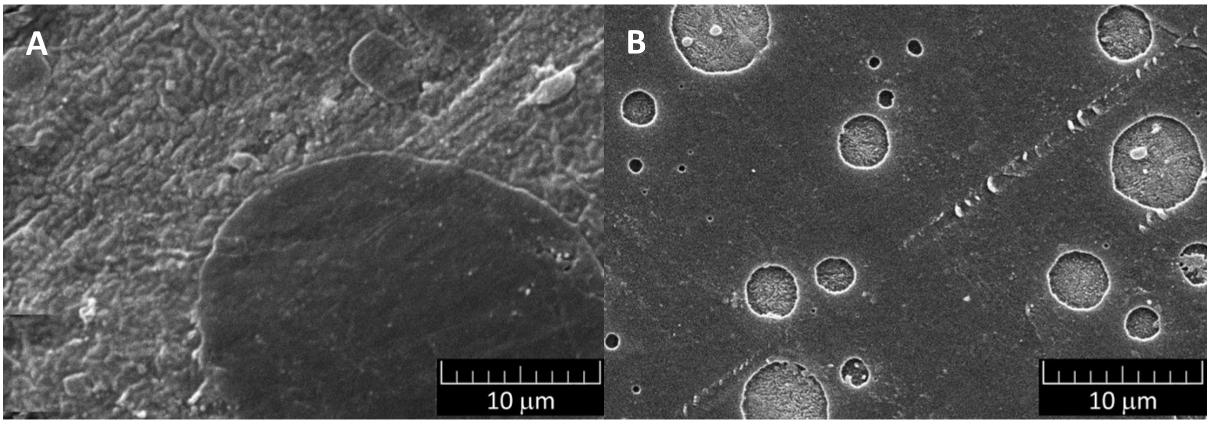

Figure 1: SEM micrographs of PLA/PE-LD 80/20 (A) and 20/80 (B) polymer blends after plasma treatment.

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Application of self-assembled films of long chain organic acids in corrosion protection

Primjena samoorganizirajućih filmova dugolančastih organskih kiselina u zaštiti od korozije

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Self-assembled monolayers (SAMs) of long-chain organic compounds have found their application in many fields [1], such as sensors, electronic devices, lubrication as well as in corrosion protection [2].

Long-chain organic acids, such as carboxylic, hydroxamic or phosphonic acids can bind to oxidized surfaces of metals and alloys which is an advantage for their practical application as most of the commercially important metals and alloys readily get covered by thin oxide layers when exposed to air. The other advantage of long-chain organic acids, especially carboxylic acids is that they are non-toxic. Most of the studies on long-chain organic acids SAMs are focusing on characterization of SAM structure and binding of head group to metal surface but there are far less studies that focus on efficiency and durability of corrosion protection provided by SAMs, especially on alloys.

In order to achieve efficient corrosion protection, self-assembled monolayer should be dense, ordered and defect free to act as a barrier against aggressive ions diffusion towards the metal surface. In principle, SAMs are easily prepared by adsorption, either from the solution or vapor phase, but in practice many factors determine whether the well ordered and compact monolayer will be formed. Film formation is affected by temperature, solution exposure time, environmental conditions, solvent, etc. The task of forming well ordered organic monolayer is especially complicated when alloys are used as a substrate.

In this work the possibility of corrosion protection of copper-nickel alloy by self-assembled films of long chain carboxylic and phosphonic acids is examined. The influence of various factors, such as molecule chain length, acid group, surface roughness, adsorption conditions on the corrosion protection are examined. By changing the experimental conditions both mono- and multilayer films are formed and their protective effect is evaluated.

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Acknowledgments: The research leading to these results has received funding from Croatian Science Foundation under grant agreement 9.01/253.

Possibility of valorization of oil shale as a source of synthetic crude oil production

Mogućnost valorizacije aleksinačkog uljnog škriljca za proizvodnju sintetičke nafte

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Results obtained in the field of modern geochemistry in the world, and in the Republic of Serbia as well, indicate that it is possible to exploit oil shale for various purposes. Studies of oil shale deposits in Serbia (Aleksinac basin, Senon groove, Valjevo-Mionica tectonic groove, Vranje basin, and Krusevac basin) were mostly completed during intensive geological and geochemical research between 1978 and 2000.

Among deposits listed above, Aleksinac basin is commercially the most promising one. It stretches over about 10 km in the direction north-northwest between the Južna Morava River and the Moravica River and covers about 20 km^2. Aleksinac oil shale is considered a very important potential alternative source of energy so that even pilot studies of its exploitation were performed. Detailed studies that have been included a large number of samples from various locations and depths. It involves retorting process (about 3000 samples), determined calorific value of representative samples or composite samples (120 samples), ashes analysis (150 samples), abundance of heavy metals and rare elements (60 composite samples); the mineral composition is determined by crystallographic analysis. Based on the results obtained, it was concluded that Aleksinac oil shale can be used for the production of synthetic crude oil, bricks, cement, and fillers in road construction. Results of a fundamental study of oil shale conducted by the researchers of the informal Belgrade school of geochemistry, shaded light on the (clarified) nature of organic substance in the Aleksinac shale. Study of the composition and structure of the organic substance – kerogen in the Aleksinac shale by oxidative alkaline degradation of kerogen concentrate [1] and introducing a new microbiological method for obtaining a concentrate of organic substance [1,2,3] resulted in a much more reliable estimate of energy potential and quality of the synthetic crude oil. Aleksinac shale contains dominantly kerogen type I and relatively small percentage of kerogen type II (based on characteristic laminated microtexture) with about 75 % C; 11 % H; 3 % N; 4 % S and 5 %O, with high atomic H/C ratio (1.40-1.70) and very low atomic O/C ratio (0.05-0.30).

Based on overall study of the results of technical analysis of Aleksinac shale samples and results of fundamental research, it could be concluded that today, as well as in recent future, obtaining of synthetic oil is unacceptable from financial, technical-technological and ecological reasons.

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Micro-, lab-, pilot- and industrial scale based biocatalytic processes for production of biofuels

Biokatalitički procesi proizvodnje biogoriva na mikro, laboratorijskoj, poluindustrijskoj i industrijskoj razini

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Nowadays as the availability and accessibility of fossil fuels is significantly declining, the need for the production of biofuels from various renewable sources is becoming increasingly interesting. Biodegradability, non-toxicity and low pollution emissions are merely some properties making biogas, biodiesel and bioethanol more environmentally friendly fuels.

Solid-state fermentation could be a suitable technology for the production of value-added products by utilization of the renewable waste materials, which makes it also economically feasible. So far, this technology was used for production of enzymes, organic acids, mushrooms, flavor and aroma compounds, pigments, polysaccharides, hormones, human food and animal feed. Different type of bioreactors have been developed and successfully used for solid-state fermentation of broad range of substrates and in production of value-added products. Solid-state fermentation on lab-, pilot- and industrial-scale will be demonstrated as part of anaerobic degradation of several waste materials such as brewer's spent grain (mono-substrate) and whey and cow manure (co-digestion). The anaerobic process was divided into a reactor for the anaerobic digestion of solids (SS-AD - Solid State Anaerobic Digestion reactor), in which hydrolysis mainly took place and into a reactor with granular biomass (GBR Granular Biomass Reactor) in which most of the biogas production took place [1].

Microreactors are widely used in different fields of chemical and pharmaceutical industry, biotechnology and medicine. The application of different microreactor systems in intensification of the biodiesel production process is widely studied. However, previous studies of the application of microreactor technology in the production of biodiesel were limited to the use of chemical catalysts. Mild reaction conditions, absence of unwanted by-products (soap), reusability, simple separation and purification of the resulting biodiesel as well as lower energy consumption are some of the many advantages that make the enzyme lipase – a biocatalyst – a better choice than traditional chemical catalysts in the process of biodiesel production [2]. Different microreactor systems utilising a commercially available lipase and a lipase produced by solid-state fermentation using the fungus *T. lanuginosus* were used for transesterification of fresh and and waste cooking oil while biodiesel was separated using integrated microseparation unit.

Selected examples are clear demonstration of environmentally friendly and economic technologies used for efficient production of biofuels on micro-, lab-, pilot- and industrial scale.

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Inclusion of nutraceutical ingredients into MOFs

Ubacivanje nutraceutskih sastojaka u MOF-ove

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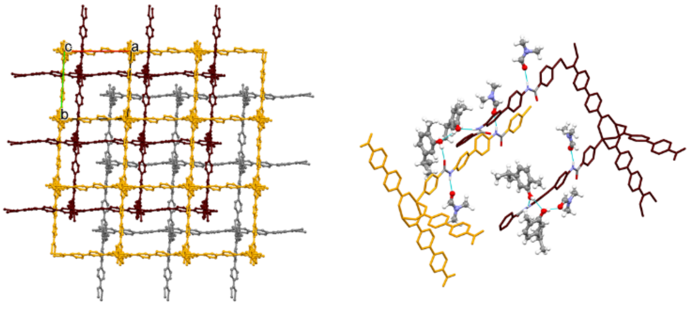
MOFs are highly versatile materials that are made by connecting metal ions with prefixed coordination geometry with rigid ligands acting as spacers, hence affording three-dimensional coordination polymers. The accurate design of the building units allows to design porous MOFs, obtaining cavities of considerable size, which usually accommodate loosely bound solvent molecules. The scope of this work is to find a systematic way to embed small molecular aggregates inside porous crystalline materials, with the multiple aims to explore the structural aspects of nanoconfinement, and of the stabilization of guest molecules inside the cavities of the structure. The feasibility of this approach stems from both the recently developed crystalline-sponge method that describes the structural determination of single molecules trapped inside a microporous framework. The guest that we are here considering for inclusion in MOFs pores are some important compounds for the human health and nutrition which occur as liquids at room temperature, such as eugenol (a major component of clove oil), carvacrol (extracted from the oregano essential oil), thymol (present in the oil of thyme); these are part of a naturally occurring class of compounds known as biocides, with strong antimicrobial attributes. In order to embed these guests in crystalline materials we needed to carefully tailor the MOF cavities; thus we designed a small library of new ligands which could afford flexible MOF architectures. We characterized a series of new materials which are able to release the guests in a controlled way, opening the way to engineer additives for active food packaging. In particular the structure and inclusion properties of PUM168 will be discussed (Figure 1). This new heteroleptic MOF shows triple interpenetration, and nevertheless can accommodate all the guests belonging to the oil family by exhibiting a remarkable flexibility; the selectivity towards mixtures will also be discussed.



PUM168

carvacrol@PUM168

Figure 1: The projection of the MOF architecture is shown on the left, and an example of MOF…guest interaction via hydrogen bonds is shown on the right.

Chirallica Ltd. - A Chemical Odyssey

Chirallica d.o.o. - Kemijska Odiseja

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Chirallica Ltd. was established in 2005 as a start-up biotech company with expertize in chiral separation and organic synthesis. Initial funds came from successful application to the RAZUM Program operated by BICRO Agency. The company had on-site production of proprietary and generic chiral stationary phases (CSP's) together with production of chiral columns for analytical and preparative use. Proprietary CSP's were the result of scientific research activities conducted within Laboratory for Stereoselective Catalysis and Biocatalysis (CAT-BIO) at Ruđer Bošković Institute in Zagreb. Generic CSP's were initially prepared and tested at CAT-BIO, and subsequent necessary R&D activities were continued at Chirallica Ltd. Along with chiral columns and bulk CSP's production, the company also implemented Simulating Moving Bed Technology (SMB) used for preparative enantioseparation on kilo scale.

Parallel with company's main activities, analytical department was established in 2007 with aim to provide efficient analytical method development and validation of pharamaceuticals. From the very beginning Chirallica Ltd. operated under ISO standards, and GMP compliance in analytical department.

The company had steady growth until 2009 when first signs of business disruption appeared as a result of global financial crisis. Chirallica Ltd. continued with its business activities until 2012 when it was abruptly terminated. Presentation will reveal key moments in the entrepreneur journey of the company, and also various business aspects will be commented.

Intellectual property in life and work

Intelektualno vlasništvo u životu i poslu

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Innovation is a key focus of the *Europe 2020* strategy which aims at creating a more competitive economy and higher employment [1]. A major tool for achieving this goal is an efficient system of intellectual property rights (IPRs) which fosters creativity and innovation [2]. The system includes copyright and related rights, trade marks, patents, designs, and other forms of intellectual property.

The IPR intensive industries, i.e. those making large use of the various types of intellectual property (including chemical and pharmaceutical industries) play an important role as far as Europe's, but also the World's economy is concerned. Data for the 2011–2013 period show that in the EU they generated 42% of total economic activity (GDP), 28% of jobs (directly) and paid significantly higher wages than other industries (46%) [2]. The IPR intensive industries have also proved to be more resilient to economic crisis.

IPRs should not be envisaged solely from the industrial point of view. The EU strategies strongly advocate bringing together industry, small and medium enterprises (SMEs), higher education institutions (HEIs), and public research organizations (PROs) for innovation to happen (the *Open Innovation* concept). Knowledge and new research results generated in HEIs and PROs should be transferred to industry and SMEs (*knowledge and technology transfer*) with governmental support (the *Triple Helix* concept).

When chemistry and related fields are considered in terms of IPRs, patents tend to come to mind first. Although organic fine chemistry and pharmaceuticals have seen a drop in the number of patent applications, they are still among the top ten fields, including biotechnology, in the number of filed applications, (EPO, 2016) [3]. Chemists and professionals in chemistry-related fields should also bear in mind the importance of copyright (e.g. PhD thesis or paper), trade mark (e.g. name of institution or project, drug name), design (e.g. drug packaging), and other forms of intellectual property.

The lecture will give a short overview of IPRs of general interest and of special interest to the field of chemistry and related fields. It will also provide examples of possible concern for the audience. It will try to place IPRs in the present economical and societal context in the hope that this will contribute, as ultimate result, to the better future positioning of Croatia on various IPRs charts.

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How to succeed: From results to publications

Kako uspjeti: Od rezultata do publikacija

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Let's say that you are an enthusiastic graduate student or a highly motivated post-doc, or maybe you are just starting out in your own independent scientific career. You are working on several projects and you have all these "cool" results that you are incredibly excited about. Obviously you really want to make sure that your efforts are noted and recognized by a wide audience so you spend many days and weeks trying to put together your first perfect Communication…and then your manuscript is rejected! Why did those reviewers not see the merits of your work? How is it even possible that they failed to recognize the value and significance of your results? Well, whether we are writing our first or 200th manuscript, a rejection is always unwanted and painful and our initial reaction upon hearing such bad news is probably to curse the reviewers, the editor and everyone associated with that wretched journal. As an associate editor I am often the bearer of bad news, so in this presentation I will try to provide a personal perspective from "the other side of the desk" that hopefully can be of some help and encouragement for when you are writing or re-writing your next manuscript.

Multicomponent approach to natural product-like compounds

Višekomponentne reakcije u sintezi spojeva srodnih prirodnim produktima

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Screening of small-molecule libraries has been the most commonly used tool in drug discovery over the past two decades. [1] However, most libraries typically represent collections of a large number of structurally similar compounds, i.e., the "chemical space" covered is infinitely small. [2] This limitation significantly hampers development of novel lead compounds needed to tackle new generations of biological targets. Contrary to that, natural products with complex molecular architectures and numerous stereogenic centers represent valuable pool of drug candidates. The concept of expanding the chemical space by developing large collections of structurally diverse natural product-like compounds is one of the main challenges nowadays. In order to achieve high degree of structural diversity, it is important to have various building blocks equipped with functional groups than can generate diverse molecular scaffolds with different stereochemistry.

Our group is currently aiming to expand the chemical space by using multicomponent reactions to generate structural variations and complexity. Multicomponent reactions (MCRs, Fig. 1a) are powerful tool for introducing chemical diversity and the rapid generation of small-molecule libraries. Among numerous types of MCRs, of special interest are those that include isocyanide functional group, particularly the Passerini and Ugi reaction. We focused on building blocks derived from natural and non-natural amino acids, carbohydrates and enediynes (Fig. 1b), and their utilization in MCRs. [3]

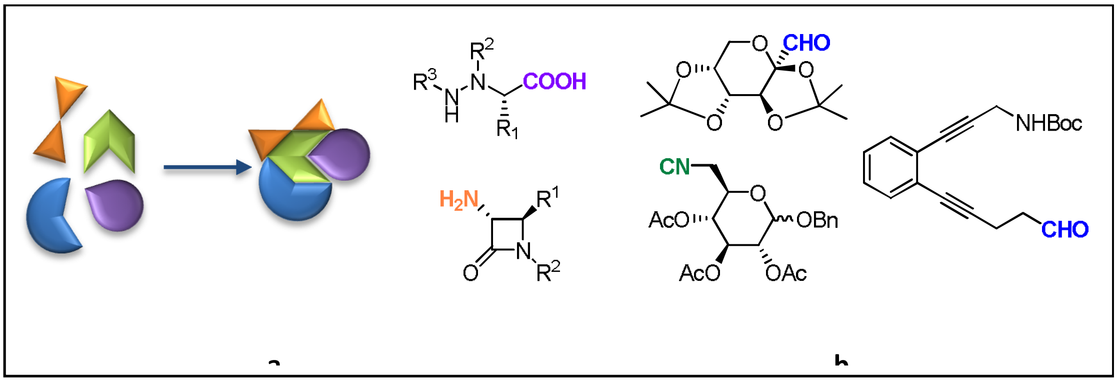

Figure 1: a) Principle of MCRs; b) Selected building blocks for MCRs.

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Selected examples of supramolecular stereochemistry

Izabrani primjeri supramolekularne stereokemije

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During our almost 3 decades long supramolecular chemistry research at the Rudjer Boskovic Institute, the stereochemical effects that occur at the supramolecular level were of permanent interest. Selected examples of supramolecular stereochemistry that will be presented include: (*i*) chiral and constitutional recognition effects appearing in transport of amino acid and dipeptide carboxylates by chiral lariat ether carriers [1], (*ii*) dia- and enantio- selectivity in the cyclopropanation of styrene with ethyl diazoacetate catalysed by novel supramolecular Cu(I) catalyst possessing helical reaction space [2], and (*iii*) the observation of the lower rim circular amidic hydrogen bonds in tetra- (O-(*N*-acetyl-PhgOMe) calix[4]arene derivatives whose opposite directionality may result in cyclo-diasteroisomerism [3]. Various stereochemical effects were also observed during our studies of self-assembly and hierarchical organization in supramolecular gels [4]. Bis(PheOH) maleic acid amide (non-gelling) photo-isomerization into fumaric acid amide (gelling) in aqueous media represents a photo-induced gelation system [5]. The stereochemical examples from gel studies related to the enantiomer/racemate gelation controversy [6], the stereochemical effects appearing in two-component gels formed by chiral gelators [7], the issue of *meso*-gelators [8], the appearance of intense optical activity of golden nano-rods adsorbed on the surface of chiral gel fibres [9] and the efficient inter-molecular central to axial chirality transfer in the self-assembled biphenyl containing amino acid-oxalamide gelators [10] will be also presented.

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Analysis of the state graduation exams - misconceptions in fundamental chemical items

Analiza ispitnih zadataka državne mature - (ne)razumijevanje temeljnih kemijskih koncepata

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Na temelju rezultata kvalitativne analize ispitnih zadataka državne mature iz Kemije od 2011. [1] do 2016. [2] analizirane su korelacije dobivenih odgovora s obzirom na učeničko (ne)razumijevanje temeljnih kemijskih koncepata. Rezultati analize ukazuju da je kvaliteta ispitnih zadataka kao i uspješnost učenika na maturi tijekom godina rasla. Više se pažnje posvećuje ispitivanju prirodoslovne pismenosti te kvaliteti postavljenih pitanja. Istovremeno rezultati pokazuju premalu zastupljenost zadataka treće kognitivne razine u kojima se traži povezivanje i primjena određenog kemijskog koncepta, a ti su zadatci redovito manje uspješno riješeni.

Kemija je na državnoj maturi izborni predmet, godišnje državnoj maturi iz Kemije pristupi oko 3500 maturanata, te isključivo služi kao bodovni kriterij za ulazak u sustav tercijarnog obrazovanja. Svjedodžba o položenoj državnoj maturi iz kemije služi kao dokaz da je učenik ostvario zadanu razinu postignuća u onim ključnim znanjima, vještinama ili kompetencijama koje je trebao steći prema programu škole koju je pohađao. Prema Ispitnom katalogu državne mature Kemije [2] temeljni su kemijski koncepti svrstani u 5 područja: *Tvari, Kemijske promjene, Energija, Brzina kemijskih reakcija, Ravnoteža kemijskih reakcija.* U šestom području ispituje se vještina prikupljanja podataka, obrade i prikazivanja rezultata. Ishodi učenja sastavni su dio sadržaja poučavanja važećeg Nastavnog plana i programa Kemije za gimnazije [3], a birani su s ciljem ispitivanja kemijskih koncepata važnih za nastavak školovanja i primjenu u svakodnevnom životu. Provjera usvojenosti odnosi se prvi put i na provjeru opažanja učenika tijekom izvedbe pokusa u nastavi kemije. Primjenom konceptualnih modela poučavanja kod učenika potiče se aktivno promatranje i zaključivanje. Podršku pri promjeni načina poučavanja te veću podršku nastavnicima pri osmišljavanju pokusa, obradi i interpretaciji rezultata opažanja treba kontinuirano provoditi stručnim usavršavanjima na svim razinama (od školske, županijske, međužupanijske i državne). Ulaganjem u unaprjeđenje nastave kemije, ostvaruju se ciljevi ugodnog radnog ozračja sudionika nastavnog procesa te motivira mlade za nastavak školovanja u području prirodnih i srodnih znanosti.

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Structural formulas and names of organic compounds

Strukturne formule i imena organskih spojeva

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Poznavati strukturu neke molekule znači znati vrstu i broj atoma koje ona sadržava, način njihovog povezivanja (konektivnost) i vrstu kemijske veze između njih te raspored svih atoma u prostoru. U upotrebi je nekoliko načina prikazivanja struktura organskih molekula, a to su projekcijska (konstitucijska) formula, sažeta (kondenzirana) formula i prikaz strukture pomoću veznih crtica. Iz ovakvih prikaza često se ne dobije točan uvid u trodimenzijsku strukturu organske molekule, pa se za prikazivanje međusobnog razmještaja atoma u prostoru koriste različiti konformacijski prikazi (Newmanova projekcijska formula, konformacijski prikazi cikličkih molekula poput cikloheksana), dok klinaste formule, Fischerove projekcijske formule i Haworthove formule dodatno koristimo kod prikazivanja stereoizomera. Svaku organsku molekulu treba imenovati tako da je na temelju imena moguće jednoznačno strukturno prikazati nju samu. Pravila za imenovanje organskih spojeva jasno su određena od strane Međunarodne unije za čistu i primijenjenu kemiju (engl. *International Union for Pure and Applied Chemistry,* IUPAC) koja su donesena 1979. i 1993. godine te objavljeni hrvatski prijevodi 1985. [1] i 2001. godine.[2]

Na temelju učeničkih odgovora u zadaćama državne mature iz kemije te natjecanja iz kemije uočene su neke nedosljednosti u prikazivanju struktura organskih molekula kao i imenovanju istih. Stoga se pokazala potreba da se ovoj problematici pristupi sustavno te da se usklade neke razlike u poimanju ovih koncepata zbog čega učenici često gube bodove. U tom je smislu osobito važno dodatno educirati nastavnike te ih upozoriti na moguća odstupanja koja su uočena i kod strukturnog prikazivanja organskih molekula i kod imenovanja organskih spojeva. Tijekom izlaganja bit će iznijete najučestalije učeničke pogreške s preporukama kako ih izbjeći.

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USMENA IZLAGANJA

ORAL CONTRIBUTIONS

Stereoselectivity in phthalimide initiated photocyclization of peptides

Stereoselektivnost u ftalimidom potaknutim fotokemijskim ciklizacijama peptida

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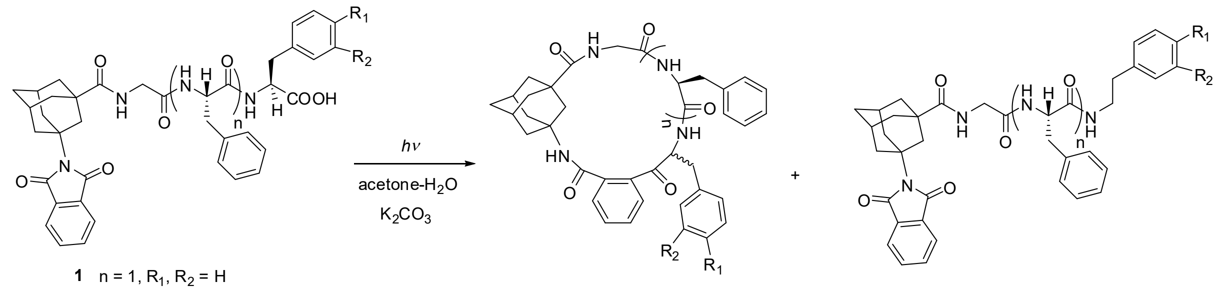
Phthalimide in the triplet excited state is a good oxidizing agent. Therefore, upon photoexcitation of the phthalimide to the triplet state, alkyl-carboxylates are easily oxidized by inter- or intramolecular single electron transfer (SET) from the carboxylate to the phthalimide [1]. The SET promotes irreversible decarboxylation leading to radical intermediates, which was implemented in different synthetic applications. For example, such a decarboxylation has been used in the photocyclization of crown ethers or peptides [1,2].

We have become interested in photoinduced decarboxylation reactions of different phthalimide derivatives of adamantane aminoacids [3,4]. Within the scope of that research, we have found an example of highly enantioselective dipeptide cyclization with a memory of chirality [5]. In the continuation of the research we investigated photocyclization of tetra- and pentapeptides **1**-**6** (Scheme 1). The photocyclizations of **1**-**6** to peptides **7**-**12** proceed in moderate yields, but with high diastereoselectivity. Interestingly, preliminary results indicate different stereochemistry in the cyclic products in tetra- and pentapeptides and suggest that the chiral information in the peptide chains leads to a complete inversion or retention of configuration.



1 n = 1, R_1, R_2 = H
2 n = 2, R_1, R_2 = H
3 n = 1, R_1 = OCH_3, R_2 = H
4 n = 2, R_1 = OCH_3, R_2 = H
5 n = 1, R_1 = OCH_3, R_2 = OCH_3
6 n = 2, R_1 = OCH_3, R_2 = OCH_3

7-12 n = 1,2, R_1, R_2 = H, OCH_3

13-18 n = 1,2, R_1, R_2 = H, OCH_3

Scheme 1: Photocyclization of tetra- and pentapeptides.

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Synthesis and structural analysis of novel isomeric amidino-substituted 2-aminophenols

Sinteza i strukturna analiza novih izomernih amidino-supstituiranih 2-aminofenola

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Recently our scientific focus has been placed on amidino-substituted benzothiazole compounds with emphasis on their synthesis, study of anticancer activities and DNA binding properties [1]. In contrast to a great number of biologically active amidino-substituted benzimidazole and benzothiazole derivatives, benzoxazoles are still rare [2]. The main reason is the lack of a general method for their preparation, which could be based on a condensation reaction of the amidino-substituted 2-aminophenols with aldehydes, carboxylic acids and carboxylic acid derivatives as commercially available substrates.

Most common method for amidine preparation is nucleophilic addition of amines or ammonia to suitably activated carboxylate equivalents such as imidates, thioimidates, and imidoyl chlorides. Imidates can generally be prepared either by base-catalyzed or acid-catalyzed (Pinner synthesis) addition of alcohol to nitrile. The addition of dry hydrochloric acid to a mixture of nitrile and an alcohol leads to the hydrochloride salt of an imino ester. This salt can further react with ammonia or with excess of an amine to form amidine.

Here, we report efficient synthesis by Pinner reaction of unsubstituted, *N*-substituted and cyclic amidine derivatives starting from 2-amino-4-cyanophenole (**1**) and 2-amino-5-cyanophenole (**2**) (Figure 1). Resulting compounds were isolated in the zwitterionic form and their structures were confirmed by ^{1}H and ^{13}C NMR spectroscopy, LC-MS and elemental analysis. In addition, zwitterionic form of **3d** is confirmed by X-ray structural analysis.

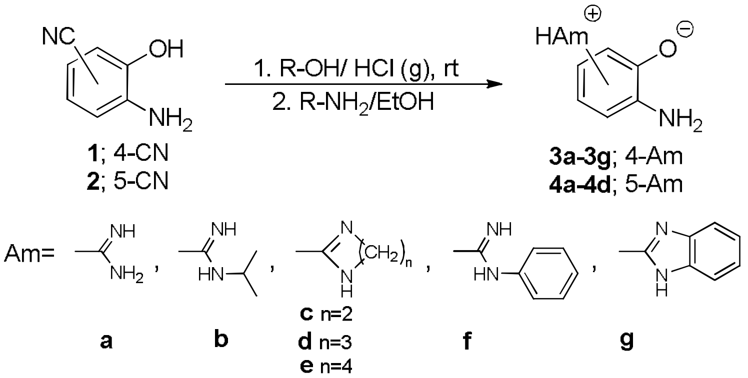

Figure 1: Synthesis of amidino-substituted 2-aminophenols.

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Organocatalytic asymmetric transformations of 3-substituted 3-hydroxyisoindolinones

Organokatalitičke asimetrične transformacije 3-supstituiranih 3-hidroksiisoindolinona

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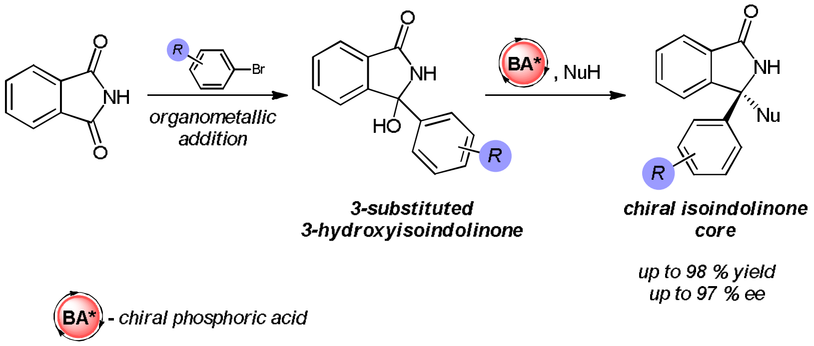
3-Substituted isoindolinones and their derivatives are common structural motifs in a variety of compounds with biological activities. For example, they have been established as precursors to anti–ischemic stroke agents, as well as antimicrobial and antitumor agents. Their activity as MDM2–p53 protein–protein, HIV–1 integrase, and protein-tyrosine phosphatase inhibitors is also well known. In addition, registered and commercially available anxiolytic, anticonvulsant and antihypertensive drugs also contain 3-substituted isoindolinone cores. Hence, it is of great importance to develop facile and effective methods for their asymmetric synthesis.

In our group, we are interested in developing asymmetric organocatalytic transformations generating cores of natural compounds. As a part of an ongoing project, we have developed chiral Brønsted-acid catalyzed asymmetric additions of nucleophiles to ketimines, that are generated *in situ* from 3-substituted 3-hydroxyisoindolinones. The asymmetric addition of thiols provided chiral *N*(acyl),*S*-acetals in high isolated yields and excellent enantioselectivities, and the application of the developed protocol was demonstrated in the synthesis of a known HIV-1 reverse transcriptase inhibitor. In a similar fashion, asymmetric Friedel-Crafts reaction resulted in high yields and enantioselectivities of products comprising triarylsubstituted stereocentres, an important motif in the cores of natural compounds.



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Interpolyelectrolyte neutralization of linear polyions in solution and at the surface

Interpolielektrolitna neutralizacija linearnih poliona u otopini i na površini

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Complexation of several linear vinylic polyions with complementary charge density in aqueous solutions of binary 1:1 salts was investigated by means of microcalorimetry, dynamic light scattering, electrokinetics and spectrophotometry. The build-up of corresponding multilayers was monitored using quartz crystal microbalance. Charged primary and secondary polyelectrolyte complexes were formed upon stepwise titrant to titrand addition. At c_{salt} / mol dm^{-3} ≤ 0.1 their flocculation near the equivalence occurred, resulting with precipitates containing approximately equal amounts of oppositely charged monomers [1–3]. However, in the case of abrupt (instead of stepwise) titrant addition in excess, the primary complex charge reversal was achieved [3]. The counterion specific aggregation and more pronounced overcharging of primary complexes were noticed at higher electrolyte concentrations [1–3]. This resulted with asymmetric interpolyelectrolyte neutralization. The monomer-counterion preferences were correlated with standard Gibbs energies and enthalpies of counterion hydration. The reactions of investigated polyelectrolytes were predominantly (or entirely) entropically driven, irrespectively of the type of reaction products formed (nano-complexes, precipitates) and the concentration of electrolyte present [1–3]. The equilibrium establishment proceeded slowly and solely in the presence of simple salt. The influence of electrolyte type and concentration on the multilayer build-up was essentially the same as in the case of corresponding reactions in solution. These results, and the fact that sequential nano-complex overcharging in solution can be achieved simply by manipulating with the amounts of monomers introduced, suggest that no fundamental differences between the processes of complex and multilayer formation exist.

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Acknowledgments

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The effect of the chain length of n-carboxylic acids onto the corrosion inhibition of copper in chloride and acidic aqueous media

Utjecaj duljine lanca kod n-karboksilnih kiselina na inhibiciju korozije bakra u kloridnom i kiselom vodenom mediju

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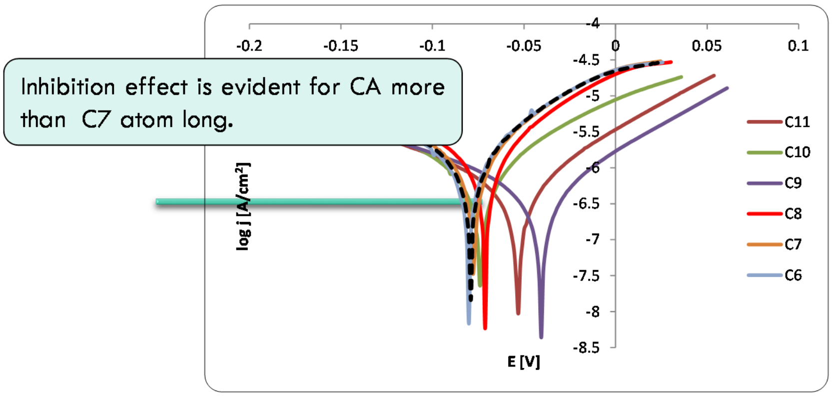
The copper metal and its alloys represent an important class of materials from which a number of industrial equipment's (desalination plants, heat exchangers, cooling systems, etc.) are made. The use of these materials relies due to their characteristics (strength, electrical/thermal conductivity, etc.), but as many metals and alloys copper suffers from its surface degradation due to the corrosion phenomena [1]. The use of n-carboxylic acids (hexyl-, heptyl-, octyl-, nonoyl-, decyl- and undecanoiccarboxylic acids) on copper surface as anticorrosive barriers was explored. The anticorrosive efficacy of these molecules in 3.5% aqueous sodium chloride media (Figure 1) and 0.1M H_2SO_4 was determined by electrochemical potentiodynamic polarization.



Inhibition effect is evident for CA more than C7 atom long.

Figure 1: Tafel plots for the copper electrode (d=1mm) immersed in 3.5% NaCl aqueous media in the presence of 1E-3M of corresponding (C_5-COOH to C_{10}-COOH) carboxylic acids.

The inhibition efficiency of these molecules as corrosion inhibitors increases almost linearly with the chain length of the used n-carboxylic acids in both of the tested corrosion media. The maximum corrosion inhibition reflected by these molecules in aqueous 3.5% NaCl is 78%, whereas in aqueous 0.1M H_2SO_4 is 82 %. According to the experimental corrosion measurements, the alkyl chain of n-alkanoic acid needs to have at least 7 carbon atoms in order to perform a pronounced inhibition of corrosion.

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Aromatic mono- and bis-amide derivatives as anion receptors in solution

Aromatski mono- i bis-amidni derivati kao receptori aniona u otopini

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Chemistry of anion recognition and complexation has developed into an important field of supramolecular chemistry, with ever-new application potentials of the corresponding systems discovered [1]. Despite a significant progress in the field, the search for receptors exhibiting peak selectivity and high binding affinity continues [2]. In order to facilitate the design of efficient anion ligands, it is of great importance to identify the interactions that lead to the complex formation and assess their individual contribution to the overall stability [3]. One of the feasible approaches towards this goal is to study series of relatively simple model compounds, gaining detailed insight into the interplay of their structure and reactivity [4]. Thus gathered knowledge can be employed in the systematic development of the novel anion receptors as it can point out the suitable type and number of the binding moieties as well as the appropriate linkers to achieve the desired properties.

In this work we present the synthesis and the anion complexation study of a series of amide derivatives differing in number and arrangement of the binding sites (amide N–H groups). The stability of their complexes with acetate, dihydrogen phosphate, and chloride was studied in dimethyl sulfoxide using ^{1}H NMR spectroscopy and conductometry. The stoichiometry of all complexes was found to be 1:1 and their stability was discussed with respect to the receptor structural properties as well as specific features of the anions.

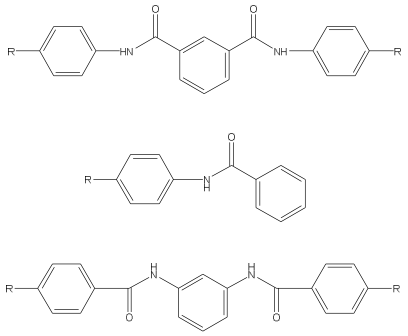

Figure 1: Structures of the studied anion receptors.

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Sparse discrimination of molecular fragments for prediction of octanol-water partition coefficient

Predikcija koeficijenta particije oktanol-voda primjenom molekulskih fragmenata i diskriminacijske analize rijetkom matricom

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In this work is applied molecular graph theory and sparse Fisher discrimination algorithm for determination of key molecular fragments in prediction of POW octanol-water partition coefficients. Computational cPOW is considered as a numerical predictor for bioavailability of molecules, i.e. its affinity toward transfer across a cell membrane. Here is focus on application of sparse linear discrimination algorithm and nonlinear decision trees applied on a set of for a set of alkanes, alkenes, acetones, aromatics, organic acids and halogenated hydrocarbons in the range of C_1-C_{12}. Corresponding experimental values are from the J. Sangster data base [1]. As predictors are evaluated molecular graph signatures (fragments) of second order as proposed by J.P. Faulon [2]. For decomposition of molecule structure into graph signatures used is Bioclipse software by O. Spjuteh *et. al.* [3]. Obtained large data matrix of signatures is evaluated by statistical parameters (the fragments they do not confirm to parametric probability density functions) and is evaluated by singular value decomposition for dimension reduction (number of effective POW predictors). All statistical and numerical evaluations are done by algorithms available in R software [4]. Obtained is high prediction accuracy with linear models (sparse linear model with relative standard error 3.57 %), some improvement is gained with chemometric decomposition (sparse PLS partial least squares with relative standard error 3.44 %). Further considerable improvement in prediction is obtained with sparse decision tree forest, accounting for interactions, yielding relative standard error 1.41%. The first three molecular fragments with the highest contribution to prediction maximum logPOW (>4) are in Faulon notation: [Cl]([Cl][Cl]([C])), [C]([C](=[C][H])p[C](p[C][H])p[C] ([C]p[C])), [C]([Cl][Cl][H][H]). Obtained results are applicable in pharamaceuticals design and toxicology studies.

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Voltammetric characterization of carotenoids in aqueous media

Voltametrijska karakterizacija karotenoida u vodenom mediju

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Carotenoids are responsible for the coloration of many plants and fruits. They possess potential membrane antioxidant activity due to their reactivity with singlet oxygen and oxygen free radicals which can prevent oxidative damage and offer protection against various diseases. So far, electrochemical investigations of carotenoids have been performed in non-aqueous media [1] with the notable exception of some studies in micelle systems [2] and as self-assembled monolayers (SAM) in aqueous phase [3]. Such conditions are closer to the natural carotenoid surrounding in the living cell and offer the opportunity to ascertain the effect of different factors e.g. pH, ion content etc. Because of that, development of novel methods for characterization of carotenoids in aqueous phase could lead to better understanding of processes in living cells and their functions.

This work presents the electrochemical oxidation of the naturally occurring pigments β-carotene and astaxanthin on a paraffin impregnated graphite electrode (PIGE) using square-wave voltammetry (SWV) in 0.1 M $HClO_4$ aqueous electrolyte. Voltammetry of microparticles (VIM) was used in a wide range of potential scan rates as this method allows determination of electroactive compounds in crystalline state. The results revealed that the oxidation of both compounds is a chemically controlled irreversible process. Oxidation peak for β-carotene was obtained at E = 0.853±0.033 V (Figure 1) and for astaxanthin at E = 1.111±0.029 V (Figure 2). It should be noted that responses for β-carotene were obtained in a mixture of β-carotene and sepiolite, electroinactive phyllosilicate clay, in ratio 1:1.

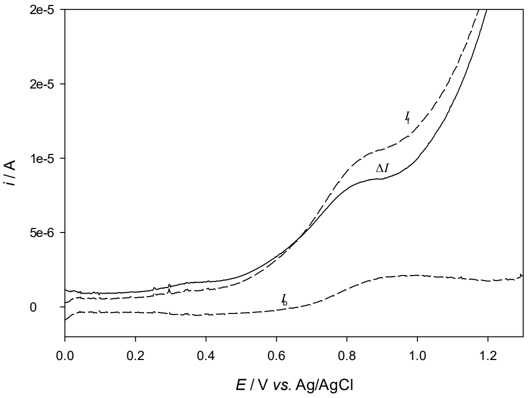

Figure 1: Square-wave voltammetry of β-carotene:sepiolite (1:1) microparticles immobilized on PIGE. Experimental conditions: E_{sw} = 50 mV, ΔE = 2 mV, f = 25 s^{-1}.

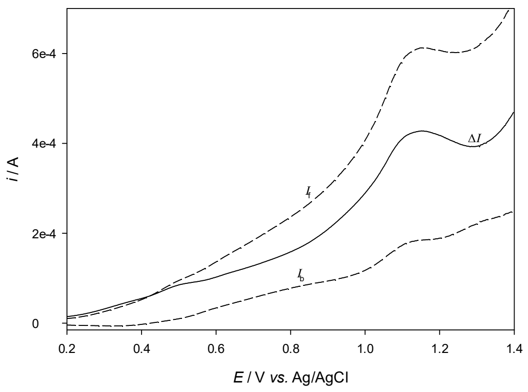

Figure 2: Square-wave voltammetry of astaxanthin microparticles immobilized on PIGE. Experimental conditions: E_{sw} = 50 mV, ΔE = 2 mV, f = 100 s^{-1}.

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Determination of inorganic arsenic species in food *by in situ* irridium trapping ETAAS method

Određivanje anorganskih specija arsena u hrani metodom ETAAS uz *in situ* iridijevu stupicu

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Information on the chemical form in which arsenic is present in food is of great importance in the assessment of food safety. Toxicity is generally associated with the inorganic forms of arsenic: arsenite (As^{3+}) and arsenate (As^{5+}) which may be present in food in a proportion from 1 % to 3 % of the total arsenic content. Of particular interest are arsenic species in rice and rice-based products due to high concentration inorganic arsenic the potential exposure of specific population [1]. The analytical methodology for the quantification of arsenic species is generally based on the combined systems of high performance liquid chromatography (HPLC) with atomic fluorescence spectrometry (AFS) or inductively coupled plasma mass spectrometry (ICP-MS) [2,3]. The analytical approach and the method selection are primarily determined by available technology, the composition of the matrix and the moieties of arsenic present in the sample.

In this work the hydride generation ETAAS with *in situ* trapping on an iridium-coated graphite tube was used for inorganic species analysis in variety of food. Sample preparation was denaturation and solubilization of the protein matrix in concentrated hydrochloric acid which allowed release of all arsenic species into solution and the subsequent extraction of the inorganic arsenic present in the acidic media using chloroform.

The method is robust and applicable for various food samples with the inorganic arsenic amount of 0.01 mg kg^{-1} to 7.5 mg kg^{-1}. We measured the concentration range of inorganic arsenic in different categories of food: rice and rice products (0.060 - 0.196) mg kg^{-1}; cereal based foods for infants and young children containing rice (0.017 - 0.119) mg kg^{-1}; sea fish (sardines, tuna and mackerel) (0.010 - 0.070) mg kg^{-1}; grains (0.010 - 0.016) mg kg^{-1} and fresh vegetables (0.010 - 0.013) mg kg^{-1}. The accuracy and precision of the method was evaluated by using different certified reference materials: NIST 1568 b Rice Flour (R = 93 %), BCR 191 Brown bread (R = 97 %), ERM CE278k Mussel tissue (R = 114 %) and IAEA 359 Cabbage (R = 92 %).

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Chemometric classification of smokeless gunpowders using FT-IR reflection spectroscopy

Kemometrička klasifikacija bezdimnih baruta pomoću FT-IR refleksijske spektroskopije

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Smokeless gunpowder is a mixture of chemical compounds used as a propellant in ammunition or in explosive devices. The main component in the gunpowder is nitrocellulose. In addition to this, some smokeless gunpowders may also contain nitroglycerin and nitroguanidine [1]. The chemical analysis of smokeless gunpowder is usually performed by finding the concentration of some of the previously mentioned components and more often by finding the content of stabilizers and plasticizers which are used in the manufacturing process (such as diphenylamine, dinitrotoluene, dibutyl phthalate) [2-4].

It has been proven that infrared spectroscopy could be successfully applied for detection of the previously mentioned components of the gunpowders as well as for differentiation of the gunpowders according to their chemical composition and origin [2]. In this work, using infrared reflection spectroscopy, we analyzed 103 samples of smokeless gunpowders produced by 6 different manufacturers from 5 different countries with majority of the samples being from former Yugoslavia. In addition to this, it is important to state that our samples correspond to 11 different calibers of ammunition.

As previously stated the aim of this study was to try analyze these gunpowder samples using chemometric processing of the data. For this purpose principal component analysis (PCA) and self-organizing maps (SOM) were used. Using both of these data analysis techniques and our expertise in the field of infrared spectroscopy we were able to find that the chemical composition of both major and minor constituents has considerable influence on the grouping of the samples on PCA plots and SOMs. With further analysis of both (1) infrared spectra as well as (2) the results obtained using PCA and SOM we were able to distinguish considerable difference in the quality of the gunpowders produced by different manufacturers.

Having in mind the results obtained here we were capable to predict the composition. It is also interesting to note, that in some cases it was possible to determine the caliber of the ammunition, since it is known that for different purposes the composition of the gunpowders varies and also the particles are shaped in a different manner [1]. The results obtained in this work show that infrared spectroscopy coupled with chemometric methods (such as PCA and SOM) are considered as promising tools for forensic examination of smokeless gunpowders.

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Aggregation-induced emission (AIE) of self-assembled benzimidazole based acrylonitrile dye

Emisija izazvana agregacijom (EIA) akrilonitrilnog bojila temeljenog na benzimidazolu

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Aggregation of organic fluorophores is mostly investigated as an undesirable side effect in many biological or chemical applications due to fluorescence quenching. However, development of novel organic luminophores with aggregation induced emission (AIE) changed the aspect of aggregation phenomena. AIE was introduced as an analytical tool in wide range of application, such as bioimaging, optoelectronics and chemosensors [1]. Reversible and multicolour pH sensing AIEgen molecules are very rare [2]. The intramolecular charge transfer (ICT) compounds, such as styryl cyanine dye **BIA** (Figure 1), are strong candidates for the design and development of AIEgen sensors due to their pronounced capacity for self-assembly and the pH sensitivity of planar benzimidazole moiety. Herein we report novel molecular system relying on the pH induced aggregation–deaggregation mechanism based on 2-benzimidazolyl substituted acrylonitrile dye (**BIA**). The effects of pH on AIE and other photophysical properties of **BIA** in dissolved, aggregated and solid states are examined. **BIA** forms three prototropic species (tri-state system) that emit in the red, green and blue (RGB) spectral regions (Figure 1). The neutral form is capable of self-assembly in an aqueous environment exhibiting stable red-orange aggregation-induced emission (AIE) at 600 nm in the physiologically relevant pH range. The aggregation and emission are pH switchable and fully-reversible.

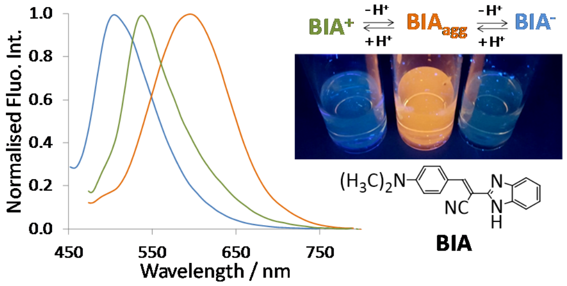

Figure 1: Normalised emission spectra and photographs taken under UV illumination of prototropic species **BIA**$_{agg}$, **BIA**$^{+}$ and **BIA**$^{-}$ in aqueous solutions.

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Semiquinone radicals as a base for novel organic (semi)conductors: how π-stacking determines magnetism and electrical conductivity

Semikinonski radikali kao temelj za nove organske (polu)vodiče: utjecaj π-interakcijâ na magnetska svojstva i električnu vodljivost

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Semiquinones are a class of stable organic radicals with a great potential for design of novel organic electronics and multifunctional materials. Since the radicals are planar, they typically form π-stacks, which stabilise crystal packing and determine magnetic and electrical properties of the crystals. Stronger π interactions thus imply stronger exchange interactions and lower energy barrier for electron transfer. Two types of stacks π-have been described: 1) Peierls-distorted with alternating short (< 3.1 Å) and long (> 3.35 Å) [1] interplanar distances (i.e. comprising dimers of radicals with paired spins), which are diamagnetic and isolators and 2) stacks of equidistant radicals which are 1D antiferromagnetic and semiconductors [2].

Despite its importance, π-stacking of planar organic radicals has been little studied from the fundamental point of view. Here we present a detailed study of different factors which influence (semi)conductivity of semiquinone systems in the solid state: 1) type of stack (Peierls-distorted or equidistant), 2) induction effect of electron-withdrawing substituents, 3) interplanar distance and 4) orientation of the stacked rings. As suitable systems we chose series of salts of three semiquinones (5,6-dichloro-2,3-dicyanosemiquinone [3], tetrachloro- and tetrabromosemiquinone [1]) with planar organic cations derived from *N*-methylpyridinium [2].

Since only antiferromagnetic compounds with equidistant radicals are good semiconductors, we focused our attention to this type of stacks. Electronegativity (i.e. electron-withdrawing) of the substituents plays a double role: *i*) it stabilises the radical by enhancing delocalisation of π electrons and *ii*) lowers the energy of the HOMO orbital, thus increasing band gap related to electronic transport. Therefore, the most stable radicals (5,6-dichloro-2,3-dicyanosemiquinone, DDQ [3]) are the least conductive, while less stable ones (tetrabromosemiquinone) are the best conductors. This effect is far more pronounced than increasing of the band gap by increasing interplanar separation, while orientation of the rings in the stacks apparently does not influence electrical conductivity.

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Supramolecular potential of halogen interactions in metal-organic systems of Co^{II} and Ni^{II} pentane-2,4-dionato complexes

Supramolekulski potencijal halogenskih interakcija u metalo-organskim sustavima kompleksa Co^{II} i Ni^{II} s pentan-2,4-dionom

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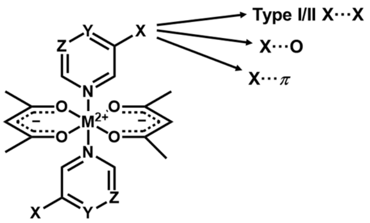
In recent years the crystal engineering potential of halogen bonds was recognized and extensive research is being carried out to maximally utilize those interactions in engineering organic and metal-organic systems. It was even shown that in some cases it is possible to predict the halogen patterns according to electrostatic potential values calculated for each potential donor and acceptor [1]. Halogen atoms can also form other, weaker supramolecular interactions such as halogen···π and C–H···halogen interactions. Although their usual role in the crystal packing is only secondary, it was shown that they can become main structure directing interactions in systems lacking strong hydrogen and halogen bonding capability [2].

We have recently reported our findings of type-I halogen···halogen and halogen···π interactions present in a series of six isostructural pentan-2,4-dionato Co(II) and Ni(II) complexes with chloro-, bromo- and iodopyrazine. It was found that halogen···π interactions play a secondary role in the packing while type-I interactions arise as the result of the packing itself [3]. In order to assess possible steric effects as well as to determine the impact of electron withdrawing power of endocyclic nitrogen atoms on the overall halogen bond pattern formation, here we opted to examine a series of halopyrimidine derivates.

To this aim we have prepared Co(II) and Ni(II) pentane-2,4-ditionato complexes with iodopyridine and bromopyrimidine. The crystal packing of iodopyridine derivates is directed by I···O halogen bonds, while in the crystal structure of bromopyrimidine derivatives halogen···π interactions were observed.



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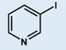
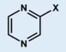
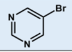
	I···O
 X=Cl, Br, I	X···π & Type I
	X···π

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Acknowledgments

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Fluorophore one-atom-controlled recognition of DNA/RNA secondary structures

Razlikovanje sekundarnih struktura DNA/RNA temeljeno na razlici u jednom atomu fluorofora

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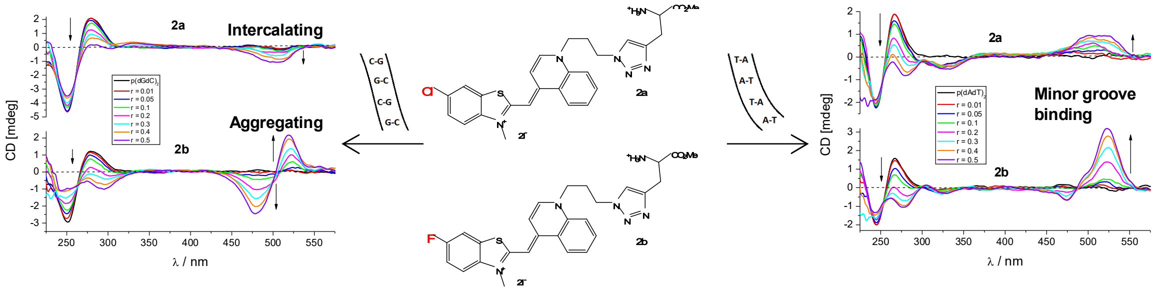
Monomethine cyanine dyes are well known molecular probes with a great increase in fluorescence efficiency upon binding to nucleic acid while nonfluorescent in the free form [1]. Here are presented two cyanine-amino acid conjugates, synthesized by a Copper-catalysed azide-alkyne cycloaddition (CuAAC) method with copper wire as a catalyst source [2]. Novel compounds differ in only one substituent on cyanine part (chlorine and fluorine substituent) and are suitable for peptide incorporation on both C- and N-end.



Scheme 1: Interactions of the cyanine-amino acid conjugates with alternating GC and AT base pairs.

Circular dichroism (CD) titrations revealed that both compounds cause strong distortion of DNA backbone (decrease of the band between 240-290 nm) combined with pronounced induced CD (ICD) band in the range where only cyanine dye absorbs (420–550 nm). While dye with chlorine atom, **2a,** intercalates (negative ICD signal) between alternating GC-DNA base pairs, fluorine analogue **2b** aggregates along GC-DNA backbone (bisignate ICD bands) in *P*-configured helicity [3]. Both dyes bind into the minor groove of the alternating AT-DNA sequence.

Recognition of AU-RNA sequence based on one-atom-difference of dyes is observed with fluorimetric titration and thermal experiments. **2b** shows doubly enhanced fluorescence emission with pApU and moderate thermal stabilization, at variance to **2a**, which does not show any stabilization of the same polynucleotide.

Presented fluorescent amino acids show recognition of secondary structure of DNA and RNA based on one-atom-difference and in future prospects should be easily incorporated into DNA/RNA targeting peptides.

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Modelling ion dynamics in ionic liquids and ionogels

Modeliranje ionske dinamike ionskih tekućina i ionogelova

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Room temperature ionic liquids (RTILs) are salts which are liquids at room temperatures. These salts, usually composed of a bulky organic cation such as 1-butyl-3-methylimidazolium and anions such as tetrafluoroborate (BMIm-BF_4) or bis(trifluoromethylsulfonyl)imide (BMIm-TFSI), are superior electrolyte materials. They are non-hazardous substances (green solvents) with good chemical and thermal stability, low vapour pressures and non-flammable nature. Hence they have wide applications in a variety of electrochemical devices and batteries. Since the last decade efforts are underway to confine these liquids in polymers or supramolecular gelators without losing the advantages of the properties of the pure RTILs so as to prevent leaks in device applications and robust for use in technology.

Recently, it was shown that the confinement of an ionic liquid (IL) BMIm-BF_4 in bis(leucinol)oxalamide matrix led to formation of stable gels over a wide range of gelator concentrations with a minimum gelator concentration (MGC) as low as about 0.7 wt%. An encouraging effect was the marginal enhancement observed in the DC conductivity at about 0.8 wt% gelator concentration of the ionogel at room temperature compared to that of the pure BMIm-BF_4 [1]. This enhancement becomes more pronounced and shifts to higher gelator concentrations with decreasing temperature.

In this contribution, we consider DC conductivity of the above and two other ionogels: BMIm-BF_4 in bis(valinol)oxalamide (MGC: 1.7 wt%) and BMIm-TFSI in bis(phenylalaninol)oxalamide (MGC: 0.4 wt%), where similar behaviour and trends are observed. For each of these three systems, frequency-dependent conductivity spectra (measured over 10^{-2} Hz to a few MHz, and a wide range of temperatures) of the pure RTIL as also of the ionogels of varying gelator concentrations were studied. We find that the conductivity isotherms for each system and composition can be collapsed to construct a master plot, which indicates that there is no change in the mechanism of conductivity or in the number density of charge carriers, but only that the mobility of ions get faster as temperature is increased [2] or vice versa. We model the shape of the spectra using the MIGRATION concept, and also the non-Arrhenius temperature dependence of the DC conductivities of each of these systems [3]. We extract information on activation energies of elementary displacements, and the length scale which marks the onset of diffusion. These results are presented and the implications for ion dynamics are discussed.

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Computational insight into the cyclotrimerization of isocyanates using bicyclic guanidine catalyst

Računalni uvid u reakciju ciklotrimerizacije izocijanata korištenjem bicikličkog gvanidinskog katalizatora

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Polyurethane foams are widely used polymers composed of organic units joined by carbamate (urethane) linkers [1]. Management of their physical properties poses significant challenge in the creation of new materials with desired properties. Since the cyclotrimerisation of organic isocyanates is one of the most sensitive steps in the whole process, identifying efficient catalysts for this chemical transformation represents an important and needed research goal.

In this work we considered triazabicyclodecene (**TBD**) as a potential catalyst for the cyclotrimerization of isocyanates. We have investigated the reaction pathway involving a sequential addition of metyl-isocyanates (**MIC**) using well established quantum chemistry methods at the MP2/6–311++G(2df,2pd)//M062X/6–31+G(d) level [2]. Our results show that the first **MIC** molecule is activated by the **TBD** catalyst through the nucleophilic attack of its imino nitrogen atom to strongly electrophilic carbon on **MIC** followed by the intramolecular **MIC**–**TBD** proton transfer, thus opening the possibility for the activation of another **MIC** molecule on the second nitrogen atom on **TBD**. After that, the two **MIC** systems combine to give a dimer, to be followed by the analogous formation of an open-chain trimer chemically bonded to **TBD**. The last step involves the cyclization of the trimer and the liberation of the final hexacyclic product concomitant with the regeneration of the **TBD** catalyst. The overall reaction pathway reveals that the investigated trimerization is thermodinamically a very favorable process ($\Delta_r G$ = –34.3 kcal mol^{-1}) with reasonable reaction barrier ($\Delta G^{\ddagger}$ = 27.7 kcal mol^{-1}) in the THF solution. In addition, it provides a convincing insight to why dimerization is not favorable from both thermodynamic and kinetic points of view, being strongly in line with experimental observations. Compared to the uncatalyzed reaction, **TBD** lowers the activation barrier by 8.4 kcal mol^{-1}, thus increasing the reaction rate by the factor of 10^6. These significant results suggest **TBD** as a much efficient catalyst than some other systems proposed in the literature based on proazaphosphatranes [3].

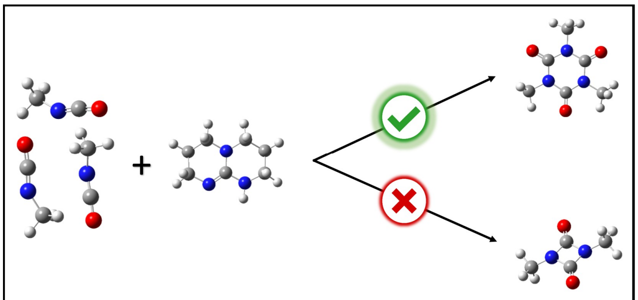

Figure 1: Schematic representation of a reaction involving three methyl-isocyanates (**MIC**) with the **TBD**

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Kinetics of chemical reactions in the solid-state: a versatile model based on dynamic cooperativity

Kinetike kemijskih reakcija u čvrstom stanju: prilagodljiv model baziran na dinamičnoj kooperativnosti

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Solid-state transformations can be described using either bulk-based or reaction-order based models [1]. Bulk-based models, such as the Avrami-Erofeyev, are particularly suitable for the analysis of phase change, as they depict the propagation of the new phase (either by nucleation, geometrical contraction or diffusion). On the other hand, reaction-order based models, such as Finke's two- and four-parameter models attempt to provide some mechanistic insight at the molecular level [2].

Since the reactants and the products typically form different phases, most chemical reactions which occur in the solid state are coupled with phase transitions. The models mentioned above might be able to fit the experimental kinetic curves (on account of having enough parameters and flexibility), but the data gained from such fits does not always have a clear physical interpretation. Specifically – does the obtained rate constant and activation energy describe the chemical or the phase transformation? Mnyukh suggests that there are at least two activation energies, one describing the nuclei, and other the interface formation and growth [3].

In order to solve this problem, we propose a new model based on the formation of the **activated reactant**, and on **dynamic cooperativity**. The model can be described with the following equations and parameters:

$$\mathrm{A} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{A}^*$$

$$\mathrm{A}^* + \kappa\,\mathrm{A} \xrightarrow{k_2} \mathrm{B} + \kappa\,\mathrm{A}^*$$

$$\mathrm{A} \xrightarrow{k_3} \mathrm{B}$$

where A is the reactant, A* the activated reactant, B the product, and κ the cooperativity function, which depends on the extent of the reaction. As a training set for the model we use the dimerization of aromatic (di)nitroso compounds, which afford a variety of kinetic curves, ranging from sigmoidal to exponential. We show that our new model affords better fits than previously used ones. Also, the obtained rate constants show that the reaction rate is dependent on the preparation method used (sublimation or photolysis), which suggests that the chemical and the phase transformations can somewhat be decoupled [4].

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Acknowledgments

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Carbon dots: Fundamentals and applications

Ugljikove točke: osnove i primjena

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Carbon dots [1-3] have attracted so much recent attention that the research and development of carbon dots have emerged to become a rapidly advancing and expanding technical field [4,5]. Carbon dots are generally defined as small carbon nanoparticles with various surface passivation schemes. A wide variety of potential technological applications of carbon dots have been pursued, including those in our laboratory for fluorescence bioimaging and sensing [6,7], bactericidal functions [8], and photocatalytic energy conversion [9,10], and others. Most of these targeted applications mimic, compete, and/or go beyond those already derived from conventional semiconductor quantum dots (QDs). In fact, carbon dots now represent a new class of QDs-like nanomaterials with properties and performance competitive or superior to those of semiconductor QDs yet benign and nontoxic, among other advantages. In this presentation, the basic concepts of carbon dots will be introduced, our recent progress in the development of carbon dots and related technologies highlighted, and their various applications discussed.

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Required physical properties of materials for crystalline coatings

Potrebna fizikalna svojstva materijala za kristalne premaze

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The process of crystallization can be used for coatings in the fields of pharmaceutical and food industries. Hartwig et al. [1] presented in their work a technique to encapsulate small amounts of liquids in the form of pastilles by means of crystallization.

In previous studies [2] it could be shown that encapsulation of bigger amounts of liquids is also feasible by crystallizing certain substances out of supersaturated solutions under defined conditions. Encapsulation of milk and condensed milk with sucrose and erythritol was exemplified – dissolvable milk containers for convenient handling were developed. In the current study fundamental requirements are determined that are essential to enable the generation of hard layers inclosing liquids. The influence of physical properties of certain solutions on the encapsulation behavior is investigated and general conclusions can be derived. Therefore a special focus is placed on following determinants:

- particular crystal morphology
- crystal growth rate
- absolute solubility
- slope of saturation curve
- viscosity
- interfacial tension

The results will be presented and discussed in detail at HSKIKI25.

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Mathematical modelling of lactol synthesis catalyzed by 2-deoxyribose-5-phosphate aldolase

Matematičko modeliranje sinteze laktola katalizirane enzimom 2-deoksiriboza-5-fosfat aldolazom

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The kinetics of enantioselective production of a valuable chiral synthon for the common statin-type side chain of a cholesterol-lowering drug was studied. The examined process is a two-step aldol reaction catalyzed by the enzyme 2-deoxyribose-5-phosphate aldolase (DERA, E.C. 4.1.2.4) in which the acceptor substrate chloroacetaldehyde reacts with the donor substrate acetaldehyde and gives an intermediate aldehyde, which subsequently reacts with a second donor acetaldehyde molecule and results with the key product lactol (Figure 1). A side reaction of the sequential two-step acetaldehyde self-addition also occurs (Figure 2).

In order to find the optimal DERA concentration for obtaining the highest selectivity, several reactions were performed in a batch reactor with same initial substrate concentrations and different initial DERA concentrations.

The kinetics of all reactions were determined using the method of initial rates and were described by Michaelis-Menten kinetic models. The kinetic parameters of the proposed models were estimated by nonlinear regression analysis using simplex or least squares method.

Based on the kinetic results, mathematical models were developed for the lactol synthesis with selectivity-optimal DERA concentration and were validated in a batch reactor. The noted enzyme deactivation was described with second-order kinetics.

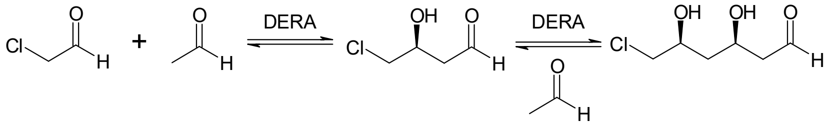

Figure 1 Aldol reaction of chloroacetaldehyde with acetaldehyde catalyzed by DERA

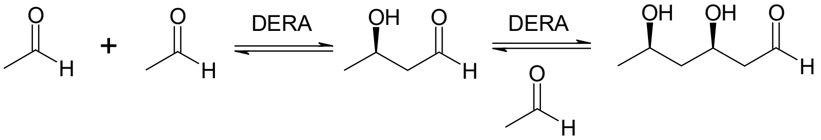

Figure 2 Self-aldol reaction of acetaldehyde catalyzed by DERA

Acknowledgments

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Investigation of mumps and measles virus proteome and lipidome

Istraživanje proteoma i lipidoma virusa zaušnjaka i ospica

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Measles (MEV) and mumps (MUV) virus are enveloped, nonsegmented, negative single stranded RNA viruses of the family *Paramyxoviridae* [1]. They are the cause of mumps and measles, respectively, both of which can be prevented by vaccination. Lipid bilayer of enveloped viruses is not directly encoded by the virus but acquired from the host cell membranes. Lipid composition of some viruses was found to resemble that of host cell plasma membrane, but in other cases significant differences were noticed [2,3]. Apart from virus-coded proteins, it has been established that various enveloped viruses incorporate also host cell proteins (HCPs) both inside the viral particle and in the lipid bilayer. Indications exist that some HCPs are specifically taken up by the viral particles by direct interactions with viral proteins, but HCPs might also be included by non-specific interactions, or as contamination arising from the presence of exosomes in virus preparations [4-6].

The aim of our research was investigation of MEV and MUV lipidome and proteome, consisting of 8 and 9 virus-coded proteins, respectively, and detection of HCPs potentially present in virus preparations. Viruses were grown in Vero cells, microfiltrated, purified by hydrophobic interaction chromatography (HIC) and eluates concentrated by ultracentrifugation. Alternatively, viruses were purified only by ultracentrifugation. Also, supernatants from non-infected Vero cells were purified and analyzed as described for virus samples. Obtained samples were resolved by SDS-PAGE, protein bands excised and *in-gel* digestion by trypsin was performed. Lipids were extracted from samples by Bligh-Dyer method and separated using 2D-HPTLC. Lipids and proteins were identified by MALDI-TOF/TOF-MS. Results implicate that there are no considerable differences between lipid composition of viral particles and Vero cells. All viral structural proteins were detected in viral samples, including fusion protein both for MUV and MEV which was not previously found. Also, various HCPs previously reported in other purified virus preparations such as actin, cyclophilin A, and annexin A2 were detected.

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Stabilization of low affinity protein-protein interactions by site-specific incorporation of unnatural amino acids

Stabilizacija proteinskih interakcija niskog afiniteta pomoću mjesno-specifične ugradnje neprirodnih aminokiselina

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The introduction of new chemical functionalities into proteins represents a promising approach for investigating and manipulating diverse biological processes. Among a number of different approaches, the expansion of the genetic code has emerged as an eminent tool for *in vivo* site-specific incorporation of unnatural amino acids (UAAs) into proteins [1]. The requirements for genetic code expansion include an orthogonal aminoacyl-tRNA synthetase (aaRS), engineered to specifically transfer the UAA, but no natural amino acids, onto its orthogonal tRNA. Being a specific substrate only to the orthogonal aaRS, an orthogonal tRNA is able to direct the incorporation of the UAA during translation in response to a unique codon, most commonly the amber stop codon, in the gene of interest.

Over the past decade, a plethora of UAAs bearing different functional groups have successfully been incorporated into proteins, both in bacteria as well as in eukaryotic cells, giving new insights into their structures and functions. The development of fast, chemoselective and high-yielding bioorthogonal reactions between UAAs and externally added chemical probes, for example, offers a unique opportunity for imaging individual proteins and labeling proteomes [1c, 2]. Their high reactivity, however, makes them unfit for investigating protein-protein interactions in their native conformations.

For this purpose, we are exploring bioreactive bromoalkyl-bearing UAAs that are inert under physiological conditions but react with nucleophilic natural amino acids such as cysteines in a proximity enhanced manner [3]. By synthesizing and incorporating the electrophilic UAAs site-specifically into proteins of interest, we were able to use these reactions *in vivo* to covalently link positions that are brought into close proximity by the formation of the protein complex. We applied this method for chemical stabilization and crystallization of low affinity protein complexes in their native conformations which has, until now, been very challenging.

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Spectroscopy of novel dicationic cyanine dyes as potential markers for mitochondrial DNA

Spektroskopija novih dikationskih cijaninskih boja kao potencijalnih markera za mitohondrijsku DNA

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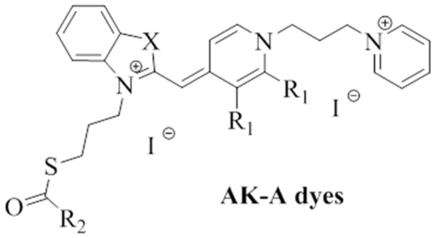
Cyanine analogues are small molecules attractive for their use as fluorescent probes. They are characterized by a dramatic increase in fluorescence emission intensity upon association with biomacromolecules. The interest in synthesis and various applications of cyanine dyes is very big due to their sensitivity, low toxicity, remarkable fluorescence enhancement upon DNA/RNA binding and specific or selective affinity to certain base pair sequences. Therefore, cyanine dyes have a widespread use in molecular biology and medicine as spectrophotometric markers in fluorescence-based techniques.

Inspired by previous results on mitochondria specific dyes [1,2], in this work are presented spectroscopy methods we have used for studying interactions of five novel benzoxazolium and benzothiazolium asymmetric dicationic monomethine cyanine dyes with DNA/RNA, in order to elucidate the mode of binding and the specific affinity for different polynucleotides. Apart from the fluorescence spectroscopy, the study includes UV/Vis spectrophotometry and circular dichroism spectroscopy, as well as the thermal melting experiments. Combined studies revealed that AK-A dyes bind with micromolar affinity to all ds-DNA/RNA. While AK-A dyes intercalate into ds-DNAs, they switch binding mode for ds-RNA, forming aggregates within ds-RNA major groove. Also, fluorimetric response of dyes is strongly dependent on a dye structure and some dyes show fluorimetric selectivity between various ds-DNA and ds-RNA, dependent on a type of polynucleotide secondary structure. AK-A dyes specifically accumulate in mitochondria with negligible antiproliferation activity on human carcinogenic lung (H460) and breast cancer (MCF-7) cells. Obtained results reveal great potential of novel dyes as imaging agents in cell biology.



$X = O, S$
$R_1 = H, \text{-CH=CH-CH=CH-}$
$R_2 = CH_3, C_2H_5, (CH_3)_2CH, C_5H_{11}$

Figure 1: Studied compounds AK-A.

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Influence of deposition conditions on properties of ZnO films for photocatalytic application

Ispitivanje uvjeta nanošenja na svojstva ZnO slojeva za fotokatalitičku namjenu

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ZnO is a semiconducting material with energy gap of 3.2 eV, capable of absorbing UV light. Due to easy and inexpensive synthesis and low environmental impact, ZnO is attractive for use in photovoltaic cells and as a photocatalyst for degradation of organic pollutants [1]. We have prepared ZnO films on a glass substrate from a solution of zinc acetate in methanol, using dip-coating and chemical bath deposition methods. Influence of calcination on transformation of initial acetates to ZnO was studied by combined differential scanning calorimetry and thermogravimetric analysis, infrared spectroscopy (FTIR) and X-ray diffraction (XRD), while the morphology was investigated by scanning electron microscopy. Photocatalytic activity of selected films was investigated by following the decomposition of 2,5-dihydroxybenzoic acid exposed to UV-A light in a laminar-flow reactor. Concentration of the acid was determined using a UV-Vis spectrophotometer.

Dip-coating results in a crystalline zinc acetate film on the glass substrate, which is converted into pure crystalline ZnO upon calcining at temperatures above 300 °C. Chemical bath deposition results in mostly amorphous structure with pronounced layered regularity, as evidenced by XRD, and FTIR spectra indicate that it is probably a mixed zinc acetate hydroxide [2]. This compound also transforms into pure ZnO above 300 °C. Two methods give films of very different morphology. Films prepared by dip-coating are smooth and consist of fine ZnO grains, while those prepared by chemical bath deposition consist of leafy layers of ZnO grains. This morphology is formed during deposition and conserved during calcining. Expectations that leafy morphology is more suited for photocatalytic applications [3] was confirmed by photocatalytic investigations, which have shown that the film prepared by chemical bath deposition degrades 2,5-dihydroxybenzoic acid more quickly than those prepared by dip-coating. Further research is needed to optimize the deposition conditions.

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Investigation of mixed glass former effect and thermally induced crystallization in Li_2O-P_2O_5-GeO_2 glasses

Istraživanje efekta miješanih staklotvoraca i termički potaknute kristalizacije Li_2O-P_2O_5-GeO_2 stakala

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In order to improve the stability, safety and required performance of lithium-ion batteries many novel glass and glass-ceramic materials are being investigated for their potential use as a solid electrolytes [1,2].

Ternary ion conducting $40Li_2O–(60-x)P_2O_5–xGeO_2$, x=0–25 mol%, glasses have been chosen as a model glass system for the mixed glass former effect and crystallization investigations. Electrical properties of these glasses were studied by impedance spectroscopy (IS) to determine the influence of the structural changes induced by gradual substitution of one glass network former, P_2O_5, by other network former, GeO_2, keeping Li^+ ion content constant. Glass-ceramics have been prepared by controlled crystallization of these glasses at different temperatures selected according to the DTA curves. Changes that occurred in structure and electrical properties of glass-ceramics were analysed.

In glasses, the dc conductivity increases for the three orders of magnitude with increasing germanium content. This conductivity enhancement was attributed to the facilitated mobility of Li^+ ions due to the depolymerisation of phosphate chains and incorporation of germanium atoms into network, confirmed by Raman and MAS NMR. Heat-treated glasses have been characterized using XRD and MAS NMR. Microstructure study showed crystalline grains embedded into glass matrix. Grain size and degree of crystallinity varies with germanium content and crystallization temperatures. Heat-treated GeO_2-free samples showed slightly higher dc conductivity values than the non-treated glasses. On the other hand, when germanium oxide was added into the system, the dc conductivities of heat-treated samples showed lower values if compared with values obtained for glasses. Decrease in dc conductivity is more pronounced for samples with high germanium content and higher degree of crystallinity. Correlated behaviour between conductivity and changes in microstructure indicates that in the heat-treated glasses a part of the Li^+ ions enters randomly distributed crystalline grains, which are not enough connected to form easy conducting pathways.

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Interactions of tripeptide derivatives of salicylic acid with calcite surfaces

Interakcije tripeptidnih derivata salicilne kiseline s površinom kalcita

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One of the focuses in the field of materials chemistry is to design the systems that could be used for the controlled introduction and release of active pharmaceutical compounds in the living organisms and tissues. At that, a promising systems for controlled drug delivery is calcite, most stable polymorph of calcium carbonate, functionalized by small, biologically active molecules, like derivatives of salicylic acid (Sal). [1] During biomineralization, $CaCO_3$ precipitates as main inorganic component of invertebrate's hard tissues. [2] Such calcitic skeletal elements regularly contain small amounts of macromolecules. It has been shown previously that the isolated fragments of proteins extracted from mineralized tissue, which exert a significant influence on the morphology and crystal structure of $CaCO_3$, contain high acidic regions, comprising mostly aspartic acid.

In this respect, we decided to investigate the interactions of calcite functionalized with highly active biomolecules, in order to uncover the roles of their flexibility and chirality in potential composites suitable for drug delivery. Hence, we prepared salicylic acid-derived aspartic acid (Asp) tripeptides. In order to investigate influence of chirality on extent of organic/inorganic interaction different enantiomers of aspartic acid, N-Sal-linker-L-Asp-D-Asp-L-Asp (Sal-LDL) and N-Sal-linker-L-Asp-L-Asp-L-Asp (Sal-LLL), were employed in tripeptides. Salicylic acid was attached to tripeptides using linkers of various length. The interactions between synthesized molecules and the calcite surface was investigated using advanced simulation techniques and by crystal growth kinetic analyses.

The Langmuir adsorption constants are calculated from kinetic data and used as an indication of extent of organic/inorganic interaction. [3] Our results indicate that Sal-LDL adsorb better than Sal-LLL on calcite surface. The highest adsorption constant was found with the longest linker of CH_2 group.

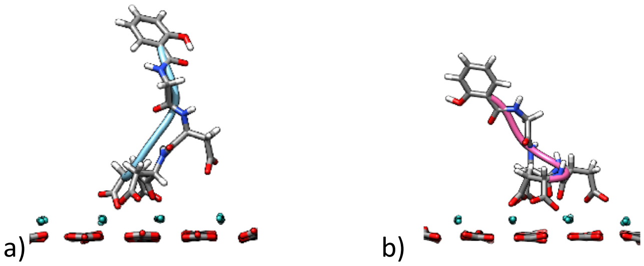

Figure 1: Structures representing the minima in the free energy surface of a) Sal-LLL and b) Sal-LDL, as found in the bulk region.

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Transformation of selected UV filters in chlorinated aqueous solutions

Transformacija odabranih UV filtera u kloriranim vodenim otopinama

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UV filters represent an important group of anthropogenic organic compounds appearing in swimming pool and marine bath waters due to human activity. Quite often they are treated as contaminants of emerging concern. Some of them may decompose when exposed to light by direct photolytic reactions or transform in the presence of chlorine and chlorinated medium (water pools, sea water). The formation of halogenated byproducts in chlorinated waters is inevitable, especially when UV filters possess phenolic and/or amino moieties.

In this work we present our research, focused on synthesis, characterization and toxicity of transformation and degradation products of selected UV-A filters (i.e. benzophenones, dibenzoylmethanes) formed under disinfection conditions in presence of chlorine. Main products which are formed include different mono- and di-chlorinated products. Their structures were confirmed by high-performance liquid chromatography-tandem mass spectrometry (HPLC–MS^2) with accurate mass measurements and by gas chromatography–mass spectrometry (GC/MS). Additionally, compounds have been characterized by independent synthesis and NMR analysis. Our results of toxicity assessment using different test organisms such as *Vibrio fischeri*, microalgae and daphnids have shown different sensitivity of testing organisms to the parent UV filters in comparison with chlorinated products as well as different toxicity for specific UV filter in comparison to the other UV filters groups.

Impact of ozone gradient on grapevine leaves

Utjecaj gradijenta ozona na listove vinove loze

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Due to complex orography and air mass circulation, the Rijeka Bay area is characterized by O_3 gradient, with concentrations raised with the altitude [1]. Therefore AOT_{40} values were often exceeded and should result in harmful effects on vegetation. Based on previous controlled experiments [2], we examined the possible effect of atmospheric ozone on grape leaves under natural O_3 gradient. Grapevine leaves (2-5) were collected from May to September 2016 at two sampling points in the proximity of two AQM stations: Site 1 in the city centre (20m asl) and Site 2 (186m asl) in the suburban settlement. Subsequent to weighing and determination of surface area, the leaves (0,5 g) were extracted in 95% ethanol and analysed on chlorophyll a (Chla), chlorophyll b (Chlb) and carotene (Car) content by UV-VIS spectrometry on 3 wavelengths (664, 649, 470 nm) [3]. In summer 2016 O_3 gradient was not that pronounced as usual [1], but stil the concentrations differed by approx. 20%, exceeding national AOT_{40} value atboth sites (22.360 and 28.061 μg m^{-3} h, respectively, at Sites 1 and 2). The concentrations of other pollutants were bellow LV. The Cha and Chb in a sample leaves collected at the end of May at Site 2 are equal to that with filtered O_3 in control experiment [2], i.e. without damage caused by ozone, while the Car content is lower approx. 50% and is kept at the same level. The concentrations of pigments obtained in July prooved the possible damage by O_3, while in subsequent months could speed up natural ageing. This is the first evidence of O_3 damage on plants in the Rijeka Bay area, in spite of weaker O_3 gradient and lacking visible signs of damage. Preliminary results indicate the need for more frequent sampling, particularly in the period included in AOT_{40} (May-July).

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Photooxidative degradation of pesticides in water: Mechanistic modelling approach

Fotooksidativna razgradnja pesticida u vodi: mehanističko modeliranje

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A worldwide concern for development of alternative water-reuse technologies continuously increases, mainly focused on industry and agriculture. The conventional water treatment technologies, mostly relying on physical and biological processes seems to be inadequate for effective removal of priority substances such as pesticides. At the same time, advanced oxidation processes (AOP) showed to be very effective for the same purpose.

This study evaluates the applicability of photooxidative degradation of four pesticides from priority substances list within the EU Water Framework directive: namely alachlor, chlorphenvinfos, diuron, isoproturon. The aim of the work was development of a flexible mathematical/mechanistic model (MM) capable to describe UV-C/H_2O_2 process with further parameters:

- conversion and mineralization kinetics of parent pollutant,
- water quality during AOP treatment; defined by chemical (COD) and biochemical (BOD_5) oxygen demand,
- changes of pH-value during AOP treatment.

After model development, extensive statistical analysis was performed. The analysis revealed high correlation between predicted and empirical data.

The applied MM model proved to be easy interpretable, transparent, flexible and accurate at the same time. Accordingly, it can be used for prediction of degradation of pesticides with complex structures by applying UV-C photo-assisted AOPs with hydrogen peroxide as oxidant.

Enzymatic cascade reaction for the synthesis of an imino aldol adduct: oxido-reduction coupled with aldol addition

Enzimatska kaskadna reakcija sinteze imino aldolnog produkta: oksido-redukcija i aldolna adicija

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Aldol adducts containing amino groups are important building blocks of many naturally occurring molecules such as iminosugars [1]. In this work the oxidation of the amino alcohol catalyzed by alcohol dehydrogenase was coupled with aldol addition catalyzed by an aldolase, to synthesize an imino aldol adduct. The reaction scheme is presented in Figure 1. Similar reaction system was found to be effective in our previous work [2].

Several enzymes were tested as catalysts for oxidation of Cbz-*N*-3-amino-1,2-propanediol to Cbz-*N*-3-amino-2-hydroxypropanal and it is confirmed that alcohol dehydrogenase from horse liver is the most efficient catalyst for this reaction step. Aldol addition is catalyzed by D-fructose 6-phosphate aldolase as the most appropriate catalysts for this reaction, according to the literature [3]. Since alcohol dehydrogenase requires a coenzyme for its activity, the regeneration was done by using NADH oxidase. Coenzyme regeneration has to be fast and efficient to shift the equilibrium of oxidation towards aldehyde synthesis. Therefore, the influence of NADH oxidase and alcohol dehydrogenase activity ratio was tested on alcohol conversion in a cascade reaction. Also, the influence of coenzyme concentration and initial substrate (amino alcohol) concentration on the cascade reaction product yield was examined. The operational stability of all enzymes was determined by following their activity during the experiments.

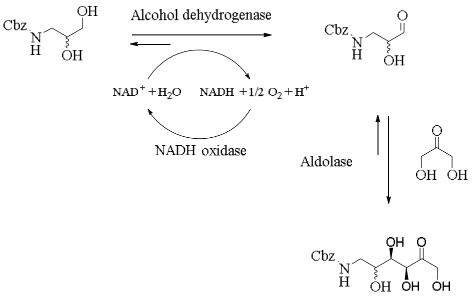

Figure 1: Cascade reaction scheme.

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Stereochemical aspects of cyclotriphosphazenes

Stereokemijski aspekti ciklotrifosfazena

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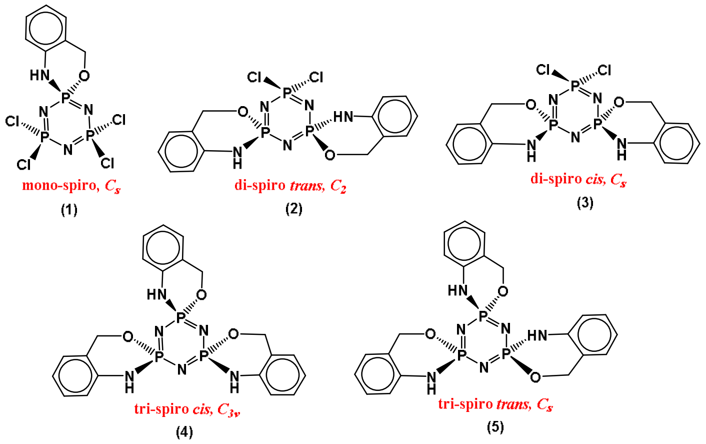
The stereogenicity of molecules is a fundamental issue in structural chemistry and has major implications in catalysis, biology and medicinal chemistry [1]. The tetra-coordinated, pentavalent phosphorus atoms in cyclophosphazene derivatives are potential stereocenters and their centers of chirality are analogous to those for tetrahedral carbon atoms [2]. Although stereogenic properties of chiral cyclophosphazenes have been extensively investigated during the last decade, some stereochemical terms such as prochirality, homo-, enantio- and diastereotopic atoms or groups and pseudo-asymmetric centers have not been fully recognized. In this study [3], a series of new cyclotriphosphazene derivatives were prepared in order to investigate systematically their stereochemical properties in terms of stereochemical principles. Furthermore, two different meso forms were obtained representing the first systematic examples of cyclotriphosphazenes including pseudo-asymmetric phosphorus centers. The specific synthetic details involve the reactions of, hexachlorocyclotriphosphazene with 2-aminobenzyl alcohol which provided the mono- (**2**), di- (**3**, **4**) and tri-spiro (**5**, **6**) derivatives (Figure 1). The new compounds were analyzed by standard spectroscopic techniques and X-ray crystallography. Their stereogenic properties were confirmed by ^{31}P NMR spectroscopy on addition of a chiral solvating agent. These results can be applied to not only phosphazene compounds but also other heterocyclic systems which contain pro and/or pseudo chiral atoms or groups.



mono-spiro, C_s
(1)

di-spiro *trans*, C_2
(2)

di-spiro *cis*, C_s
(3)

tri-spiro *cis*, C_{3v}
(4)

tri-spiro *trans*, C_s
(5)

Figure 1: 2-Aminobenzyl alcohol derivatives of cyclotriphosphazene (**1**-**5**).

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From discrete or polymeric heterometallic complexes to the mixed-metal oxides

Od diskretnih ili polimernih heterometalnih kompleksa do mješovitih metalnih oksida

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Mixed-metal oxides are an important class of advanced materials, due to their stability, low cost, low toxicity, useful photophysical properties and wide range of technological applications. They are mostly utilized as catalysts and structural ceramics, but recently, the use of mixed-metal oxides as sensors, actuators, and smart materials has also been explored. It is known that the effect of crystallinity, particle size, structure and morphology of these materials could highly affect their properties. These can be tuned in part by changing the synthesis methods.

The possibility of using coordination polymers through the thermal decomposition process as molecular precursors in the synthesis of nanomaterials with high surface and specific morphology has been considered only recently. This method of obtaining oxide materials, compared with conventional methods, has several advantages: (*i*) the obtained material is more homogeneous because the metals are mixed at the molecular level; (*ii*) the resulting materials have relatively high specific surface areas because the crystalline oxides are formed under significantly milder conditions than those in, for instance, solid-state reaction processes; (*iii*) the existence of bridging or chelating ligands in the precursors prevents metal separation during oxide formation; (*iv*) there is much greater control of the metal stoichiometry in the final oxide. The $C_2O_4^{2-}$ group easily decomposes to gaseous CO_2 and CO at low temperatures, and hence, the oxalate-based solids can serve as a convenient source of oxides [1].

Utilizing the preparation of the oxide materials *via* thermal decomposition, several oxalate-based compounds were tested as molecular precursors. Discrete heterotetranuclear oxo-bridged compound $[Cr_2(bpy)_4(\mu\text{-}O)_4Nb_2(C_2O_4)_4]\cdot 3H_2O$ (**1**; bpy = 2,2'-bipyridine) showed to be a good candidate for molecular precursor-to-material conversion, yielding the rutile-type $CrNbO_4$ oxide after heat treatment at 900°C. The thermal processing of heterodimetallic one-dimensional (1D) compound $\{[CaCr_2(bpy)_2(C_2O_4)_4]\cdot 0.83H_2O\}_n$ (**2**) proved to be a simple, one-step synthesis route for the preparation of the β-$CaCr_2O_4$ phase at 1100 °C in nitrogen flow. The r.t. structure of β-$CaCr_2O_4$ is isomorphic with calcium ferrite, unlike most chromate structures, which usually crystallize as spinel oxides. A three-dimensional (3D) oxalate-based coordination polymer $\{[Co(bpy)_3][Mn_2(C_2O_4)_3]\cdot H_2O\}_n$ (**3**) was used as a single-source precursor for the formation of spinel oxide $CoMn_2O_4$ heating at 800 °C.

The conversion *via* thermal decomposition of compounds **1**–**3** was explored by thermal analysis (TGA and DTA), IR spectroscopy and powder X-ray diffraction (PXRD).

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From the topochemical postulate to molecular switches

Od topokemijskog principa do molekulskih prekidača

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A rapidly increasing interest in the solid-state reactions due to their application is followed by a desire to design new intelligent materials. It is known that the efficacy of the solid-state reaction is governed by the topochemical postulate which says that the reaction is possible only if topochemical postulate is satisfied. As a part of the study of the effects of topochemical factors on the solid state organic compounds, we report the results of research including the photo-dissociation of aromatic C-nitroso compounds [1]. The discovery that nitroso dimers in crystals undergo photodissociation has at least two perspectives, the study of topochemical effects in the solid-state chemical reactivity, and the possibility to apply this effect in the molecular OFF-ON switches in molecular electronics. In this special case a topochemical postulate will be fulfilled only in case when the monomer crystal structure affords close contacts between the reactive centers of neighboring molecules. Dimerization of 4-bromnitrosobenzene and 4-iodonitrosobenzene was studied under three different topochemical environments: (i) strong topochemistry in the cryogenic conditions where the starting monomers have been obtained by photolysis of crystals of the corresponding dimers at 14 K, (ii) looser topochemistry in the freshly sublimed crystals of monomers and (iii) randomly distributed monomer molecules in thin layers prepared by cryogenic deposition on CsI plate. It was demonstrated that the change in topochemistry and modifying structure at the molecular level drastically modifies the reaction rate and affect a bulk physical property (reactivity) of a solid.

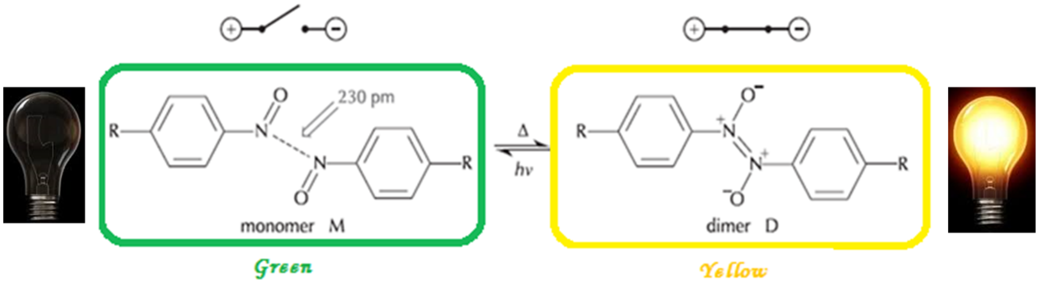

Figure 1: Photothermal bond formation and bond breaking: the molecular OFF-ON switch.

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Acknowledgements

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One-pot three-component mechanosynthesis of imine cocrystals with halogen bond donors

Kokristali imina s donorima halogenske veze dobiveni trokomponentnom mehanokemijskom sintezom u jednom koraku

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A century long interest in *o*-hydroxy imines can be attributed to their photo- and/or thermochromic properties in the solid state [1] which can be tuned by means of cocrystallization [2,3].

Herein we report one-pot mechanosynthesis which combines the formation of covalent bonds and halogen bonds [4] to obtain imine cocrystals with halogen bond donors. In order to explore the potential of pyridyl fragments as halogen bond acceptor species in comparison/competition with hydroxy and methoxy groups [3] we used imines derived from *o*-vanillin (**ov**) and aminopyridines (**3amp** and **4amp**) and as halogen bond donors we selected commonly used perfluorinated compounds: 1,2-, 1,3- and 1,4-diiodotetrafluorobenzene (**12tfib**, **13tfib** and **14tfib**) as well as 1,3,5-triiodotrifluorobenzene (**135titfb**). We obtained eight cocrystals by one-pot grinding of a mixture of **ov**, aminopyridine and halogen bond donors in 1:1:1 or 2:2:1 molar ratios. To observe mechanosynthesis, as well as to facilitate the characterization of the new cocrystal by single-crystal X-ray diffraction, mechanochemical experiments were accompanied by crystallization. All reactants and products were characterized by means of powder X-ray diffraction. In all obtained cocrystals the molecules are connected by means of I···N halogen bonds between halogen bond donor iodine atoms and pyridine nitrogen atoms.

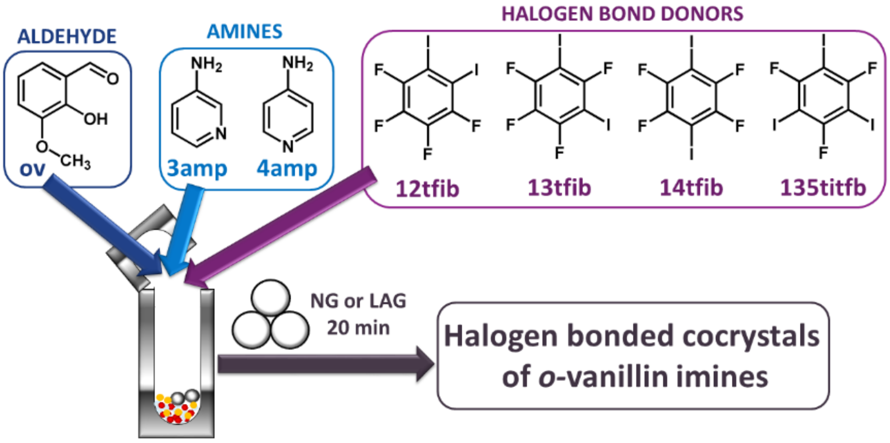

Figure 1: A schematic view of the methodology used for one-pot mechanosynthesis of the cocrystals.

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Beauty of crystal faces: The story of growing single crystals

Ljepota kristalnih ploha: Kako uzgojiti jedinični kristal

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Croatian association of crystallographs and Croatian crystallography community in cooperation with PLIVA and Chemistry department of Faculty of science in Zagreb has devised and organized second Croatian contest in growing single crystals for students of elementary and secondary school titled "The Beauty of Crystal faces". This contest was intended for students of 7th and 8th grade of elementary school and all four grades of secondary school. The main goal of the contest was preparation of single crystal as big as possible in one of three categories: 1) inorganic salt crystallization, 2) organic salt crystallization and 3) challenging category in which student first had to prepare the substance from which they will grow their single crystal. The students of primary and secondary school were competed separately and duration of experiment was limited to two months. One of primary goals of the contest was to bring closer the world of science to students and interest them about crystals, crystal growth as well as to teach them scientific approach to a real problem. Through the contest students had to adopt fundamental techniques and procedures used in chemical laboratory such as using laboratory dishes and chemicals, filtration, decanting, handling acids and bases and writing high-quality laboratory notebook, which is important component of every experimental work.

The response to the content was unexpectedly good: there were more than 100 schools applied with more than 700 students divided in about 170 teams. This contest indicated that a lot of students already have great interest toward chemistry, science in general and experimental work.

Figure 1: Assessment and grading of submitted crystals prepared by students

From thioureas and guanidines to amides and olefins - a journey through mechanochemical organic landscapes

Preko tiourea i gvanidina do amida i olefina - putovanje kroz mehanokemijske organske krajolike

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Global awareness of the negative environmental impact of chemical industry has prompted members of chemistry community to engage in finding solutions for a sustainable future. The emergence of green chemistry, as an expanding research field, has paved the way to the development of environmentally more benign processing of chemicals. One of the most investigated areas of chemical science in the last decade has been synthesis and reactivity in the solid-state with emphasis on the application of mechanochemical methods. Ranging from manual treatment in mortar using a pestle, high-intensity milling in shaker and planetary mills or agitation during twin screw extrusion, these methods provide a unique environment for solvent-free chemical reactions and allow for the discovery of new types of reactions, unknown phases or polymorphs in crystalline solids, isolation and characterization of species unstable in solution etc.

In this presentation, recent advancements in mechanochemical synthesis of organic molecules will be discussed. The solid-state reactivity of iso(thio)cyanates towards amines has been exploited as a platform to develop a solvent-free environmentally-friendly approach to synthesis and structural characterization of (thio)ureas and guanidines used as chiral organocatalysts, sensors and biologically active compounds [1-2]. The construction of the amide bond in dipeptides [3] and olefin metathesis under mechanochemical conditions [4], as well as trapping of reactive intermediates enabled by solid-state ball milling [5], will also be highlighted.

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Antioxidative and antiproliferative activity of methoxy and amidino substituted benzamides and benzimidazoles

Antioksidativna i antiproliferativna aktivnost metoksi i amidino supstituiranih benzamida i benzimidazola

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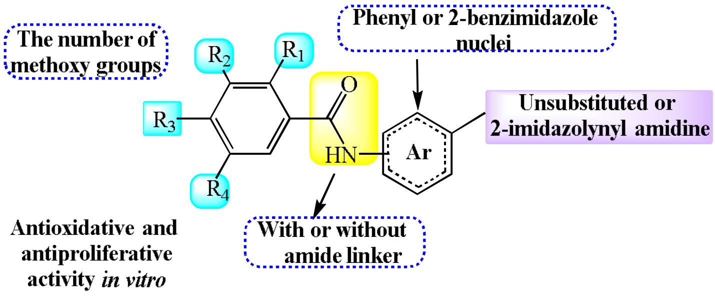
A variety of biochemical and pathophysiological processes in the human body could produce oxygen free radicals and other reactive oxygen species as by-products which may cause oxidative damage of most important biomolecules such as nucleic acids, lipids and proteins. Thus, oxidative damage of biomolecules eventually leads to several chronic diseases including cancer, diabetes, aging and other degenerative diseases [1].

Herein we present the synthesis and potential antioxidative and antiproliferative activity of novel methoxy amidino substituted bezamides and benzimidazoles. For the synthesis of novel targeted compounds, classical organic synthesis reactions were used [2]. Their antioxidative potency has been evaluated by *in vitro* spectrophotometric assays and preliminary structure-activity relationships among the synthesized compounds are discussed [3]. The compound bearing three methoxy groups and imidazolynyl amidine groupe exhibited the most prominent reducing activity as well as free-radical scavenging activity. Furthermore all novel compounds were tested against three human cell lines: HCT 116 (colon carcinoma), H 460 (lung carcinoma) and MCF-7 (breast carcinoma).



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This work was funded by the Croatian Science Foundation (project HRZZ-5596).

Gaining knowledge and developing skills during teaching optional subject Chemistry laboratory

Stjecanje znanja i razvoj vještina tijekom izvođenja nastave fakultativnog predmeta Praktikum kemije

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U sklopu projekta "Osnaživanje gimnazijskog obrazovanja provedbom kurikularne reforme STEM i ICT područja" Prve gimnazije Varaždin, financiranog od strane Europske unije iz Europskog socijalnog fonda, razvijeno je 7 novih fakultativnih kurikuluma iz STEM područja. Svrha projekta bila je razviti kurikulume te stvoriti materijalne uvjete za njihovu provedbu kako bi učenici gimnazije stekli nova znanja i razvili vještine, a s ciljem uspješnijeg nastavka školovanja te lakšeg ulaska na tržište rada. U projekt su bili uključeni i partneri – fakulteti Sveučilišta u Zagrebu: Fakultet organizacije i informatike, Prirodoslovno-matematički fakultet i Prehrambeno-biotehnološki fakultet Zagreb, čija je zadaća bila pružanje stručne pomoći i podrške, provedba edukacija i recenzija te razvoj i uspostava platforme za e-učenje.

U sklopu projekta razvijen je kurikulum fakultativnog predmeta Praktikum kemije [1], napisan priručnik za učenike i protokoli za vježbe za ovaj predmet te je izrađen online kolegij na CARNet lms – Loomen platformi. Nastava fakultativnog predmeta Praktikum kemije počela se izvoditi u školskoj godini 2016./2017. Učenici tijekom izvođenja nastave tog predmeta razvijaju vještine rada u laboratoriju te integriraju sadržaje kemije, fizike, informatike i matematike u praktičnom radu i mjerenjima kakva se ne izvode u sklopu redovne nastave. Tijekom realizacije nastave učenici koji su odabrali fakultativni predmet samostalno pripremaju uzorke za analizu, izvode eksperimente, prikupljaju kvantitativne podatke koje zatim obrađuju, grafički prikazuju, analiziraju te izvode zaključke. Strategija učenja i poučavanja temelji se na učenju otkrivanjem [2], stjecanje trajnih znanja i razvijanju vještina korisnih za svakodnevni život, nastavak prirodoslovnog obrazovanja, ali i za znanstvenu aktivnost. Učenici aktivno usvajaju sadržaje, potiču se na kreativnost i kritički način razmišljanja te na osmišljavanje i provođenje vlastitog istraživanja u školskim uvjetima.

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Representation of the project "Modern technologies and educational methods for gaining skills and competencies at high schools": STEM for everybody

Predstavljanje projekta "Suvremena tehnologija i edukacijske metode za stjecanje vještina i kompetencija u gimnazijama": STEM za SVaKoG*

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Gimnazija Bjelovar je uspješno aplicirala na otvoreni poziv na dostavu projektnih prijedloga koji se odnose na Promociju kvalitete i unaprjeđenje sustava odgoja i obrazovanja na srednjoškolskoj razini. Cilj ovog poziva bio je uspostava programskih, kadrovskih i materijalnih uvjeta u gimnazijama koji će omogućiti stjecanje dodatnih kompetencija u području matematike, prirodoslovlja i informacijsko-komunikacijskih tehnologija. Nositelj projekta bila je Gimnazija Bjelovar, a partneri u provedbi projekta bili su: Gimnazija Petra Preradovića iz Virovitice, Srednja škola Marka Marulića Slatina i Visoka Tehnička škola u Bjelovaru. Projekt se provodio 12 mjeseci u periodu od 23.10.2015.-23.10.2016. U projektnim aktivnostima, uz nastavnike iz STEM (Science, Technology, Engineering and Math) i ICT područja, sudjelovali su i učenici, te ravnatelji i stručni suradnici. Glavna projektna aktivnost bila je razvoj kurikula fakultativnih predmeta: Računalna kemija, Linearno programiranje, Razvoj aplikacija i unaprjeđenje postojećeg kurikula Nacrtne geometrije. Provedena je analiza postojećih planova, programa i kurikula. Održano je 7 edukacija za 30 nastavnika s temama: Kurikul temeljen na ishodima učenja, Metode učenja i poučavanja u kontekstu HKO-a, Ocjenjivanje u kontekstu ishoda učenja, Korištenje novih tehnologija radi povećanja interaktivnosti nastavnog procesa, Poticanje poduzetničkog načina razmišljanja kod učenika: prepoznavanje prilika i istraživanje rješenja, Radionica o alatima i metodama izrade digitalnih nastavnih sadržaja, Radionica o međunarodnim projektima namijenjenim osuvremenjivanju STEM nastave. Realizirano je studijsko putovanje 8 nastavnika u Nizozemsku. Šest nastavnika iz četiri partnerske ustanove sudjelovalo je na edukaciji Future Classroom Lab-u u Bruxellesu. Cilj provedenih edukacija i studijskog putovanja nastavnika u Nizozemsku bio je jačanje nastavničkih kompetencija za izradu novih kurikula i provedbu novih nastavnih sadržaja te primjenu suvremenih metoda poučavanja i novih tehnologija. Nakon provedenih edukacija izrađena su 4 projektom predviđena kurikula fakultativnih predmeta za gimnazije. Izrađeni kurikuli su zasnovani na ishodima učenja i izrađeni prema principima Europskog kvalifikacijskog okvira (European Qualification Framework, EQF), Preporuci Europskog parlamenta i Vijeća EU od 23. travnja 2008.) i HKO-a (Osnove za Hrvatski kvalifikacijski okvir, MZOŠ 2009.) te će doprinijeti daljnjem razvoju i provedbi Hrvatskog kvalifikacijskog okvira. Za svaki fakultativni predmet izrađeni su nastavni materijali, ispitni materijali, priručnici za učenike i nastavnike u digitalnom obliku. Sve aktivnosti, kao i materijali razvijeni u ovom projektu javno su dostupni na internetskoj stranici projekta. [1]

Reference

[1] http://stemzasvakog.wixsite.com/stemzasvakog

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*STEM za SVaKoG – "**S**uvremena **t**ehnologija i **e**dukacijske **m**etode za **s**tjecanje **v**ještina i **k**ompetencija u **g**imnazijama"

Science Plus
Project-Based Learning in STEM/ICT subjects

Znanost plus
Projektna nastava u STEM/ICT predmetima

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U sklopu projekta Znanost plus koji se provodio 12 mjeseci, razvilo se 15 novih fakultativnih predmeta iz STEM/ICT [1] (Science, Technology Engineering and Mathematics/Information Communication Tehnology odnosno znanost, tehnologija, inženjerstvo, matematika/informacijsko komunikacijska tehnologija) područja. U projektu je sudjelovalo 32 nastavnika iz Prirodoslovne škole Vladimira Preloga u Zagrebu i Gimnazije Andrije Mohorovičića iz Rijeke. Partneri u projektu bili su Gimnazija Andrija Mohorovičić iz Rijeke, Pliva d.o.o. i Prirodoslovno-matematički fakultet, Sveučilišta u Zagrebu.

Cilj projekta je bio uvesti fakultativne predmete koji će povećati zanimanje učenika za STEM/ICT područje te povećati kompetentnost učenika gimnazijskog usmjerenja na tržištu rada. Specifičnost novih predmeta je obrađivanje interdisciplinarnih nastavnih sadržaja kroz projektnu nastavu [2] koja u središte nastavnog procesa stavlja učenika dok je nastavnik moderator. Među učenicima je provedena anketa o zainteresiranosti za pojedine sadržaje. Rezultati ankete pokazuju kako su učenici najviše zainteresirani za sadržaje iz područja primijenjene kemije i biologije. Na području kemije razvila su se četiri nova fakultativna predmeta: Kemija istraživanjem, Odabrana poglavlja kemije, Kemija okoliša i Kemija hrane. Središnje tema pojedinog predmeta su voda, tlo i hrana iz kojih proizlaze projektne teme koje će birati učenici. Cilj je projektne nastave osposobiti učenike za praktičnu primjenu znanja i vještina te za argumentirano društveno djelovanje u zaštiti okoliša i zdravlja. Rezultate svog istraživanja na projektu učenici će prezentirati u školama, roditeljima i lokalnoj zajednici.

Tijekom provedbe projekta nastavnici su se educirali na Agronomskom fakultetu i na Fakultetu kemijskog inženjerstva i tehnologije, Sveučilišta u Zagrebu, te u Hrvatskom zavodu za javno zdravstvu i Visokom učilištu Algebra. Nakon završene edukacije napisani su priručnici za učenike i nastavnike koji će provoditi projektnu nastavu. Od školske godine 2017./2018. učenici će moći birati neke od 15 fakultativnih predmeta prema osobnim interesima.

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POSTERSKE PREZENTACIJE

POSTER PRESENTATIONS

Radical scavenging potency of 4-hydroxyphenylpropionic acid: a theoretical approach

Studija potencijala hvatanja radikala 4-hidroksifenilpropionskom kiselinom

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Health benefits of polyphenol-rich diet are related to intestinal metabolites, rather than to polyphenolic compounds originally present in food [1,2], which usually possess very low bioavailability and low systemic concentration [3,4]. Particular intestinal metabolites are produced in high μM concentrations and may promote health *via* several possible *in vivo* mechanisms [5]. 4-hydroxyphenylpropionic acid (4-HPPA) is among the most abundant products of polyphenols degradation in large intestine [5]. Its concentration in colon may reach value of 200 μM [5], which could be sufficient to exert biological activity and effective direct radical inactivation.

Radical scavenging mechanisms of 4-HPPA, in water and pentyl ethanoate as a solvent, were studied by DFT method using Gaussian 09 package [6]. Geometry optimizations and frequency calculations were carried out using the M06–2X/6-311++G(d,p) level of theory, in conjunction with the SMD continuum solvation model. Hydrogen atom transfer (HAT) and sequential proton loss electron transfer (SPLET) mechanisms were found to be thermodynamically probable and competitive processes in both media. The Gibbs free energy change for reaction of inactivation of radicals indicates 4-HPPA as a potent scavenger.

4-HPPA possesses potential for inactivating radicals of different characteristics by direct scavenging *via* HAT and SPLET mechanisms. Because 4-HPPA is produced in high μM concentrations and is usually better absorbed than its precursor molecules, it may contribute to health benefits associated with regular intake of polyphenol-rich diet.

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Acknowledgments

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The role of guaiacyl moiety and carboxyl group in radical scavenging by dihydroferulic acid

Uloga gvajakolne i karboksilne skupine u hvatanju radikala dihidroferuličnom kiselinom

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Thermodynamics of $2H^+/2e^-$ radical scavenging mechanisms of dihydroferulic acid, a naturally occurring plant compound and colon catabolite of (poly)phenols, was studied by DFT method using SMD/M06–2X/6–311++G(d,p) level of theory with the Gaussian 09 program package [1].

Until recently, radical inactivation by (poly)phenolic compounds has been investigated by considering involvement of only phenolic –OH group(s) *via* $1H^+/1e^-$ mechanisms. Here, we studied the role of guaiacyl moiety (reaction path *a* [2]) and carboxyl group (reaction path *b* [3]) (Figure 1) in radical scavenging by dihydroferulic acid *via* double hydrogen atom transfer (dHAT), double electron transfer-proton transfer (dET-PT) and double sequential proton loss electron transfer (dSPLET) mechanisms in polar and non-polar solvents [4].

Obtained results indicate that dihydroferulic acid possesses potential for inactivating radicals of different characteristics ($HO^•$, $HOO^•$, $CH_3O^•$, $CH_3OO^•$, $PhO^•$, $Cl_3COO^•$ etc.) what can be ascribed to $2H^+/2e^-$ mechanisms such as dHAT and dSPLET, rather than to a single $1H^+/1e^-$ processes. We found that reaction path *a* is less energy demanding than reaction path *b*.

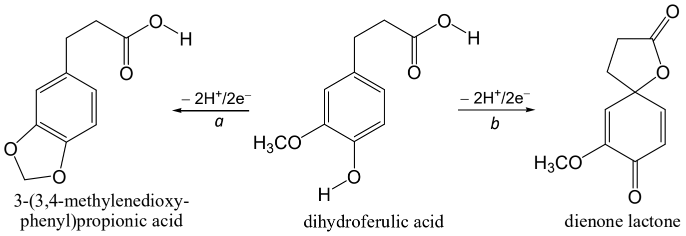

Figure 1: Reaction paths studied.

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This work has been supported by The Foundation of the Croatian Academy of Sciences and Arts, under the project No. 10-102/244-1-2016. – "Investigations of the antioxidant mechanisms of polyphenols and their metabolites."

Determination of electroneutrality point temperature dependence for various materials in an aqueous electrolyte solution

Temperaturna ovisnost točke elektroneutralnosti različitih materijala u vodenoj otopini elektrolita

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Electrical interfacial layer forms upon the contact of aqueous electrolyte solution with a surface of solid colloid or nanoparticles. Inside the electrical interfacial layer, apart from the accumulation of the electrolyte ions, potential determining ions OH^- and H^+ accumulate as well. There are several different models that describe process of accumulation of ions on interfaces [1-2]. For an inert surfaces accumulation of potential determining ions is achieved through distribution between the bulk of the solution and interfacial layer, while for metal oxides it is achieved by a process of protonation and deprotonation of the charged surface group. The electrical interfacial layer is characterized by electroneutrality point. At the electroneutrality point (pH_{eln}) all electrical properties at the surface diminish. The values of surface potentials and the net surface charge density equal zero. In the case of negligible or symmetric counter ion association electroneutrality point has the same values as the isoelectric point and point of zero charge ($pH_{eln} = pH_{iep} = pH_{pzp}$).

Determining temperature dependence of electroneutrality point (isoelectric point or point of zero charge) enables the evaluation of the difference in standard distribution enthalpy of H^+ and OH^- on inert surface. This data enables us to better understand the behavior of the electrical interfacial layer and creation of the suitable mathematical and physical models. To achieve a better understanding, experimental results obtained for different inert as well as non-inert materials, i.e. metal oxides, were compared. For this purpose, two inert (Teflon and diamond) and one metal oxide (TiO_2) surfaces were studied.

Colloid particles in general have very different physical properties, so one method for evaluation of thermodynamic parameters of interfacial processes cannot be applied for all material. In this respect, we have chosen three distinct methods: potentiometric mass titration, streaming potential measurements and calorimetry. Potentiometric mass titration is a standard method for determining point of zero charge. Streaming potential measurement is a reliable method to determine electrokinetic potential. Lastly, calorimetry is a standard method for observing changes in enthalpy of the system during chemical reactions or physical processes. Differences in standard distribution enthalpy of H^+ and OH^- ions on the diamond, Teflon and TiO_2 surfaces were calculated and compared.

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Computationally guided search for novel benzimidazole derivatives with enhanced antiproliferative activity

Dizajn benzimidazolnih derivata izražene antiproliferativne aktivnosti temeljen na rezultatima računalnih metoda

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The experimental search for novel benzimidazole derivatives with enhanced antiproliferative activity was successfully guided by QSAR modelling. Robust 3D-QSAR models were derived using available database of the compounds with previously measured activities in the same laboratory, under the same conditions. Using the QSAR analysis of the obtained models, the molecular descriptors with the highest influence on the activity were identified. The QSAR analysis revealed that the antiproliferative activities against four cell lines, H460, HCT 116, MCF-7, and SW 620, should be increased if the new compounds are charged at pH range from 5 to 7 and if their hydrophobicity is increased comparing to the dataset compounds. Novel amino and diamino substituted benzimidazo[1,2-*a*]quinolines with introduced quarter amino groups and aliphatic chains were designed according to the QSAR analysis and their antiproliferative activities were computationally predicted. Using uncatalyzed microwave assisted amination, 14 novel compounds were synthesized and their antiproliferative activities were assessed against H460, HCT 116, MCF-7, and SW 620 tumor cell lines *in vitro*. Novel compounds showed antiproliferative activities in micromolar and submicromolar inhibition concentrations. Experimental measurements of antiproliferative activities enabled undisputed validation of QSAR models, very good agreement between experimentally measured activities and computational predictions was obtained. Based on the identified molecular descriptors with the highest influence on antiproliferative activity, possible mode of action is proposed.

Dimerization mechanism of aromatic nitroso compounds in solid state

Mehanizam dimerizacija aromatskih nitrozo spojeva u čvrstom stanju

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Kinetics of the solid-state reactions can be described by using the classical Avrami's-Erofeev approach [1]. Avrami's model represents only empirical description of the reaction kinetics, thus it's inconvenient for the deeper mechanistic interpretations. Recently, Finney and Finke have proposed a new four-step autocatalytic model (FF model) and applied it for explanation of particular solid-state reactions mechanisms [2].

However, we found that neither Avrami nor Finke models are adequate for analyzing the kinetic data for dimerization of aromatic nitroso compounds in the solid state, the reaction that we use as a model for studying solid-state reaction mechanisms. The starting nitroso monomers are obtained by photolysis of the corresponding dimers (azodioxides) under cryogenic conditions. Re-dimerization of these compounds occurs upon heating and affords data that can be interpreted as a combination of sigmoidal and exponential behavior [3]. The former is characteristic for solid-state transformations and can be described by Avrami's, A→B→C or by FF models. The latter represents chemical reactions accompanied by (bi-)exponential growth curves. Dimerizations of the same compounds in different molecular arrangement, i.e. in crystals of monomers obtained by mild sublimation, is for several orders of magnitude slower. This observation can be explained by different distances between nitrogen atoms of the starting neighbouring nitroso molecules that appear in sublimed or photolysed crystals [4].

Bis(4-nitrosophenyl) derivatives with various spacers between the phenyl rings follow different kinetics. Dimerization of the methane derivative at 200 K occurs in parallel reactions yielding *cis* and *trans*-isomers. At higher temperature (270 K) *trans*-isomers transform to *cis*-isomers *via* monomer intermediates. On the other hand, derivative with the -CH_2CH_2- spacer follows standard exponential-like dimerization to *trans*-isomers.

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Quartz-water interface – complementary experimental and molecular dynamics study

Istraživanje međupovršine kvarc-voda putem molekulske dinamike i eksperimenta

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Properties of interfacial water differ significantly from those present in the homogeneous bulk water, whereby the presence of surface charges and the accumulation of ions at the solid-water interface can induce long-range ordering of water molecules and the formation of electrical interfacial layer. This, in turn, gives rise to a variety of different physical and chemical processes, such as heterogeneous catalysis, mineral dissolution, membrane chemistry etc. Using a model system, consisting of (0001) quartz surface and alkali metal (Na$^+$, K$^+$) halide (Cl$^-$, I$^-$) solutions at three different pH conditions (pH = 3, 6, and 9), we have characterized the behavior of water at quartz-water interfaces using complementary combination of molecular dynamics (MD) simulations and two experimental techniques, namely inner surface potential measurements (obtained by Single Crystal Electrode [1]), from which zeta-potential is obtained.

Our strategy enabled us to compare experimental and theoretically calculated results in a direct manner, *i.e.* theoretically obtained zeta-potentials (obtained *via* non-equilibrium molecular dynamics (NEMD) simulations [2]) were compared with the measured zeta-potential data, thus enabling us to both critically assess the applicability of a chosen silica-water force field [3] and to describe the nature of the model quartz–water interface in appreciable detail. More specifically, we find that interactions between the surface silanol ($\equiv$SiOH) and siloxide groups ($\equiv$SiO$^-$) with water and solvated ions have a dominant role in inducing a multidimensional layering profile of water. In this respect, we find that the interface region comprises of a “compact layer” of solvent next to the quartz surface that is not properly described in classical electric double layer theories, whereby the depth of the diffuse solvent layer is sensitive to the ionic strength, pH conditions and the identity of solvated ions.

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Conformational analysis of the bis(D,L-isoleucinato)copper(II) complex in aqueous solution

Konformacijska analiza kompleksa bis(D,L-izoleucinato)bakra(II) u vodenoj otopini

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Copper is as an essential element indispensable for optimal catalytic activity of numerous enzymes such as Cu,Zn-superoxide dismutase, cytochrome *c* oxidase and tyrosinase [1]. Bis(amino acidato)copper(II) complexes are known since the second half of 19th century, but their structure and properties started to be systematically investigated a century later. They are interesting for studying because they can be used as model compounds for determination of the copper binding sites in metalloproteins, and owing to their stereochemical diversity.

The crystal and molecular structure of the bis(L-isoleucinato)copper(II) monohydrate complex was solved in 1969 (orthorhombic space group $P2_12_12_1$) [2], while the monoclinic polymorph (space group *C*2) was characterized 40 years afterwards [3]. Both polymorphs have *cis*-configuration. It is assumed that both *cis*- and *trans*-isomers are stable in aqueous solution [3], even though the *trans*-one has never been isolated. On the contrary, the bis(D,L-isoleucinato)copper(II) complex was reported only in polycrystalline form; its IR [4] and ESR [5] spectra showed that it could exist as a *trans*-isomer, but its crystal structure has not yet been reported.

Each chelate ring in bis(D,L-isoleucinato)copper(II) can have 18 conformations, when considering two conformations of the five-membered ring (with C_{β} in an axial or equatorial position) and nine conformations of the isoleucine residue (defined by the N_{am}-C_{α}-C_{β}-$C_{\beta1}$ and C_{α}-C_{β}-C_{γ}-C_{δ} torsional angles which can take values of $\approx$ 60°, –60° and 180°).

To calculate the conformational analysis for bis(D,L-isoleucinato)copper(II) in aqueous solution we used two methods: the molecular dynamics (MD) and the density functional theory (DFT) with the polarizable continuum model (PCM). The MD simulations are done using the FFWa-SPCE force field, developed to study the properties of the bis(amino acidato)copper(II) complexes in aqueous solution, solid state and in vacuo [6]. The goal of this work is to investigate the relative energies of the *cis*- and *trans*-conformers of bis(D,L-isoleucinato)copper(II) and to compare two methods` predictions of the most stable groups of conformers in aqueous solution.

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Gallium(III) binding properties of aroylhydrazones derived from nicotinohydrazide

Kompleksacija galija(III) aromatskim hidrazonima izvedenim iz nikotinohidrazida

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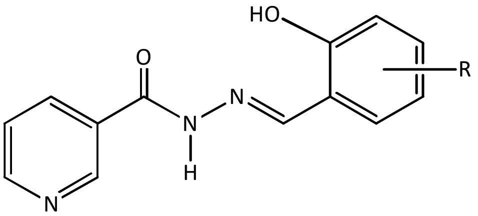
One strategy that has been explored to evade the bacterial resistance to drugs is to target the iron metabolism of bacteria, since iron is critical for all bacteria growth. Three major concepts have been evaluated to exploit limitations in the bacterial iron metabolism: reducing the availability of free iron with iron-chelating agents; inhibiting iron metabolism in the infected host, and the "Trojan Horse strategy" which takes advantages of natural iron-uptake systems to deliver antimicrobial compounds inside the cells that then kill them [1].

Biological systems have difficulties to differentiate between Fe^{3+} and Ga^{3+} ions due to their nearly identical ionic radii, same charge, preferred coordination number and chemical behavior. However, Ga^{3+} lacks the redox activity of iron (3+/2+ redox chemistry) and the substitution of Ga^{3+} into metalloenzymes can result in a loss of enzymatic function, with cellular toxicity as a result, which has marked Ga^{3+} the "Trojan Horse" in biological systems.

Recent studies have shown that biologically active salicylidene acylhydrazide is an excessively strong complexing agent for gallium and that chelation of Ga(III) to the hydrazone increase the stability of the compounds against acid-induced hydrolysis [2]. In this study we prepared structurally similar aromatic hydrazones (Scheme) and investigated their binding properties toward gallium(III) ions. Complexation was monitored in methanol/water 1/1 mixture by spectrophotometric batch titrations at pH = 2.52 due to ligands' hydrolysis.



R = H (**1**); 3-OCH_3 (**2**); 4-OCH_3 (**3**); 5-OCH_3 (**4**)

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Chemometric analysis of IR spectra: who needs the HPLC?

Kemometrijska analiza IR spektara: kome treba HPLC?

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The aim of this study was to assess the possibility of kinetic parameters estimation for the succinimide substitution reaction only by chemometric analysis of IR spectra acquired during in-situ measurements, without the need for prior instrument calibration, sampling or any other analytical technique, like HPLC.

Measurements were performed in-situ, at 100 °C, in 100 ml reaction vessel by measuring IR spectra of melted reaction mixture during 25 hours, using process FT-IR spectrometer equipped with optical fibers and diamond ATR probe.

To determine kinetic parameters from spectroscopic data, IR spectra were analysed by a number of chemometric methods, including Principal Component Analysis (PCA), Evolution Factor Analysis (EFA) and Multivariate Curve Resolution (MCR) by Alternate Least Squares regression (ALS), alone and in combination with kinetic mathematical models of different complexity levels.

Reaction yield estimated by simultaneous ALS and the highest complexity level kinetic model fits was very close to experimentally obtained yield (91% vs 89%) which validated the adopted approach.

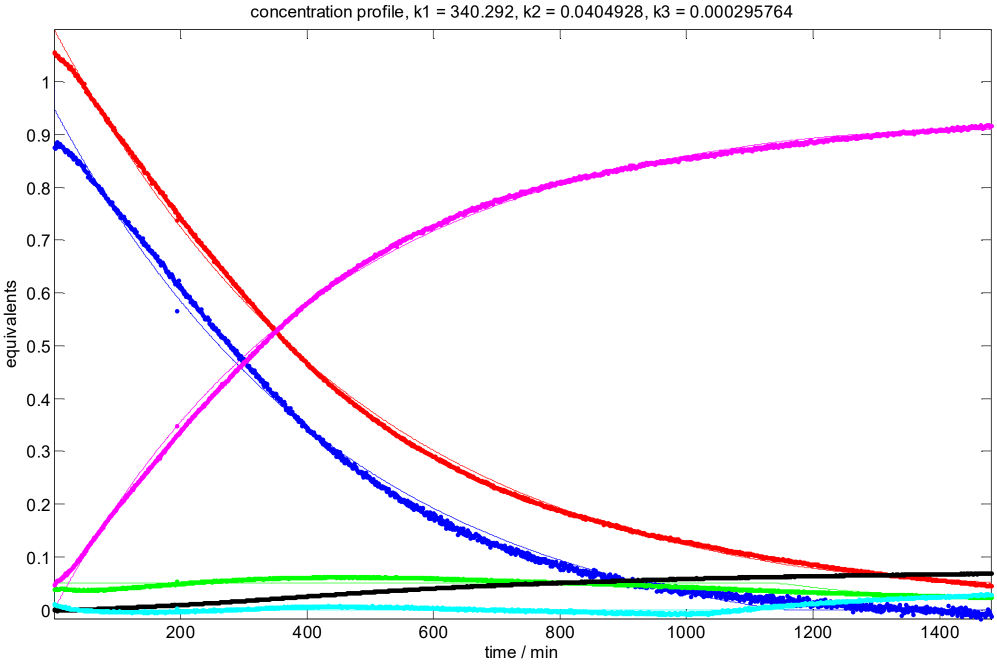

Figure1: Concentration profiles estimated by simultaneous ALS and the highest complexity level kinetic model fits. Colours: red and blue are for reactants, pink - product, black– impurity, green– intermediate, cyan– catalyst. Smooth lines are kinetic model fit results, dotted curves are ALS fit results.

The chlorination of barbiturates. Quantum-chemical study of the reaction mechanism

Kloriranje barbiturata. Kvantno-kemijska studija reakcijskog mehanizma

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Barbiturates are drugs that act as central nervous system depressants. They are used as anxiolytics, hypnotics, anticonvulsants and intravenous anesthetics. The chlorination of barbiturates by hypochlorous acid (HOCl) is very important reaction in biochemistry and environmental chemistry. The barbiturates show high stability over a extended period of time and resistance to both biological and chemical degradation, which is why they accumulate in the environment retaining their pharmacological properties. In order to explain why barbiturates are chemically inert to chlorination by HOCl, standard quantum chemical methods have been used to describe the reaction of most common barbiturates used in medical practice. The chlorination reaction of pharmaceutically relevant 5,5-disubstituted barbiturates has been compared with the parent barbituric acid.

It has been shown that barbituric acid easily undergoes chlorination to give the C5-chlorinated product (Figure 1). Chlorination of 5,5-disubstituted barbiturates is not possible in the C5-position, but only in the N-position. However, calculated energy barriers for those processes are prohibitively high ($\Delta G^{\#}_{298} > 200$ kJ/mol). To undergo N-chlorination, the tautomerization of corresponding barbiturates to their iminol forms is required (Figure 2). As expected [1], the calculated energy barrier for chlorination of the iminol form is lower than the direct N-chlorination of the amide form, but exceeds 150 kJ/mol, which indicates the recalcitrant properties of barbiturates under chlorination conditions.

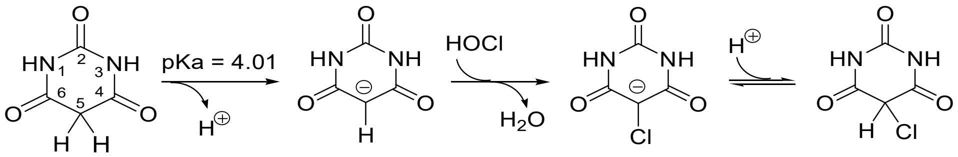

Figure 1: Chlorination of barbituric acid in the C5-position.

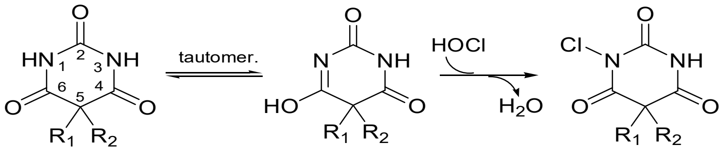

Figure 2: Tautomerization and N-chlorination of 5,5-disubstituted barbiturates.

$R_1 = R_2 = $ Et (Veronal®)

$R_1 = $ Et, $R_2 = $ Ph (Luminal®)

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Nucleofugalities of butyrate and isobutyrate in various solvents

Nukleofugalnosti butirata i izobutirata u različitim otapalima

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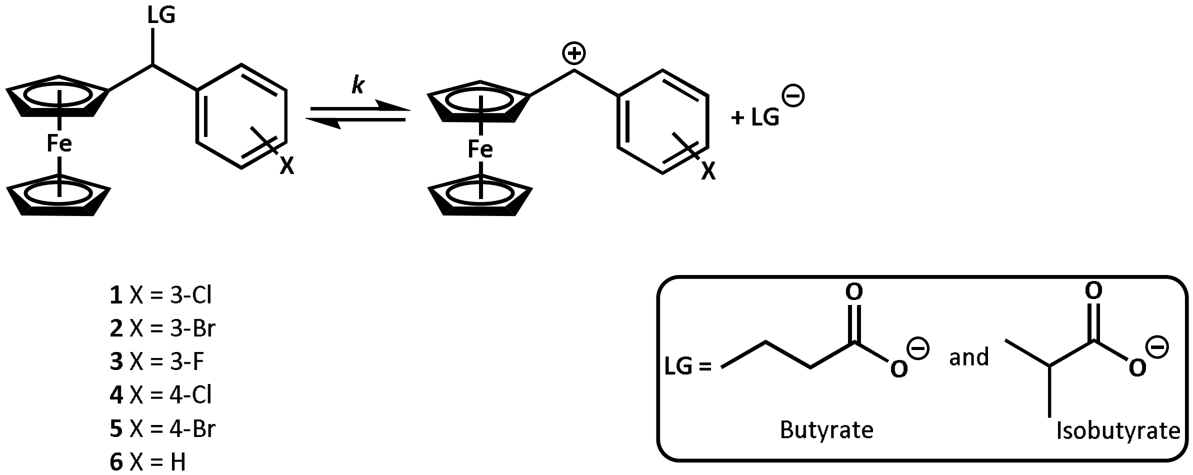
Nucleofugalities (the leaving group abilities) of butyrate and isobutyrate in various aqueous protic and aprotic solvents have been derived from the S_N1 solvolysis rate constants of the corresponding X-benzylferrocenyl derivates (Scheme 1., **1**-**6**,) by applying the LFER Equation (1) [1,2]:

$$\log k = s_f\,(E_f + N_f) \qquad (1)$$

In this equation k is a first order rate constant for S_N1 reaction at 25°C, s_f (slope of the log k/E_f correlation line) and N_f (nucleofugality, negative intercept on the abscissa of the log k/E_f correlation line) are nucleofuge specific parameters, while E_f is the electofugality parameter of the corresponding benzylferrocenyl electrofuge determined earlier.

Comparison with neutral and other anionic leaving groups reveals that butyrate and isobutyrate are relatively poor leaving groups, whose nucleofugalities (N_f values) are similar with the nucleofugalities of pyridine and its 4-substituted derivates [3,4], benzoate [5], and acetate [6]. Also, it has been found that the N_f values of butyrate in all examined solvents are slightly higher than N_f values of isobutyrate.



1 X = 3-Cl
2 X = 3-Br
3 X = 3-F
4 X = 4-Cl
5 X = 4-Br
6 X = H

Scheme 1. Solvolysis of X-benzylferrocenyl butyrate and isobutyrate

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Surface potential of calcite in aqueous medium

Površinski potencijal kalcita u vodenom mediju

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Reactions at the calcite/aqueous electrolyte solution interface have an enormous impact on numerous natural processes. Contact of solid calcite particles or macroscopic calcite single crystal surfaces with aqueous electrolyte solutions results in the accumulation of ions at the interface and the formation of an electrical interfacial layer (EIL) [1]. Calcite single crystal electrodes (SCrEs) enable the evaluation of the inner surface potential (Ψ_0) of defined (104)-oriented calcite single crystal surfaces [2]. These surfaces are the most stable one and they control the reactivity of natural calcite particles.

In this study, the surface potential of the (104) calcite/electrolyte solution interface was investigated at different experimental conditions. For that purpose two types of calcite SCrE were constructed. The stability of the calcite SCrEs and the reproducibility of measurements with these systems were tested. Measurements of surface potentials were performed at non-equilibrium and equilibrium conditions of well-defined calcite/electrolyte solution/atmosphere systems.

At non-equilibrium conditions, a series of potentiometric titrations was carried out to examine the surface potential of calcite in aqueous sodium chloride environment as a function of pH. Additionally, the influence of Ca^{2+} and CO_3^{2-} concentration on the surface potential of calcite was investigated. Furthermore, the measurements of calcite SCrE potential at conditions where calcite dissolution is expected was used for monitoring the calcite dissolution process. The topography of the calcite single crystal surface used for surface potential measurements was examined by atomic force microscopy (AFM).

Equilibrated aqueous suspensions of calcite were prepared in order to investigate the pH-dependency of the surface potential of calcite and at the same time avoiding or minimizing any possible dissolution or growth effects. Equilibrium conditions and composition of solutions required to achieve a certain pH and ionic strength were a priori calculated on the basis of thermodynamic modeling using PhreeqC 3.2 [3].

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Acknowledgments

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Adsorption of polyelectrolytes on cerium oxide nanoparticles

Adsorpcija polielektrolita na nanočestice cerijeva oksida

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The research interest in cerium(IV) oxide (ceria) nanoparticles has been increasing recently due to their potential applications in various fields such as biomedicine and catalysis. In that sense, the biocompatibility of ceria nanoparticles should be stressed since there are no reports on health risks which may be associated with such particles [1]. In many cases a stable dispersion of cerium oxide nanoparticles in a biological environment is needed and for reaching that aim polyelectrolyte coated particles are very promising. Therefore, the objective of this study was to synthesize and characterize ceria nanoparticles and to systematically investigate their interactions with polyelectrolytes. As a model polyelectrolyte negatively charged strong polyelectrolyte sodium poly(styrene sulfonate) (PSS) [2] was used.

For that purpose, cerium oxide nanoparticles were synthesized [3] and, after rinsing and drying procedure, characterized by means of X-ray powder diffraction (XRD), dynamic light scattering (DLS) and zeta-potential measurements. Average diameter of ceria nanocrystals was estimated from XRD measurements using Scherrer equation and it was found to be 6 nm. Isoelectric point of ceria nanoparticles was measured at two ionic strength values ($I_c = 1\times10^{-2}$ mol dm^{-3} and 1×10^{-3} mol dm^{-3}) and the obtained values were $\mathrm{pH_{iep}} = 5.8 \pm 0.2$ and $\mathrm{pH_{iep}} = 5.9 \pm 0.1$, respectively. Hydrodynamic radius of the synthesized cerium oxide nanoparticles was obtained by dynamic light scattering at various experimental conditions. It was shown that the particle size depends on pH and on ceria mass concentration and obtained results were in the range between 40 and 70 nm.

Adsorption of sodium poly(styrene sulfonate) on ceria nanoparticles was also examined using zeta-potential and DLS measurements. As expected, at pH = 3 adsorption of negatively charged PSS on positively charged ceria nanoparticles leads to overcharging of the surface. The influence of PSS concentration on zeta-potential was tested and it was shown that already at $c(\mathrm{PSS}) = 5\cdot10^{-4}$ mol dm^{-3} overcharging took place. DLS was used for determination of the particle size of ceria nanoparticles coated with PSS and it was shown that in the examined pH range measurable difference in particle size between uncoated and coated samples was obtained.

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Solvolytic reactivity of pentafluorophenolates

Solvolitska reaktivnost pentafluorfenolata

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The reactivity (nucleofugality) of the pentafluorophenolate leaving group [1] has been determined experimentally from first order solvolytic rate constants (k) of X,Y-substituted benzhydryl pentafluorophenolates (Scheme 1) by using three-parameter LFER equation (1) [2].

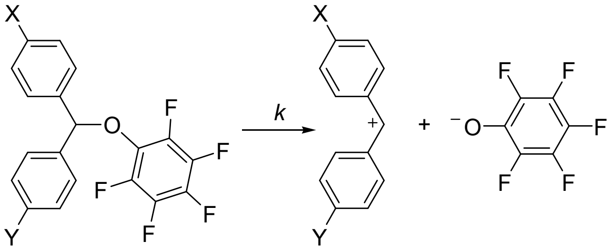
$$\log k = s_f\,(E_f + N_f) \qquad (1)$$

The parameters in this equation are: the nucleofuge-specific parameters N_f (the negative intercept on the abscisa of the log k/E_f correlation line) and s_f (the slope of the correlation line), and E_f, the electrofugality parameter – an independent variable that quantifies the solvolytic reactivity of a certain electrofuge.

Comparison with nucleofugalities of other leaving groups [2–4] reveals that pentafluorophenolate is a moderate leaving group ($N_f = –0.97$ in 80% aqua ethanol) with an unusually high reaction constant ($s_f = 1.29$ for 80% ethanol).

Besides the main purposes of estimating solvolytic reactivities of various substrates and comparing reactivity of leaving groups in a wide range of reactivity, equation (1) can also be employed in investigating the solvolytic behavior of various types of substrates and leaving groups. Thus, it enables to observe variation and even inversion in relative reactivities of phenolates and carboxylates due to different reactivity of electrofuges [1–3].

Furthermore, correlation of $\Delta^{\ddagger}G°/\Delta_rG°$ for solvolysis of benzhydryl phenolates and carboxylates indicates that phenolates solvolyze over the lower Marcus intrinsic barrier than corresponding carboxylates.



1: X = Y = MeO
2: X = MeO, Y = PhO
3: X = MeO, Y = Me
4: X = MeO, Y = H
5: X = Me, Y = Me
6: X = Me, Y = H
7: X = F, Y = H
8: X = Y = H

Scheme 1: Solvolysis of X,Y-substituted benzhydryl pentafluorophenolates.

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pH dependent effect of stirring on the electrode potentials of the metal oxide single crystal electrodes

Utjecaj miješanja otopine u ovisnosti o pH na potencijal metal-oksidnih monokristalnih elektroda

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During the potential measurements of the metal oxide single crystal electrodes [1,2] certain influence of stirring of the solution on the measured potentials was observed. The effect of stirring on the (glass) electrode potential was known from previous research [3–5]. However, theoretical explanation of this effect never converged into the wide accepted model. The general lack of interest for this phenomena is mostly due to the fact that the magnitude of this effect is negligible in daily pH measurements. However, in some cases, when measuring the potentials on SCrE, the measured signal magnitude might be low enough (*i.e.* $E < 5$ mV) to make those stirring effects the factor which shouldn't be neglected.

For the purposes of more precise SCrE potential measurements, necessary for the investigation of the mechanisms contributing to the electrode potentials, the effect of stirring was investigated as a function of pH. It was observed that not only the magnitude of the stirring influence varies with pH, but the direction of those changes also reverses at certain pH. The plot of $\Delta E_{\text{stirr.}}$ *vs.* pH is linear, with variable slopes dependent on the SCrE material used. The potential response of the SCrE to stirring was measured. The signal shapes that were obtained by switching stirring on and off indicate involvement of more than one simultaneous and possibly independent contributing mechanisms.

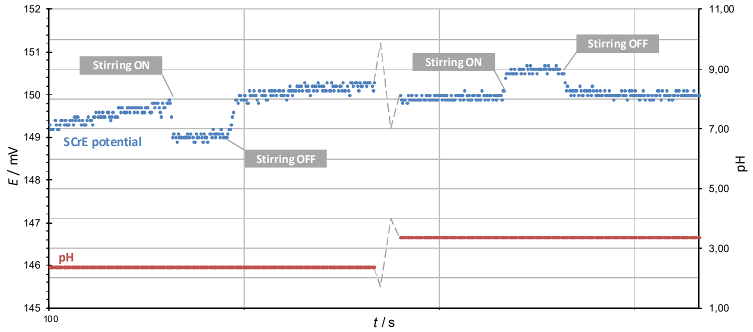

Figure 1: An example of difference in potential responses of the Fe_2O_3 (001) SCrE to stirring, at two pH values.

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Characterization of oximes containing heterocyclic aromatic and/or non-aromatic substructures

Karakterizacija oksima s alifatskim i/ili aromatskim heterocikličkim podjedinicama

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The better characteristics of compounds essential for their biological efficacy can be revealed by the systematic variations of their structure. For example, selectivity can be tuned by the modification of substituents or change of the base, usually heterocyclic moiety. Compounds which possess an oxime functionality ($R^1R^2C{=}N{-}OH$) usually have a broad scope of useful applications, equally in organic chemistry, materials science [1] as well as one in medicinal chemistry (e.g. treatment of acute intoxication by organophosphorus compounds [2]).

Oximes containing heterocyclic aromatic (imidazole) and non-aromatic (quinuclidine) substructures as well as *Cinchona* alkaloid derivatives were synthesized. To quantify the effects of R^1 and R^2 group modifications, pK_a values were measured and partition-coefficients determined. The variation of the substituents did not only result in the change of the molecular shape, but also had substantial impact on the acidity of the oxime hydroxyl group and basicity of the heterocyclic nitrogen atom. Molecular modelling was used to define conformational space of flexible compounds, to describe structural changes and determine electronic effects as a function of the group R.

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Advances in QSAR analysis of anti-trypanosomal activity

Napredak u QSAR analizi aktivnosti protiv *Tripanosome*

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Trypanosomiasis, also known as sleeping sickness, is a vector-borne parasitic disease transmitted by tsetse fly (*Glossina genus*) and caused by kinetoplastid *Trypanosoma*. We have investigated quantitative structure–activity relationship (QSAR) of anti-trypanosomal activities of natural compounds polyphenols [1], as well as synthetic compounds: pyridyl benzamides, 3-(oxazolo [4,5-b]pyridin-2-yl)anilides [2], and 6-arylpyrazine-2-carboxamides [3]. Anti-trypanosomal activity was modelled by using mono-dimensional (1D), to three-dimensional molecular (3D) descriptors. In order to find a thriving QSAR models for anti-trypanosomal activities, genetic algorithm-multilinear regression (GA-MLR) and artificial neural networks (ANN) were employed. The GA-MLR QSAR models have excellent statistical robustness with good external predictive ability. For the polyphenols, the obtained models displayed relevance of the frequency of occurrence of two oxygen atoms at topological distance, as well as stability of molecules. The most relevant structural features for the pyridyl benzamides is the presence of oxygen-halogen at a topological distance 6. Derivatives of 3-(oxazolo[4,5-b]pyridin-2-yl)anilide with enhanced anti-trypanosomal activities should have furan ring and atoms at a topological distance of 7. Inhibitory activity of 6-arylpyrazine-2-carboxamides has correlation with the presence of *N-sec*-butylformamide and substituted benzene. The results obtained will be useful for further research of more effective plant-derived agents and future synthesized compounds against the *Trypanosoma*.

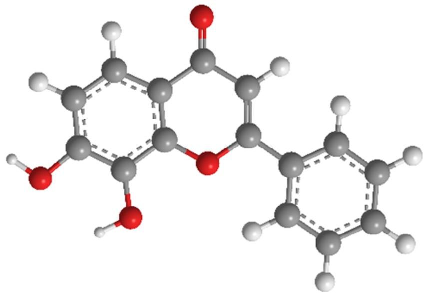

Figure 1: Molecular structure of the most active polyphenol (7,8-Dihydroxyflavone) against *Trypanosoma brucei rhodesiense*.

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The counteranion specific effects on interpolyelectrolyte neutralization in aqueous solutions and at surfaces

Utjecaj protuaniona na interpolilelektrolitnu neutralizaciju u vodenim otopinama i na površinama

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The interpolyelectrolyte neutralization of poly(diallyldimethylammonium)(PDADMAC) and (poly(N-ethyl-4-vinylpyridinium) (P4VPEt) cations with poly(styrene sulfonate) (PSS) anion in aqueous solutions of binary sodium salts was studied by means of dynamic light scattering (DLS), microcalorimetry, spectrophotometry and quartz crystal microbalance with dissipation monitoring (QCM-D). The reactions upon stepwise titrant to titrand addition in solution proceeded as described by Fuoss and Sadek [1]. At first, charged primary (the excess of titrand monomers at surface) and then secondary complexes (the excess of titrant monomers at surface) were being formed, whose coalescence resulted with precipitate formation. In contrast, sequential deposition of polycation-polyanion pairs was realized by exposing the SiO_2 surface to reactant solutions.

At lower salt concentrations, no influence of the counterion type could be noticed. The insoluble, metastable polyelectrolyte complexes formed in solution, contained almost equal amounts of oppositely charged monomers and the multilayer thickness was only weakly influenced by the type of the salt present. The anion-specific aggregation and more pronounced overcharging of positive polyelectrolyte nanocomplexes was observed at higher electrolyte concentrations. This led to asymmetric interpolyelectrolyte neutralization (*i.e.* direction dependent monomer ratio in metastable precipitates). The polycation affinity towards explored counteranions decreased in the order: $ClO_4^- \approx I^- > NO_3^- \approx Br^- > ClO_3^- > Cl^-$ for both PDADMAC and P4VPEt. The type of the anion introduced also effected the composition of the negative nano-complexes, obtained during titration of the polyanion with investigated polycation solutions, though the effect was much less pronounced than in the opposite direction. The reactions of investigated polyelectrolytes were predominantly (or entirely) entropically driven at ionic conditions explored. The thickness of P4VPEt-PSS and PDADMAC-PSS multilayers was in complete accord with the results of experiments in solution.

The equilibrium establishment in solutions containing equal amounts of oppositely charged PDADMAC-PSS and P4VPEt-PSS polyelectrolytes proceeded slowly and resulted with formation of virtually insoluble polysalts. Though being slow, the transformation of investigated metastable products into equilibrium ones, proceeded much faster than in the case of previously investigated poly(allylammonium)(PAH) - PSS pair [2].

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Selection of chemical conductivity model in the study of ion-association reaction

Odabir kemijskog modela provodnosti u istraživanju reakcije ionske asocijacije

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In this paper conductometric experimental data were processed using chemical models based on well-known equations Fuoss-Hsia, Lee-Wheaton and Pitts. These equations were derived from different ionic models and derived with various mathematical approximations so their accuracy and reliability was estimated by applying the same conductometric data. The models were compared and evaluated based on the results and their deviations from the experimental points as well as by obtained standard thermodynamic quantities of the association reaction. A three–parameter adjustment usually fails to provide uniform values for the association distance *R* [1]. So it is not possible to know the size and nature of the ion pair. Therefore, three fixed values for this parameter were chosen: R = a (a is the sum of the crystallographic radii), R = a + d (d is the diameter of the solvent molecule) and R = q (q is the Bjerrum critical distance) [2]. By repeated calculation three solutions for Λ_o and K_A were obtained at each temperature, and three sets of thermodynamic quantities of the association reaction were derived at 298,15 K. The most acceptable results are those that lead to the best agreement between the models. The best agreement between the models regarding all above mentioned quantities is obtained when R = q.

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Conformational analysis of β-lactamase inhibitors

Konformacijska analiza inhibitora β-laktamaza

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Due to the resistance, bacterial infections are now recognized as a major public health issue and an important social challenge [1]. Bacterial resistance to antibiotics causes a dramatic increase of mortality associated with infections, and also presents a significant economic burden. β-lactam antibiotics belong to the class of antibiotics with a broad spectrum of activity (*e.g.* penicillin derivatives). The mechanism of their bactericidal action includes inhibition of enzymes involved in the cell wall synthesis. Unfortunately, efficiency of these important antibiotics is significantly reduced by bacterial β-lactamases. In order to overcome β-lactamase-mediated resistance, β-lactamase inhibitors were introduced into clinical practice while the search for new ones is ongoing. These inhibitors greatly enhance the efficacy of β-lactam antibiotics in the treatment of serious infections.

Conformational landscape of compounds reflects molecular properties including reactivity [2]. It is consisting of all possible conformations (including conformers that correspond to a distinct local potential energy minimum and bioactive conformations). In order to identify the most important parts of the conformational landscape responsible for the activity, a full conformational analysis for a set of known β-lactamase inhibitors as well as for the new quinuclidinium based compounds will be performed. This analysis includes systematic variations of torsional angles around single bonds in molecules and calculation of electronic energies providing surface written in the form of the *n* dimensional data. Combinatorial algorithm will be used to determine all local minima (conformers) from these multidimensional surfaces and sets of conformers including their relative abundance *in vacuo* and in solution will be presented.

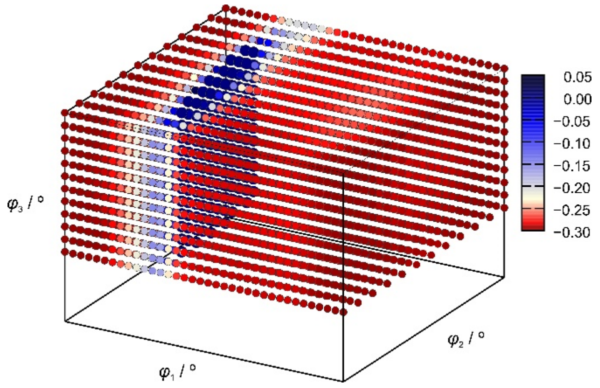

Figure 1: Conformational landscape of β-lactamase inhibitor sulbactam spanned by three torsional coordinates.

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Reaction mechanism of biologically relevant reactive aldehydes with different amino acids

Reakcijski mehanizam biološki relevantnih reaktivnih aldehida s različitim aminokiselinama

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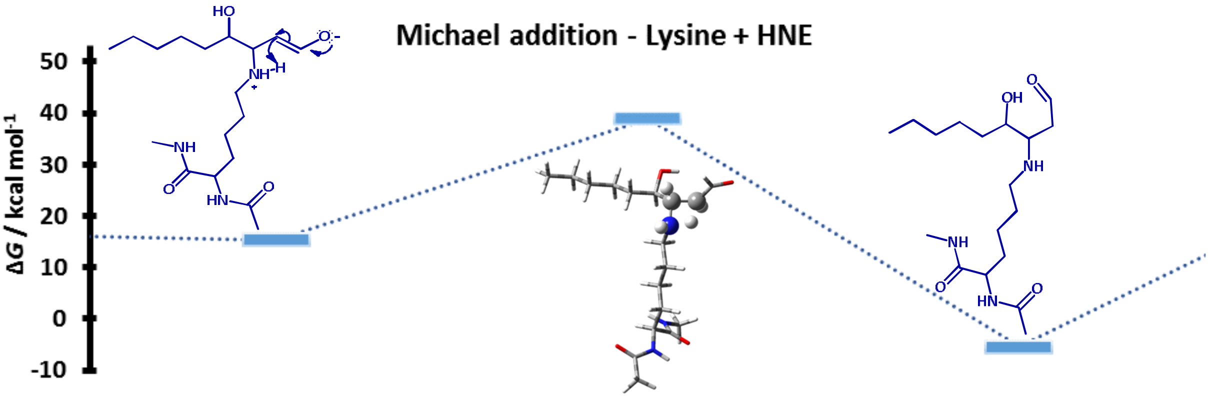
Reactive aldehydes, such as 4-hydroxy-2*E*-nonenal (HNE) and 4-oxo-2*E*-nonenal (ONE) are formed during oxidative stress in cellular membranes. They readily react with membrane proteins and lipids in phospholipid bilayers in turn modifying cellular function [1,2,3]. In order to understand the details of chemical reactions relevant in biological membranes, we performed model calculations in inert solvent dichloromethane using SMD/MP2/6–311++G(d,p)//B3LYP/6–31G(d) level of theory. In particular, we present a detailed reaction mechanism of reaction between HNE and ONE with four different amino acids (lysine, arginine, histidine and cysteine). Two different mechanisms between nucleophilic amino acids and electrophilic reactive aldehydes are identified - Michael addition and Schiff base formation. Michael addition mechanism has three steps: zwitterion formation, proton transfer and cyclization to a hemiacetal derivative resulting in thermodynamically stable products. On the other hand, Schiff base formation occurs in two steps with elimination of water as a rate determining step. Overall, free energy reaction barriers for Schiff base formation are larger as compared to those in Michaecl addition reaction. Interestingly, both HNE and ONE have similar free energy barriers in both reaction pathways with a single exception in Michael addition of ONE and arginine amino group, where a substantial decrease of free energy reaction barrier is predicted in agreement with experiments [4].



Potential energy profile of proton transfer in Michael addition

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Mechanism of the reaction between 5-fluorouracil and hypochlorous acid

Mehanizam reakcije između 5-fluorouracila i hipokloraste kiseline

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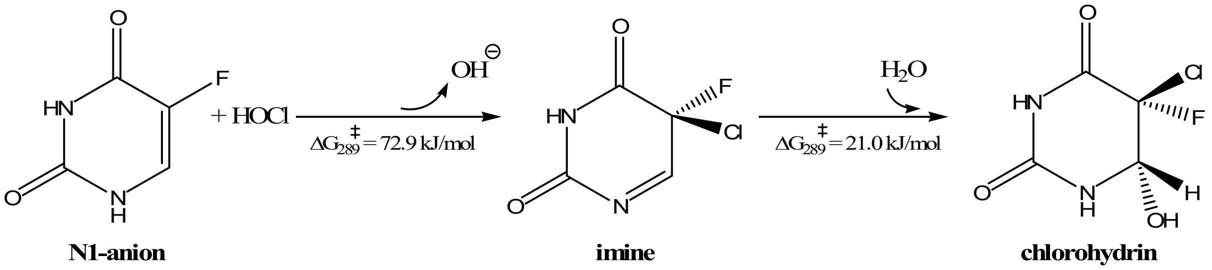
The reaction between hypochlorous acid (HOCl) and 5-fluorouracil (5-FU) is the fundamental process which can occur in activated neutrophils in cancer patients [1] or during chemical treatment of (hospital) wastewaters [2,3]. Therefore, the chlorination of 5-FU is of utmost importance in medicinal and environmental chemistry. In this work, it is experimentaly shown that the first product of 5-FU chlorination process is chlorohydrine, which undergoes further chlorination. Structural characteristics of products are determined using ^{1}H, ^{19}F and ^{13}C NMR spectroscopy. Reaction mechanism of chlorination cascade of 5-FU is investigated using quantum chemistry methods. M06–2X/6–311++G(3df,2pd)//M06–2X/6–311+G(d) level of theory is applied. The solvent effects are described by the implicit SMD solvation model, using the optimal number of the explicit water molecules. It is shown that 5-FU is chlorinated at the C5 position in the pyrimidine ring. The two-steps reaction in which the first reaction is the addition of Cl^{+} on N1 anion of 5-FU, yielding the imine intermediate, is determined as the most feasible mechanism. The free energy barrier which corresponds to the addition of chloronium ion is 72,9 kJ/mol. The addition of water on the imine intermediate ($\Delta_r G^{\ddagger}$ = 21,0 kJ/mol), which results in the chlorohydrine, is the second reaction step. The results obtained with quantum chemical methods are in agreement with experimental data. Standard bioassays are preformed in order to determine ecotoxicity of chlorination products of 5-FU. Results of these study play a key role in predicting the environmental fate of 5-FU.



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Microwave - assisted quaternization of various pyridine derivatives and their antibacterial activity

Reakcije kvaternizacije derivata piridina pod utjecajem mikrovalnog zračenja i njihova antibakterijska aktivnost

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Numerous pyridinium derivatives have been investigated concerning their biological and pharmacological activities. Their importance lies in their effective antimicrobial, antiviral, antihypertensive and immunostimulating activities. Some of pyridinium aldoxime derivatives are potential antidotes against organophosphate poisoning.

In this study, reactions of quaternization under microwave heating of pyridine, α-picoline, pyridine-4-aldoxyime, pyridine-2-aldoxime, nicotinamide, isonicotinamide and pyridoxal oxime with different electrophiles: 2-bromo-4'-nitroacetophenone, 2-amino-4-chloromethylthiazole hydrochloride, methyl iodide, 1,3-diiodopropane and 1,3-dibromopropane are reported. The synthesis yield by microwave dielectric heating is improved and reaction time shortened compared to conventional heating.

Some of the synthesized compounds were tested regarding their potential antibacterial activity against two Gram-positive and two Gram-negative bacteria. Antibacterial assessment showed a relatively high efficacy of 1-[2-(4-nitrophenyl)-2-oxoethyl]pyridinium bromide against G-positive and G-negative bacteria.

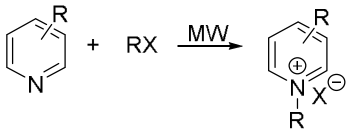

Figure 1: Quaternization of pyridine derivatives.

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Green synthesis of colloidal silver with honey and carob gum

"Zelena" sinteza koloidnog srebra pomoću meda i karuba gume

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As possible applications of colloidal silver as an effective antibacterial agents, there were found lot of methods of preparation of colloidal silver with natural reducing agents, harmless for human health, which often have a positive effect on human health.

The paper examined the possibility of preparation of colloidal silver by reduction of silver ions from the silver nitrate solution with honey and addition of carob gum as colloidal stabilizer.

For green synthesis of colloidal silver applied honey was from chub tree from Međimurje area, and as a protective agent carob gum was used, which stops the growth of colloidal silver, extracted from the carob seeds which originate from the Dalmatia area. Silver colloidals were prepared at different pH value (6.5-8.0) and were tested for Tyndall effect by passing the laser beam and UV-Vis spectrophotometer in the range of 300-600 nm. Spectrograms were compared with colloidal silver prepared with reduction of silver ions with sodium borohydride, which applied as standard sample. Colloidal silver prepared with green synthesis has pronounced Tyndall effect and UV-Vis spectrograms show the existence of a characteristic peak of the colloid, but with different intensities and different wavelengths depending on the concentration of the applied reducing agent.

Figure 1: Appearance of Tyndall effect in prepared colloid.

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Ferrocenoyl-adenine conjugate: Regioselectivity of the acylation reaction

Ferocenoil-adenin konjugati: Regioselektivnost reakcija acilacije

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The interest in ferrocene-modified purine and pyrimidine derivatives during the last two decades was motivated by the unique properties displayed by ferrocene, in particular its redox ability, membrane permeability and low toxicity. In ferrocenyl-nucleobases, the iron-containing ferrocenyl moiety mimics the ribose fragment of nucleosides [1]. Our research group has developed a one-step synthetic route to prepare ferocenoyl derivatives of nucleobases, the Fc–C=O fragment has been linked to "standard" pyrimidine bases. The ferrocenoyl units introduced into different *N*-positions of the pyrimidine ring systems and the regioselective of substitution in products has been confirmed by NMR spectroscopic analysis and quantum chemical calculations [2].

In continuation of our research on ferrocenyl-nucleobases with carbonyl groups as a linker, ferrocenoyl-adenine conjugate were synthesized. Most of the reactions result in the formation of a mixture of *N*7- and *N*9-substituted products (Figure 1). The ratio of these isomers depends on reaction conditions (solvents, temperature of deprotection and coupling reaction, base catalyst). The position of substitution in products and the reaction regioselectivity will be explored by spectroscopy methods (1D and 2D-NMR, FTIR) and quantum chemical calculations (DFT level of theory).

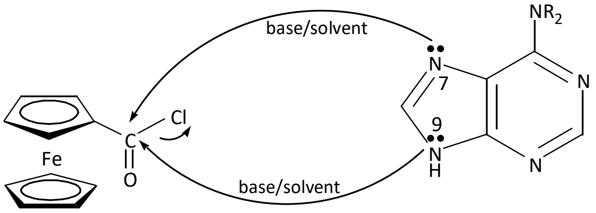

Figure 1: Formation of a mixture of *N*7- and *N*9-substituted products.

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Mechanochemical *N*-alkylation of imides

Mehanokemijska *N*-alkilacija imida

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Development of environmentally friendly organic reactions is an important goal of modern chemistry [1]. Among other, reduction of impact of chemical reactions on the environment could be achieved by developing methods for chemical synthesis that would reduce energy consumption. Recently, important progress has been made in development of solvent-free organic reactions, by using high-energy ball milling technique, which can enable more efficient and faster approach to known chemicals [2].

In the continuation of our interest in solid-state synthesis [3], we studied a mechanochemical *N*-alkylation reaction of imides with alkyl halogenides. Mono and bis (in the case when two amide nitrogen sites were available for alkylation) alkylated products, were successfully synthesised in a rapid two-step procedure carried out in a single pot. Sequential milling procedure was shown to be advantageous in terms of use of smaller amounts of reagents. *Ex-situ* IR spectroscopy indicated that reaction proceeds through potassium salts of imides, formed *in situ* by neat grinding of imide with K_2CO_3 as a base, which further react with alkyl halides in liquid assisted grinding (LAG) to obtain corresponding *N*-alkylimides. Phthalimido protected amines prepared in this way were also employed in solvent-free Gabriel synthesis of primary amines, by using ethylene diamine as a safe replacement for hazardous hydrazine, typically used as a nucleophile in the deprotection step. *N*-benzylphthalimides derived from reaction of phthalimide with various benzyl bromides were efficiently transformed to corresponding benzyl amines.

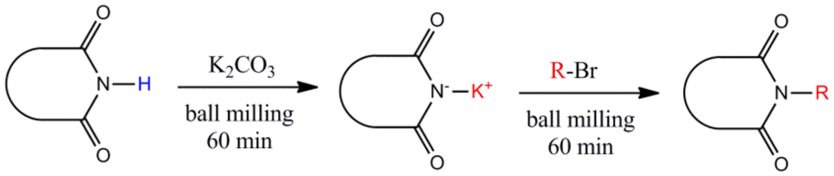

Figure 1: Two-step one-pot *N*-alkylation of imides in ball mill.

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The influence of *N*-heterocyclic carbene ligand on the properties of ruthenium olefin metathesis complexes

Utjecaj liganda *N*-heterocikličkog karbena na svojstva rutenij-olefin metateznih kompleksa

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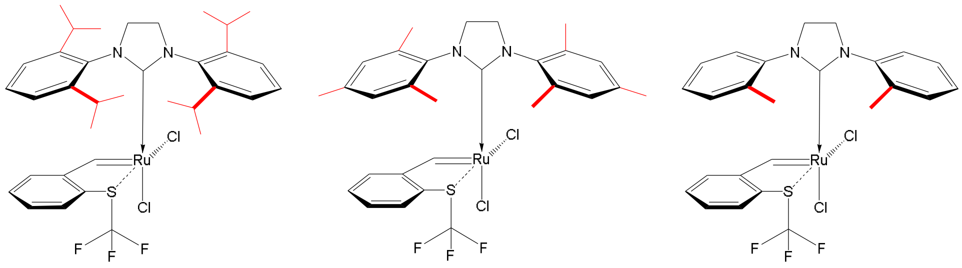
Olefin metathesis is an important and widespread C-C bond formation reaction. The ongoing increased use of this reaction may be directly attributed to the development of active, air stable ruthenium catalysts. A significant aspect of this area is the ability to control the initiation of the ruthenium catalyst for applications related to the preparation of thermosets, 3D printing, etc. In this regard, precatalysts chelated by sulfur ligands, which exhibit an uncommon *cis*-dichloro configuration and are completely latent at this configuration, have been shown to be readily activated by heat or light [1]. Activation of these catalysts is achieved by isomerization of the *cis* – dichloro configuration to the *trans* form [2]. Moreover, control over the activation rate could be tuned by changing the substituent on the sulfur atom either by *steric*, or *electronic* effects [3]. To date, **S-CF$_3$** is the most active complex among the sulfur chelated catalysts [4]. In an attempt to evaluate the effect of the *N*-hetreocyclic carbenes ligands on the stability and activity of S-chelated ruthenium metathesis catalysts, a series of complexes consisting *N*-hetreocyclic carbene ligands with different steric and electronic properties were synthesized (Figure 1). Herein, we present our results concerning the structures of the ruthenium complexes and their metathesis activity at ambient conditions and upon heat and UV irradiation.



NHC- IPr **NHC- Mes** **NHC- Tolyl**

Figure 1: Ruthenium complexes with different NHC ligands.

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Chiral Brønsted acid-catalyzed Friedel-Crafts addition of indoles to 3-hydroxyisoindolinoes

Adicija indola na 3-hidroksiisoindolinone katalizirana kiralnim Brønstedovim kiselinama

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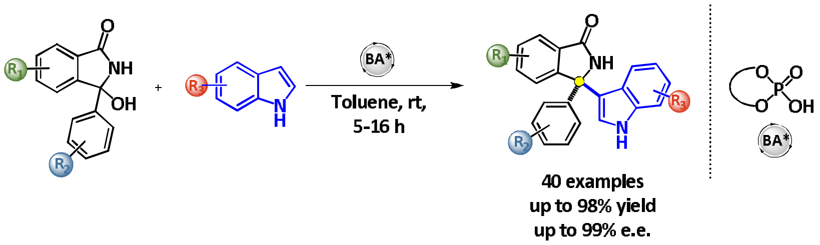
The 3,3-disubstituted isoindolin-1-one motif is common to a variety of compounds with potent biological activities. They have been established as anti-ischemic stroke agents, MDM2–p53 protein–protein, HIV–1 integrase, and protein–tyrosine phophatase inhibitors, as well as antimicrobial and antitumor agents [1-5]. Due to the presence of isoindolin-1-ones as key structural units in a number of synthetic and natural bioactive molecules, the methodology for the *asymmetric organocatalytic synthesis* of 3,3-disubstituted isoindolin-1-ones is underexplored. Rare examples include asymmetric organocatalytic hydrogenations [6], thiol additions [7], and metal–catalyzed arylations [8]. Here we report a chiral Brønsted acid-catalyzed Friedel-Crafts addition of indoles to *in situ* generated ketimines from 3-hydroxyisoindolinoes. The transformation is fast, proceeds at room temperature, and affords isoindolinone cores with quaternary carbon centres in excellent yields (up to 99 %) and enantioselectivities (up to 95:5 e.r.). Obtained products contain stereogenic carbon centre with three aromatic substituents, a common and valuable motif in natural compounds.



40 examples
up to 98% yield
up to 99% e.e.

Figure 1: Friedel-Crafts addition of indoles to *in situ* generated ketimines from 3-hydroxyisoindolinoes.

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Synthesis of enediyne peptidomimetics by Passerini reaction

Sinteza endiinskih peptidomimetika Passerinijevom reakcijom

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A significant area of organic chemistry is chemical synthesis performed through one–pot mode [1]. Such reactions, known as multicomponent reactions comprise three or more starting reagents and give a single product. The main advantage of multicomponent reactions are an easy access to libraries of complex and structurally diverse compounds starting from relatively simple components. Isocyanide–based multicomponent reactions, e.g. Passerini and Ugi reactions are of special importance, because they provide diverse peptide-like compounds. The Passerini reaction is one of the oldest multicomponent reaction used for the construction of α-acyloxyamides–depsipeptides. The reaction involves coupling of aldehyde, carboxylic acid and isocyanide in a nonpolar solvent [2].

We are interested in utilizing multicomponent reactions for the synthesis of conformationally constrained peptidomimetics. The enediyne structural motif (Figure 1) found in natural products with strong anticancer activity [3] was shown to induce β-turn or β-sheet conformation when incorporated into peptides. Therefore, we decided to use the Passerini reaction for the synthesis of a new class of enediyne-based depsipeptides. Enediyne aldehyde **1,** prepared by two consecutive Sonogashira reactions, was coupled with different isocyanides and carboxylic acid in dichloromethane on room temperature (Figure 1). Enediyne depsipeptides **2** were obtained in up to 92 % yields.

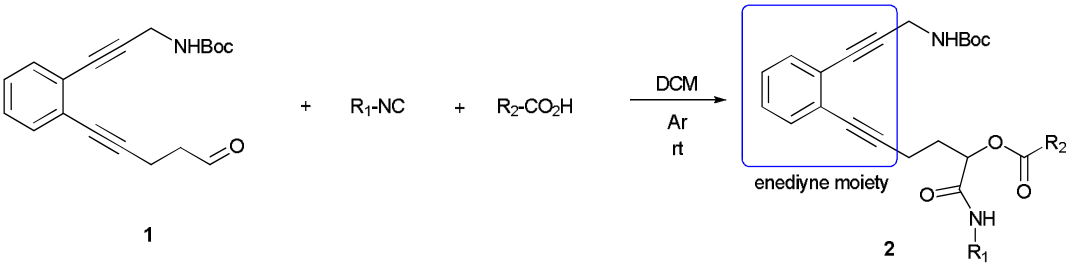

Figure 1: Multicomponent synthesis of enediyne-based peptidomimetics.

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Synthesis of enantiopure 3,5-disubstituted hydantoins *via* transformation of β-lactam ureas

Sinteza enantiomerno čistih 3,5-disupstituiranih hidantoina transformacijom β-laktamskih urea

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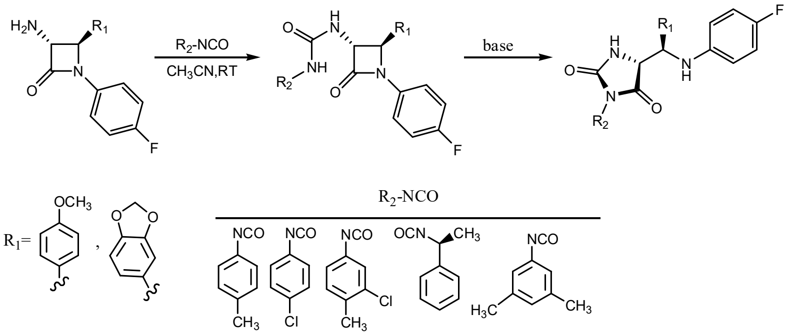
Hydantoins are an important class of heterocyclic compounds, and they can often be found as a structural motif in various drugs and natural compounds [1]. Hydantoin ring is found in biologically active marine alkaloids isolated from different marine organisms [2]. In addition, optically pure hydantoins are used as chiral auxiliaries in stereoselective synthesis and as metal ligands in catalysis [3].

In conducted research the 3,5-disubstituted hydantoins are prepared from enantiomerically pure β-lactam ureas (Scheme 1). In the first step, enantiomerically pure *trans*-3-amino-β-lactams in reaction with structurally different isocyanates are converted into *trans*-3-amino-β-lactam ureas (up to 99% ee, and 90% yield). In the next step preparation of 5-substituted hydantoins is carried out by an intramolecular transformation of *trans*-3-amino-β-lactam ureas. The conversion is carried out in methanol in the presence of different bases (K_2CO_3, NaOMe, NaH).

Special attention was paid to the stereochemistry during transformation of *trans*-3-amino-β-lactam ureas to corresponding hydantoins with respect to the 5- position of hydantoin on which racemization easily occur. The racemization is largely dependent on the reaction conditions. The advantage of the proposed method compared to the synthesis from derivatives of α-amino acids is ability to introduce an additional chiral center on the side chain, and the use of mild reaction conditions.



Scheme 1

References

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Ferrocene-containing mannosides as inhibitors of E. coli adhesion

Ferocenski manozidi kao inhibitori adhezije *E. coli*

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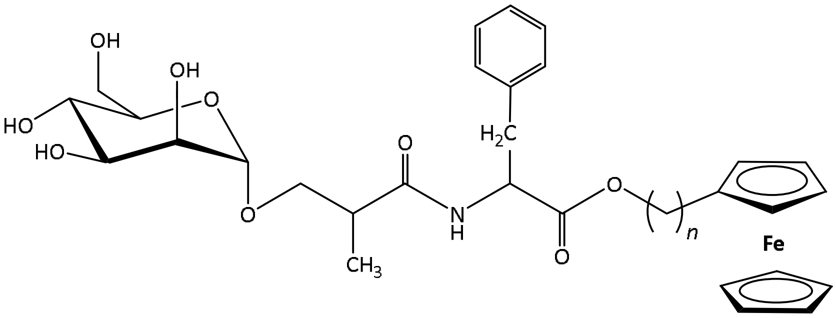
E. coli adhesion to the bladder epithelium is mediated through recognition of the tissue-surface mannosylated proteins with bacterial lectin FimH. The inhibition of this recognition-dependent interaction has been recognized as a promising strategy for the development of an anti-adhesion therapy. The mannosides with either aryl- or elongated alkyl-functionalized aglycon portions have been shown to be potent inhibitors of FimH-mediated adhesion [1].

So far, we have synthesized and tested two types of mannose-containing ferrocenes, which differ according to the type of the bonding between glycon and aglycon portions (the carbohydrate and organometallic moieties were connected *via* chiral linker through amide or ester bond) and the length of the constitutive alkyl chain (n = 0-5)[2-4]. The bioconjugate with butyl spacer and amide linkage has proved as the most efficient ferrocene-containing inhibitor of hemagglutination.

Herein, we present the synthesis and hemagglutination inhibition potential of compounds **1** and **2** containing amide groups and butyl or pentyl spacer. Considering that the hydrophobic entrance of the mannose binding site of FimH is flanked by aromatic tyrosine residues, the insertion of aromatic phenylalanine unit into the aglycon portion of the novel compounds is expected to improve the affinity of the ferrocene-containing mannosides for FimH.



1, $n = 4$
2, $n = 5$

Figure 1: Ferrocene-containing mannosides **1** and **2**

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Synthesis and conformational analysis of peptidomimetics composed of ferrocene-1,1'-diamine and natural amino acids

Sinteza i konformacijska analiza peptidomimetika sačinjenih iz ferocen-1,1'-diamina i prirodnih aminokiselina

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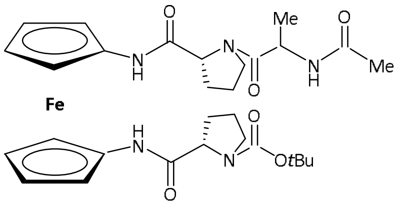
1,*n*-Disubstituted ferrocenes were established as molecular templates for the design of turns and β-sheet-like structures as the almost free rotating cyclopentadiene rings are separated by about 3.3 Å which is ideal for interstrand hydrogen bonding in their conjugates with natural amino acids or peptides. It was clearly demonstrated that hydrogen bond donating/accepting properties of turn-inducing ferrocene scaffolds regulate the hydrogen bonding patterning of the derived peptides: the 10-membered interstrand hydrogen-bonded rings were established in the conjugates of the amino acids or peptides with dicarbonyl-functionalized ferrocene core [1], the 12-membered rings were formed in their conjugates with -NH-Fn-CO- moiety [2], while conjugation with diamino-functionalized ferrocene lead to the 14-membered hydrogen-bonded rings (also labelled as two simultaneous 10-membered β-turns) in the corresponding symmetrically disubstituted conjugates [3].

Herein, we report the synthesis of orthogonally protected and desymmetrized peptides **1** and **2** composed of turn-nucleating ferrocene-1,1’-diamine unit and homo- or heterochiral amino acid sequences. The effects of the backbone chirality and *N*-terminal protecting group on the conformational properties of the novel peptidomimetics are explored by IR, NMR and CD spectroscopy. The spectroscopic studies were augmented with DFT calculations.



1 (Ac-L-Ala-L-Pro-NH-Fn-NH-L-Pro-Boc)

2 (Ac-D-Ala-L-Pro-NH-Fn-NH-L-Pro-Boc)

Figure 1: Orthogonally protected ferrocene peptides **1** and **2**.

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Synthesis and characterization of homo- and heteroannularly substituted ferrocenoyl-cytosine derivatives

Sinteza i karakterizacija homo- i heteroanularno supstituiranih derivata ferocenoil-citozina

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Pyrimidines and purines substituted by ferrocenyl moiety present interesting organometallic conjugates as their structures incorporate both biologically and electrochemically active components. The first syntheses of ferrocenyl-nucleobases were reported by Chen in 1980 [1,2].

In our previous study were prepared ferrocenoylated N1-pyrimidine nucleobases (uracil, thymine and 5-fluorouracil). The synthetic procedure to obtain exclusively the N1-regioisomer does not require any protection of the N3-position in the nucleobase. The nucleophilic addition of pyrimidine bases to the carbonyl group of FcCOCl proceeds by a concerted S_N2-like mechanism with the absence of the generally assumed tetrahedral intermediate [3].

This report will refer to the preparation procedure of homo- and heteroannularly substituted ferrocenoyl-cytosine derivatives. Regioselectivity of these reactions have been analyzed in details by NMR spectroscopy and quantum chemical calculations.

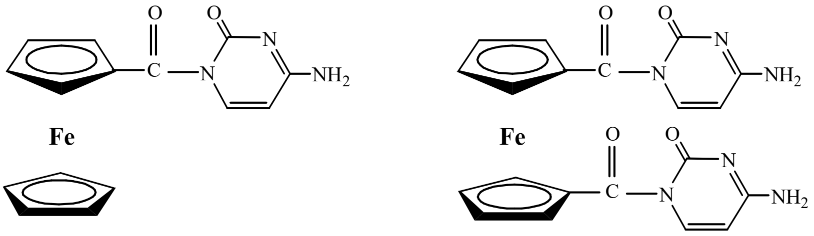

Figure 1: Homo- and heteroannularly N1-ferrocenyl substituted cytosine.

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Photochemistry of thiophene and pyridine derivatives of butadiene

Fotokemija tiofenskih i piridinskih derivata butadiena

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Through the years a detailed study of reactivity of stilbene and as continuation butadiene derivatives was conducted in our group. The energy that is needed for cycloaddition reactions to take place in these conjugated systems can be supplied by photochemical excitation [1,2] or thermal one [3,4]. These previously studied butadiene derivatives showed diverse behavior in excited state and gave new polycyclic structures as products. Products with bicyclo[3.2.1]octane skeleton were present in almost all of the irradiation experiments. These structures are widely present in a vast number of biologically active compounds [5] and are hard to obtain in ground state chemistry.

Research was further extended to include new heterocyclic rings into the butadiene structure. Thiophene and pyridine rings were included, and new compound were successfully synthesized and characterized (Figure 1).

Compounds **1** and **2** were investigated and in excited state gave polycyclic products that were completely characterized. As the yields of the transformations were good and all of the polycyclic products were isolated and characterized the next step was to determine the quantum yields for these cycloaddition reactions.

To determine the quantum yields chemical actinometry was utilized. We used ferrioxalate actinometer as well as potassium iodide actinometer to gain valid reproducible results. In order to conduct these measurements GC-MS and HPLC-MS systems were used.

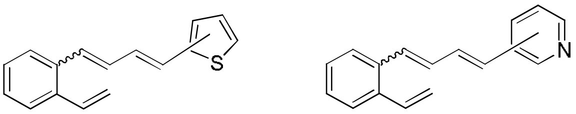

Figure 1: Molecular structure of 2/3-[4-(2-vinylphenyl)buta-1,3-dienyl]thiophene (**1**) and 3/4-[4-(2-vinylphenyl)buta-1,3-dienyl]pyridine (**2**).

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Synthesis of new tripyridyl amphiphilic porphyrins for PDT *via* methylation and *N*-oxidation of 3- and 4-pyridyl groups

Sinteza novih tripiridilnih amfipatskih porfirina za PDT metiliranjem i *N*-oksidacijom 3- i 4-piridilnih skupina

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Photosensitisers are compounds whose activation by light of a specific wavelength can lead to the destruction of tumour cells and of various microorganisms through oxidative stress. Among the most common photosensitisers are compounds with porphyrin structure that can generate cytotoxic singlet oxygen and other reactive oxygen species, as well as release fluorescence. Therefore, they have significant theranostics potential with possible applications in photodynamic therapy (PDT) and in diagnostics for molecular imaging [1]. Porphyrin photosensitisers selectively accumulate in tumour tissue thanks to the mechanism known as the "enhanced permeability and retention effects", and it has been suggested that compounds with amphiphilic properties could facilitate this process [2,3].

Recently we reported the synthesis of 5-(4-octadecanamidophenyl)-10,15,20-tris(*N*-methylpyridinium-3-yl)porphyrin trichloride and evaluation of *in vitro* PDT activity of this amphiphilic porphyrin on HeLa cells [4]. The lipophilic part of the molecule proved to be important for the overall PDT activity, but also for the indicated bifunctional activity. Therefore, in order to investigate further the effect of the lipophilic moiety, several amphiphilic porphyrins, with saturated and unsaturated long alkyl chain (C18), were prepared. The amphiphilicity was achieved in the last synthetic step by methylation of 3- and 4-pyridyl groups. Another series of amphiphilic zwitterionic porphyrins was prepared by *N*-oxidation of 3- and 4-pyridyl groups. Porphyrin *N*-oxides have been previously investigated as potential hypoxia-selective agents [5], but derivatives with long alkyl chains have not yet been reported. All prepared porphyrins were characterised by ^{1}H and ^{13}C NMR one- and two-dimensional spectroscopy, ESI-Q-TOF and MALDI-TOF/TOF mass spectrometry, and their photophysical properties evaluated by UV-visible and fluorescence spectroscopy. Their synthesis will be described, and the distinct features of their characterisations will be presented and discussed.

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Mechanochemical synthesis of aryl ketones

Mehanokemijska sinteza arilnih ketona

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Friedel-Crafts (FC) acylation is industrially important transformation of aromatics to aryl ketones for preparation of for chemical feedstock, synthetic intermediates and fine chemicals [1]. Environmentally more friendly, solvent-free mechanochemical [2,3] reaction conditions for the preparation of ketone functionalized aromatics were developed (Scheme 1). Reaction parameters such as catalyst, time, ratio of reagents, milling support, frequency of milling, size and number of milling balls, solvents for liquid assisted grinding were studied to establish the optimal reaction conditions [4]. The scope of the reaction was explored by employment of different aromatic substrates in combination with anhydrides and acyl halides. It was established that FC reactive aromatics could be effectively functionalized by FC acylations carried out in ball-milling conditions without the presence of solvent. Reaction mechanism was also studied by *in situ* Raman spectroscopy [5].

Scheme 1: FC acylations by ball milling.

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Choline chloride based deep eutectic solvent as a convenient solvent for synthesis of Schiff bases

Eutektičko otapalo na bazi kolin-klorida kao pogodan medij za sintezu Schiffovih baza

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Coumarins are a class of compounds widely distributed in plant kingdom, but lots of synthetic work has been done on them in the last few decades as well. Most synthetic routes utilize various toxic solvents and catalysts, leaving a significant environmental impact and tendency today is to reduce such negative impact whenever possible. For such purpose, deep eutectic solvents are often used. Deep eutectic are often used as green media for many synthetic routes and are often characterized as environmentally friendly [1-3]. Their application in organic synthesis and extraction, as well as an extensive analysis of their properties were described in some recent reviews [1-6]. The aim of our work was to synthesize a novel coumarinyl Schiff bases utilizing choline chloride/malonic acid based deep eutectic solvent as reaction media. Previously, a series of Schiff bases was synthesized [7] in our laboratory conventionally, but we have noticed their formation when deep eutectic solvents are applied. No need for specific catalyst, like acetic acid which is often used in these kinds of reactions, was noticed, since this eutectic solvent acted as a catalyst as well. Not only did we get a novel compounds, we applied an environmentally friendly approach, utilizing a solvent made of biodegradable components, with low toxicity and vapor pressure which can be easily recycled and reused.

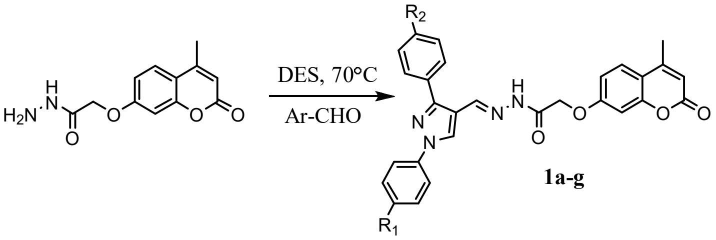

Figure 1: Synthesis of Schiff bases in deep eutectic solvent (a) R_1-Cl, R_2-NO_2; b) R_1-F, R_2-Cl; c) R_1-CH_3, R_2-Cl; d) R_1- CH_3, R_2-Br; e) R_1-CH_3, R_2-OCH_3; f) R_1-Cl, R_2-I; g) R_1- CH_3, R_2-I).

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Application of new chiral phospine Rh(I) complexes in enantioselective catalytic hydrogenation reactions

Primjena novih kiralnih fosfinskih kompleksa Rh(I) u reakcijama katalitičkog enantioselektivnog hidrogeniranja

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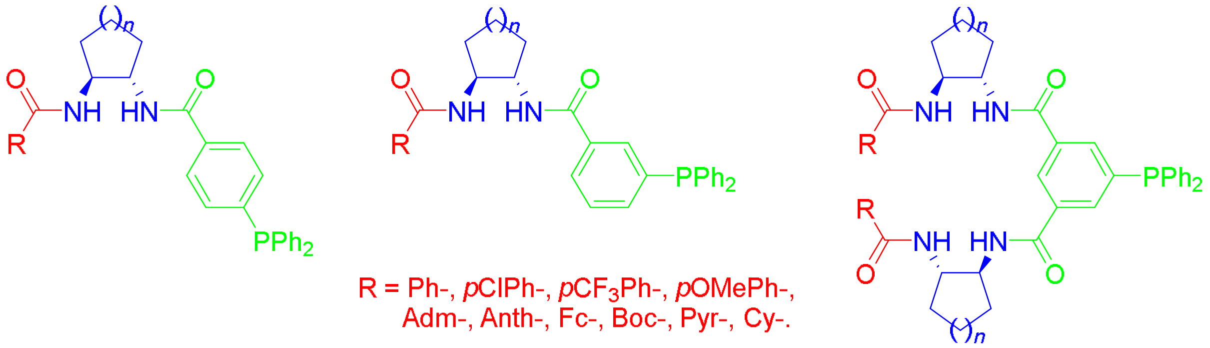
Asymmetric catalysis is of crucial importance in science and industry. Traditionally, chiral induction in asymmetric catalysis is achieved by the vicinity of a chiral source and the reaction center. However, we have shown that chiral induction can also be achieved by a distant source of chirality; a maximal selectivity of 84 % ee was achieved by using aminoacid based phosphine ligands [1]. In our quest to increase the enantioselectivity we have shifted our attention from chiral aminoacids to chiral cyclic aliphatic diamines, since they are know to induce very high selectivity [2].

We have prepared a series of novel monodentate ligands comprised of three building blocks (Figure 1). The metal binding building block is a triphenylphospine with different substitution patterns: *para-*, *meta-* and *dimeta-*. The next building block is a disubstituted chiral diamine, cyclohexanediamine or cyclopentanediamine. Finally, the last building block is designed to study the steric and electronic influence on selectivity in catalysis by incorporating different voluminous substituents or differently *para*-substituted benzoic acids. Rhodium complexes of the ligands were generated *in situ* and used as catalysts in asymmetric hydrogenation of model substrates, acetamidoacrylate **S1** and acetamido-cinnamate **S2**. The best result was achieved with the anthracene cyclohexanediamine *m*-phospine ligand which gave 91 % ee for **S1** and 96 % ee for **S2**. Further plans are to test our ligands on a wider range of model and commercially important substrates.



R = Ph-, *p*ClPh-, *p*CF_3Ph-, *p*OMePh-, Adm-, Anth-, Fc-, Boc-, Pyr-, Cy-.

Figure 1: General ligand structure.

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Stereochemistry of hexacoordinated transition metal complexes with iminodiacetamide ligands

Stereokemija heksakoordiniranih kompleksa prijelaznih metala s iminodiacetamidnim ligandima

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Hexacoordinated transition metal complexes of tridentate ligands **L** with **ML_2** stoichiometry can form several geometrical isomers: meridional, *trans*-facial, and delta or lambda *cis*-facial. The configuration of isomers is affected by steric and electronic properties of the ligands and coordinating ability of the counterions [1]. Derivatives of iminodiacetamide (imda) are studied as tridentate ligands and in all known complexes the iminodiacetamides act as O,N,O' chelators. The Cambridge Structural Database (CSD) contains crystallographic data for less than 20 metal complexes with iminodiacetamide or its *N*-substituted derivatives. All reported complexes of *N*-substituted imda derivatives are *trans*-facial isomers [2].

In this communication we present the synthesis and characterization of phenyl iminodiacetamide derivatives (**L1**-**L6**) and their **ML_2** complexes with transition metals, **M** = Zn(II), Co(II), Ni(II) or Cd(II). The amide nitrogen atoms were substituted with phenyl groups in order to increase their solubility in common organic solvents and enable characterization of complexes in solution. To test the effect of the ligands electronic properties on the complex configuration, ligands were prepared with electron donor or electron withdrawing groups on the *para*-position of phenyl rings (R). The complexes were characterized in solid state (single crystal X-ray diffraction, IR, TG) and in solution (^{1}H and ^{13}C NMR, IR, UV-Vis).

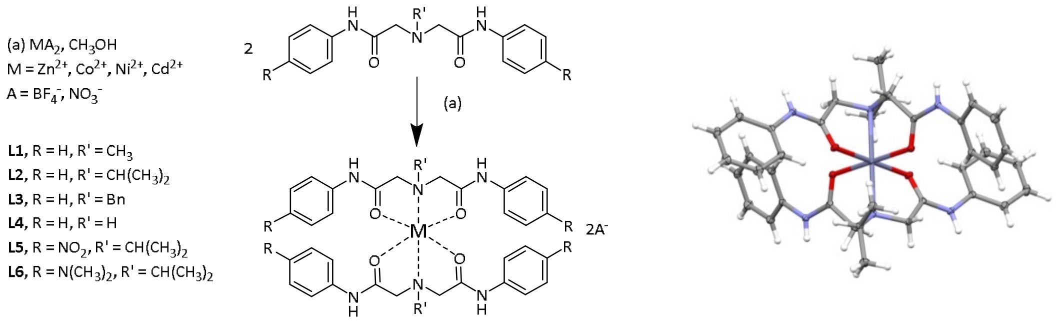

Figure 1: Synthesis of transition metal complexes (left) and crystal structure of *trans*-fac Zn(**L2**)$_2$ complex (right).

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Synthesis and conformational study of desmuramyl di-, tri- and tetrapeptides

Sinteza i konformacijska analiza desmuramil di-, tri- i tetrapeptida

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Muramyldipeptide (MDP), *N*-acetylmuramyl-L-alanyl-D-isoglutamine, is the smallest structural unit of peptidoglycans displaying immunostimulating (adjuvant) activity. Structure-activity relationship studies of muropeptides suggest that the desmuramyl dipeptide part (L-Ala-D-isoGln) is responsible for the adjuvant activity [1]. Primary structure modifications as well as their conformational changes may be responsible for changes in biological activity of peptides. Increase of lipophilicity in the N- and C- terminus of the dipeptide, such as introduced adamantly group at the N-terminal amino acid, can significantly improve pharmacological properties of desmuramyl peptides.

Synthesis as well as conformational computational and experimental NMR analysis of corresponding desmuramyl dipeptide, tripeptide and tetrapeptide derivatives in zwitterionic and non-zwitterionic form was performed. L-Alanyl-D-isoglutamine was obtained by the removal of N- and C- protecting groups from commercially available dipeptide. Tri- and tetrapeptides were obtained by consecutive attachment of corresponding amino acids (1-adamantyl-glycine and serine) to desmuramyl dipeptide, using optimized coupling methodology (EDC/HOBt coupling reagents in the mixture of solvents CH_2Cl_2/1,4-dioxane 1:1). (*S*)-1-adamantyl-glycyl-L-alanyl-D-isoglutamine was prepared in four synthetic steps using more efficient method than previously reported [2,3].

The most stable conformers of synthesized peptides were determined. A systematic conformational space search was performed by means of molecular and quantum mechanical study in solution, which was modelled as a polarizable continuum. Hydrogen bonds were determined by using the QTAIM population analysis method. Calculated conformers were compared with those obtained in solution by NMR study in deuterated water and DMSO.

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Amine-modified mesoporous silica-carbon composites with periodic composition for carbon dioxide capture

Mezoporozni kompoziti silika-ugljik modificirani aminom s periodičkim sastavom za hvatanje ugljikovog dioksida

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Carbon dioxide emissions from fossil fuel combustion have attracted more attention due to its important impact on the atmosphere, such as air pollution and global warming. Several methods have been proposed to capture CO_2. Adsorption is considered to be one of the most promising technologies due to low power consumption, relatively low cost and applicability in wide range of temperatures and pressures. The success of this approach depends on the development of efficient adsorbent with high selectivity and adsorption capacity for CO_2. Several materials have been used for this purpose such as porous adsorbents, mesostructured sorbents, zeolites, metal oxides, metal-organic frameworks. Proper modification of the sorbents can potentially enhance the sorption by chemisorption interaction with CO_2. Mesoporous carbon adsorbents are widely used for CO_2 capture due to their accessibility, low cost and low sensitivity to moisture. Recent investigations have shown that not only the pore volume determine the activity of sorption, but also the sizes of the pores. However, the preparation of the mesoporous carbon materials with large pores is difficult due to shrinkage of the structure during the synthesis, so silica can serve as a template for stabilization of the structure. Important sorption parameters can be adjusted during synthesis of silica-carbon composites by varying the ratio between silica and carbon content before the amine modification.

Mesostructured support composites with periodic compositions Si:C were synthesized by soft template approach and modified by impregnation using TEPA as amine-modifying agent. The prepared amine-modified silica-carbon composites were characterized by TG, XRD, low temperature N_2- adsorption, TEM, FTIR, XPS. The CO_2 sorption isotherms were measured at three different temperatures, adsorption capacities were investigated and the heats of adsorption were determined. The carbon dioxide capture from flue gas was tested, as well as the ability for regeneration. Although the specific surface areas, pore volumes and pore diameters of the amine-modified composites are smaller than those of the unmodified supports the adsorption capacity for carbon dioxide is improved because of the contribution of the chemisorption along with the physical adsorption. The amine-modified carbon-containing materials exhibit better performance as sorbents for carbon dioxide than the modified silica. Improved carbon dioxide capture with increasing the carbon content in the amine-silica–carbon composites is observed.

Acknowledgements

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Synthesis of *N*-heterocycles by the three-component Ugi reaction

Sinteza *N*-heterocikla trokomponentnom Ugijevom reakcijom

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Multicomponent reactions (MCRs) have attracted significant attention in organic chemistry because of their exceptional ability to implement a wide range of components in one-pot reactions, affording numerous, very diverse products. MCRs are usually very useful in the synthesis of natural products and diverse heterocyclic scaffolds. In particular, isocyanide-based MCRs (IMCRs) are attractive in terms of functional group tolerance and the high levels of chemo-, regio-, and stereoselectivity obtained [1]. Among them, the Ugi four-component reaction (U-4CR) which combines a carbonyl compound, an amine, a carboxylic acid, and an isonitrile is the most prominent. Of particular interest are intramolecular Ugi reactions where one component is a bifunctional building block. These procedures are an efficient tool for the synthesis of nitrogen-containing heterocycles, a versatile building blocks for stereoselective syntheses. On the other hand, these Ugi reaction products possess noteworthy pharmacological activities [2,3].

In the course of our research, we are interested in utilizing α-amino acids and their derivatives as bifunctional components in the Ugi three-component reaction. Herein, we report the succesful use of two different bifunctional amino acid-derived components, Fmoc-Lys-CHO and H-Glu-OMe. In the first case, lysine-derived amino aldehyde undergo intramolecular reaction yielding imine liable to isocyanide addition. In the second set of Ugi reactions, H-Glu-OMe is used, which acts as an amine and a carboxylic acid component. In both cases final products were obtained in moderate to high yields and have the potential for multiple postmodifications.

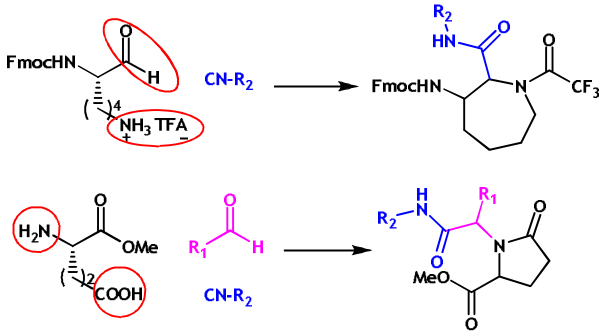

Figure 1: Three-component Ugi reactions utilizing bifunctional α-amino acids.

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New aniline photocage for carboxylic acids

Nova anilinska fotouklonjiva zaštitna skupina za karboksilne kiseline

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Photocleavable protecting groups (PPGs, photocages) are extensively used in chemical and biological sciences. It was shown that they can be used for light-controlled small molecule release (NO, H_2S, CO, HNO) in biological systems [1], photocontrolled targeted drug delivery [2] and in molecular imaging and cell biology [3].

Very important area for application of PPGs is organic synthesis. Typical protecting groups used in organic synthesis (e.g. Boc, Fmoc) require some specific reagents/conditions for their removal. On the other hand, for removal of PPGs only iradiation is required (usually UV), which is big advantage in comparison with the standard protecting groups. Three main classes of PPGs described in the literature are based on: 2-nitrobenzyl, carbonyl or benzyl moieties [4]. However, these PPGs suffer from some limitations in their application, e. g. for 2-nitrobenzylalcohols the decaging reaction is slow. Therefore, research for new PPGs is very important topic of current research in organic photochemistry.

Wang *et al.* have recently reported an interesting example of photocage for alcohols, based on *m*-hydroxyaniline ethers [5]. We decided to further develop this type of protecting group and expand their application for the protection of carboxylic acids. A systematic study of photochemical reactivity was conducted on *o*-, *m*- and *p*-substituted aniline-based PPGs. We have found out that a range of structurally different carboxylic acids can be easily converted to *o*-hydroxymehtylaniline esters ih high yield. The photodeprotection was accomplished under mild conditions (aqueous CH_3CN), using 300 nm light. After the photodecageing, only aqueous workup (extraction) was required to obtain pure acid, without the need for the product chromatographic purification or crystallization. Furthermore, we have demonstrated that aniline alcohol can be regenerated from the photodeprotection reaction and reused.

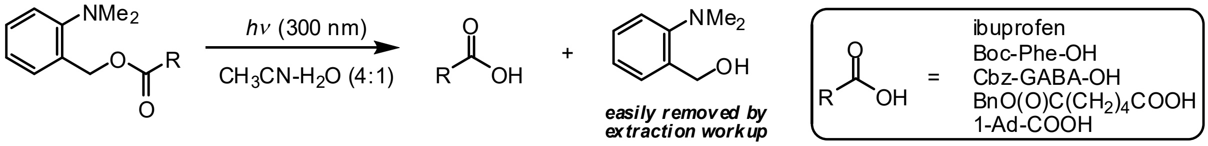

Figure 1: Photodeprotection of carboxylic acid protected with new aniline photocage.

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Using click chemistry for the synthesis of peptidomimetic immunomodulators

Korištenje klik kemije za sintezu peptidomimetskih imunomodulatora

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Click chemistry refers to fast reactions that give very high chemical yields, use easily removable solvents and mild conditions while byproducts are easily removable as well [1]. Staudinger ligation, copper free and copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) have been increasingly used for fluorescent labeling of biomolecules as well as for the synthesis of small biologically active compounds [2].

Peptidogycans are polymeric components of bacterial cell walls and their monomers stimulate strong immune response. It has been shown that a minimal structural unit of peptidoglycan monomer showing a significant adjuvant activity is muramyldipeptide (MurNAc-L-Ala-D-*iso*Gln, MDP) [3]. The aim of this work was the synthesis of mannosylated derivatives of desmuramylpeptides, MDP analogues lacking the original carbohydrate moiety, for further biological evaluation. Mannose moiety serves for targeting the mannose receptors on surface of the immune cells thereby enhancing the specificity of interactions with the cells thus affecting the type of immune response [4]. In order to improve the lipophilicity of mannosylated desmuramyldipeptides, some of which have been previously shown to improve the pharmacological properties of MDP, the peptide part was conjugated with the adamantyl moiety over a triazole ring. Adamantyl substituted triazoles were prepared *via* CuAAC, conjugated with desmuramyldipeptides and linked to mannose *via* different short linkers to improve flexibility and accessibility of mannose towards mannose receptors.

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Acknowledgements

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Sythesis of novel lipophilic mannosides and their complexation with β-cyclodextrin

Sinteza novih lipofilnih manozida i njihovo kompleksiranje s β-ciklodekstrinom

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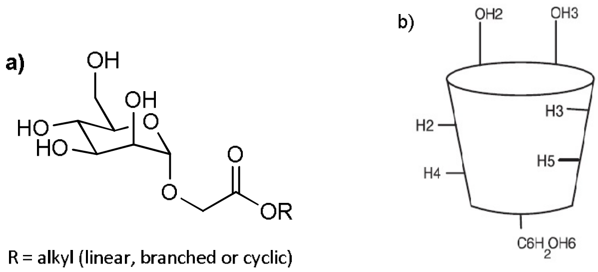
Cyclodextrines (CDs) have been studied due to their ability to host wide variety of hydrophobic compounds in water and increase their solubility in water, hence bioavailability [1]. Recently, we reported the synthesis of adamantyl glycosides and the thermodynamic parameters of their complexation with β-CD in water [2] Our present investigations have been directed to the complexation of amphiphilic glycosides, namely, adamant-1-yl, cyclohexyl and benzyl 2-(α-D-mannopyranosyloxy)acetates with β-CD in water and in organic solvent.

In this work we present the synthesis of novel amphiphilic mannosylated derivatives of acetic acid with different alkyl parts (Figure 1). The esters were prepared by the reaction of acetylated mannopyranose and corresponding esters of bromoacetic acid with linear, branched or cyclic alkyl parts. Their complexation with β-CD was studied by means of titration calorimetry and NMR spectroscopy. Solvents used in calorimetric experiments were strongly hydrogen bonded (water, alcohols) in which the inclusion of similar guests in β-CD is still largely unexplored. The thermodynamic parameters of complexation (reaction enthalpies, standard reaction entropies, binding constants) were determined. Obtained results provide a deeper insight in correlations between guest structure and its complexation thermodynamics in examined solvents.



R = alkyl (linear, branched or cyclic)

Figure 1: a) general structure of guest molecules and b) simplified presentation of β-cyclodextrin cavity.

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Acknowledgments

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Metal-ion-assisted synthesis of cyclic homopeptides

Sinteza cikličkih homopeptida potpomognuta metalnim ionima

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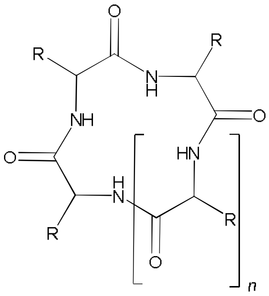
In the recent years cyclic peptides have attracted attention since they find applications in many fields from drug discovery to nanomaterials. These compounds are difficult to prepare due to the fact that the activated peptide must adopt an entropically disfavoured conformation before forming the desired product [1]. The most important factor for successful peptide macrocyclization is ring size. Peptides that contain less than seven aminoacids are troublesome to cyclize [2]. In this work we describe the synthesis of small cyclic homopeptides containig 4-6 aminoacids.

Cyclic peptides are also known as versatile ion-binders [3] but their binding affinities are often reduced by the inadequate orientation of amide functional groups. To overcome these problems, cyclopeptides will be conjugated to a molecules with rigid geometry [4], such as calixarenes. Cyclic homolysine and cyclic homoserine will be bind to calixarenes exploiting functional groups on peptide's side chain,. Influence of the lenght of side chains on affinities of this conjugates towards different anions will be investigated.

Linear precursors were sinthesized using standard solution phase peptide synthesis and HOBt, HBTU as a coupling reagents. A three-dimensional orthogonal protection scheme was required to build the linear peptides, to deprotect the *N*- and *C*-termini and to cyclize them in a head-to-tail fashion. To promote the cyclization, different alkali metal ions were used depending on the size of the desired cyclic peptide. These ions coordinate amidic oxygen atoms along the chain forcing the linear peptide to form a strong turn structure and to bring the *N*- and *C*-termini closer, allowing in that way cyclization to occur.



R: CH_2OtBu, $CH_2CH_2CH_2CH_2NHBoc$, n: 1,2,3

Figure 1: Structure of cyclic homopeptides.

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Passerini reaction of carbohydrate derivatives

Derivati ugljikohidrata u Passerinijevim reakcijama

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Carbohydrates represent the most abundant class of natural products with distinctive role in different biological processes and they are highly valuable pool of chiral molecular scaffolds [1]. Multicomponent reactions (MCRs) offer an attractive one-pot strategy for generating a library of highly functionalized and complex organic compounds in modern synthetic chemistry. Utilization of carbohydrates and their derivatives in MCRs is based on their polyfunctional character and stereochemical diversity [2,3]. The Passerini reaction is an isonitrile-based MCR that yields α-acyloxy carboxamides from an aldehyde, an isonitrile, and a carboxylic acid.

Our initial efforts were directed toward exploitation of 2-isocyanoglucosyl derivative in the Passerini reaction with various aldehydes and carboxylic acids. Next, we used for the first time a highly strained D-fructose-derived aldehyde in the Passerini reaction with commercially available and sugar-derived isocyanides and notices a highly diastereoselective character of this reaction.

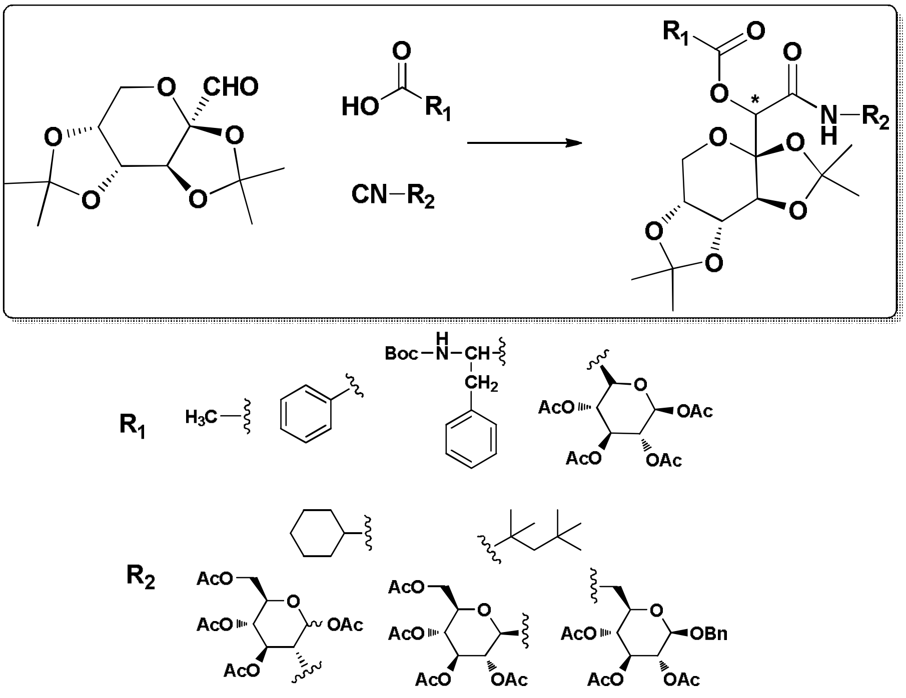

Figure 1: Passerini reaction.

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Plasticizer influence on the anionic surfactant sensor response

Utjecaj plastifikatora na karakteristike odgovora senzora za anionske tenzide

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The surfactant sensitive electrodes are based on direct potentiomery and usualy based on PVC liquid membrane. PVC liquid membrane consists of the ionophore, lipophilic ionic sites, lipophilic salts (as electroactive compounds) and plasticizer (additive with a low molar mass). Plasticizer makes the rigid PVC matrix more softer and flexible. Plasticizer offers some additional benefits to the PVC sensing membrane; it disolves ionophore and enhances the species mobility inside the membrane. The plasticizer, as a part of PVC sensing membrane, should possess some important properties; 1) it should be insoluble in water, 2) it should prevent the ionophore leakage to the analyte, 3) it should be inert to ion exchange. The typical weight ratio of PVC and plasticizer in the sensing membrane is 1:2.

The aim of this work was to investigate the influence of six different plasticizers on the surfactant sensor response. Six different plasticizers, 2-nitrophenyl-octyl-ether (P1), bis(2-ethylhexyl) phthalate (P2), bis (2-ethylhexyl) sebacate (P3), 2-nitrophenyl phenyl ether (P4), dibutyl phthalate (P5) and dibutyl sebacate (P6), were incorporated into the PVC-based surfactant sensors, and their influence on the determination of anionic surfactants (sodium laurylsulfate (SDS) and sodium dodecylbenzenesulfonate (DBS)) was investigated. The sensors containing plasticizers P1 - P5 exhibited a sub-Nernstian slope value ranged from -46.4 to -54.8 (mV/decade of activity), while P6 exhibited a super-Nernstian slope value -66.3 (mV/decade of activity). Due to the best analytical performances and its low price, the sensor containing dibutyl phthalate (P5) presented the best properites on the response characteristics of the surfactant sensor. The sensor was tested on real commercial samples.

Acknowledgements
This work was supported by the Croatian Science Foundation under the project IP-11-2013.

Croatian chemical and laboratory terminology (KELANA)

Hrvatsko kemijsko i laboratorijsko nazivlje (KELANA)

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The national project *The Database of Croatian Special Field Terminology (STRUNA)* [http://struna.ihjj.hr], coordinated by the Institute of Croatian Language and Linguistic, and supported by the Croatian Science Foundation, started in 2009. Meanwhile, within the terminology database STRUNA around 33,000 specialized entries have been defined within eighteen projects. From 2012, STRUNA is a part of the *Croatian Terminology Portal* [http://nazivlje.hr], a focal point for all available contemporary terminological resources in the Croatian language.

In order to standardize the chemical terminology, some Croatian chemists joined STRUNA within the project the *Development of Croatian Chemical Terminology (KENA)* (2009–2010) [www.struna-kena.com]. During the realization of KENA project about 2,500 terms from all disciplines of chemistry and chemical wood processing were collected and terminologically processed. The need for further enlargement of the related part of the Croatian terminology resulted with the new project the *Croatian Chemical and Laboratory Terminology (KELANA)* (ongoing from 2016) [http://www.irb.hr/kelana]. The project KELANA includes a continuation of collecting novel terms related to the theoretical, inorganic, analytical, physical, organic and applied chemistry, novel terms related to different kit, equipment, apparatus and instrument items used in laboratory activities, as well as those related to the basic pilot and industrial equipment of chemical plants.

Solid-state chemistry of p-iodonitrosobenzene

Kemija čvrstog stanja *p*-jodnitrozobenzena

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Aromatic *C*-nitroso compounds dominantly exist as *Z*- or *E*-azodioxides (dimers) in solid state [1]. Under cryogenic conditions, crystals of azodioxides can be photolysed to corresponding nitroso monomers, which again dimerize at elevated temperatures. Crystals of nitroso monomers can be also prepared by sublimation of azodioxides. By warming the sample to room temperature, sublimed monomers undergo dimerization reaction affording azodioxides.

p-Iodonitrosobenzene can exist in two solid forms, as monomer and *E*-dimer. Solid-state chemistry of *p*-iodonitrosobenzene exhibits an interesting and somewhat different behavior when compared to other nitrosobenzene derivatives (e.g. *p*-bromonitrosobenzene). Dimerization reaction of *p*-iodonitrosobenzene after sublimation is very slow and ends in the early stage [2]. This can be explained by regular arrangements of molecules in the crystal lattice of *p*-iodonitrosobenzene with most of the nitroso groups near the iodine atoms rather than to each other. In addition, *E*-azodioxy dimer of *p*-iodonitrosobenzene, which can be isolated by crystallization from solution, reverts on heating to the crystals of monomers [3].

In the present work, we studied kinetics of solid-state thermal dissociation of *E*-azodioxy dimer of *p*-iodonitrosobenzene at different temperatures by IR spectroscopy. From the temperature dependence of the reaction rate constants, activation energy for thermal dissociation was calculated. In addition, we investigated solid-state photodissociation of *E*-dimers of *p*-iodonitrosobenzene under cryogenic conditions and kinetics of the subsequent re-dimerization reaction.

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Acknowledgments

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Crystallization of new copper halide polymorphs from supramolecular gels

Kristalizacija novih polimorfa bakrovih halogenida iz supramolekulskih gelova

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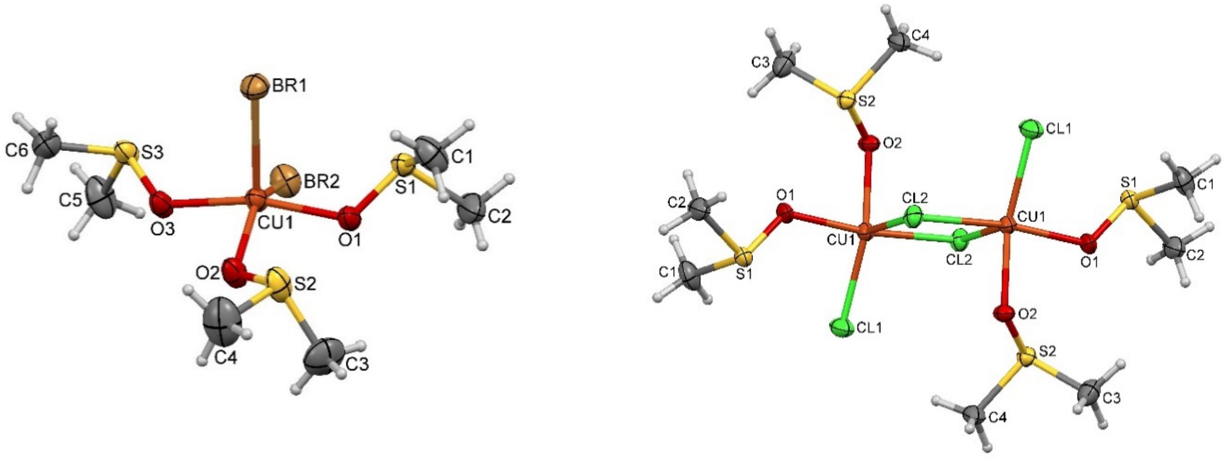
The self-assembly of low-molecular-weight organogelators (LMWGs) renders supramolecular gels by the operation of hierarchical non-covalent forces. The unique features of supramolecular gels and their dynamic nature have stimulated numerous curiosity-driven studies, as well as the discovery of potentially innovative and highly technological applications. Particularly interesting is the exploitation of supramolecular gels as media for the crystal growth of molecular species since it is possible to attain different polymorphs and crystal habits, one of the key issue in pharmaceutical industry. Gel phase crystallization represents a *prime de facto* example of orthogonal self-assembly of the crystals and gel network, which are generally microphase separated and retain a distinct identity [1].

We have recently described the CuX_2-induced (X = Cl, Br) and water-mediated metallogel formation by a pyridine containing anthraquinone-based ligand in dimethyl sulfoxide (DMSO) [2]. This system withstands the presence of a significant excess of Cu(II) ions and we have exploited this unusual feature as a medium for a metal salt crystal growth. Indeed, the crystals of two copper halide polymorphs are produced spontaneously upon aging the Cu(II)-metallogel after one week at room temperature. X-ray crystal structure analysis showed that one Cu(II) complex is mononuclear, while the other is dihalo-bridged Cu(II) complex. In both of them, $[CuBr_2(DMSO)_3]$ and $[CuCl(DMSO)_2(\mu\text{-}Cl)]_2$, polyhedron around the Cu(II) ion could be best described as distorted square pyramid (Figure 1).



a) b)

Figure 1: Molecular structures of $[CuBr_2(DMSO)_3]$ (a) and $[CuCl(DMSO)_2(\mu\text{-}Cl)]_2$ (b), with the atom numbering schemes. Displacement ellipsoids for non-hydrogen atoms are drawn at the 30 % probability level.

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Synthesis and complexation properties of calix[4]arene glycoconjugates

Sinteza i kompleksacijska svojstva glikokonjugata kaliks[4]arena

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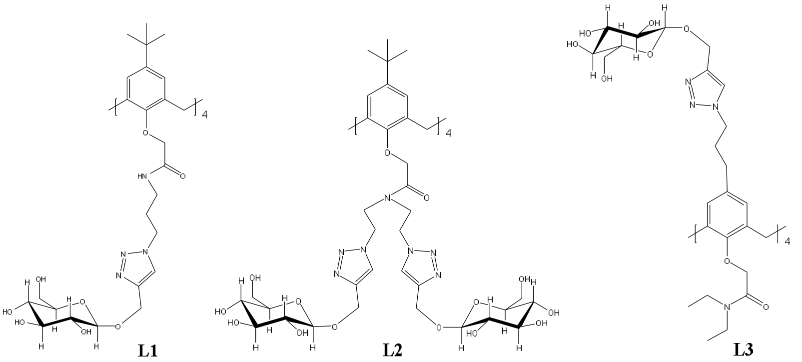
Calixarenes are a class of supramolecular cavitands that can be easily functionalized to give receptors for ionic and neutral species. In many papers published so far their use has been tested in a wide range of applications, from simple host-guest interactions to biomimetics and catalysis. Structural evolution of these compounds has led to more selective receptors with improved physico-chemical properties. Most of the synthesized calixarene ionic receptors are not sufficiently soluble in water which makes their use quite limited [1]. Water-soluble calixarenes usually own this property to the introduced easily-ionized sulfonic groups. In the scope of this work novel neutral and water-soluble ligands **1**–**3** (Figure 1) were designed and prepared, and their complexation with alkali-metal cations was investigated. Glucose was embedded in the structure as hydrophilic domain whereas secondary and tertiary amides served as cation-binding sites. The latter motifs were used since the calixarene derivatives comprising such groups were previously proven to form highly stable complexes [2]. Complexation reactions with alkali-metal cations were studied in water, methanol, and formamide thus giving insight into the solvation as well as intra- and intermolecular hydrogen bonds effects. Several techniques were used, such as UV spectrophotometry, isothermal titration calorimetry and NMR spectroscopy.



L1 **L2** **L3**

Figure 1: Structure of **L1-3**

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Influence of self-assembly of the bis(amino acid) fumarate on polymerization induced by gamma and ultraviolet rays

Utjecaj samoorganizacije na polimerizaciju bis(amio) fumarata induciranu gama i UV zrakama

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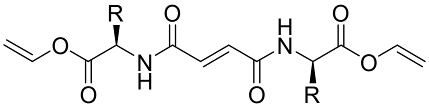
Supramolecular gels are a new class of self-assembled nanomaterial which design is a great challenge in the past decades because of their gel properties, specific applications, and preparation of new materials [1]. We investigated the influence of self-assembly organogelators [2,3] on polymerisation in gels by UV and gamma irradiation. For UV irradiation we used high-pressure Hg lamp (100W) and photoinitiator benzophenone and for gamma irradiation using ^{60}Co source at a total dose of 200 kGy and the dose rate of 14 kGy/hGy min^{-1}. Synthesis part of this work was to prepare a methyl ester of bis(Leu)fumarate and vinyl esters of bis(L-Leu or L-Val)fumarate (**1** and **2**) by the reaction of fumaryl chloride with vinyl ester of the appropriate amino acid. Amino acid vinyl esters were prepared by the Pd-catalyzed transvinylation with vinyl acetate. These compounds are gelator of various organic solvent. After preparation of supramolecular gels of bis(Leu or Val)fumarate in toluene, the resulting material was exposed to UV or gamma rays.



1. R = *i*-Pr; **2.** R = *i*-Bu

Figure 1: New bis(L-Leu and L-Val)fumaramide gelators

The obtained materials after irritation are polymers with a different network pattern of bis(L-Leu)fumarate and bis(L-Val)fumarate as a direct link of different self-assembly. Morphological study by SEM shows that the morphology of gel-network and polymer-network did not change significantly upon polymerization as confirm of the initial self-organized aggregates. Using FTIR spectroscopy data for solid matter and polymer matter we noticed that the characteristic stretching at 996 cm^{-1} (ascribed to fumaryl) and 947 cm^{-1} (characteristic for vinyl esters) are disappearing. Bis(Leu)fumarate polymer using UV irradiation mostly polymerizable through fumaric double bound but bis(Val)fumarate polymer through vinyl esters. UV irradiation of the methyl ester of bis(L-Leu)fumarate in a solution gave cyclobutane ring in [2+2] cycloaddition reaction.

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Dinuclear ferrocene derivatives as a model system to study the effect of variable spacer length on hydrogen bond patterns

Dinuklearni ferocenski derivati kao modelni sustavi za proučavanje utjecaja različite duljine razmaknice na uzorke vodikovih veza

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Ferrocene-containing derivatives with only one ferrocene unit and two small peptide chains attached to each cyclopentadienyl ring show a great potential for formation of intra- or interchain hydrogen bonds because of a restricted rotation of these rings. An engagement of two ferrocene units imposes additional conformational flexibility in comparison to the mononuclear ferrocenes. The first oxalamide-bridged dinuclear ferrocene compound with acetyl groups did not show any preference for intramolecular hydrogen bonding [1]. In addition, these compounds did not exhibit any self-assembly and gelation properties, although some of the mononuclear ferrocene-containing and bis(amino acid)-oxalamide derivatives have already been proven as gelators [2,3].

If we want to predict the self-assembly and gelation properties of oxalamide-bridged dinuclear ferrocene peptides, firstly we need to fully understand the supramolecular structure and its relationship with molecular structure of single molecules. In order to make a clear distinction between affinities of potential hydrogen bond donor and acceptor sites toward inter- or intramolecular hydrogen bonding we performed a detailed conformational study by means of computational chemistry methods (DFT, QTAIM). The results were compared with those obtained by previously conducted experiments. In the course of this research, an improved procedure for syntheses of higher analogues of oxalamide-bridged dinuclear ferrocene compounds is described. In comparison with the first oxalamide-bridged compound [1] these analogues differ in spacer length and sizes of the oppositely attached peptide chains. The total number of potential hydrogen bond donors and acceptor sites increases in both compounds, thus resulting in the formation of multiple intramolecular hydrogen bonds. Nevertheless, some of these sites remain free and able to trigger unidirectional self-assembly and gelation behavior due to intermolecular hydrogen bonding.

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Synthesis and complexation properties of fluorescent calix[4]arene derivatives

Sinteza i kompleksacijska svojstva flourescentnih derivata kaliks[4]arena

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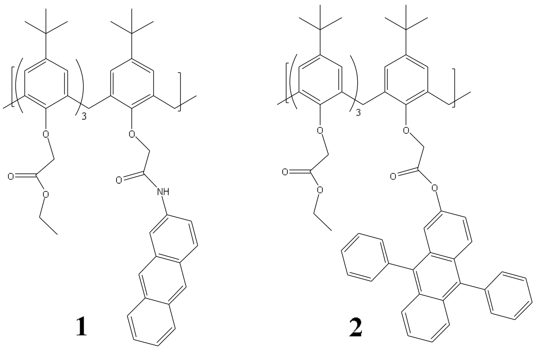
Calixarenes are macrocyclic oligomers consisted of four or more phenolic residues linked by methylene bridges in the *ortho* position. By their relatively easy functionalization, a vast number of efficient receptors for various ionic and neutral species have been prepared [1]. Calixarenes bearing fluorescent moieties could be considered as potential sensitive fluorimetric ion sensors due to the high sensitivity of fluorimetry [2,3]. In the scope of this work novel fluorescent antracene- and diphenylantracene-based calix[4]arene derivatives **1** and **2** were designed and synthesized. Their complexation with alkali-metal cations was investigated as well. Antracene and diphenylantracene moieties were introduced at a lower calixarene rim and served as fluorescent groups positioned close to the cation-binding site. Due to the low solubilities of the prepared calix[4]arene derivatives in solvents of moderate permittivities, their complexation was studied in methanol–dichloromethane and acetonitrile–dichloromethane solvent mixtures (φ = 0.5). Stability constants of the corresponding complexes were determined (in some cases only assessed) by means of fluorimetry, UV spectrophotometry, and isothermal microcalorimetry. The latter technique also provided information on reaction enthalpies and entropies. The obtained thermodynamic quantities were discussed regarding the structural characteristics of the ligands and solvation properties of the solvents used.



1 **2**

Figure 1: Structures of calix[4]arene derivatives **1**–**2**

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Supramolecular architectures of halogen bonded cocrystals containing $CoCl_2L_2$ metal-organic units

Supramolekulska arhitektura kokristala povezanih halogenskom vezom koji sadrže $CoCl_2L_2$ metalo-organske jedinice

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The assembly of metal-organic units is an attractive target for crystal engineering by halogen bonding, due to their potential to provide new magnetic, optical or electrical properties [1]. Herein we present $CoCl_2L_2$ complexes (L = 1,10 phenantroline, **phen**, or 2,2' bipyridine, **bpy**) as halogen bond acceptors and show their potential as building blocks for the construction of multicomponent materials by both liquid assisted grinding and conventional solution-based method. For cocrystal synthesis we selected commonly used, perfluorinated halogen bond donors: iodopentafluorobenzene (**ipfb**), 1,4-diiodotetrafluorobenzene (**14tfib**), 1,3-diiodotetrafluorobenzene (**13tfib**), 1,2-diiodotetrafluorobenzene (**12tfib**), 1,1,2,2,3,3,4,4-octafluoro-1,4-diiodobutane (**ofib**) and 1,3,5-trifluoro-2,4,6-triiodobenzene (**135tfib**). Single crystal X-ray diffraction experiments have shown that cocrystals display different supramolecular architectures governed by Cl···I halogen bonds between halogen bond donor iodine atoms and metal complex chlorine atoms (varying from 3.088 to 3.471 Å). Halogen bonded architectures in the cocrystal can be grouped into discrete molecular complexes (0D), chains (1D), two- and three-dimensional networks (2D and 3D). As expected, discrete complexes are formed using **ipfb,** a monotopic halogen bond donor, as well as **12tfib,** a ditopic donor. Halogen bonded chains were found in cocrystals with ditopic donors (**14tfib**, **13tfib**, **ofib**) as well as with **135tfib**, tritopic halogen bond donor. 2D and 3D networks are formed only using ditopic halogen bond donors **13tfib** and **ofib**. In all cocrystals halogen bonded aggregates are further connected by C-H···F, C-H···Cl, C-H···C, C-H···I, C-F···C, I···C or I···I contacts.

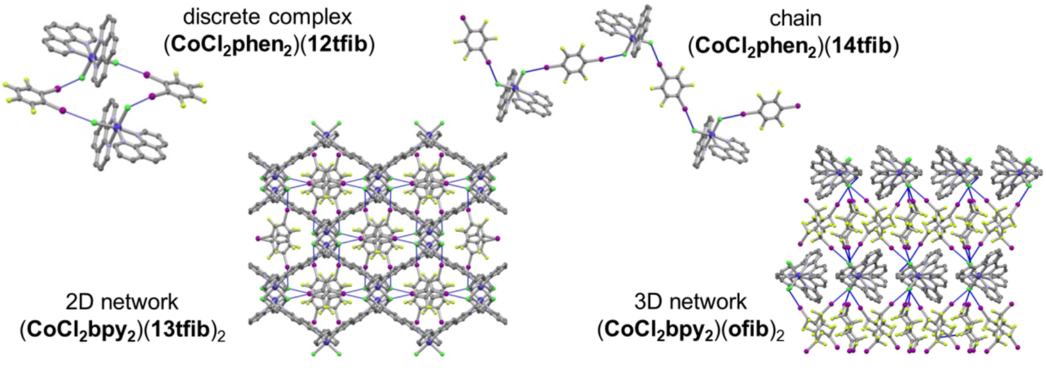

Figure 1: Examples of different supramolecular architectures in prepared $CoCl_2L_2$ cocrystals.

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Interactions between iodide ions and quinoid rings

Interakcije između jodidnih iona i kinoidnih prstenova

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A series of cocrystals of tetrachloro- and tetrabromoquinone with organic iodide salts has been prepared and structurally characterised. Derivatives *N*-methylpyridinium were chosen as cations, due to their planarity and similar size to the quinones, while their electronic properties are radically different. While the iodide usually acts as an electron donor, reducing the quinone into the semiquinone radical [1,2], sometimes the co-crystals of the neutral quinone and the iodide appear.

In the studied crystals, the common motive, or supramolecular synthon [3], has been identified: a sandwich-like I^-···quinone···I^- moiety with close contacts between the iodide anion and carbon skeleton of the quinoid ring (Fig. 1). Distances between the iodide and the ring centroid range between 3.6 and 3.85 Å, which is slightly shorter than sum of van der Waals radii for C and I. Interactions between π system aromatic ring and an anion are rarely observed, since aromatics are usually electron-rich; in the case of electron-depleted quinoid rings, anion···π contacts are more likely to form. In the studied cases, however, there is also a partial electron transfer between the iodide and the quinone which is noted by a change of colour: the neutral quinone is yellow, while the co-crystals and the semiquinone crystals are black.

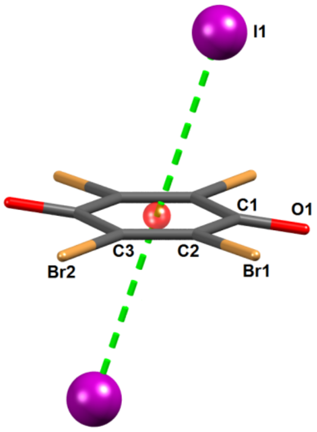

Figure 1: The I^-...quinone...I^- supramolecular synthon appearing in the studied structures.

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Imines derived from 2-hydroxy-1-naphthaldehyde as halogen bond acceptors

Imini izvedeni iz 2-hidroksi-1-naftaldehida kao akceptori halogenske veze

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It has recently been shown that imines derived from *ortho*-vanillin and aromatic amines containing halogen bond acceptor moieties can form a variety of bonding motifs with halogen bond donors [1]. Since we have previously shown different bonding capabilities of select aromatic amines based on their substituent groups [2], our next goal was to investigate motif retention in a more robust building blocks. We synthesized a series of imines derived from 2-hydroxy-1-naphthaldehyde (**n**), and performed mechanochemical and solution cocrystallization experiments with 1,4-diiodotetrafluorobenzene (**tfib**). Eight aromatic amines have been selected for imine syntheses: 3-aminoacetophenone (**3aa**), 4-aminoacetophenone (**4aa**), 3-aminobenzonitrile (**3abn**), 4-aminobenzophenone (**4ab**), 4-aminobenzonitrile (**4abn**), 4-nitroaniline (**4noa**), 3-aminopyridine (**3ap**) and 5-amino-2-methoxypyridine (**5a2mp**).

Mechanochemical, powder X-ray diffraction and DSC experiments have shown that of our eight Schiff bases, only those with acetophenone or pyridyl fragments participate in cocrystal formation. Single crystal X-ray diffraction experiments have shown that, as expected [3], pyridine nitrogen atoms in the (**n3ap**)$_2$(**tfib**) cocrystal form strong halogen bonds with **tfib** (d(I···N) = 2.92 Å, ∠(C–I···N) = 175°). On the other hand, in the (**n5a2mp**)(**tfib**) cocrystal, halogen bonds are formed instead between **tfib** and methoxy oxygen groups (d(I···O) = 3.15 Å, ∠(C–I···O) = 167°) and between **tfib** and the π-system of the naphthaldehyde fragment (d(I···C) = 3.44 Å, ∠(C–I···C) = 166°).

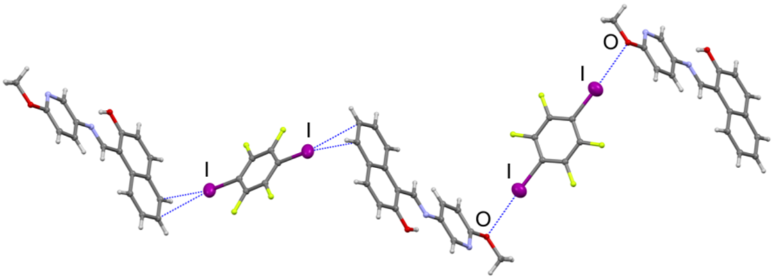

Figure 1: Part of the halogen bonded chain in the (**n5a2mp**)(**tfib**) cocrystal.

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Synthesis and enantiomeric recognition studies of a pyridino-18-crown-6 ether containing a benzothiazole unit

Sinteza i enantiomerno prepoznavanje piridino-18-kruna-6 etera koji sadrže benzotiazolnu jedinicu

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Enantiomeric recognition is an important phenomenon in Nature, because many biological processes are based on enantioselective reactions such as the metabolism of amino acids. Enantiopure pyridino-18-crown-6 ethers are effective ligands for enantiomeric recognition [1,2]. Optically active sensor molecules possessing a fluorescent signalling unit provide a sensitive tool for the examination of their enantiomeric differentiation ability by the use of fluorescence spectroscopy [3].

We synthesized a new enantiopure pyridino-crown ether based sensor molecule [(*S,S*)-**1**] containing a benzothiazole fluorophore unit (Figure 1). The enantiomeric recognition ability of (*S,S*)-**1** toward the enantiomers of PhEt, NapEt, PhgOMe and PheOMe (Figure 1) was studied in acetonitrile using UV–vis and fluorescence spectroscopies.

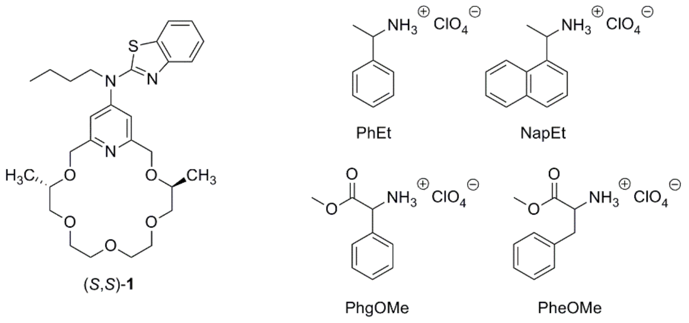

Figure 1: New enantiopure pyridino-18-crown-6 ether and the optically active primary ammonium salts used in the enantiomeric recognition studies.

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Copper(II) complexes with *n*-arylalkyliminodiacetamide ligands

Bakrovi(II) kompleksi s *n*-arilalkiliminodiacetamidnim ligandima

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The amide linkage is the most fundamental chemical bond in all proteins [1]. The binding of metal ions by amides, peptides and proteins is of great interest because of the importance of metal ions in biological systems [2]. Beside their obvious biological significance, amide ligands have many other valuable properties and many of them already found their practical application. They are used as pharmacological agents owing to their relatively good solubility and low toxicity. Amides also show potential for metal ion recognition. Furthermore, the amide moiety provides various possibilities of hydrogen bonding motifs which can be used to control the self-assembly processes between metal complexes in supramolecular coordination chemistry [3,4]. Recently, we discovered interesting supramolecular architectures in the structures of Cu(II) and Ni(II) complexes with *N*-arylalkyliminodiacetamides as hydrogen bond donors and nitrate ions as hydrogen bond acceptors [5,6]. In order to obtain similar architectures with other oxo-ions such as perchlorate ions (same charge, different symmetry) we synthesized a few novel copper complexes with *N*-arylalkyl derivatives of iminodiacetamide, namely $[Cu(Bnimda)_2](ClO_4)_2$ (**1**), $[Cu(Peimda)_2](ClO_4)_2$ (**2**) and $[Cu(Ppimda)_2](ClO_4)_2\cdot 2H_2O$ (**3**) (Bnimda, Peimda, Ppimda; Bn = benzyl, Pe = 2-phenylethyl; Pp = 3-phenylprop-1-yl).

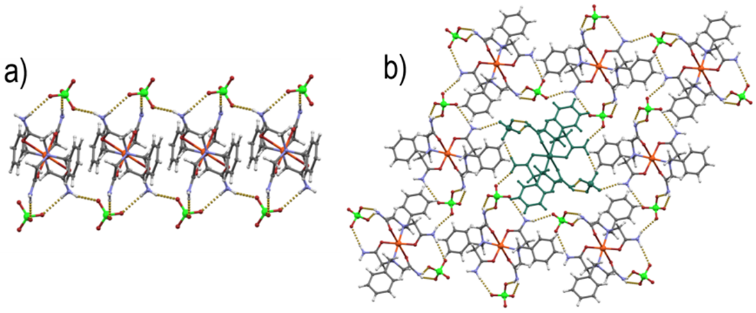

Figure 1: Crystal packing in **1.** a) Hydrogen bonded chains along the crystallographic *a* axis viewed along the crystallographic *b* axis; b) Interconnection of chains into a 3D structure viewed along the crystallographic *b* axis.

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Chiral oxamides as highly efficient gelators for ionic liquids

Kiralni oksamidi kao učinkoviti gelatori ionskih tekućina

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Chiral bis(amino acid and amino alcohol) oxamides belong to a class of efficient gelators of various organic solvents and water [1,2]. Their gelation ability is the result of unidirectional self-assembly into fibrous aggregates due to strong and directional intermolecular hydrogen bonding provided by oxamide units and the lack of molecular symmetry due to the presence of two chiral centers, which is known to prevent crystallization and favors aggregation. Additionally, bis(amino acid) oxamides show rather rare ambidextrous gelation behavior: they can gel both lipophilic, highly polar solvents and water due to their bolaamphiphilic structural features with well-separated lipophilic amino acid substituents and hydrophilic carboxylic acid or alcoholic OH groups located above and below the planar oxamide unit.

Recent study [3] showed that (*S,S*)-bis(leucinol)oxamide is highly efficient gelator for imidazole-based ionic liquid, capable of producing highly conductive supramolecular ionogel. This finding is very important since ionic liquids and materials based on ionic liquids are identified as "ideal" electrolytes for different applications due to their unique combination of properties such as negligible vapor pressure, non-flammability, chemical and thermal stability, high ionic conductivity, and wide electrochemical window.

In order to gain a deeper insight into the gelation properties of oxamide compounds towards ionic liquids we have expanded our survey to include gelation tests of series of amino-alcohol oxamides, namely ((*S,S*)-bis(leucinol)oxamide, (*S,S*)-bis(phenylalaninol) oxamide, (*S,S*)-bis(valinol)oxamide and (*S,S*)-bis(phenylglycinol)oxamide) and three ionic liquids, 1-butyl-3-methylimidazolium tetrafluoroborate, 1-butyl-3-methylpyridine bis(trifluoromethylsulfonyl)imide and 1-butyl-3-methylimidazolium bis(trifluoromethyl-sulfonyl)imide. The results have showed that (*S,S*)-bis(valinol)oxamide is the most efficient gelator since it forms gel with all three ionic liquids, whereas bis(phenylglycinol)oxamide does not make gel with any of the tested ionic liquids. The minimum gelator concentration varies from w = 0.3 to 1.7 % indicating high gel-forming ability of the oxamide-based gelators. In addition, all prepared ionogels have very high ionic conductivity, comparable to those of the respective neat ionic liquid which classifies them to quasi-solid materials with a potential for application as novel electrolytes.

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Photocatalytic degradation of phenol on the immobilized TiO_2 layer

Fotokatalitička razgradnja fenola na imobiliziranom sloju TiO_2

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The advanced oxidation processes (AOPs) are widely used in wastewater treatment to eliminate persistent organic pollutants, which cannot be completely removed with an conventional wastewater treatment methods (like adsorption, flocculation, air stripping, *etc*). Among these advanced technologies, TiO_2 heterogeneous photocatalytic oxidation with u*ltraviolet (*UV) irradiation source is one of the most promising [1-3].

The purpose of this work was optimization of the phenol photodegradation with immobilized TiO_2 layer using a simple photocatalytic reactor under UV irradiation. Phenol was chosen as a model compound to degrade, since it is frequently found in various industrial effluents and has a toxicity effect [4].

The photocatalytic TiO_2 layer was prepared using chitosan [β-(1-4)-2-amino-2-deoxy-D-glucose] for immobilization on glass fibre woven roving. Photocatalytic degradation was investigated in a batch reactor of annular type with recirculation. The source of UV irradiation (commercial 8W UV lamp; λ=254 nm) was placed in the central part of the photoreactor. Intensity of the UV lamp was measured using a radiometer (UVX Radiometer from UVP with the corresponding sensor UVX-25 for UV-C radiation). The influence of various operating conditions, such as temperature, initial reactant concentration, pH value, flow rate recirculation and irradiation time of the UV lamp on photodegradation of phenol was investigated at constant amount/thickness of the photocatalytic layer. Samples from the reactor were analyzed using HP 1090 HPLC using a 5 μm, 250x4.6 mm Zorbax SB-C18 column and diode array *detector (*DAD).

Several kinetic models were proposed and appropriate kinetic parameters were estimated to determine kinetics and reaction mechanism. The results obtained in this study have demonstrated the feasibility of the immobilized TiO_2 layer as potential heterogeneous photocatalyst for organic pollutants decontamination in the industrial wastewater.

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Binder-solid interactions in fluidized bed melt granulation

Interakcije vezivo-prašak pri granuliranju u fluidiziranom sloju taljenjem

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Fluidized bed melt granulation is an emerging process technology by which powders are enlarged using solid, low melting point binders. In this research, granulation of two pharmaceutical excipients, lactose monohydrate and microcrystalline cellulose, has been investigated. Melting of solid polyethylene glycol enables the formation of liquid bridges between particles which are necessary for enlargement to occur. *In-situ* granulation tests were performed in a lab-scale processing unit, fluidized bed granulator. Particle size distributions indicate a significant enlargement of lactose monohydrate/polyethylene glycol system. Additionally, granulation has substantially improved powder flowability which contributes to better tabletting. Enlargement of microcrystalline cellulose using polyethylene glycol as a binder was unsuccessful. Therefore, study of granulation phenomenon is directed towards detection of powder-binder interface parameters for microcrystalline cellulose/polyethylene glycol and lactose monohydrate/polyethylene glycol systems. Contact angle measurement technique using a goniometer has been applied for characterization of two interfaces of interest. Contact angles of three test liquids with well known surface energies were determined on substrates of microcrystalline cellulose, lactose monohydrate and polyethylene glycol. Two parametric models were used for quantitative prediction of interactions. Surface free energies of each phase, interfacial energies of interest and corresponding values of thermodynamic work of adhesion and spreading coefficients were estimated using Owens-Wendt and Wu models. Adhesion parameters indicate weak interactions between microcrystalline cellulose and polyethylene glycol with high possibility of phase dewetting and consequently on the inability for granulation of this system. Additionally, interface parameters indicate the possibility for establishment of considerable interactions between lactose monohydrate and polyethylene glycol.

Copolymerization reactivity ratios and properties of copolymers of 2-*N*-morpholinoethyl methacrylate with styrene or dodecyl metacrylate

Omjer kopolimerizacijske reaktivnosti i svojstva kopolimera 2-*N*-morfolinoetil-metakrilata sa stirenom i dodecil-metakrilatom

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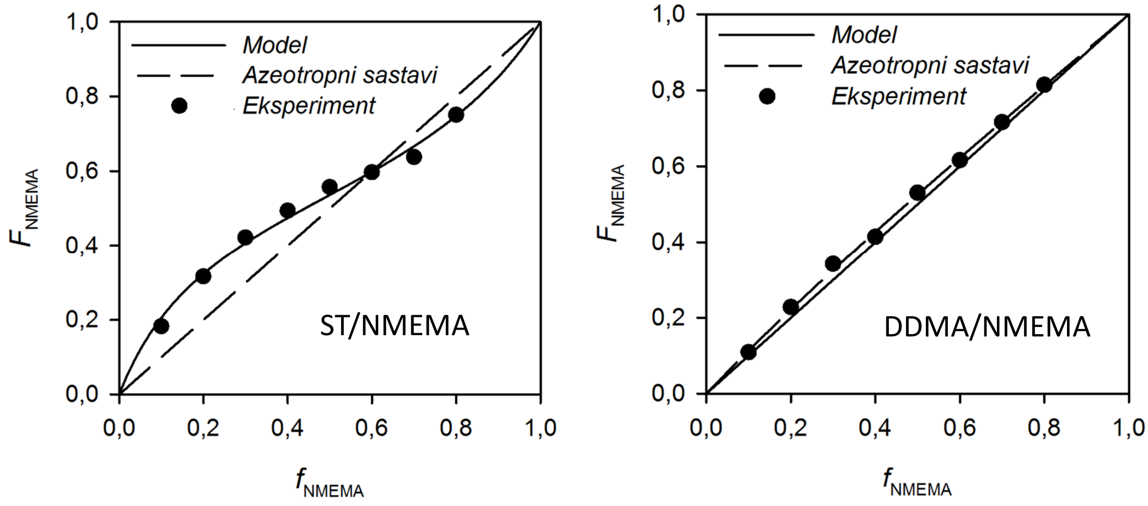
Monomer 2-*N*-morfolinoetil-metakrilat (NMEMA) sastavnica je kopolimera koji se koriste za dostavu lijekova. Sastavom kopolimera utječe se na topljivost i tijek otpuštanja aktivne tvari. Kako bi se priredili kopolimeri željenih svojstva, odnosno sasatav i strukture, potrebno je poznavati kopolimerizacijeske reaktivnosti monomernih sastavnica. U ovom radu određeni su omjeri kopolimerizacijskih reaktivnosti 2-*N*-morfolinoetil-metakrilata u binarnim sustavima sa stirenom (ST) ili dodecil-metakrilatom (DDMA). Kopolimerizacija NMEMA sa ST ili DDMA provedena je izotermno pri 70 °C do niskih konverzija (< 10 mas. %) u toluenu. Kao inicijator upotrebljen je *tert*-butil peroksi-2-etilheksanoat (c = 0,02 mol dm^{-3}). Kopolimeri su priređeni u širokom rasponu sastava (90 – 20 mol. % NMEMA, uz korak od 10 mol. %). Omjeri kopolimerizacijske reaktivnosti izračunati su linearnom metodom prema Kelen – Tüdosu (KT) i nelinearnom metodom prema Tidwell – Mortimeru (TM). Za sustav ST/NMEMA iznose: r_{ST} = 0,35, r_{NMEMA} = 0,57 (KT); r_{ST} = 0,35, r_{NMEMA} = 0,56 (TM), dok su za sustav DDMA/ NMEMA: r_{DDMA} = 0,83, r_{NMEMA} = 1,03 (KT); r_{DDMA} = 0,86, r_{NMEMA} = 1,06 (TM). Omjeri kopolimerizacijske rektivnosti za sustav ST/NMEMA manji su od 1 što ukazuje na neidealnu kopolimerizaciju s azeotropnom točkom te slabo izraženu sklonost prema stvaranju alternirajućeg kopolimera. Za razliku od prethodnog, omjeri kopolimerizacijske reaktivnosti za sustav DDMA/NMEMA bliski su jedinici što ukazuje na gotovo idealnu kopolimerizaciju. Nadalje, priređenim kopolimerima određeni su toplinska postojanost (TG metodom) te fazni toplinski prijelazi (DSC metodom).



Omjer molarnih udjela NMEMA u reakcijskoj smjesi i kopolimeru prilikom kopolimerizacije s ST (lijevo) ili DDMA (desno).

Influence of impeller off-bottom clearance on mechanism and crystal growth kinetics of borax in PBT-SBT dual impeller crystallizer

Utjecaj udaljenosti donjeg miješala od dna na mehanizam i kinetičke parametre rasta kristala boraksa u kristalizatoru s dvama PBT-SBT miješalima

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In the last few decades, an interest in batch crystallization had increased significantly due to the numerous advantages of this separation method. Even though the number of scientific papers dedicated to the subject is continuously increasing, only a few of them deal with the impact of mixing on the process of crystallization. Additionally, the number of those researches in which mixing is performed by dual or even a multi-impeller system is almost negligible. Since mixing ensures favorable conditions for mass and energy transfer, an impact of this operation on every aspect of a crystallization process should be investigated. For this reason, the aim of this work was to find how the off-bottom clearance influences mechanism and crystal growth kinetics.

Batch crystallization of disodium tetraborate (borax) by controlled cooling was conducted in a crystallizer of 15 dm^3, which was equipped with four baffles. Saturated solution was prepared at 30°C and was cooled at the rate of 6 °C/h. Since liquid height to vessel diameter ratio (H/d_T) equaled 1.3, mixing was performed by using two impellers of a standard diameter (D/d_T=0.33). Radial SBT impeller was mounted above an axial PBT impeller on a single shaft (PBT-SBT dual impeller system). Impeller spacing (S/D) was kept constant and equal to S/D=1 while the off-bottom clearance was varied in the range of 0.2 to 1.3. Impeller speed, at which crystallization was conducted, ensured the state of a complete suspension (N/N_{JS}=1). Solution concentration was monitored continuously by *Na*-ion selective electrode. Linear crystal size over process time was determined by microscopic analysis of the slurry samples with *Motic Images Advanced 3.*2 software. In order to explain obtained results, it was also necessary to analyze the fluid flow generated by impellers. For this purpose, the overall fluid flow pattern was photographed according to the method developed by S. Ibrahim and A. W. Nienow.

Results of this investigation indicate that the change of off-bottom clearance reflects on the values of linear crystal size over process time and consequently on the crystal growth kinetics. It was found that the overall crystal growth coefficient, k_g, increases with an increase of impeller off-bottom clearance. A deviation from this trend is only present when the flow generated by the lower impeller is transformed due to the vicinity of the crystallizer bottom. An analysis of numerical values of the order of overall crystal growth process, g, did not imply a regular dependence of this parameter on the off-bottom clearance. To determine the crystal growth mechanism, a model proposed by Mersmann was used. By this model, in all tested conditions, crystal growth was integration limited.

Hydraulic Design of Four-Product Dividing Wall Columns – technical challenges and solutions

Hidrauličko projektiranje kolona s razdjelnom stijenkom za četiri proizvoda – izazovi i rješenja

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Dividing Wall Column (DWC) is a distillation technology that minimizes energy and equipment as well as plot area requirements of three and more component separations by distillation. By virtue of its design, it is the most sustainable among distillation technologies. Although its potential has been proven and well established in practice, the number of industrial applications of DWCs is still limited. This is mainly due to DWC being an atypical distillation column, meaning there are certain design and operation-related concerns and potential constraints that may discourage inexperienced practitioners and make them reluctant to consider design and implementation of a DWC in prospective applications [1].

In the meantime, many process engineers have developed skills and are capable of using available commercial software packages to simulate performance of a DWC. However, what is not readily available in commercial software packages is a proven hydraulic design method needed to translate performance simulation results into shell dimensions and detailed internal equipment layout, or to examine appropriateness of an existing column shell in a retrofit case. This must be done with certain rigor if one wishes to arrive at a reliable basis for evaluation of cost-effectiveness of both new DWC designs and retrofits.

To contribute to filling the know-how gap hindering wider application of DWC technology, the present paper addresses all relevant aspects of packed DWC dimensioning, using engineering tools available in public domain. Emphasis is on equipment choice and a predictive model that enables accurate estimation and proper balancing of the pressure drop in parallel sections. The latter being the key to successful design and operation of DWCs. Capability of quantification in this respect opens the door for exploration of possibilities for expansion of the application window of DWCs, both as a new design to enhance potential benefits and as an energy saving retrofit option.

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Microencapsulation of dronedarone hydrochloride

Mikrokapsuliranje dronedaron hidroklorida

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Dronedarone hydrochloride is an anti-arrhythmic drug for the regulation of cardiac arrhythmia. Dronedarone is a benzofuran containing heterocyclic compound and is a structural analog of amiodarone, but with slight structural modifications where the iodine group is replaced by a methane-sulfonyl group. The intention behind the replacement of iodine group is to reduce the risk of non-target organ adverse effects caused by amiodarone therapy. Microencapsulation is a process by which tiny droplets of liquid or solid material are coated with a continuous film of polymeric or lipid material. The size, structure and form of microcapsules depend on preparation techniques, materials used and the process conditions in which they were produced. One way of obtaining the microcapsules is spray drying. Due to its simplicity, flexibility and speed of production, spray-drying has found a wide application in the pharmaceutical industry. The aim of this study was to produce microcapsules of dronedarone hydrochloride with extended-release profile by spray drying.

In this study three different encapsulation materials were used; gum arabic, gelatin and cellulose acetate phthalate. Experiments were conducted in a laboratory spray-dryer. The influence of different process conditions on the quality of the obtained microcapsules (drying air temperature, flow rate of atomizing air) was tested. The effectiveness of microencapsulation process was tested spectrophotometrically by determining the content of dronedarone hydrochloride in microcapsules. The morphology of the microcapsules was tested using scanning electron microscope. Dronedarone hydrochloride release rates were obtained and described with appropriate kinetic models.

The results indicate that diversity of coating materials and process conditions enables control of dronedarone hydrochloride release in microencapsulation process.

Effects of application of ultrasonic power on the crystallization behavior of maleate salt of active pharmaceutical ingredient

Utjecaj ultrazvučnog zračenja na proces kristalizacije maleatne soli aktivne farmaceutske supstance

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Simultaneous robust control of granulometric crystal properties (size, shape, size distribution) has become increasingly important in industrial practice [1] since it has an impact on filtration, residual moisture, downstream processes costs and, finally, bulk properties (density, flowability, compressibility)[2].

The maleate salt of active pharmaceutical ingredient (API) has characteristic very narrow metastable zone width (very close solubility and supersaturation curve) accompanied with lack of operating space for crystallization control. From a reason of very intensive nucleation, such conditions result with needle like particles and broad size distribution. Since monitoring and control approaches can result in better understanding of the process and significant improvement of product quality, process was monitored in real-time by Focused Beam Reflectance Measurement (FBRM) instrument.

With a purpose to produce more uniform particles, the effect of continuous and pulsed ultrasonic treatment of different amplitudes and duration on the morphology of maleate salt of API was investigated. Suspension of the salt in appropriate solvent was prepared and was treated with the ultrasonic amplitudes of 30, 40, 50 and 60 % during 2.5 and 5 min. The difference in the quality of initial crystals and crystals obtained after ultrasonic irradiation is evident from the microscopic pictures of the product obtained from each experiment. Increasing the ultrasonic time exposure of the particles (5 min instead 2.5 min) resulted with no significant change in particle size distribution.

Furthermore, on the basis of good morphological results obtained with sonocrystallization and the fact that the metastable zone width is very narrow and unvafourable, influence of the ultrasound irradiation at the nucleation point and during crystallization process of maleate salt of API was investigated. It was found that ultrasonic waves directly influence the morphology of the maleate salt of the API during crystallization process and product of better and improved quality was manufactured.

This work shows important research developments and arising challenges in the field of industrial crystallization.

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Direct nucleation control of fumarate salt of API using FBRM and spectroscopic methods

Direktna kontrola nukleacije fumaratne soli API-a pomoću FBRM-a i spektroskopskih metoda

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Particle size is a crucial characteristic of the active pharmaceutical ingredient (API), and particle size distributions (PSD) are an important consideration for pharmaceutical manufacturers [1]. PSDs, the range of the individual particle sizes that make up a substance, should be narrow, so that most individual particles fall within a specific, tightly defined size range. The PSDs of API may influence key performance factors such as bioavailability, dissolution, stability, uniformity of content, etc. [2].

Optimization of crystallization process of fumarate salt of the API using Focused Beam Reflectance Measurement (FBRM) technology and analytical methods such as a Raman and ATR-UV/Vis spectroscopy is described and discussed. FBRM is used as in-line analytical method for observing particle size and counts of particles in the suspension in real time. Spectroscopic methods were used to observe concentration of API in solution during crystallization process to determine supersaturation level in order to define optimal conditions for crystallization control. That approach has resulted in gaining larger particles referring to d_{90} parameter and narrower PSD. A crystallization of fumarate salt of API in *n*-butanol shows all the benefits of a combination of the FBRM probe with various analytical methods during crystallization process. Characterizing particle properties effectively, in particular mean particle size and particle size distribution, allows processing problems to be solved and product quality to be improved.

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Process safety assesment using adiabatic and reaction calorimetry for sodium borohydride as reducing agent in methanol

Sigurnosna procjena reaktanta natrij borhidrida kao reducensa u metanolu korištenjem adijabatske i reakcijske kalorimetrije

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Process safety assessment is a key aspect of process development with a goal of safely transfering a process to production, without any kind of hazard or risk. The main focus of research was made on the thermal risk that comes out of unwanted, secondary reactions which occur when process conditions are uncontrolled, whether the cooling of the reactor has failed, or taking into account different rates of heat and mass transfer during the process scale-up.

Reaction calorimetry (RC-1), adiabatic calorimetry (ARRST) and process simulators (Dynochem, Visimix) are usefull tools in obtaining data and process understanding. Reaction calorimetry is a technique for gathering valuable kinetic data of exothermic and endothermic events which give insight into process safety and hazard analysis by quantifying the enthalpy of the reaction. Adiabatic calorimetry is used for testing the process in conditions that are uncontrolled, by heating the reaction mixture with a constant heat ramp while monitoring exothermic events.

In our research, exothermic reaction with significant pressure generation that occurs when using sodium borohydride as a reducing agent in methanol as a solvent was examined. Sodium borohydride is a commercially available reagent which is commonly used for the selective reduction of organic molecules. It is readily soluble in water and alcohols during which hydrogen and heat ($\Delta_r H > 300$ kJ/mol) are being released. The reaction measurements were conducted using Mettler Toledo RC-1 reactor at 0-5°C under atmospheric pressure. Using adiabatic calorimetry it was concluded that no unwanted reactions occur which allowed the prediction of safe conditions in case of unstable reaction conditions.

With the data obtained from those tools, process simulators are used to build reaction models that include wanted and unwanted reactions, allowing us to build scenarios that could bring the process into dangerous and unstable conditions.

Electrochemical Behaviour of Aluminium Alloy in Chloride Solution in Presence of Pyrazole

Elektrokemijsko ponašanje aluminijske legure u otopni NaCl u prisustvu pirazola

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Aluminum and its alloys are widely used metals in industry owing to their many great characteristics including: good electrical and thermal conductivities, low density and high ductility [1, 2]. The main problem with corrosion of aluminum and its alloys is local destruction of the passive film which causes the occurrence of pitting corrosion in chloride solutions. Electrochemical investigations show that aluminium alloy has certain corrosion activity in 0.51 mol dm^{-3} sodium-chloride solution. Effects of pyrazole on corrosion inhibition of aluminum have been investigated in 0.51 mol dm^{-3} NaCl solution using potentiodynamic polarization and polarization resistance method. The results show that pyrazole acts as a corrosion inhibitor. Protection efficiency increases with increasing concentration of pyrazole [3, 4]. The calculated value of DG_{ads} indicates that the adsorption of the pyrazole on the surface Al alloy is a spontaneous process that is a combination of physical adsorption and chemisorption.

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Modelling, monitoring and control of batch crystallization processes

Modeliranje, nadziranje i vođenje šaržnih procesa kristalizacije

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Crystallization is an important technique for separation and purification of substances as well as for product design in chemical, pharmaceutical and biotechnological process industries. A common control strategies used in batch crystallization are often operated by tracking predetermined recipes, e.g. temperature, feed flow, and/or heat input profiles, which are largely based on operators' experience [1].

The FDA's initiative to encourage the use of Process Analytical Technology (PAT) and the availability of various robust in situ sensors like ATR-UV/vis spectroscopy and FBRM (*Focused Beam Reflectance Measurement*) has greatly improved the monitoring and control of pharmaceutical crystallization processes [2].

Crystallisation is a multi-variable system with multi-input and multi-output (MIMO), often with high interaction amongst the process variables. Thus a modern approach to control is possible using a model-based MIMO control system. Model Predictive Controllers (MPC) can handle such highly interacting multivariable systems efficiently due to their coordinated approach.

An internal feedback mechanism exists between supersaturation generation and kinetic phenomena through the evolution of crystal population and solute concentration. This feedback mechanism determines the production rate and the quality attributes, e.g. purity, size distribution, and morphology, of the crystals. The goal is to produce crystals with a certain quality as far as possible using the minimum amount of energy. From the control point of view a crystalliser the main quality criteria are the properties of produced crystals, the size and size distribution. The quantity of the produced crystals and delivery of the crystalliser can be also controlled.

This review gives an overview of the recent approach to the modeling, monitoring and control of crystallization processes with emphasis on the application of PAT for continuous real-time monitoring of the key process variables.

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Comparison of Catalytic Properties of Cu/13X Catalyst in the Wet Peroxide Oxidation of 4-(2-Hydroxyethyl)phenol in Batch and Fixed Bed Reactor

Usporedba katalitičkih značajki Cu/13X katalizatora u reakciji oksidacije 4-(2-hidroksietil)fenola vodikovim peroksidom u šaržnom i cijevnom reaktoru

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4-(2-Hydroxyethyl)phenol is one of the phenolic compounds commonly found in olive oil mill wastewater (OOMW) – the liquid waste generated in the olive oil production process. This wastewater represents a special challenge for treatment because it contains a number of harmful organic contaminants such as lignin, tannins and polyphenolic compounds whose proven toxicity towards the microorganisms used in the aerobic biological processes make direct conventional biological treatment inapplicable [1]. Its high polluting charges are measured in BOD_5 and COD levels up to 35 g dm^{-3} as well as the presence of phenols and polyphenols that can constitute up to 20 wt. % of total organic content. Therefore, the current research focuses investigation on developing viable treatment processes that will reduce or eliminate toxic content of the OOMW and improve its biodegradability. Catalytic wet peroxide oxidation (CWPO) is simple, cost effective and environmentally friendly process that is based on non selective oxidation of organic compounds by hydroxyl radicals that are formed upon the decomposition of hydrogen peroxide over a suitable catalyst. Finding a suitable catalyst has become a focal point of most studies [2]. This study deals with investigation of applicability of zeolite based catalyst for such purposes. Zeolites have been widely used as catalysts in a number of different oxidation reactions yielding excellent catalytic properties because of what they were selected for evaluation in this process [3,4].

Cu/ 13X zeolite catalyst (d_P= 0.4 - 0.6 mm) was prepared, characterized, thermally stabilized by high temperature calcination in air and used in the catalytic screening in wet peroxide oxidation of model wastewater (tyrosol aqueous solutions) to evaluate its catalytic properties. The experiments were performed in a suspension batch and adiabatic continuous fixed bed reactors under mild reaction conditions with low energy consumption ($T = 323\text{-}343$ K, 500 mg dm^{-3} organic compound(s), stoichiometric oxidant amount, 1.25 g of catalyst). It was found that the prepared catalyst showed promising activity in both reactor systems yielding over 50 % conversions of targeted organic contaminants at with no significant leaching of active metal component of the catalyst.

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Cooling of the plain bearing of ball mill drive in the production of Portland cement

Hlađenje kliznog ležaja kugličnog mlina u tehnološkom procesu proizvodnje Portland-cementa

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The purpose of this study is to examine the characteristics of industrial shell and tube heat exchanger (MIT05) with fixed tube bundles, 2-pass tube side, for cooling of mineral oil that lubricated plain bearings ball-mill raw material in the production of Portland cement [1-5]. Through the tube bundle, which consists of 44 copper pipes with the outer diameter of 10 x 1 mm and the length of 404 mm, in two passes, streaming cooling water inlet temperature 21 °C, with volume flow of 1 m^3h^{-1}. Mineral oil flows inside the shell and around the tube, with volume flow of 8 L/min. The pipes are laid out in a triangular fashion and pitched 13 mm apart. There are 6 baffles inside the shell. The results of examination indicate the laminar flow (Re < Re,c) inside the tubes and shell. Until the oil temperature, $\Delta t_{U,}$ rises by 5,5 ^{o}C the the available surface area of heat transfer is greater than required and meets the set requirements. As the oil temperature, $\Delta t_{U,}$ rises up of 5,5 ^{o}C the surface required to exchange heat also rises compared with available surface, while the multi-tube exchanger no longer fulfills the requirements for cooling the mineral oil. By increasing the flow of cooling water is coming to an increase in the tube-side mass flow rate of water and the transition from laminar flow in the transitional area (2300 < Re < 10 000). This increases the overall heat transfer coefficient and reduces the required surface heat exchanger to transfer the same amount of heat.

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Optimization of fuel purification process using nanosuspension

Optimizacija procesa pročišćavanja goriva nanosuspenzijama

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Sulfur and nitrogen oxides, formed as products of fuel combustion, are air pollutants that can lead to the appearance of acid rain and, therefore, represent one of the main sources of environmental pollution [1]. Environmental concerns about the presence of sulfur and nitrogen compounds in fuels have prompted the European Union (EU) and American Environmental Protection Agency (EPA) to establish strict regulations regarding the presence of sulfur and nitrogen in fuels [2].

Extractive desulfurization and denitrification are presented as competitive and advantageous methods of removing sulfur and nitrogen compounds from fuels. They are conducted at mild operating conditions (ambient pressure and temperature) with solvents which are selective with a better ability of removing undesirable components. Improvements towards green technology and the development of new, environmentally friendly designed solvents offer many possibilities and represent an important subject in further progress. New, designed solvents DES, which satisfy the principles of green chemistry, have shown higher efficiency in fuel purification processes, extracting biologically active compounds, metabolites and macromolecules compared to extraction with classic volatile organic solvents [2,3]. In addition to their suitable physical properties, the main advantages of DES are their nontoxicity, affordable price and a simple synthesis method in which cheap, renewable and biodegradable components are applied under mild conditions to form a eutectic mixture.

In this study, DESs were used as media to form nanosuspensions (NS) with different nanoparticles (Al_2O_3, SiO_2 and TiO_2) in order to improve transport properties in the extraction process. In recent years, it has become known that NSs possess enhanced thermal properties due to Brownian motion of well dispersed nanoparticles inside fluids. Improvements of mass transfer by diffusion and/or convection can be expected due to heat and mass transfer analogy. The experiments are focused towards preparation of stable nanosuspensions, their implementation and achieving improvements in the extraction of thiophene (sulfur compound) and pyridine (nitrogen compound) from fuel. Optimal extraction time, most effective stirring and stability time of nanosuspension were determined. Results of extraction process using stable nanosuspensions were compared to extraction using same DES.

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Preparation and characterization of amorphous material obtained *via* Spray drying technology

Priprava i karakterizacija amorfnog materijala dobivenog sušenjem raspršivanjem

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Drying is perhaps the oldest, most common and most diverse of chemical engineering unit operations. Over four hundred types of dryers have been reported in the literature while over one hundred distinct types are commonly available. [1] Spray drying, amongst other technologies, is a well-established technology for the production of amorphous products. It offers the possibility to modify powder characteristics such as particle size, particle morphology, crystallinity and the amount of residual solvent. [2]

In this work, 5-(4-(4-(5-Cyano-1H-indol-3-yl)butyl)piperazin-1-yl)benzofuran-2-carboxamide hydrochloride (Figure 1) was used as a model molecule for preparation and characterization of stable amorphous form of the active pharmaceutical ingredient by means of spray dryer technology. For the purpose of feed solution preparation, solubility of crystalline structure was determined in variety of pure solvents as well as mixture of solvents and most suitable system was chosen. Feed solution of the active pharmaceutical ingredient, dissolved in mixture of acetonitrile and water, was dried at different process conditions such as inlet temperature, nitrogen flow rate used for atomization and feed solution flow rate. Influence of process conditions on physical and chemical properties of final dried product was examined on a variety of analytical and physical methods. The results showed that a stable amorphous structure of the high purity active pharmaceutical ingredient is obtained with a spray drying, and that the optimal conditions of the process are defined. The amorphous structure is stable at temperatures below 200 °C when it is transformed into a new crystal structure. Conditions of high relative air humidity lead to partial transformation.

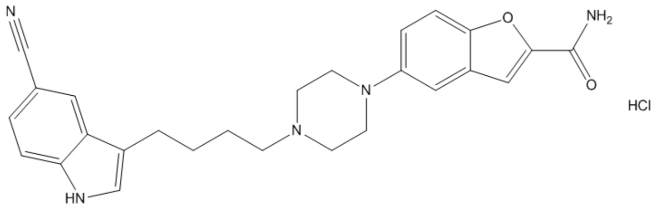

Figure 1: Structure of 5-(4-(4-(5-Cyano-1H-indol-3-yl)butyl)piperazin-1-yl)benzofuran-2-carboxamide hydrochloride.

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Third generation biodiesel – from microalgae to fuel

Biodizel treće generacije – od mikroalgi do goriva

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World's energy demands are constantly growing and fossil fuel supplies will soon become insufficient. Solar panels and wind turbines cannot make up for all the energy needed, especially not in the transport sector. That sector is where biodiesel and biofuels in general are most valuable. Biodiesel is an alternative to fossil diesel, can be used in the same engine in a blend or by itself and has been known since the first diesel engine appeared. Chemically, it is a mixture of fatty acid methyl esters and it is most commonly produced by transesterification of oil with methanol and with basic salt as a catalyst.

Depending on the type of oil used, biodiesel is often divided in three generations: first generation biodiesel is produced from fresh oil, while waste cooking oil is used for second generation biodiesel. Third generation biodiesel is made from microalgae and this paper will describe the process from growing microalgae to producing biodiesel.

Microalgae samples were collected from two lakes – Jarun (Zagreb) and Bajer (Vrbovec) and one culture was cultivated from domestic waste water. They were grown in the laboratory for 40 days and then washed with distilled water and dried in a spray drier. After drying, oil was extracted from biomass in Soxhlet apparatus. Algal oil was then treated with methanol and NaOH in transesterification reaction to produce biodiesel. Extraction with deep eutectic solvent (ChCl:EG, 1:2,5) was conducted to remove free glycerol from biodiesel. Properties of the final product were then analyzed to check whether it complies with the ISO standards for biofuels.

Extraction of essential oil and absolute from Immortele

Ekstrakcija eteričnog ulja i absoluta iz smilja

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Helichrysum italicum, commonly named as Immortelle or Everlasting is widely distributed in the Mediterranean basin where it grows naturally in the dry, sandy and stony areas. Immortelle is used in traditional medicine due to its anti-inflammatory, antibacterial and antiallergic antioxidant activity. It is used both in cosmetics and in pharmaceutical preparations. Recently, its repellent and insecticidal activity has been proved. Immortelle essential oil can be obtained from all aerial parts of the plant. The composition of the essential oil is influenced by the vegetative cycle and the soil type as well as the geographical location.

The aim of this work was to extract essential oil and absolute from Immortelle. The aerial parts of Immortelle were harvested at the end of its flowering stage at the beginning of October. Immortelle essential oil was produced by hydrodistillation while immortelle absolute was produced by simple solvent extraction and Soxhlet extraction with ethanol and n-hexane. Homogeneous samples of the flowering top and stems were distilled or extracted separately. The yield of the essential oil obtained by hydrodistillation was 0.15% (w/w). The maximum yield of absolute obtained by Soxhlet extraction was 6.78 % (ethanol) and 1.37 % by solvent extraction (n-hexane). Isolated and purified products were analyzed by FTIR and GCMS. Immortelle essential oil and absolute exhibited a very complex composition, depending on the method and solvent used as well as the freshness of the plant. All products obtained by atmospheric hydrodistillation and extraction are characterized by a high amount of sesquiterpenes. Vacuum hydrodistillation results with high concentration of esters.

Preparation of zein/shellac nanoparticles

Priprema nanočestica zeina i šelaka

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Zein and shellac are both biopolymers, recognized as safe, biodegradable, edible, non-toxic materials, so they represent a great resource for development of new functional colloids, which could be used in food and pharmaceutical industry.

Zein is plant protein, obtained from corn (*Zea mays*), usually as co-product of bioethanol or starch industry. It is water insoluble yellow powder, which can be dissolved in various organic solvents. Nowadays, its use, as a coating material, packaging material or material for encapsulation, has been investigated [1-3]. Shellac is animal resin and it is a purified product of natural material Lac, which is secreted by parasitic insect *Kerria laca*. It is also water insoluble and used for food and drug coating [4].

In this paper zein, shellac and zein/shellac nanoparticles were prepared, by antisolvent precipitation from concentrated aqueous ethanol (90%) solutions. Zein, shellac or their mixtures of different mass ratio (1/0, 8/2, 1/1, 4/6 and 0/1) were first dissolved in the aqueous ethanol in order to prepare biopolymer solutions. Thereafter, the ethanol solutions were sheared into a bulk of water, in order to prepare nanoparticles. The influence of pH on zeta-potential and particle size were investigated. Isoelectric point of thus prepared nanoparticles was determined.

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Biosorption and biodegradation of carbon compounds from pharmaceutical industrial wastewater

Biosorpcija i biorazgradnja ugljikovih spojeva iz farmaceutske industrijske otpadne vode

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Biological wastewater treatment with activated sludge is commonly used technology for contaminants removal from wastewater. It has significant efficiency and decreases ecological footprint. Activated sludge consists primarily of bacteria which are connected in activated sludge flocs. Its main role is the removal of carbon compounds from wastewater with biosorption and biodegradation. Biosorption is a process where carbon compounds from wastewater are attached on the surface of biomass cell structure or accumulated within the structure of a floc [1]. Microorganisms from activated sludge can metabolize captured carbon compounds to the final main products, carbon dioxide and water. In this way biodegradation becomes substantial process for the removal of organic contaminants [2].

The aim of this work was to study biosorption and biodegradation of organic contaminants from pharmaceutical industrial wastewater with activated sludge. The experiments were conducted in batch conditions with initial concentration of pharmaceutical wastewater, $S_0 = 5473 \pm 85.6$ mg dm^{-3}, and different initial concentrations of activated sludge, which ranged between 2.82 and 5.98 g dm^{-3}. During the experiments, chemical oxygen demand (COD), concentration of biomass, dissolved oxygen and pH-value were monitored. Microscopic analysis was also conducted. In biosorption, the equilibrium was reached within 30 minutes and process efficiency was 20.5 %. Biodegradation process was described with Endo-Haldane model. Biokinetic parameters were estimated to be $\mu_{\mathrm{max}} = 0.19$ h^{-1}, $K_{\mathrm{S}} = 113.09$ g dm^{-3}, $K_{\mathrm{i}} = 8.05$ g dm^{-3}, $k_{\mathrm{d}} = 4.23 \cdot 10^{-3}$ h^{-1} and $Y = 0.19$ g g^{-1}. Overall efficiency of biodegradation process was 74.4 %.

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Potentiostatic electrodeposition of copper In the presence of surfactants

Elektrostatska depozicija bakra u prisutnosti površinski aktivnih tvari

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Nearly 500 pounds of copper is produced in the world each second. Along with the increased production, copper quantities in the environment have increased. Wastewater pollution by heavy metals including copper, remains today one of the biggest environmental problems to solve in industrialized countries, which still poses a threat to society.

Various conventional methods are used to remove heavy metals from wastewater. Electrodeposition is usually applied for the recovery of copper. The recovery process is considered of great importance for reducing environmental emissions and for substantial savings. Potentiostatic copper electrodeposition at a graphite electrode from synthetic 0.05M copper (II) sulfate solution was studied at pH3. An excellent recovery of copper (99%) at -500mV with deposit easily removable from the electrode by scratching and tapping without removing the cathode material has been achieved [1-2].

In the present work, the effect of the presence of surfactants on electrochemical copper recovery process, by potentiostatic electrodeposition from acid copper chloride solutions of pH3 on a graphite electrode, has been investigated using cyclic voltammetry, electrochemical impedance spectroscopy and chronoamperometry.

The effect of the concentration of surfactants on current-potential curves shows that increasing the concentration of surfactant to a certain limit enhances the deposition by increasing the deposition rate. Impedance spectroscopy was done to characterize the kinetics of nucleation and electroplating of copper deposits at different medium. The morphology and the composition of copper deposits in the presence of surfactants were characterized by SEM and FTIR measurements.

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Liquid-liquid equilibrium in the systems *n*-hexane/*i*-octane – pyridine – [choline chloride – ethylene glycol]

Ravnoteža kapljevina-kapljevina u sustavima *n*-heksan/*i*-oktan – piridin – [kolin klorid – etilen glikol]

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With the aim of developing green technologies, the research has recently focused on the deep eutectic solvents (DES), which are considered as 'green' solvents due to their great physical and chemical properties [1], such as low melting point, negligible vapor pressure, non-flammability, reuse and cheap synthesis from biodegradable and non-toxic compounds [2,3]. Accordingly, deep eutectic solvents took their application in liquid-liquid extraction [4,5,6] as one of the possible alternative methods for fuel denitrification. In this work the influence of deep eutectic solvent composition on liquid-liquid equilibrium was investigated. Liquid-liquid equilibria for the six ternary systems consisting of a hydrocarbon (*n*-hexane or *i*-octane), pyridine and a deep eutectic solvent (choline chloride – ethylene glycol in molar ratios 1:2, 1:3 and 1:3.5) were experimentally determined at 25°C and atmospheric pressure. In addition, physical properties of DES investigated that are important for their application, i.e. density, viscosity, pH value, refractive index, thermal conductivity, thermal diffusivity, thermal capacity and electrical conductivity are measured. The equilibrium data were presented with tie lines; the data are well correlated with NRTL and UNIQUAC activity coefficient models.

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Comparison of the quality and fatty acid profile of VOOs produced by different technological processes

Usporedba kvalitete i profila masnih kiselina u djevičanskim maslinovim uljima proizvedenim različitim tehnološkim procesima

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Virgin olive oil (VOO) is unique vegetable oil that is obtained directly from olive fruit using only mechanical processing. That way it contains a great number of valuable bioactive compounds that are responsible for its specific taste and aroma, but also for health promoting beneficial properties. The type of technological process for olive oil production has strong influence on quality and chemical composition of produced oil. In this paper we studied the influence of different technological processes on the quality and fatty acid profile of VOOs produced in Dalmatia. We took in consideration traditional processing using hydraulic press, modern centrifugal system by two phases and laboratory olive oil plant (Abencor mc2) with controlled producing parameters. In all obtained samples we analyzed basic quality indicators (FFA - free fatty acids expressed % of oleic acid, PV – peroxide value expressed as mmol O_2/kg, K-numbers (UV spectrophotometric indices K_{232} and K_{270}) [1], total phenolic content (TPC) expressed as mg of gallic acid per kg of oil [2], fatty acid composition [3,4] and also sensory analyses according official EC [1] and IOC methodology [5]. All oils produced by centrifugal process and by laboratory oil mill were in category of extra virgin olive oil, while majority of samples obtained by traditional hydraulic press were in lower categories. Also sensory analyses confirmed lower quality for traditionally produced olive oils. Oils produced by laboratory plant had stronger positive sensory attributes (fruitiness, bitterness and pungency). Values for TPC showed notable differences among oil samples depending on processing type, as well as fatty acid profile for certain olive oil which is discussed in this paper.

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Dissolution kinetics of omeprazole tablets produced via wet granulation

Kinetika otpuštanja omeprazola iz tableta dobivenih mokrim granuliranjem

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Tablets are the most frequently used dosage forms for drug delivery. Controlled-release profile of active ingredient is a highly important end-use property of many tablets. Modifications of excipients significantly affect the final properties of tablets. With this, the targeted dissolution profile of active ingredient could be reached. Our primary goal is to investigate the effect of properties of mixtures for tableting on the uniformity of content and the dissolution pattern of the drug. In addition, our intention here is to describe the release profile of omeprazole, the drug that works for controlled decreasing of the stomach acid amount.

Various mixtures for tableting were prepared of: omeprazole (active pharmaceutical ingredient), PanExcea, magnesium stearate and saccharose (excipients). One mixture was built up of saccharose granulated in a fluid-bed. Four mixtures were using saccharose granulated in an inclined disc unit, and the last was prepared by granulation of all components in a fluid-bed unit. Mixtures were compressed using a single punch tableting machine. Tablets were characterized using standard tests on: weight, thickness, diameter, hardness, friability, moisture content and uniformity of drug content. Dissolution kinetics was studied on the tablets that fulfill high quality requirements.

The results revealed a significant effect of pretreatment processes on the characteristics of tablets. Granulation of all components in a fluid-bed environment results in tablets with less friability, of greater hardness and with a more uniform composition of omeprazole. Thus, tablets showed less erosion occurrence and slower release profile of omeprazole. Dissolution kinetics of omeprazole tablets was efficiently described using Higuchi and Hopfenberg models.

Novel 5-amidino benzimazoles as selective cytostatic agents against lung cancer cells

Novi 5-amidinobenzimazoli kao selektivni agensi protiv karcinoma pluća

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Lung cancer is one of the most common malignant tumors in the world. Dysregulation of p38 mitogen-activated protein kinase (MAPK) levels in patients are associated with advanced stages and short survival in cancer patients (e.g., prostate, breast, bladder, liver, and lung cancer) [1]. The benzimidazole derivatives have shown various biological activities such as anticancer, antimicrobial, antivirus, anti-inflammatory and antioxidant [2]. Moreover, the amidino moiety is among the strongest neutral bases with high proton affinity and has therefore found wide application in biologically active compounds [3].

We designed and synthesized novel 1,2,3-triazolyl linked 5-amidino benzimidazoles (Figure 1) in order to evaluate their cytostatic activities. Environmentally benign synthetic protocols using microwave- and ultrasound irradiation were used to prepare 1,4-disubstituted-1,2,3-triazoles, as key precursors in the synthesis of novel 5-amidino benzimidazoles. Some representatives have shown selective inhibitory effects against non-small lung carcinoma (A-549) and cervical carcinoma (HeLa).

Further biological evaluations of the most selective compounds indicated their mechanism of action *via* the p38 MAP kinase pathway.

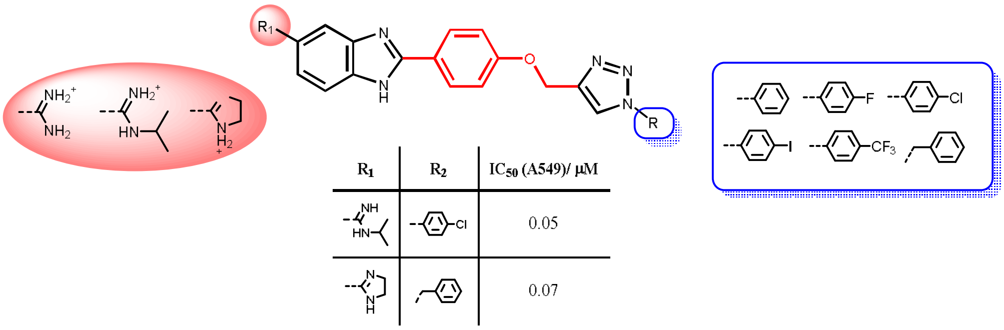

Figure 1: 1,2,3-triazolyl linked 5-amidino benzimidazoles.

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Bacterial adhesion on polyelectrolyte multilayers

Adhezija bakterija na polielektrolitne višeslojeve

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It is known that bacteria readily adhere to various surfaces and, therefore, bacterial adhesion can be controlled by different material surface properties. The factors that affect the intensity of bacterial adhesion include surface roughness, surface charge, and degree of hydrophobicity, Lewis acid-base character, and hydrogen-bonding capacity [1]. Environmental factors including pH, temperature, nutrient composition and population characteristics may enhance the adhesion and biofilm maturation. In our study we focus on the surface charge. Using layer-by-layer technique we prepared various surfaces with different terminating layers. We used the silica surface on which poly(allylamine hydrochloride)/sodium poly(4-styrenesulfonate) (PAH/PSS) polyelectrolyte multilayers were formed. The surface charge was examined by the zeta potential measurements of silica particles covered with polyelectrolyte multilayers, whereby ionic strength and polyelectrolyte concentrations significantly influenced the build-up process. The corresponding surface roughness and hydrophobicity were determined by atomic force microscopy and tensiometry. For adhesion experiments, we used the bacterium *Pseudomonas aeruginosa*. The extent of adhered bacteria on the surface was determined by scanning electron microscopy. The results showed [2] that the extent of adhered bacteria mostly depends on the charge of terminating polyelectrolyte layer, since relatively low differences in surface roughness and hydrophobicity were obtained. This study has shown the importance of combining surface characterization with microbial testing to understand the bacteria-surface interactions. The application of polyelectrolyte multilayers with tunable electrostatic properties enables the preparation of the surfaces with desirable properties in terms of bacterial adhesion.

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Synthesis and antiproliferative *in vitro* study of novel lipophilic 3-hydroxypyridin-4-ones

Sinteza i antiproliferativni *in vitro* učinak novih lipofilnih derivata 3-hidroksipiridin-4-ona

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3-Hydroxypyridin-4-ones are nowadays widely investigated for their broad spectrum of biological activities (antibacterial, antidiabetes, antiprotozoal, antineurodegenerative and anticancer) [1]. Recently, we prepared and investigated several *N*-aryl substituted 3-hydroxy-2-methylpyridin-4-ones as well as their ester adamantyl derivatives for their *in vitro* antitumor properties on several cancer cell lines [2]. All tested compounds showed antiproliferative activity ranging from moderate to strong on all inspected cell lines with lipophilic adamantane containing derivatives being active at low micromolar IC_{50} concentrations. Further studies of those derivatives in terms of their mechanism of action is now in progress. In this work, for the purpose of the structure-activity relationship study (SAR), novel lipophilic ether (adamantyl and cyclohexyl) derivatives of *N*-aryl substituted 3-hydroxy-2-methylpyridin-4-ones were prepared (Figure 1) and their *in vitro* antitumor properties evaluated on the related panel of cancer and leukemia cell lines. The compounds were synthesized starting from corresponding pyridinones and adamant-1-yl or cyclohexyl bromoacetates by Williamson synthesis. Antitumor properties of novel compounds will start to elucidate the key elements (ester or ether bond between lipophilic unit and pyridinone part, the nature and/or the position of lipophilic unit) needed for high antiproliferative activity of observed pyridinone derivatives. *In vitro* testing included cytotoxicity evaluation and additional testing of the most potent candidates to determine the mechanism of action more precisely.

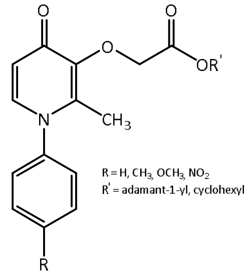

Figure 1: The structure of lipophilic ether derivatives of *N*-aryl 3-hydroxy-2-methylpyridin-4-ones.

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Acknowledgments

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Experimental study of new guandiniocarbonyl-pyrrole-aryl conjugates as potential inhibitors of human dipeptidyl peptidase III

Eksperimentalni studij novih guvanidinokarbonil-pirol-aril derivata kao potencijalnih inhibitora humane dipeltidil peptidaze III

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Dipeptidyl peptidase III (DPPIII) is a zinc dependent peptidase which catalyses hydrolysis of the 2nd peptide bond from the *N*-termini of its substrates, and is characterized by poor substrate specificity. Its fundamental physiological role is yet unknown. However, research suggested its role in several processes of interest in drug development, thus specific inhibitors would be of significant help in performing these studies. Some guanidiniocarbonyl-pyrrole analogues showed promising DPPIII inhibition properties (Figure 1, LEFT) [1]. Therefore we designed and prepared new series (Figure 1) and studied their interactions with hDPPIII by UV/Vis, fluorimetry (Figure 1, RIGHT), kinetic and ITC experiments.

Obtained results (Figure 1, RIGHT) reveal surprisingly different fluorimetric response of close analogues **A-D** upon binding to inactive enzyme mutant, pointing out that small structural differences of compound can strongly influence positioning of fluorophore within binding site and thus yield corresponding fluorimetric response. Further kinetic studies with wt hDPPIII revealed also different impacts of **A-D** on enzymatic activity.

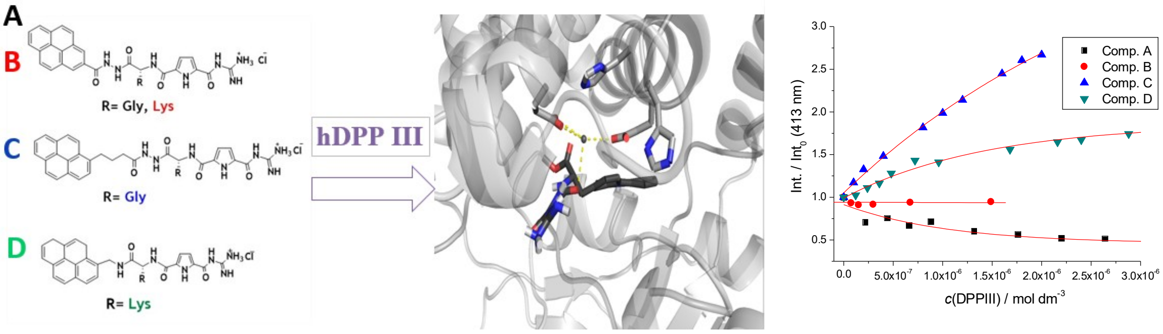

Figure 1: LEFT: Studied compounds **A-D** and starting model compound within hDDPIII binding site [1]. RIGHT: Fluorimetric response of conjugates **A-D** upon binding to enzymatically inactive DPPIII mutant (rel. fluo. int. of titration at *λ* = 413 nm normalized by starting Int$_0$). Done at pH 7, Na cacodylate buffer, *I* = 0.05 M.

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Pyrimidine and furo[2,3-*d*]pyrimidine derivatives: synthesis, cytostatic and antibacterial evaluations

Pirimidinski i furo[2,3-*d*]pirimidinski derivati: sinteza, citostatska i antibakterijska ispitivanja

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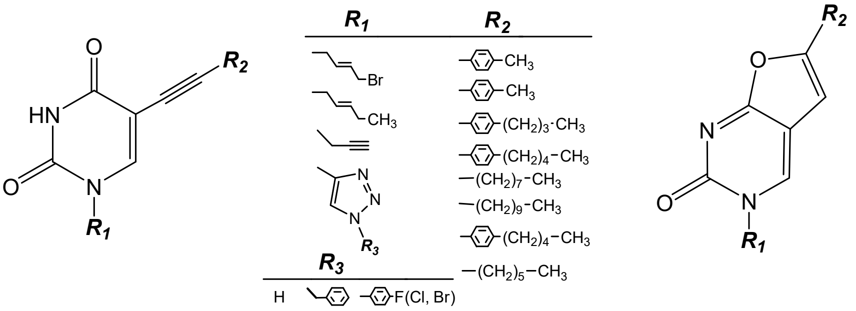
Furo[2,3-*d*]pyrimidine are purinomimetics which were subjected to biological investigations to assess their potential therapeutic usefulness. Furopyrimidines attract considerable attention due to their great practical significance through exerting pharmacological potential as antiviral, antimicrobial, and antitumor agents, and is one of the most recently explored scaffolds to have potential anticancer activity through inhibition of various protein kinases [1]. Furthermore, it was found that some 1,2,3-triazole tethered pyrimidines and furopyrimidines showed pronounced antiviral and cytostatic activity [2]. In continuation of our efforts towards the fused pyrimidines [3,4] we prepared C-5 alkynylated pyrimidines and C-6-alkylated furo[2,3-*d*]pyrimidines substituted at *N*-1 or *N*-3 with butenyl, propargyl and 1,2,3-triazolyl substituents. The novel *N*-substituted and C-5 alkynylated uracil derivatives have been synthesized by *N*-alkylation of pyrimidine bases and subsequent Pd-catalysed Sonogashira cross-coupling reaction. 1,2,3-Triazolyl derivatives were afforded *via* 'click' reaction and furo[2,3-*d*]pyrimidines by *in situ O*-heteroannulation of C-5 alkynylated derivatives. The novel compounds were evaluated against tumor cell lines (HeLa, CaCo-2, Raji and K562) and on the growth of gram positive and gram negative bacterial strains.



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Synthesis and biological activity of novel amidine derivatives of 7-cloro-4-aminoquinoline

Sinteza i biološka aktivnost novih amidinskih derivata 7-klor-4-aminokinolina

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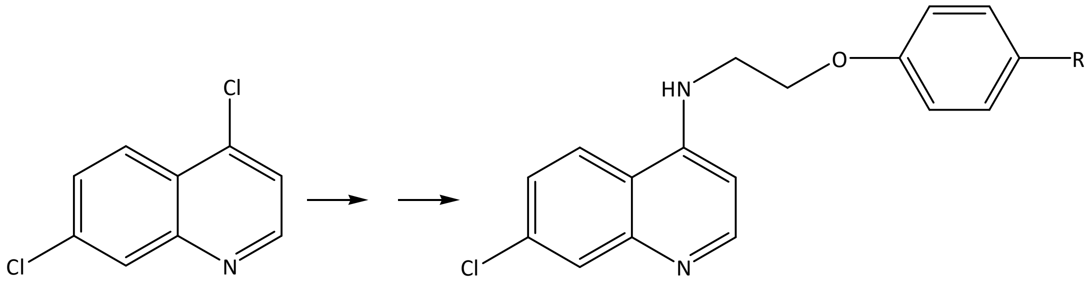
Significant progress against cancer has been made in recent years, nevertheless in EU 1.25 million people dies every year because of cancer. Cost related with cancer in EU is more than 100 billion euros per year. Most of the anticancer agents available today suffer from poor efficiency and selectivity or high toxicity in non-cancer cells. One of the strategies in overcoming these problems is focusing on the molecules that act simultaneously on multiple targets, either by combination of two (or more) drugs or by combining two (or more) active pharmacophores in a single-hybrid molecule with dual activity [1,2].

Continuing our research on the preparation of biologically active molecules we have synthesized and evaluated antitumor activity of a new class of hybrid molecules prepared by joining two pharmacophores which are present in a number of natural and synthetic agents: 7-chloroquinoline and phenyl-amidine.

Starting with commercially available 4,7-dichlorquinoline and ethanolamine we have prepared 2-(7-chloroquinolin-4-ylamino)ethanol, which was first transferred to *N*-(2-bromoethyl)-7-chloroquinolin-4-amine, which in reaction with 4-hydroxybenzonitrile form the corresponding nitrile. Resulting nitrile was used as starting material for the synthesis of various amidines via Pinner reaction. The newly synthesized compounds were also evaluated for their *in vitro* cytotoxic activity against normal epithelial (MDCK1), cervix adenocarcinoma (HeLa), colon adenocarcinoma (CaCo2), and leukemia (K562 and RaJi) cell lines using MTT assay. All investigated compounds showed dose-dependent cytotoxic activity, while leukemia cells were most sensitive. Their effect on normal cells were limited or none. Thus, observed results suggest that these compounds are very good candidates to explore their antitumor potential more deeply.



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Synthesis and biological evaluations of 1,2,3-triazolyl-tethered 4-quinolone–ferrocene conjugates

Sinteza i biološka ispitivanja konjugata 4-kinolona i ferocena povezanih 1,2,3-triazolilnom poveznicom

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1,2,3-Triazoles have attracted considerable attention in recent years because of their wide range of biological activities against various viruses, malignant cells, microorganisms and their inhibitory activities against several enzymes [1]. Advances in the rational design of metalbased therapeutic agents have increased after the discovery of cisplatin, which has been the main impetus for the expansion of metal complexes in cancer and other pathologies. The introduction of a ferrocenyl (Fc) moiety into a drug molecule has now been recognized as a useful approach for the development of more effective therapeutic applications [2].

Novel 4-quinolone–ferrocene conjugates linked *via* 1,2,3-triazolyl scaffold were synthesized by regioselective Cu(I)-catalyzed 1,3-dipolar cycloaddition of corresponding azide and alkynyl derivatives. Azido intermediates were synthesyzed from hydroxyl or bromoethyl analogs, while alkynyl derivatives of quinolones were prepared by alkylation in the presence of base. Although *N*-alkylation process of the quinolone system is both thermodynamically and kinetically favored, the introduction of trifluoromethyl group at C2-position makes this reaction kinetically less favored. Results of biological evaluations for newly synthesized compounds will be presented.

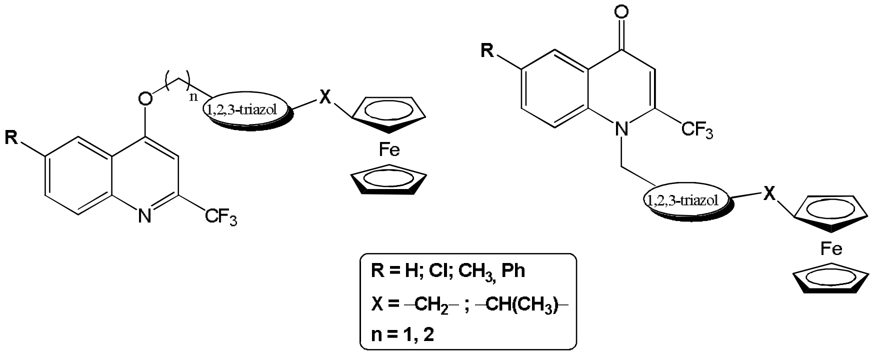

Figure 1: 1,2,3-triazolyl-tethered 4-quinolone–ferrocene conjugates.

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The influence of amino acids relevant for pathological biomineralization on the precipitation of calcium oxalate monohydrate

Utjecaj aminokiselina relevantnih za patološku biomineralizaciju na taloženje kalcijeva oksalata monohidrata

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Urolithiasis, a form of pathologic biomineralization, is a disease which causes the formation of urinary stones in different parts of kidney or bladder [1]. Recently, increasing number of kidney stones in industrial countries is observed and the interest of scientists to explain their pathogenesis with a special focus on calcium oxalate stones is renewed. Calcium oxalates crystallize in the form of hydrated salts: thermodynamically stable calcium oxalate monohydrate (COM, $CaC_2O_4{\cdot}H_2O$, whevellit) [2,3] and metastable dehydrate (COD, $CaC_2O_4{\cdot}2H_2O$, weddellit) [4,5], and trihydrate (COT, $CaC_2O_4{\cdot}3H_2O$) [6,7]. The kidney stones formation under biological conditions can be triggered by various metabolic disorders such as: hipercalciuria, hypocitraturia, hiperoxaluria, and the change in the urine acidity. The mechanisms and the conditions under which they crystallize are still not completely clarified.

In this work, the spontaneous precipitation and characterization of calcium oxalate monohydrate under conditions of hiperoxaluria is reported. The experiments were conducted in a simple model system and with the addition of amino acids reportedly important for pathologic biomineralization [8,9]. The precipitations were carried out with solutions $c_i(Ca^{2+}) = 7.5 \text{ x } 10^{-3}$ mol dm^{-3} and $c_i(C_2O_4^{2-}) = 6.0 \times 10^{-3}$ mol dm^{-3}. The amino acids selected for the addition are often found in the urine of healthy people and in the organic matrix which is an integral part of kidney stones.

The reactant solutions were mixed under controlled hydrodynamic and thermodynamic conditions. Changes in the composition and morphology of precipitated calcium oxalate monohydrate were observed by means of PXRD, EPR, SEM, IR and TGA.

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Phenanthridine-pyrene conjugates as fluorescent probes with peculiar kinetic behaviour

Konjugati fenantridina i pirena kao fluorescentne probe s neobičnom kinetikom

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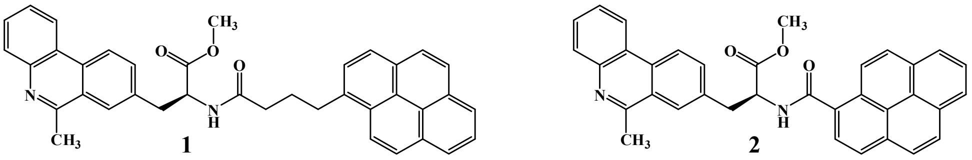
Phenanthridine derivatives are promising fluorescent probes whose properties can be modified by different substituents attached to the aromatic core. On the other hand, pyrene derivatives are one of the earliest known fluorescent probes for biomolecules. Also, it is known that two or more pyrenes form an excimer [1], where fluorescence band of single pyrene molecule is significantly shifted to longer wavelengths upon inter- or intramolecular stacking of pyrene moieties. Some of the compounds from both described classes show intriguing biological activity. It has been reported recently that some pyrene-guanidiniocarbonyl pyrrole derivatives exhibit strong pH-dependent affinity towards ds-DNA which can be modified by the flexibility of the linker connecting those two units [2]. Also, one of them binds to human dipeptidyl peptidase III enzyme with a micromolar affinity which can be monitored by significant changes in fluorescence spectra of the compound [3]. Moreover, previous studies have shown that two phenanthridine units can also form an excimer, characterized by specific fluorescence band [4].

Two phenanthridine-pyrene conjugates, differing only in linker connecting them, have been prepared. New conjugates exhibit excimer formation: **1** and **2** show new fluorescence emission bands at 495 nm and 485 nm, respectively, which are significantly red-shifted compared to fluorescence of single phenanthridine or pyrene molecule. To the best of our knowledge, it is the first reported phenanthridine-pyrene excimer. Further on, excimer band is not kinetically stabile and shows strong fluorescence decrease upon consecutive excitations.



1 **2**

Figure 1: Two novel pyrene-phenanthridine conjugates.

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Continuous flow-ultrasonic synergy in click reactions for the synthesis of novel 1,2,3-triazolyl appended L-ascorbic acid derivatives

Sinteza novih 1,2,3-triazolnih derivata L-askorbinske kiseline clik reakcijom u mikroreaktoru uz upotrebu ultrazvuka

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Flow chemistry technique performs a chemical reaction in a continuously flowing stream in a network of interconnecting tubes. Although click reactions are traditionally conducted in batch process, the progress toward increased sustainability that requires novel approaches with reduced environmental impact opened up in recent years continuous-flow as a novel alternative to conventional batch-based synthesis. Microreactor technology has the potential to revolutionize the pharmaceutical industry because the number of potential drug candidates that can be prepared and screened can be considerably increased, hence the likelihood of developing new drugs is considerably enhanced [1].

Realizing the benefits of flow chemistry and in continuation of our study towards the synthesis of 1,2,3-triazole-containing heterocycle pharmacophores [2,3], we report herein the first Cu(I)-catalyzed 1,3-dipolar cycloaddition of azido functionalized L-ascorbic acid derivative and selected alkynes to provide target 1,2,3-triazolyl appended 4,5-didehydro-5,6-dideoxy-L-ascorbic acid library, as molecules with unique biological properties, using innovative ultrasound and continuous flow hybrid system (Figure 1). Implementation of ultrasound with flow chemistry accelerated hour-scale reaction conditions in batch to the minute range in micro-flow device and considerably improved the yields for the flow syntheses. Moreover, the synergistic use of microreactor technology and ultrasonic irradiation highlights the sustainable eco-friendly aspect of utilized method.

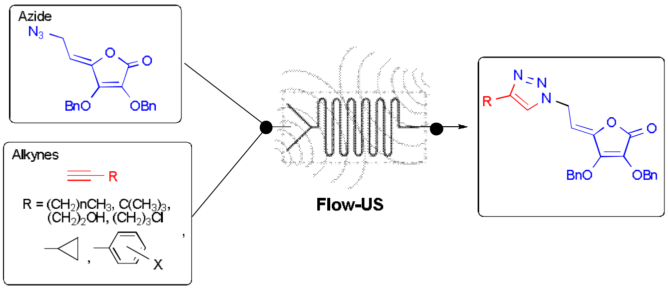

Figure 1: Synthesis of C-6-substituted 1,2,3-triazolyl 4,5-unsaturated L-ascorbic acid derivatives utilizing ultrasonic (US) assisted continuous flow in click reactions.

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QSAR based synthesis of novel primaquine ureidoamides

Sinteza novih ureidoamida primakina na temelju QSAR studije

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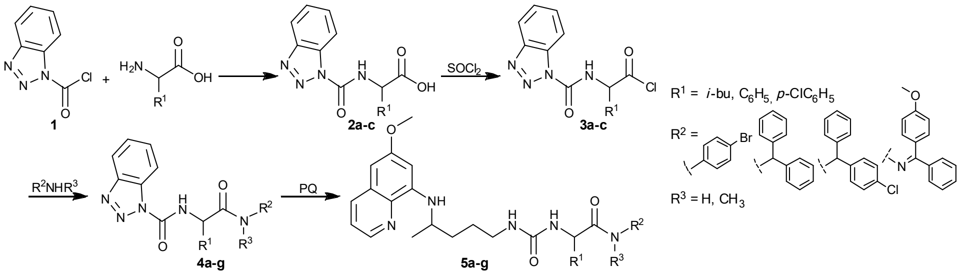
Novel ureidoamides **5a-g**, bearing primaquine (PQ) and amino acid moieties, were designed and prepared after a detailed QSAR study. QSAR model was developed based on the results of antimalarial screening of our previously synthesized compounds against the erythrocytic stages of *Plasmodium falciparum* strain [1].

Compounds **5a-g** were prepared by the aminolysis of *N*-(1-benzotriazolecarbonyl)-amino acid amides **4a-g** with PQ, while amides **4** were obtained from *N*-(1-benzotriazolecarbonyl)-amino acid chlorides **3a-c** and the corresponding amines or hydrazones. Three amino acids (L-leucine, D-phenylglycine, DL-*p*-chloro-phenylglycine), four amines (*p*-bromoaniline, diphenylmethanamine, (4-chlorophenyl)(phenyl)methanamine)), *N*-methyl-1,1,diphenylmethanamine and one hydrazone (4-methoxybenzophenone hydrazone) were used. The synthesis of similar ureidoamides was described by our group in several papers [2,3], as well as the synthesis of starting *N*-(1-benzotriazolecarbonyl)-amino acids **2a-c**, their chlorides **3a-c** [4] and 1-benzotriazole carboxylic acid chloride (BtcCl, **1**) [5]. Scheme outlines the general route leading to compounds **5a-g** and their synthetic precursors. The structures of newly prepared compounds **5a-g** was confirmed by IR, ^{1}H, ^{13}C NMR and MS spectroscopy. The evaluation of their biological (antimalarial, antiproliferative, antioxidative and antimicrobial) activity is in progress.



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Chemical composition and biological activity of volatile oil from wild edible Mediterranean plant Centaurea scabiosa

Kemijski sastav i biološka aktivnost hlapljivog ulja divlje jestive mediteranske biljke *Centaurea scabiosa*

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Centaurea scabiosa is wild edible plant used in food and nutrition in Mediterranean area. A whole juvenile plant is used in local cuisine of Dalmatian region, Croatia [1-5]. Volatile oils may comprise variety of biologically active compounds [6,7]. Aim of this work was to investigate the volatile oil chemistry of *C. scabiosa* species and its biological activity: antioxidant potential, inhibition of cholinesterases and toxicity on human cells. The chemical composition of essential oil was assessed using GC/MS technique. Antioxidant capacity of essential oil was determined using DPPH and FRAP methods [8,9]. Inhibition of both acetylcholinesterase and butyrylcholinesterase was determined using Ellman method [10]. Toxicity of *C. scabiosa* volatile oil was measured on primary fibroblasts through the MTT assay [11]. The major compounds found in essential oil were heptacosane, caryophyllene oxide, alloaromadendrene epoxide, α-cyperone and α-bisabolol. Essential oil in stock concentration of 1 g/L showed moderate inhibition of both cholinesterases while antioxidant potential was low on both tested methods. *C. scabiosa* volatile oil showed no toxicity on primary fibroblasts at the highest tested dose of 0,125 g/L in 0,5 % DMSO.

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Carvacrol protects human cervical cancer cells against cisplatin-induced cytotoxicity through multiple ERK-dependent mechanisms

Karvakrol štiti ljudske stanice raka vrata maternice od citotoksičnosti inducirane cisplatinom kroz više ERK-ovisnih mehanizama

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Carvacrol, a natural compound, has been shown to possess anticancer activity. We investigated ERK MAPK signaling as a possible mechanism of cytotoxic activity of carvacrol against HeLa cervical cancer cells and occurrence of a drug−phytochemical interaction between cisplatin (CP) and carvacrol. HeLa cells were treated with carvarcol (550 µM) or CP (20 µM), alone or combined, without or with addition of the MEK inhibitor PD325901 (150 µM). Both carvacrol and CP activated ERK and showed cytotoxicity against HeLa cells. However, PD325901 increased cytotoxicity in carvacrol-treated cells, but increased survival of CP-treated cell. Co-treatment with carvacrol and CP increased HeLa cell survival compared to CP treatment, while MEK inhibition further increased their survival. The cell survival was negatively associated by the expression of Bax, cleaved caspase-9 and cleaved PARP. Co-treatment with CP and carvacrol suppressed apoptosis compared to CP-treated cells, while MEK inhibition resulted in further decrease in apoptosis. Additionally, carvacrol increased CP-induced expression of autophagy protein LC3B-II but not Beclin 1, which was enhanced by PD325901 treatment, suggesting ERK-dependent mechanism of autophagy. Nevertheless, other ERK-dependent and independent pathways were involved in cytoprotective activity of carvacrol, including IκBα/NF-κB and Akt/mTOR, depending on the type of the treatment. The results of the current study suggest that both carvacrol and CP showed cytotoxicity against HeLa cells, with the opposite role of ERK in the two treatments. In addition, carvacrol induced CP resistance in HeLa cells through ERK-mediated induction of autophagy and inhibition of apoptosis.

Synthesis of novel 2-arylbenzothiazole derivatives and biological evaluation of antioxidant, antibacterial and antitumor activity

Sinteza novih 2-arilbenzotiazolskih derivata i biološka ispitivanja antioksidativne, antibakterijske i antitumorske aktivnosti

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Studies of benzothiazole derivatives became a rapidly developing and increasingly active field due to their interesting pharmacological properties. Benzothiazole analogues offer a high degree of structural diversity that is useful in search of new therapeutic agents [1].

In connection with our previous studies focused on synthesis and antitumor activity of 2-arylbenzothiazole derivatives [2-4] we now put our attention on the synthesis of a series of novel 2-hydroxyphenyl- and 2-methoxyphenylbenzothiazole compounds (Figure 1). Different substituents at 6-position of the benzothiazole skeleton were introduced through condensation reactions involving 5-substituted-2-aminothiphenols and the corresponding benzaldehydes. Antiproliferative effects of compounds **1**-**12** were evaluated on a panel of tumor cell lines *in vitro* and normal human fibroblasts. Antibacterial properties were determined against two G+ and two G- bacterial strains. In addition, *in vitro* antioxidant potencies were measured by use of DPPH, FRAP and ABTS tests. Preliminary structure-activity relationships for synthesized compounds are presented herein.

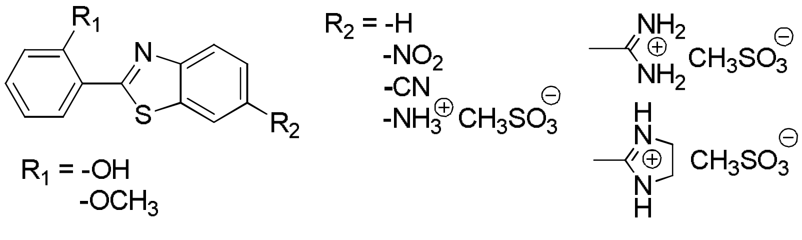

Figure 1: Structures of evaluated 2-arylbenzothiazole derivatives **1**-**12.**

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Antioxidative activity and metal and pH sensing properties of heteroaromatic benzamides

Antioksidativna aktivnost heteroaromatskih benzamida kao senzora za metalne ione i pH

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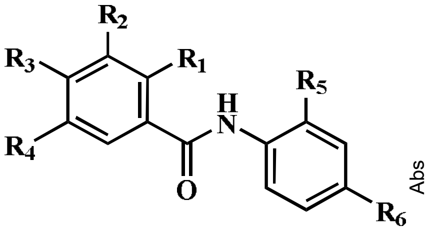
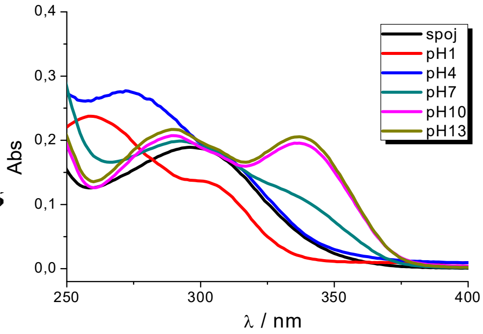
Within this work, we present the synthesis, spectroscopic characterization and antioxidative activity of novel methoxy and/or hydroxy derivatives of amino substituted benzamides. For the synthesis of novel targeted compounds, classical organic synthesis reactions were used [1]. Amino substituted derivatives were prepared by reduction of nitro analogues while hydroxy substituted benzamide derivatives were obtained by the removal of methoxy protecting groups with BBr_3. Structures of newly prepared compounds were confirmed by means of ^1H and ^{13}C NMR, UV/Vis and fluorimetric spectroscopy.

To explore and confirm the possibility of synthesized derivatives for their application as metal or pH sensors, UV/Vis and fluorimetric titrations of aqueous compounds solutions with aqueous solutions of metal chloride salts or different buffers were performed [2]. Additionally, the antioxidant properties of chosen compounds were determined by DPPH and FRAP methods [3].



R_1, R_2, R_3, R_4 = H, OCH_3, OH, CN
R_5 = H, NO_2, NH_2, NH_3^+Cl-
R_6 = H, OCH_3, NO_2, NH_2, NH_3^+Cl-



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Proteome changes of food borne pathogens treated with disinfectants based on pyridoxal oxime derivatives

Promjene u proteomu patogenih bakterija prisutnih u hrani nakon tretiranja s antimikrobnim spojevima na bazi piridoksal oksima

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Antimicrobial agents based on quaternary ammonium salts (QAC) have been extensively used as disinfectants in food-processing industries and medicine. It is suggested that these substances exhibit antimicrobial properties by adsorption to the outer cellular wall and by further penetration into bacterial cells. This results in inhibition of microbial growth and finally in cell death. It was also observed that QAC are decidedly more active against Gram-positive bacteria [1,2]. Recently, series of different pyridoxal oximes were synthesized in a form of bromide and chloride quaternary salts and their antimicrobial activity was tested against *Bacillus subtilis* and *Escherichia coli*, which were used as model organisms for Gram-positive and Gram-negative bacteria that cause food contamination [3].

In this work, quantitative gel-free proteomic investigations by LC-ESI MS/MS were used to identify changes in proteomes of these two bacteria after growth under the inhibition with four different disinfectants based on pyridinium oxime derivatives. Up- and down-regulated proteins were identified and their cellular localizations and functions were determined by gene ontology searching. Proteome changes presented here demonstrate different mechanism of action of these disinfectants. In Gram-positive food pathogen *B. subtilis,* the inhibitory substances seem to act mainly at the cell surface and cause the most changes in the integral membrane components, while in the Gram-negative pathogen *E. coli,* intracellular proteins were more affected. This research contributes to the investigations of the virulence and pathogenicity of food borne bacteria and their survival under stress conditions, and can also lead the way for further development of new inhibitors of microbial growth and studies of mechanism of their actions.

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Adamantyl derivatives of ferrocene: their effect on the model lipid membranes and their antioxidant abilities

Adamantanski derivati ferocena: utjecaj na modelne lipidne membrane i antioksidacijska svojstva

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The aim of this study was to design and synthesize new adamantyl derivatives of ferrocene and explore their effects on fluidity of model lipid membranes as well as their antioxidant abilities. Homoannularly and heteroannularly substituted adamantyl derivatives of ferrocene, were synthesized and incorporated into liposomes. Differential scanning calorimetry and fluorescence anisotropy measurements were employed for investigation of membrane fluidity.

The liposomes have been described as an artificial model membrane system and are often used for different biochemical and biophysical studies [1,2]. In our previous investigations dealing with the synthesis of adamantane derivatives and investigations of liposomes as drug delivery systems as well as model membranes we have demonstrated the significance of the interaction of adamantane molecule and phospholipids in lipids bilayer [3-5]. Recent studies have shown the wide application of ferrocene as a structural feature in organic and medicinal chemistry [5].

The obtained results have shown that the adamantyl derivatives of ferrocene significantly affect the structure of the lipid bilayer and cause decrease in membrane fluidity. The antioxidant potential of synthesized compounds was assessed using DPPH method and it was shown that examined compounds possess considerable antioxidant activity.

In conclusion, results of preliminary investigations have demonstrated that the adamantyl derivatives of ferrocene possess certain activities and justify further research of their potential biomedical application.

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Exclusion of the cognate substrate from the leucyl-tRNA synthetase editing pathway

Isključenje pripadnog supstrata iz korektivnog mehanizma leucil-tRNA-sintetaze

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Aminoacyl-tRNA synthetases (aaRS) are enzymes that use ATP to couple tRNAs with their cognate amino acids. Aminoacylated-tRNAs (aa-tRNAs) are substrates for ribosomal protein synthesis, whose fidelity thus relies on the accuracy of aa-tRNA formation. These enzymes exercise amino acid substrate specificity at the level of binding and/or the chemical steps of aminoacylation. Some aaRS cannot discriminate well against near-cognate amino acids in the synthetic pathway alone and thus utilize hydrolytic editing to minimize the error [1].

Leucyl-tRNA synthetase (LeuRS) pairs leucine with tRNA^{Leu}. The main threat to the accuracy of leucylation is posed by non-proteinogenic amino acid norvaline [2]. To prevent error in protein synthesis, LeuRS rapidly hydrolyses Nva-tRNA^{Leu} in the separate editing domain. Cognate Leu-tRNA^{Leu} evades the hydrolytic correction, yet the mechanism by which is excluded is still not clear. We found a 10^4-fold slower hydrolysis of Leu-tRNA^{Leu} as compared with Nva-tRNA^{Leu}, while the K_d values describing LeuRS interactions with Leu-tRNA^{Leu} and Nva-tRNA^{Leu} were similar. This indicates that LeuRS positions Leu-tRNA^{Leu} in an unproductive conformation for editing. To address this issue, we employed molecular dynamics (MD) simulations for the wild type LeuRS and the mutant T252A, which hydrolyses Leu-tRNA^{Leu}, with the substrate analogues leucyl- and norvalyl-2'-adenosine bound in the editing active site. The simulations suggest that binding of leucine in a conformation defined by N-Cα-Cβ-Cγ torsion angle of approximately ±180°, which is primarily observed in the WT and not in the T252A, results in a decrease in time during which the systems reside in the productive conformation [3]. As norvalines side chain is not branched, its conformation does not influence the system productivity. To ascertain the chemical nature of discrimination and the role of highly conserved T252 we simulated MD for the T252S and T252V mutants. The results indicate that both mutants likely resemble the wild-type enzyme in discrimination against leucine. The kinetic characterization of these mutants is underway.

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Assessment of pozzolanic activity of natural zeolite and waste construction brick

Procjena pucolanske aktivnosti prirodnog zeolita i otpadne građevinske opeke

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This study investigated the pozzolanic activity of natural zeolite tuff from Donje Jesenje (Croatia) site and waste construction brick as a replacements for Portland cement according to HRN EN 196-5 [1]. The chemical composition of Portland cement type CEM I, zeolite tuff and waste construction brick was determined by EDXRF device. Pozzolanic activity examinated on cement samples with the addition of zeolite tuff and waste brick in the amount of 20 and 30 wt. %. Samples were kept 8 days in water bath at 40 °C.

Determination of total alkalinity, and the concentration of CaO in an aqueous solution above the solid samples, confirmed the pozzolanic activity of the samples since the experimental points are located below the saturation curve in the diagram of isothermal solubility of calcium hydroxide (Fig 1).

Results confirmed the possibility of applying the pozzolanic activity tests in determining of optimal content of pozzolanic material in cement which is especially important for pozzolanic cement industry.

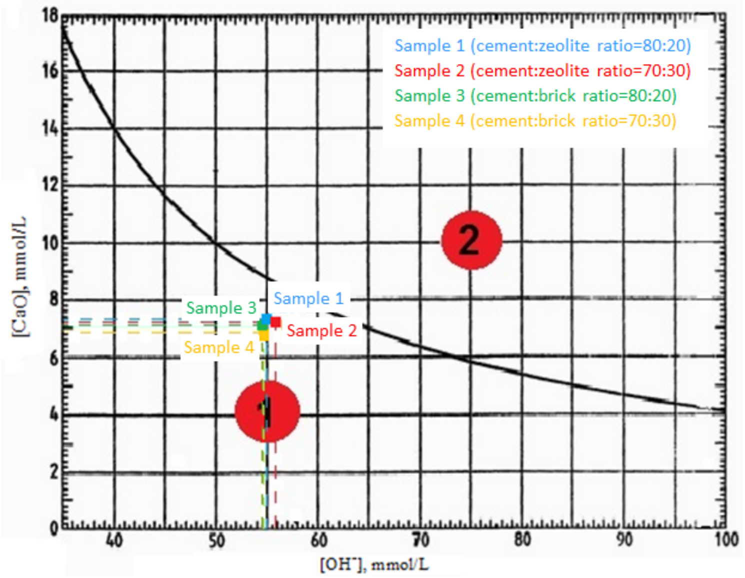

Fig 1: Diagram of isothermal solubility of $Ca(OH)_2$ in dependance on the total alkalinity of the solution above the solid sample (1-area of active pozzolan, 2- area of inactive pozzolan)

Reference

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Gels obtained by reacting diglycidyl eter terminated poly(dimethylsiloxane) with various diamines

Gelovi dobiveni reakcijom diglicidil eterom terminiranog poli(dimetilsiloksana) s različitim diaminima

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Poly(dimethtlsiloxane), PDMS is the most common of semi-inorganic polysiloxane polymers. PDMS is a versatile material with many excellent chemical, physical, and electrical properties including tissue equivalent characteristics [1]. Curing of PDMS oligomers terminated with reactive groups with appropriate reactants may produce gels. Various primary diamines that react with epoxy group [2] at relatively low temperatures were used as curing agents for diglycidyl eter terminated poly(dimethtlsiloxane), PDMS-DGE. Transparent gels that differed in quality and firmness were obtained. The influence of diamine type and reaction conditions on gels was studied by vibration spectroscopy, solvent extraction and thermal analysis. Diamine type was a primary factor defining properties of a gel. The gel prepared with ethylenediamine, EDA, had largest mass loss on extraction in hexane. The loss of mass decreased in order ethylenediamine, triethylenetetramine, diethylenetriamine while the gel prepared with 1,3-diamino-2-propanol, DAP, was the most stable. The gel prepared with EDA was the softest and that with DAP was the firmest. At 50 ºC curing reaction was faster and its extent greater than at room temperature so the gels had somewhat better properties than those obtained at room temperature. Vibration spectroscopy confirmed that differences in properties of gels depended on curing agent used [3] and indicate the role of additional hydroxy group of DAP in stabilizing the gel by hydrogen bonding.

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NMDAR Receptor Targeting Sensor for Detection Glutathione (GSH) and Peroxynitirite ($ONOO^-$)

Senzor za ciljanje NMDAR receptora za detekciju glutationa (GSH) i peroksinitirita ($ONOO^-$)

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Synaptic activity is related, by way of the NMDA receptor (NMDAR), to the glutathione (GSH) antioxidant system [1]. Glutathione (GSH) in known to play key roles in maintaining cellular redox balance. One of the harmful consequences of GSH system dysfunction in the brain is NMDA receptor (NMDAR) hypoactivity. NMDA hypoactivity is implicated in in many brain disorder, including schizophrenia (SZ), bipolar disorder (BD) and autistic spectrum disorder(ASD). Therefore, the development of imaging tools for GSH in NMDAR is necessary.

In this work, fluorescence probe 1, bearing ifenprodil-like tails that have affinity for NMDA receptors [2], was designed and prepared. Also, the two-photon fluorescent probe 1 contains sulfonyl group as a GSH binding site [3] and naphthalimide unit as the two-photon fluorophore. So, this probe can be employed for selective detection of GSH located near the NMDAR.

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Influence of solvents on polymer materials for 3D printing of microreactors

Utjecaj otapala na polimerne materijale za 3D tiskanje mikroreaktora

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Additive manufacturing (AM), also referred to as 3D printing technology, is describing all technologies that build 3D objects by adding layer-upon-layer of material. Additive manufacturing is being used to fabricate molds, prototypes and functional parts with complicated geometry. The main advantage of this type of manufacturing, in comparison with the classic manufacturing, is direct product preparation from 3D model on additive manufacturing equipment, without additional tools [1]. Depending on the technology, materials used for the production of an object can be in powder, liquid and solid form. The most commonly used are polymeric materials (ABS – acrylonitrile/butadiene/styrene, PLA – polylactide, PET – poly(ethylene terephthalate, etc.), but also, less frequently metals and their alloys, ceramics and composite materials are used.

Microreactors are reaction systems fabricated in microscopic scale by using, at least partially, methods of microtechnology and precision engineering [2]. The selection of materials for microreator manufacturing greatly depends on the desired application and on several of the parameters: the type of reaction that is carried out, chemical compatibility with solvents and reagents, the type of microreactor, the mechanical requirements of the microreactor, price, availability on the market, ease of production etc.

In this paper the effects of solvents (water, ethanol and acetone) on materials used in three additive manufacturing techniques – selective laser sintering (SLS), fused depostition modeling (FDM) and stereolithography (SLA) were investigated. Solvent effect was tested by using swelling tests to see which material is suitable for microreactor production. Also, material characterization was investigated with Fourier transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC).

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Radiolytical synthesis of iron oxide nanoparticles in the presence of PEO, PVP, CTAB and DEAE-dextran

Radiolitička sinteza nanočestica željezovih oksida u prisutnosti PEO-a, PVP-a, CTAB-a i DEAE-dekstrana

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Magnetic iron oxide nanoparticles (NPs) have applications as sensor, as contrast agents for MR imaging, in drug delivery and for hyperthermia cancer treatments. γ-irradiation is a powerful technique to synthesize NPs of controlled size and shape in solution, with advantage of inducing solvated electrons and radicals, able to reduce metal ions, homogeneously through the sample. The use of polymers or surfactants can influence the nanoparticle size, morphology, stability and dispersivity. The goal of this work was to study the influence of selected polymers/surfactant on the radiolytical synthesis of iron oxides. Iron(III) precursor solutions were γ-irradiated in the presence of poly(ethylene oxide) (PEO), polyvinylpyrrolidone (PVP), cetyltrimethylammonium bromide (CTAB) and diethylaminoethyl-dextran hydrochloride (DEAE-dextran) [1]. γ-irradiation of iron(III) chloride/PEO aqueous solution produced rigid PEO hydrogels with embedded iron oxide NPs (Fig. 1a). Addition of 2-propanol increase the reducing power of γ-irradiation resulting in the formation of magnetite NPs (Fig. 1b); however 2-propanol reduced PEO crosslinking and thus less rigid hydrogels or suspensions were formed. PVP in Fe(III) solution produced magnetic suspension with a small amount of δ-FeOOH (feroxyhyte). γ-irradiation of Fe(III)/CTAB aq. solution favoured the formation of rod-like goethite NPs (Fig. 1c). Surprisingly, γ-irradiation of Fe(III)/DEAE-dextran aq. solution with 2-propanol produced almost pure δ-FeOOH magnetic nanodiscs (Fig. 1d). This result present the first report of γ-irradiation synthesis of δ-FeOOH and the first report of obtaining δ-FeOOH in nanodisc morphology [2].

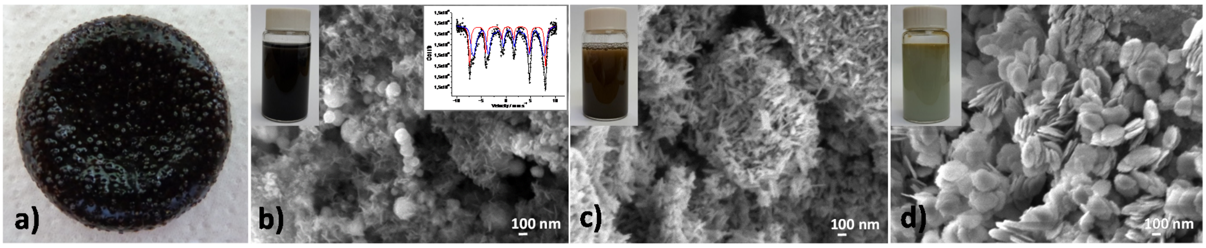

Figure 1: SEM images, photos and Mössbauer spectrum of different iron oxide nanoparticles and composite gel prepared by γ-irradiation of Fe^{3+} aqueous solutions in the presence of PEO (a, b), CTAB (c) and DEAE-dextran (d). Nanocomposite gel (a); magnetite NPs (b); rod-like goethite NPs (c); δ-FeOOH magnetic nanodiscs (d).

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Stability of conducting polymer poly(3,4-ethylenedioxytiophene) in water suspension under simulated solar irradiation

Stabilnost elektrovodljivog polimera poli(3,4-etilendioksitiofen) u vodenoj suspenziji pod simuliranim sunčevim zračenjem

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Conducting polymers are today used in fuel cells, computer displays, microsurgical tools and are now finding applications in the field of photocatalysis. Common photocatalysts such as TiO_2, ZnO and other semiconducting metal oxides have low activity under visible irradiation due to their wide band gap. Conducting polymers with extended π conjugated electron systems have high absorption coefficient in the visible light region. Conducting polymers are also attributed with valence and conduction bands but they have lower band gap energy so visible light irradiation can easily excite sufficient number of electrons which occupy the conduction band and stimulate the e^-/h^+ generation. In that way, when combined with metal oxide photocatalysts, they act as their activators and enhance their photocatalytic activity in the visible part of spectrum. In order to be used in photocatalysis of wastewaters conducting polymers need to have high chemical stability under UV and visible irradiation.

For that reason in this study poly(3,4-ethylenedioxytiophene) (PEDOT) was synthesized by chemical oxidative polymerization at two temperatures (25 and 40 °C) and at three polymerization times (24, 48 and 72 h). Obtained samples were subjected to 90 min of simulated solar irradiation in water suspension, simulating one photocatalytic cycle. Stability was tested by thermogravimetric analysis (TGA) before and after simulated photocatalysis and by measuring total organic carbon (TOC) after photocatalysis to determine the amount of possible low molecular products which could indicate polymer degradation.

From TOC results it was evident that although all samples have stable structure, samples synthesized at 25 °C showed somewhat higher stability. TGA results showed that samples retain the same level of thermal stability after simulated photocatalysis. It was also evident that washing procedure after polymerization needs to be improved as excess oxidant and non-reacted monomer were present in all samples.

Acknowledgements
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Correlation between geometry and formation of spontaneously chiral twist-bend nematic phase

Ovisnost nastanka spontano kiralne “twist-bend” nematičke faze o geometriji molekula

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Since the twist-bend nematic phase (N_{TB}) has been predicted for bent-shaped molecules [1], a series of studies reported the evidence of chiral molecular organization within the N_{TB} phase. This chiral organization is consistent with an oblique helicoidal structure and is obtained even when the molecules are achiral. Despite an effort to determine how variations in molecular structure affect incidence of the N_{TB} phase, a general and comprehensive relationship between molecular structure and the formation of the N_{TB} phase is still elusive [2,3].

Herein we report a comprehensive study, which includes synthesis, mesomorphic properties and molecular modeling, of novel carbonyl- or ethenyl- linked symmetric dimers (Figure 1.a). These new sets of dimers primary differ in the nature of linkage group. Transition properties for ethenyl-linked dimers show that all compounds display both, the uniaxial nematic and N_{TB} phase. In contrast to ethenyl series, the N_{TB} phase was observed only in the homologues with the shortest terminal chains, regardless to the spacer length.

Comparison of mesomorphic properties of these two series complemented with computational studies of conformational space around the linkage group revealed that intramolecular torsion in conjunction with molecular curvature plays important role in formation of a spontaneously chiral twist-bend nematic phase. (Figure 1.b).

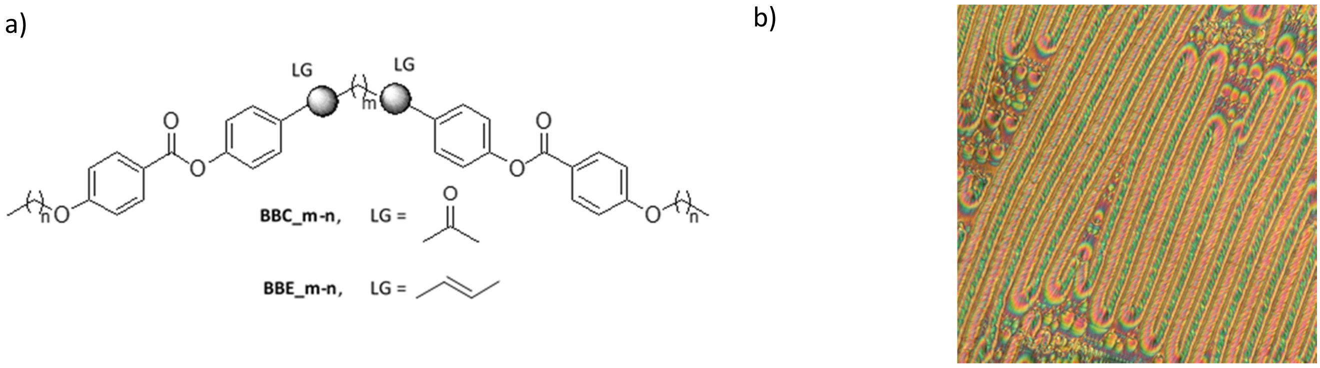

Figure 1: a) The structure of novel symmetric ethenyl BBE_m-n and carbonyl linked BBC_m-n dimers; b) POM rope texture of the N_{TB} phase of BBE_7-2 at 98 °C

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Synthesis and characterization of nanosized $MnFe_2O_4$ with applications as electrode materials in asymmetric supercapacitors

Sinteza i karakterizacija nano-$MnFe_2O_4$ za upotrebu kao materijali za elektrode u asimetričnim superkondenzatorima

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$MnFe_2O_4$ nanosized powders were prepared by solution combustion synthesis. Mole ratio of the initial compounds was calculated in the way that the ratio of oxidizing to reducing power of the components of the combustion reaction is 1:1. Different powders were prepared using different fuels, namely – glycine, glycerol and their mixture at different ratios. It was shown that single phase spinel material could not be prepared when pure glycine is used as a fuel. The materials prepared with a mixture of glycine and glycerol (75:25, 50:50, 25:75) as well as powders prepared with pure glycerol fuel are single phase as was proven by the XRD analyses. Morphological characterizations of synthesized materials were carried out through transmission electron microscopy (TEM) and low-temperature nitrogen adsorption. Results by the both methods clearly show that the type of fuel used in the synthesis strongly affects the size and shape of the particles as well as the porosity of the materials. Samples obtained with pure glycerol have mean particle size of 11 nm and specific surface area of 104 m^2g^{-1}. The isotherm for this sample is of typical IV-type with H1 hysteresis, which is an evidence for the high porosity and cylindrical-type pores with mean diameters around 8 nm. The pore volume is relatively large with narrow pore size distribution below 20 nm. On the other hand sample synthesized with highest glycine concentration in the mixture (75:25) show large particles with mean size of 59 nm, specific surface area of only 7 m^2g^{-1} and its isotherm is of II-type according to IUPAC classification. This isotherm is typical of nonporous materials with very low pore volume. The pore size distribution is large and includes meso- and macro- pores. Electrochemical performance of the synthesized $MnFe_2O_4$ materials as electrodes in asymmetric supercapacitors was investigated in two electrode cell with activated carbon (TDA Research, USA) as negative electrode and composite of activated carbon with 50 % $MnFe_2O_4$ as positive electrode. The carbon and composite electrodes are fabricated in the form of disk with PTFE binder and ABG 1001. The electrolyte is 6M KOH. The cells are subjected to charge/discharge cycling under galvanostatic conditions within the range 0.2-1.2V at different current loads (30 – 320 mAg^{-1}) using Arbin BT2000 apparatus. The electrochemical behavior of material prepared with pure glycerol is superior to materials prepared with a mixture of glycine and glycerol at different ratios, showing highest specific capacity and electrochemical efficiency among all studied samples.

Acknowledgements

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The influence of phosphonic acid film application method on its efficiency in corrosion protection of cuni alloy in seawater

Utjecaj metode nanošenja filma fosfonske kiseline na njegovu djelotvornost u korozijskoj zaštiti CuNi legure u morskoj vodi

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The preparation of self-assembled monolayers (SAMs) on metal or metal-oxide substrates is an important research topic in the field of surface engineering [1]. Reproducible preparation of well-defined and stable monolayers requires appropriate choice of both the self-assembling molecule and the preparation method. Phosphonic acids are a class of molecules particularly known for their spontaneous self-assembly on oxidized substrates. They easily chemisorb on many metals and alloys and show good resistance to hydrolysis. While phosphonic acids have become popular surface modifiers for metal oxides in various fields, especially in the past decade [2-6], there is still a lack of consensus on deposition protocols. Very limited study of phosphonic acid SAMs on cupronickel alloy have been performed, mainly with the dip-coating method [7], which is time consuming, requires high amounts of working solution and is not always practical for application in industry.

The aim of this work is to investigate the possibility of cupronickel alloy protection by self-assembled monolayers of octadecylphosphonic acid (ODPA) prepared by different techniques: dip-coating, electrochemical method and spraying. Each one of these techniques has some advantages: dip-coating method is simple, electrochemical method is less time consuming, but spraying is more practical than the above mentioned methods.

The protective properties of such formed monolayers are examined in artificial seawater by electrochemical polarization methods and electrochemical impedance spectroscopy while the structure of the film is determined by contact angle measurements, scanning electron microscopy and Fourier transform infrared spectroscopy. The results of electrochemical investigations show that by using an adequate preparation method and conditions (temperature, time, applied potential etc.) it is possible to form protective layer of phosphonic acid that significantly reduces cupronickel corrosion rate in seawater.

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Imidazole-based polydiacetylenes as colorimetric and fluorescent chemosensor

Polidiacetileni temeljeni na imidazolu kao kolorimetrijski i fluorescentni kemosenzori

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Polydiacetylenes (PDAs), a class of the conjugated polymers, have been widely explored as stimuli responsive colorimetric and fluorescent sensors. There are various imidazole- and imidazolium-beared chemosensors based on polydiacetylenes. Imidazole is amphoteric, *i.e.* it can function as both an acid and as a base.

Firstly, we developed imidazolium head groups containing polydiacetylenes for the detection of anionic surfactants. When exposed to anionic surfactants, the PDA undergoes selective and unique color as well as fluorescence changes. Also, we developed a new PDA based system that serves as a colorimetric and fluorescence turn-on sensor for naked-eye detection of CO_2. Reaction of carbon dioxide promotes a blue to red color transition.

In addition, we designed the novel PDA, PDA-I-I, derived from imidazolium- and imidazole-monomers that can be employed to instantaneously detect and rapidly destroy most bacterial cells. This observation suggests that the positively charged imidazolium head groups of PDA-I-I electrostatically interact with the negatively charged bacterial surface and that this interaction disrupts the cell membrane that causes bacterial cell death. Lastly, we reported PDA-based colorimetric chemosensor including imidazole on its head group for pH and HCl gas. When hydrogen chloride gas is introduced to PDA-Im-coated glass, its color changes from blue to red.

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Surface morphology modification of materials used for 3D printing

Modifikacija morfologije površine materijala koji se koriste u 3D tiskanju

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Polylactide (PLA) and acrylonitrile butadiene styrene (ABS) are the two most commonly used polymers in 3D printing using fused deposition modeling (FDM) technology. PLA is biodegradable thermoplastic polymer of biological origin and is very interesting as a substitute for plastic materials of petrochemical origin. ABS is thermoplastic polymer of petrochemical origin with the ability to be easily injection molded and extruded which makes it interesting for 3D printing by FDM technology.

In order to develop new materials for 3D printing of microreactors, these two polymers were blended with high-density polyethylene (PE-HD) and low-density polyethylene (PE-LD) in several ratios. In previous studies polymer blends were tested for thermal, morphological and mechanical properties and it has been shown that the addition of polyethylene can significantly modify the mechanical properties of materials used in 3D printing [1].

The aim of this study was to investigate the possibilities of designing hydrophobicity of PLA/PE-HD, PLA/PE-LD, ABS/PE-HD and ABS/PE-LD polymer blends to gain more control over fluid flow inside microchannels of 3D printed microreactors. Polymer blends surfaces were etched by using inductively coupled plasma (ICP) and coated by fluorocarbon-based material (CF_x) plasma deposition treatment in the second step. It has been shown that the surface morphology of PLA polymer blends can be highly modified by etching and CF_x coating. Treated surfaces showed contact angle up to 36° higher than the contact angle measured on untreated surface. Surfaces achieving high contact angles (> 120°) create "island like" surface morphology. Furthermore, it has been revealed that the longer time of etching has significant impact on the contact angle values as well as surface morphology of the PLA polymer blends, while the longer time of CF_x coating has no significant impact on the surface characteristics.

Opposite of the PLA polymer blends surface behaviour, it has been shown that the surface of ABS polymer blends cannot be significantly changed by ICP etching and CF_x coating. Also, no characteristic "island like" surface morphology was created on the ABS polymer blends surfaces.

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Electrochemical intercalation of graphene into polypyrrole layer for supercapacitors application

Elektrokemijsko ugrađivanje grafena u sloj polipirola za primjenu kod superkondenzatora

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Graphene is a monolayer of carbon atoms arranged in to a honeycomb two-dimensional crystal structure. It has excellent properties, such as high mobility of charge carriers, unique transport performance, high mechanical strength, extremely high thermal conductivity and high specific surface area [1]. These properties render graphene suitable for composite material formation or applications such as the active electrode material for energy power sources.

Conductive polymers are materials containing conjugated double bonds along the backbone of the polymer, which provides good electrical conductivity. These materials are suitable for supercapacitor applications due to the fast redox reaction and electrochemical activity in wide potential range. The presence of graphene within the structure of conductive polymer can additionally improve the electrical conductivity as well as the porosity of the material which facilitates the overall redox reaction process [2]. Composite materials based on conductive polymers and graphene can be prepared by chemical or electrochemical methods. However, an advantage of electrochemical polymerization is that the films are deposited directly on the electrode substrate, the film thickness can easily be controlled and the films are free from impurities [3].

In this work graphene was prepared by electrochemical exfoliation of natural graphite flakes in sodium dodecyl sulfate and sodium dodecyl benzene sulfonate aqueous solutions. The obtained solutions were used as supporting electrolyte for the electrochemical synthesis of polypyrrole. It is expected that graphene structure will be incorporated within the polypyrrole layer resulting in improved pseudocapacitive properties. The obtained nanocomposite materials were characterized by means of cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS,) ultraviolet-visible spectrophotometry (UV/Vis), Fourier transform infrared spectroscopy (FTIR), electrochemical quartz crystal nanobalance (EQCN) and scanning electron microscopy (SEM).

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Experimental investigation of shape-memory properties of the Cu-Zn-Al alloys with low content of Al

Eksperimentalno ispitivanje osobina pamćenja oblika Cu-Zn-Al legura sa niskim sadržajem Al

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Shape memory alloys (SMAs) are group of alloys which can recover their shape when they are heated above a certain temperature [1,2]. The shape memory effect is based on martensitic transformation (MT) which is a diffusionless and reversible phase transformation [3]. Two Cu–Zn–Al alloys with variable content of Zn (25 and 30 wt%) and constant Al content (4 wt%) prepared by induction melting of pure metals and hot rolled into strips of 0.5 mm thickness were thermally processed by using three different heat treatments: direct quenching, step-quenching and up-quenching with boiling water and room temperature water as the quenchants. The effects of composition and different methods of heat treatment on the microstructure and transformation temperatures of the investigated Cu–Zn–Al alloys were investigated using SEM-EDS and DSC techniques.

Based on the results of microstructure and thermal analysis investigations following conclusions are made: 1) Microstructure of the as-cast Cu–25%Zn–4%Al alloy consists of β phase in the base and a considerable amount of irregular dendritic α particles with an FCC structure distributed in the β matrix. Cu–30%Zn–4%Al alloy in the as-cast state has single-phase microstructure which includes large polygonal grains of β phase; 2) Direct quenching and up-quenching produce fully martensitic microstructure in the Cu–25%Zn–4%Al alloy. Martensite was also induced by step-quenching, but microstructure of the step-quenched Cu–25%Zn–4%Al sample also includes small precipitate particles of α phase; 3) It was determined that martensite to austenite transformation for the Cu–25%Zn–4%Al alloy occurs in the temperature range from approximately 30 to 60 °C. Comparison between obtained values of As and Af temperatures revealed small influence of applied heat-treatment processes on austenite start and finish temperatures.

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Synthesis of uniform plate-like {001} calcite crystal seed

Sinteza uniformnog pločastog {001} kalcitnog kristalnog sjemena

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Calcium carbonate crystals are interesting model for studying the additive-controlled processes that are important for pharmaceutical industry and for understanding the crystallization in biological systems [1]. Calcite, the most stable calcium carbonate polymorph, can crystallize with notable variety of habits under different environmental conditions. Indeed, it is known that the addition of inorganic ions such as Mg^{2+}, SO_4^{2-} or Li^+ can exert profound effect on the morphology of calcite precipitated in aqueous systems [2]. Previously, it has been shown that increasing amounts of lithium ions enhance the formation of {001} calcite form [3]. Such crystals could be used as a good model for determination of adsorption mechanisms of organic molecules on the {001} calcite surface.

The aim of this study was to prepare the plate-like and uniform calcite crystal seed, with well-developed {001} faces. For that purposes, the influence of the lithium ions concentration, in the range from c = 0.0 to 1.0 mol dm^{-3} and a mode of agitation have been systematically studied as a critical parameters of this specific $CaCO_3$ precipitation process. Calcite samples were characterized by means of FTIR/ATR spectroscopy and PXRD. In addition, the SEM and AFM microscopy were used for identification and surface analysis of {001} faces, while the chemical composition of the precipitate has been determined by the ion chromatography. The results indicated that the addition of lithium ions has a significant influence on the polymorphic composition, as well as on the morphology of calcite crystals. It has been shown that the uniform, plate-like calcite is preferably precipitated after the addition of Li^+ at concentration, c = 0.3 mol dm^{-3}.

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Nanoscale zero-valent iron – Characterization and analytical application

Neutralno željezo na nanoskali - Karakterizacija i analitička primjena

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Nanomaterials have gained the greatest interest over other materials as the adsorbents of analytes such as transition metals and semimetals from complex environmental samples. [1] Utilization of zero-valent iron nanoparticles (nZVI) is widely adopted in analytical preconcentration and extraction procedures due to large surface area, chemical stability, durability, corrosion resistance, and cost effectiveness. Reductive immobilization of trace quantities of potentiallly toxic metal species on iron nanoparticles is in focus of many studies directed toward environmental and health effects. Removal efficiency is often determined by imaging of solid particles by scanning emission microscopy, or by X-ray diffraction. The studies which concern the changes of solution, especially aqueous solution are rarely described in literature. [2] Therefore, in this work we have developed the ICP-OES method for quantitative analysis of chromium (VI) removal from water by nanoscale iron.

Zero valent iron nanoparticles (nZVI) were synthesized in ethanolic medium by the method of ferric iron reduction using sodium borohydride as a reducing agent. A systematic characterization of nZVI was performed using XRD and SEM studies. The extraction capabilities of synthesized particles were tested and optimized to mass fraction used in the experiments on model aqueous solutions containing hexavalent chromium species. The efficiency of Cr(VI) removal from aqueous solutions was measured by ICP-OES analysis on selected chromium emission lines. Reductive immobilization of hexavalent chromium on bare nanoparticles and nanoparticles which were modified by addition of 1,5-diphenylcarbazide was performed. [3] Separation of particles from solution was achieved using solid phase extraction (SPE). The sensitive plasma spectrometry measurements of starting and residual chromium content showed that better removal efficiency (96 %) was obtained in lower concentration range (1-5 mg L^{-1}) of Cr(VI) and with the addition of 1,5-diphenylcarbazide reagent.

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Ion-polaron charge transport in alkali zinc phosphate glasses containing WO_3 and MoO_3

Prijenos naboja kod ionsko-polaronskih alkalijskih zinkovih fosfatnih stakala koja sadrže WO_3 i MoO_3

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Glass systems of the composition (30-0.5x)M_2O-(30-0.5x)ZnO-40P_2O_5-xTMO ($0 \leq x \leq 60$ mol. %) were studied (M = Na, Li; TMO = WO_3, MoO_3). These glasses show interesting electrical properties due to potential coexistance of two different conduction mechanisms. Generally, at high alkali metal oxide content ionic conduction is predominant whereas at high transition metal oxide content polaronic conduction is prefered. In glasses with equal content of both alkali and transition metal oxide a conductivity minimum should be observed. This effect is known as ion-polaron effect and it has been a subject of investigation for decades. [1]

Structure of glasses was investigated by Raman and infrared spectroscopy (IR). Glasses with high alkali metal oxide content contain mostly metaphosphate units (Q^2) which depolymerize with the addition of TMO. Also, in these glasses, at very high content of TMO, the TMO starts acting as both network modifier and network former. [2, 3]

Electrical and dielectric properties of glasses have been studied by impedance spectroscopy in wide frequency and temperature ranges. The results have shown that these glasses show a minimum of conductivity with increasing TMO content. Conductivity minimum in all series of glasses suggest that the coupling of ionic and polaronic conduction mechanisms occur which can be attributed to ion-polaron effect.

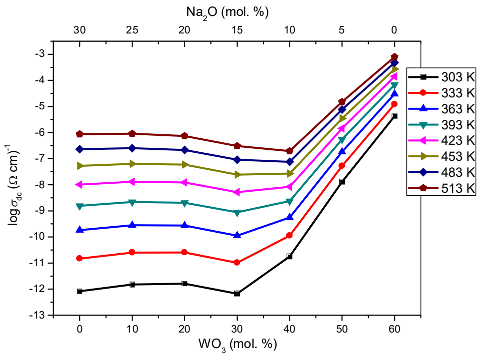

Figure 1: Dc conductivity trend of sodium-tungsten series.

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Electrical transport in iron (boro)phosphate glasses containing HfO_2 and CeO_2

Električni transport u željeznim (boro)fosfatnim staklima s HfO_2 i CeO_2

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Phosphate glasses containing transition metal oxide such as Fe_2O_3 exhibit polaronic conductivity as a result of electron hopping from Fe^{2+} to Fe^{3+} ions, which is described by *small polaron hopping* model. The electrical and dielectric properties of three series of glasses (11 samples), HfO_2-Fe_2O_3-P_2O_5, CeO_2-Fe_2O_3-P_2O_5, and HfO_2-Fe_2O_3-B_2O_3-P_2O_5, were investigated using impedance spectroscopy over a wide frequency (0.01 Hz-1 MHz) and temperature range (303-513 K), whereas fraction of ferrous ions was determined by Mössbauer spectroscopy. Detailed analysis of conductivity and permittivity spectra was done to gain a better insight into factors that possibly influence polaron transport.

In all three glass systems with wide variation of Fe^{2+} content a maximum in conductivity is observed at slightly below $Fe^{2+}/Fe_{tot} \approx 0.5$ which confirms that electrical transport is strongly controlled by polaron concentration via fraction of ferrous ions, Fe^{2+}/Fe_{total}, and overall Fe_2O_3 content. Conductivity spectra for all glasses were analyzed in the model-free approach with various scaling procedures and in addition were also modelled with MIGRATION concept. It is found that in each series of glasses the shape parameter describing conductivity dispersion remains the same indicating that the mechanism of conductivity is unchanged. Sidebottom scaling of conductivity spectra which takes into account experimental dielectric strength parameter showed that it is possible to obtain super-master curve, whereas with Summerfield scaling additional shift is required on the frequency axis. Observed feature implies that for all our systems not only does the charge carrier concentration change with composition, but also the typical length of a polaron hop. Furthermore, characteristic spatial extent of localized hopping of polarons is calculated from scaled experimental permittivity spectra and it shows a decreasing trend with increasing polaron concentration. Obtained values lie in the range of values for polaron radius calculated from equation proposed by Bogomolov.

This study revealed that electrical transport in these polaronic glasses is, in addition to polaron concentration, also influenced by polaronic hopping distance which is changing with composition due to an alteration in distribution of iron ions in the glass matrix.

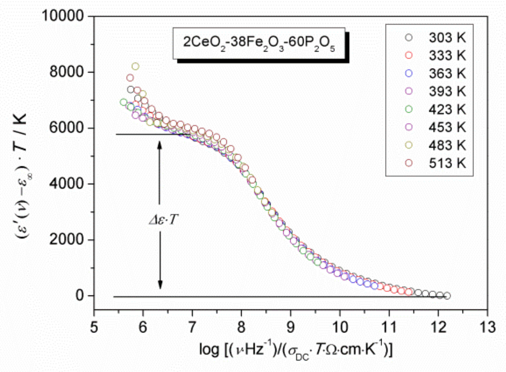

Figure 1: Scaled permittivity spectra of the $2CeO_2$–$38Fe_2O_3$–$60P_2O_5$ glass using Summerfield procedure.

Morphology, interfacial and mechanical properties study of silica reinforced iPP/SEBS(-*g*-MA) composites

Istraživanje morfologije, međupovršinskih i mehaničkih svojstava iPP/SEBS(-*g*-MA) kompozita ojačanih silikom

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The effects of different silica and elastomeric content on morphology, interfacial properties, and mechanical properties of polypropylene/silica 96/4 composites modified with 5, 10, 15, and 20 vol% of poly(styrene-*b*-ethylene-*co*-butylene-*b*-styrene) SEBS and SEBS grafted with maleic acid (SEBS-*g*-MA) were investigated. Four silica fillers differing in size (nano- *vs.* micro-) and in surface properties (untreated *vs.* treated) were chosen as fillers. Elastomers SEBS and SEBS-g-MA were added as impact modifier and compatibilizer at the same time.

The morphology of binary blends and ternary polymer composites was studied by different microscopy techniques. While in binary iPP/SEBS(-*g*-MA) blends prevails typical two phase morphology with iPP as matrix, the ternary composites revealed the wide spectrum of morphologies rather than one exclusive, depended primarily on interfacial properties. [1,2]

Both iPP/silica/SEBS(-*g*-MA) composites preferred compartmentalized morphology (as the variety of core-shell m.) with hydrophilic silica while with hydrophobic silica there is a wide spectrum of different morphologies. The spherulitic morphology of polypropylene matrix in iPP/silica/SEBS(-*g*-MA) composites was abrupt with the addition of silica and the final morphology was a result of two competitive effects: nucleation effect of filler and solidification effect of elastomer. Tensile and impact strength properties were mainly influenced by combined competitive effects of stiff filler and tough SEBS(-*g*-MA) elastomer. Both elastomers showed great impact modifying properties.

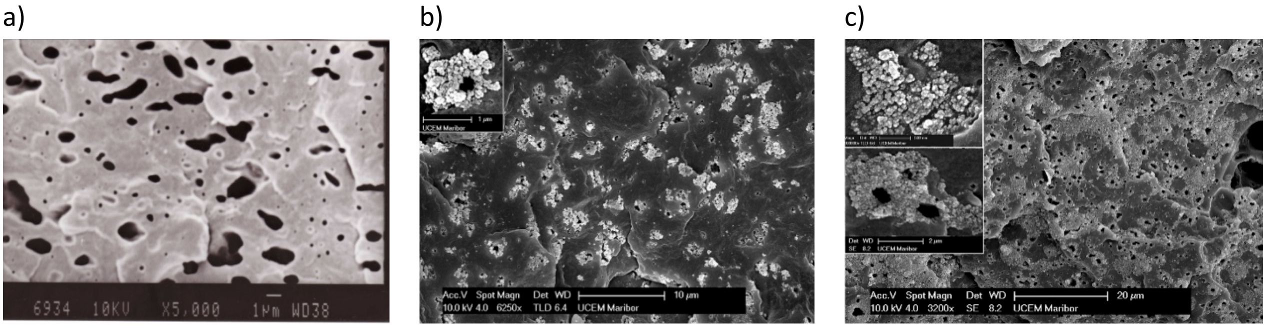

Figure 1: a) SEM pictures showing different morphologies: iPP/SEBS binary blend 80/20; b) iPP/silica 96/4 + 20% SEBS; c) iPP/silica 96/4 + 20% SEBS-g-MA

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Toxicity determination of chemotherapeutic agents in the water by Vibrio fischeri bacteria

Određivanje toksičnosti kemoterapeutika u vodi bakterijom *Vibrio fischeri*

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The growth of human consumption from year to year increases the use of pharmaceuticals in everyday life. This has extremely negative effect on environment, especially the water, causing the pollution. The problem occurs in the treatment of waste waters because such waters, contaminated with pharmaceuticals, are very difficult to process with conventional methods of treatment. All these facts and the lack of legal regulations that define the maximum permissible concentrations of pharmaceuticals in the environment, encouraged scientists and numerous experts on research and development of modern technologies for wastewater treatment.

The aim of this study was to determine toxicity of pure active chemotherapeutic agents of antiparasitics (albendazole, febantel, praziquantel), antibiotics (cefdinir, nitrofurantoin), a bisphosphonate for treating and preventing osteoporosis (alendronate), a rheumatoid (hydroxychloroquine), an antiemetic (metoclopramide), and a NMDA receptor antagonists (memantine). It si important to determine the toxicity of pure active components because it helps determining their toxicity in the environment and also helps to track the toxicity of their metabolites and degradation products. To determine the toxicity, bioluminescent method DIN 38412 –L-34 was applied where test organisms used were *Vibrio fischeri* bacteria. They are sensitive to organic contaminants whose presence causes an inhibition of bacteria luminescence. [1]

Measurements have shown that all pharmaceuticals with higher concentrations cause inhibition of bacterial culture. Which concentration will be taken as the limit one, depends on the severity of the observed effect. For the most pharmaceuticals the action after their usage is not known therefore it is necessary to implement more and more of this kind of measurements, especially for antibiotics and estrogens, which are suspected to persist in environment, either due to disability of biodegradation or due to continuous discharge.

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Sorption of pharmaceuticals on waste sludge generated from pickling of steel pipes

Sorpcija farmaceutika na otpadni mulj nastao kiselinskim dekapiranjem čeličnih cijevi

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In last decades quantities of used and manufactured human and veterinary pharmaceuticals are increasing. After consumption, because of their physical-chemical properties, they end up in the nature. Consequently many of them pass through all of the natural filters and also wastewater treatment plants, and reach surface and ground waters. Those pharmaceuticals could cause adverse effects in ecosystems and can lead to pollution of sources for drinking water. Today, scientists all around world are trying to find the solution for removing of pharmaceuticals from wastewaters. Some using methods are physical separation (reverse osmosis/nanofiltration), biological treatment (membrane bioreactors), advanced oxidation processes (Fenton, photo-Fenton, ozonation, etc.), and sorption (activated carbon, industrial by-products, agricultural waste, etc.) [1,2]. In order to reduce cost, less expensive materials as a sorbent, like different sludges, waste slurry, fly ash, blast furnace slag, anode dust, red mud were investigated [1-4].

In this work, sorption of two different pharmaceuticals from wastewater, dexamethasone and ciprofloxacin separately, on waste sludge generated from pickling of steel pipes before galvanization process were studied. In order to follow the sorption of pharmaceuticals on sludge UV/VIS spectrometry was used. Sorption parameters of both pharmaceuticals on waste sludge were determined. All experiments were performed also with heat-treated sludge with the aim to demonstrate the influence of heat treatment on its sorption potential.

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Anaerobic digestion of sewage sludge from the treatment of industrial waste water

Anaerobna digestija otpadnog mulja iz obrade industrijskih otpadnih voda

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The rapid population growth in recent decades, leads to an increase in living standards. Continuous development of society causes large and adverse changes in the environment. Awakening awareness of the importance of sustainable development, results in the emergence of new branches of engineering aimed at the development of new and improvement of existing technologies with respect to the closed production cycle. Construction of plants for biological treatment of wastewater results in increase in amount of sludge. The purpose of sludge treatment is to decrease its amount and the cost of storage. By anaerobic digestion the sludge is stabilized and biogas, a renewable source of energy, is produced. Co-digestion is an anaerobic digestion at least two types of substrates in order to increase process efficiency, to yield methane as high as possible. [1,2]

This paper characterizes the sludge which is obtained in the process of aerobic treatment of industrial wastewater. Based on the results of the BMP tests, the cosubstrate has been chosen as well as the ratio I/(S+KS) for the process of anaerobic digestion. In the experiments the volume of biogas was measured, volume ratio of methane, carbon dioxide and nitrogen was determined, and physico-chemical and microbiological analyses were carried out. The most efficient process was carried out with the cosubstrate cardboard and the ratio I1/(S+K) = 1.0.

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Recycling copper slag to iron oxide and water glass (silica): part I

Recikliranje bakrene troske u željezov oksid i vodeno staklo (siliku): 1. dio

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A new approach is proposed for the recycling of copper slag in the iron oxide concentrate, and the solution of silicon in the alkali metal hydroxide which can be used for the production of water glass and silica. The process is optimized in two parts, containing a total of 5 stages, namely:

Part I: a) air oxidation of copper slag; b) hydrothermal treatment of the slag with sodium hydroxide solution; c) separating the solid phase (iron oxide concentrate) from the liquid phase by hot filtration.

Part II: d) Formation of the gel by hydrolysis of a silicate liquid phase by changing the pH; e) Preparation of amorphous SiO_2 (silica gel).

Part I. The processes used for slag manipulation were elucidated and optimized for silicon extraction. It was established that the increase in the oxygen partial pressure in the oxidizing gas does not change the mechanism nor significantly intensifies the oxidizing process. The slag oxidation passes through a four-stage mechanism as follows: (i) oxidation of magnetite and formation of metastable spinel (γ-Fe_2O_3); (ii) transformation of γ-Fe_2O_3 into the stable α-Fe_2O_3; (iii) oxidation and decomposition of fayalite ($2FeO.SiO_2$); (iv) decomposition of the residual fayalite and polymorphic transformations in the silicate and iron phases. XRD analysis of the slag oxidized in a furnace at different temperatures confirmed that the decomposition of fayalite begins at temperatures above 400°C. At 800°C the observed phases were hematite (Fe_2O_3) and magnetite (Fe_3O_4) with small crystallite sizes. The silica phase was amorphous. No peaks of fayalite were observed. A decisive factor for the extraction of SiO_2 during hydrothermal treatment was the concentration of NaOH. Its increase reduced the amount of residual SiO_2 more than half and significantly decreased the formation of analcime ($NaAlSi_2O_6.H_2O$) in the solid phase iron oxide concentrate.

For characterization of the resulting solids are used XRD, SEM and IR analysis.

Acknowledgements

The results were obtained with the financial support of the NSF of Bulgaria project No E 02/1/12.12.2014 entitled “Study of the interaction of complex composite-silicates of metallurgical slag with alkaline solutions” funded by the Fund “Scientific Research” of Bulgaria.

Synthesis of poly(3,4-ethylenedioxitiophene)/TiO_2 nanocomposite; photocatalytic efficiency under the simulated solar light

Sinteza poli(3,4-ethylenedioxythiophene) / TiO_2 nanokompozita; Fotokatalitička učinkovitost pod simuliranim sunčevim zračenjem

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In this study nanocomposite photocatalyst of conducting polymer poly(3,4-ethylenedioxytiophene) (PEDOT) and TiO_2 has been synthesized with the aim of extending photocatalytic activity of TiO_2 into the region of visible light irradiation. PEDOT/TiO_2 photocatalysts were synthesized by chemical oxidative polymerization with two oxidants; $FeCl_3$ and ammonium persulfate (APS). Photocatalysts were characterized by Fourier-transform infrared spectroscopy (FTIR), thermogravimetric analysis (TGA) and scanning electron microscopy. Photocatalytic activity has been tested on removal of C.I. Reactive Red 45 (RR45) dye in aqueous solution by UV-A and simulated solar irradiation. UV/Vis spectrophotometric and total organic carbon (TOC) measurements were performed for determination of color removal and the extent of mineralization.

It was found that nanocomposite synthesized with $FeCl_3$ was the most efficient with superior photocatalytic activity when compared to pure TiO_2. It was able to remove color in just 15 min under the solar irradiation with mineralization extent of 85% after 90 min.

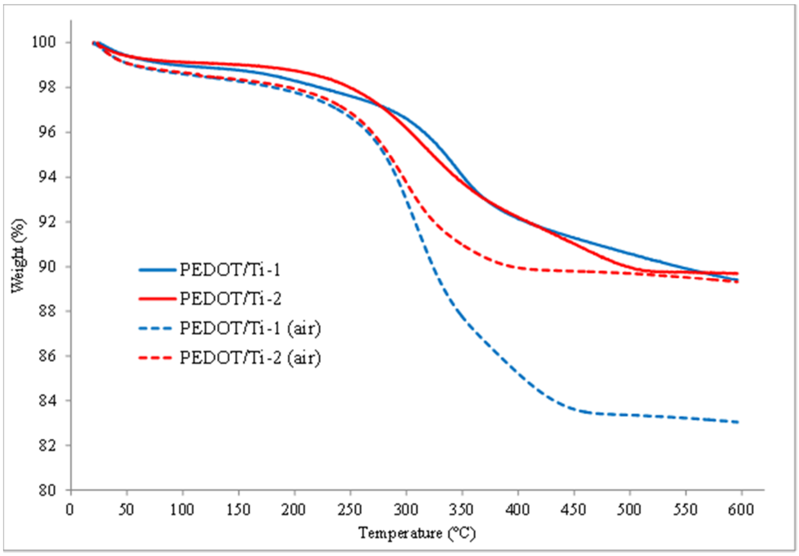

Figure 1. TG curves of composite photocatalysts synthesized with APS oxidant (PEDOT/Ti-1) and with $FeCl_3$ oxidant (PEDOT/Ti-2) recorded under N_2 and air atmosphere.

Acknowledgements

This work was financially supported by Croatian Science Foundation (HRZZ).

CD spectroscopy distinguishes structurally related mycotoxins

Razlikovanje strukturno sličnih mikotoksina metodom CD spektroskopije

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Mycotoxins are secondary metabolites produced by moulds abundant in the different environments. Among these, aflatoxin B_1 (AFB_1) is considered one of the most toxic and is human cancerogen [1]. Structurally related furofurane derivatives (Fig. 1) sterigmatocystin (STC) and 5-methoxysterigmatocystin (5-MET-STC) are direct biosynthetic precursors in AFB_1 producing Aspergilli, but also the final products of biosynthesis occurring in the different types of moulds [2]. Despite similarities in their chemical structures, their toxic properties differ and thus suggesting the differences in their physicochemical properties in water solutions.

In this study we showed CD spectra of AFB_1, STC and 5-MET-STC in organic and water based solvents for the first time. While the CD signal in organic solvent is of low intensity and quite similar for all of the three compounds (Fig. 2A), STC showed distinctive CD signal of unusually high intensity in water (Fig. 2B). In contrast to its structural analogues we suspect such signal of STC is due to its ability to aggregate in water as was confirmed with other methods we applied that will be presented and discussed. The significance of these results is yet to be explored, but they made the basis of a new approach in the analysis of STC in water based solutions, in addition to understanding its behavior in biological systems.

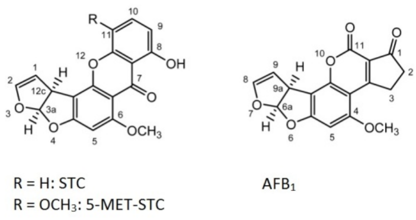

Figure 1: Chemical structures of AFB_1, STC and 5-MET-STC

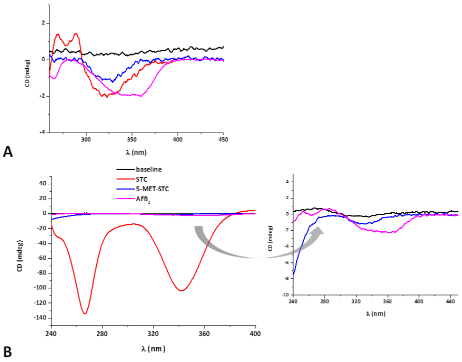

Figure 2: CD SPECTRA of AFB_1, STC and 5-MET-STC (2×10^{-5} M) in acetonitrile (A) and cacodylate buffer (pH=7, *I*= 0,05 M) (B)

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Biosorption capacity of activated sludge from pharmaceutical wastewater treatment plant

Biosorpcijski kapacitet aktivnog mulja iz postrojenja za obradu farmaceutskih otpadnih voda

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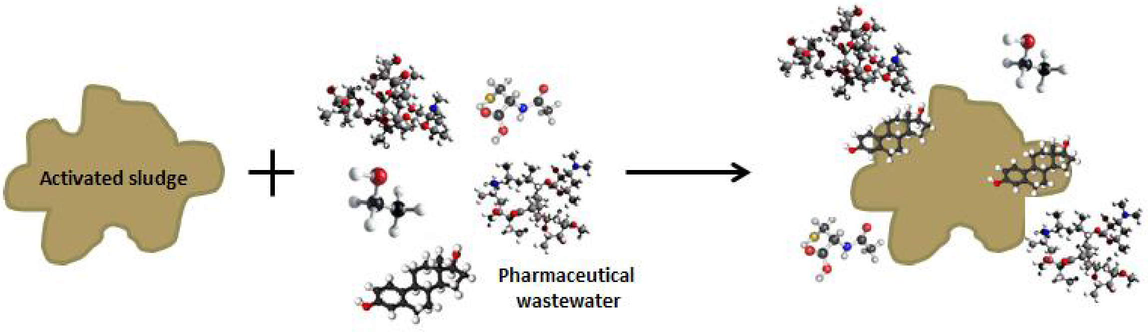
Increase in the world's population and urbanization, especially in developing countries, leads to higher amount of wastewater. Their discharging without prior treatment can easily cause environmental pollution issues. Biological processes have been widely used for wastewater treatment because of their low cost and effectiveness. Nowadays, biosorption technique is increasingly gaining importance due to the appearance of biologically resistant xenobiotics. Generally, biosorption is a physico-chemical process for removal of substances from wastewater by biological material.

In this study the biosorption capacity of activated sludge from pharmaceutical wastewater treatment plant was determined. The initial concentration of activated sludge, with particle sizes 90-125 µm, ranged between 2.82 to 5.98 g L-1 while the initial concentration of substrate was 5.41 g O2 L-1. The toxicity impact index of the pharmaceutical wastewater was TII50 = 84.21. During the experiments, the COD, pH value, electrical conductivity, concentrations of dissolved oxygen and biomass were measured. Microscopic analyses were performed to monitor the quality of activated sludge particles. The highest biosorption efficiency was 25.5 %. No activity of activated sludge was recorded due to microscopic analyses and oxygen uptake rate values which were between 1.62 mg L-1 h-1 and 8.32 mg L-1 h-1.

GRAPHICAL ABSTRACT



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Trophic index (TRIX) at selected stations of Central and South Adriatic

Prikaz trofičkog indeksa TRIX-a na izabranim postajama Srednjeg i Južnog Jadrana

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As one of the indicators related to the marine ecosystem condition in the National list of indicators, trophic index (TRIX) is included [1]. The TRIX index is a logarithmic formula of four state variables, which are directly related to productivity: chlorophyll-a (Chl, mg/L), oxygen as the absolute percentage deviation from oxygen saturation (DO, %), and nutrient salts such as dissolved inorganic nitrogen (DIN, mg/L) and total phosphorous (TP, mg/L). The trophic index TRIX was developed by Vollenweider in 1998 for the coastal area of Emilia-Romagna (northern Adriatic Sea) [2] and it has been used in this research. Accordingly, sea water can be classified on a scale from 0 to 8, based on degree of eutrophication as: oligotrophic (0-4); mesotrophic (4-5); eutrophic (5-6) and extremely eutrophic (6-8).

In this research trophic index (TRIX) has been used to assess the ecological status of coastal area of Southern and Central Adriatic. Data were obtained from two coastal stations (Dubrovnik-station A1 and Kaštela Bay-station A2) characterized by large loadings on the ecosystem (excessive of nutrient intake through wastewater, agriculture, industrial water etc.) and from another two coastal stations with less loadings on ecosystem (Podstrana-station A3 and Pelješac peninsula station A4). As reference stations, those located at the open sea (R1, R2 i R3).

TRIX calculated value based on the data obtained at the research station, range from 2.80 to 3.60. According to obtained TRIX values (< 4) sea water at research station can be classified as oligotrophic.

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Possibility of brewer's spent grain application in production of modified wheat flours by extrusion process

Mogućnost upotrebe pivskog tropa u proizvodnji modificiranih brašna pšenice postupkom ekstruzije

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Brewer's spent grain (BSG) is the major by-product of the brewing industry, which contains about 17% cellulose, 28% non-cellulosic polysaccharides. It is available in large quantities throughout the year, but its main application has been limited to animal feeding. Nevertheless, due to its high content of protein and fiber (around 20 and 70% dry basis, respectively), it can also serve as an attractive adjunct in human nutrition. The aim of this research was to investigate the potential of BSG application in production of modified wheat flours by extrusion process [1-2]. Mixture ratios (wheat flour: BSG) investigated in this study were: 85 : 15, 70 : 30 and 55 : 45. Mixtures with 30 % moisture content were extruded in the laboratory single screw extruder at temperature profile 70/90/110 °C, using a screw with compression ratio 1:1 and die with 5 mm diameter. The research included determination of physical and rheological properties of non-extruded and extruded samples.

The obtained results showed that the addition of BSG in wheat flour and extrusion process decreased all viscosity parameters. Furthermore, extrusion caused the reduction of falling number and sedimentation values, but the increment of water absorption index and dough development time. Dough stability for all extruded sample was 0, probably due to gluten "dilution" and degradation during the extrusion.

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Assessment of the contamination of soil, cabbage and potato samples in Kastriot, Kosovo

Procjena zagađenja tla te uzoraka kupsa i krumpira u Kastriotu, Kosovo

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Some heavy metals are considered to be of special interest since they are considered essential for the human organism when found in trace amounts. However, the biotoxic effects of many of them in the human biochemistry are of a great concern. Therefore, there is a need for proper understanding of the conditions, such as the concentration and oxidation states, which make them harmful and toxic.

Assessing the concentration of potentially harmful heavy metals in the soil and food is imperative in order to evaluate the potential risks to residents and consumers. Our research reviews certain heavy metals, their distribution and statistical calculations from the soil to food chain such as potatoes and cabbages.

To identify the concentrations and sources of heavy metals, and to assess the soil environmental quality, samples were collected from 3-7 km around Kosovo's power plants. In the same sampling points we collected the samples of cabbages and potatoes. Measurements were done using inductively coupled plasma atomic emission spectroscopy (ICP-AES) technique and for the digestion of food samples we used microwave digestion system. From the obtained results we can conclude that the soil samples are quite polluted with heavy metals whereas the potato and cabbage samples are mostly in average concentration.

Biodegradation of lignocellulosic waste by composting process

Biorazgradnja lignoceluloznog otpada procesom kompostiranja

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Agro-industrial wastes such as tobacco waste and olive pomace contain considerable amount of organic matter, high concentration of nicotine and phenols, respectively, and can`t be disposed on the landfills. Furthermore, these wastes also contain high concentration of lignin, cellulose and hemicelluloses [1]. These macromolecules can be degraded by composting process and with inoculation of different aerobic microorganisms which posse's ligninolytic enzymes such as *Phanerochaete chrysosporium* and *Trichoderma reesei* [1-2]. Composting is an environmentally friendly and effective biodegradation process of organic waste. It is a biological treatment in which aerobic mesophilic and thermophilic microorganisms transform organic matter into CO2, H2O and compost. Many factors influences on composting process such as moisture, C/N ratio, pH value, particle size and supply of air. Tobacco waste and olive pomace have low and high C/N ratio, respectively, and pH value of olive pomace is very low and moisture is above 60 %.

The aim of this research was biodegradation of lignocellulosic material by composting process conducted in a closed thermally insulated column reactor with an effective volume of 10 dm3 with airflow 0.6 dm3 min-1 kg-1VS, initial C/N ratio 30/1 during 28 days. Two different composting experiments were conducted without and with inoculation of different microorganisms which were isolated from tobacco waste and olive pomace such as *Pseudomonas aeruginosa, Candida rugosa, Aspergillus fumigatus* and *Cellulomonas*. Also, *Phanerochaete chrysosporium* and *Trichoderma reesei* were inoculated because according to the literature have high capability for degradation of lignocellulosic materials [2-3]. During the process, temperature changes in reactor, pH value, C/N ratio, moisture content, volatile matter content, FTIR analyses of substrate, COD of condensate, concentration of phenols, evolved CO_2 and NH_3 and the number of mesophilic and thermophilic microorganisms were determined.

It was found that the biodegradation of lignocellulosic materials with inoculation of mixed cultures was faster and obtained conversion was about 10 % higher. An FTIR analysis shows that some peaks where groups of lignin appear after 28 days disappeared which didn`t happened in the experiment where mixed culture was not inoculated. The highest biodegradation and emission of CO_2 was during thermophilic phase. No significant emission of ammonia was detected until day twenty.

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The variability of the trace elements and phytate content of different winter wheat genotypes

Varijabilnost koncentracija mikroelemenata i fitata u zrnu različitih genotipova ozime pšenice

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World population is in signifficant portion exposed to Fe and Zn insufficiency in their nutrition, andtherefore total and bioavailable concentrations of these micronutrients are very important component of the foodquality.

The purpose of conducted research was to answer is there genotype variability according to Fe and Zn concentrations and bioavailability. ThereforeFe and Zn, but also phytates as important bioavailability inhibitors, were being tested in whole grain of 343 winter wheat genotypes.Range (24,33 - 95,75 mg/kg) and average (38,79 mg/kg) of Fe were signifficantly higher than of Zn concentrations (range 13,30 – 38,93 and average 21,35 mg/kg).Analysed genotypes varied more in Fe (variation coefficient 25,4%) than in Zn concentration (21,1%), though much higher variation coefficient (45,3 %) was established for phytates (11,37 g/kg in average, range 3,62 – 23,68 g/kg).

Phytates/Fe ratio was 25 in average (range 6,7 – 59,9) and phytates/Zn was 55 (range 16,5 – 140). Moderate and increasing bioavailability indicate ratios phytates/Zn and phytates/Fe 15 or lower,and has been determined for 65 genotypes for Fe (19% analysed genotypes).It has not been determined for Zn, butphytates/Zn ratioof 7 genotypeswas lower than 20.

Cluster analysis isolated 4 genotypes with concentrations of Fe & Zn higher and phytates/Fe & phytates/Zn ratios lower than average. Another 49 genotypeswere also atributed with phytates/Fe and phytates/Zn ratios lower than average, but with a slightly lower concentrations of Fe and Zn. Additional 13 genotypes have 2 or 3 characteristics that point to bioavailability higher than average. The biggest cluster has 175 genotypes characterized with average Fe, Zn and phytate concentrations. Within 102 reamining genotypes could be expectedvery low Fe and Zn bioavailability.

The results prove variability of analysed genotypes of winter wheat according to the characteristics that significantly influence the content of bioavailable Fe and Zn in whole wheat grain.

Composting of olive mill waste and tobacco waste in a closed reactor

Kompostiranje komine maslina i duhanskog otpada u zatvorenom sustavu

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In Croatia a large amount of agro-industrial wastes, like olive and tobacco waste, are generated during production of olive oil and cigarettes, respectively. These wastes are characterized by high values of chemical oxygen demand (COD), biochemical oxygen demand (BOD), phenols, suspended soils, low pH value, high electrical conductivity and cannot be disposed on the landfill. These wastes can be treated by composting process. Composting is an environmentally friendly and effective technology to treat or manage organic wastes. It is a biological treatment in which aerobic mesophilic and thermophilic microorganisms transform the biodegradable organic matter into CO_2, H_2O and a stable organic matter-compost. Many factors like moisture, C/N ratio, airflow and pH value have influence on composting process and thereby they have to be in optimal range.

The objective of this work was to conduct composting process of mixture of olive (OW) and tobacco (TW) waste in column reactors with effective volumes of 1 dm^3 and 10 dm^3, respectively, during 28 days. The airflow in reactors of 1 dm^3 and 10 dm^3 was set at a 0.08 $dm^3\ min^{-1}$ and at a 0.84 $dm^3 min^{-1}$, respectively. Three different experiments were conducted in smaller reactor (1 dm^3) with different initial C/N ratio from 25/1 to 35/1 and from the obtained results the best was set up in a larger reactor of effective volume 10 dm^3. The initial moisture in both processes was 60 % and pH value about 6. During composting process samples were collected periodically and the most relevant physical-chemical (pH - value, moisture content, dry matter (DM), volatile solids content (VS), N content) and microbiological characteristics were determined [9, 10]. Carbon dioxide (CO_2) and ammonia (NH_3) was absorbed in 1 mol dm^{-3} sodium hydroxide (NaOH) and in 4 % H_3BO_3, respectively. CO_2 and NH_3 was analysed daily by titration 1 mol dm^{-3} and 0.1 mol dm^{-3} HCl.

From obtained results of composting of olive and tobacco waste in a smaller reactor, the C/N ratio between 30/1 and 35/1 gave the best results, higher conversion in less time. It was found that emission of carbon dioxide depended on temperature while emission of ammonia mainly depended on pH value in composting mass. The most of carbon dioxide was evolved in the thermophilic stage of composting process due to the highest activity of microorganisms.

Three-factor approach for modulating the content of phenols and taste attributes of Oblica cv. (*Olea europaea* L.) virgin olive oil

Trofaktorijalni pristup modulaciji sadržaja fenola i svojstava okusa djevičanskog maslinovog ulja kultivara Oblica (*Olea europaea* L.)

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Phenols are responsible for virgin olive oil (VOO) taste characteristics, and significantly determine VOO oxidative stability and shelf life, as well as its nutritive value. The content of phenols in VOO depends on many agronomic and technological factors [1], and olive fruit ripening degree and paste malaxation duration and temperature are among the most important. The aim of this study was to investigate the main effects and interactions of these three key factors on the content of phenols and related taste sensory characteristics of Oblica cv. (*Olea europaea* L.) VOO. Olives were picked at three ripening degrees as green (RD1), semi-ripe (RD2) and ripe (RD3), and processed by malaxation at 22 / 30 °C, for 30 / 60 min. The obtained oils were subjected to HPLC-DAD analysis of phenols [2], and sensory analysis by the official IOC method [3].

The highest variability was observed for ripening degree, where later harvest caused the particular oleuropein and ligstroside aglycons, phenolic acids, acetoxypinoresinol, and vanillin to decrease. The amounts of the two major aglycons, 3,4-DHPEA-EDA and *p*-HPEA-EDA mostly increased, but only at 30 ^{o}C. The effect of higher malaxation temperature was significant for phenolic acids and flavonoids which mostly decreased, and for vanillin and the majority of secoiridoids which increased. The main effect of malaxation duration was relatively weak. For the majority of phenols the effects of the factors significantly interacted. Among many specific and unique outcomes, several clear patterns were noted. For the majority of phenols, the positive effect of higher malaxation temperature was found to intensify with ripening, peaking in RD3, most strongly for 3,4-DHPEA-EDA and *p*-HDEA-EDA. Ripening degree also interacted with malaxation duration. At RD1, except for vanillin and *p*-HPEA-EDA, a negative effect of longer duration was observed, while at RD3 longer malaxation caused a reversed effect and all phenols increased, but exclusively at 22 ^{o}C.

Desirable taste sensory attributes correlated positively with particular main phenols. A decrease of bitterness and pungency, and an increase in sweetness was observed along ripening. Bitterness and pungency were enhanced by the higher malaxation temperature.

This work has been supported in part by Croatian Science Foundation under the project UIP-2014-09-1194.

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Potentiometric monitoring of anionic surfactants degradation using photooxidative UV/H_2O_2 processes

Potenciometrijsko praćenje razgradnje anionskih tenzida fotooksidativnim UV/H_2O_2 procesom

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The history of advanced oxidation processes (AOP) began with Fenton chemistry (1894). Until then AOP´s have become of great interest. In last few decades the importance of hydroxyl radical (HO·) reactions wastewaters treatment has been recognized and viewed as potentially convenient and economical way to generate oxidizing species for treating chemical wastes [1].

This study reports about the decomposition of sodium dodecylbenezene sulfonate (NaDBS) and secondary alcane sulphonate using photooxidative UV/H_2O_2 process. The decomposition was monitored by potentiometric titration using PVC based self-made electrode for end-point detection [2]. Advantage of this method is in determination of surfactants formed in partial digestion [3] of anionic surfactants using cost effective analytical technique (Figure 1). Even the difference of two C-atoms between the titratable anionic surfactants exhibited two inflexion points. The first one related to the anionic surfactant which formed a heavily soluble ion-pair (greater number of C-atoms) [2].

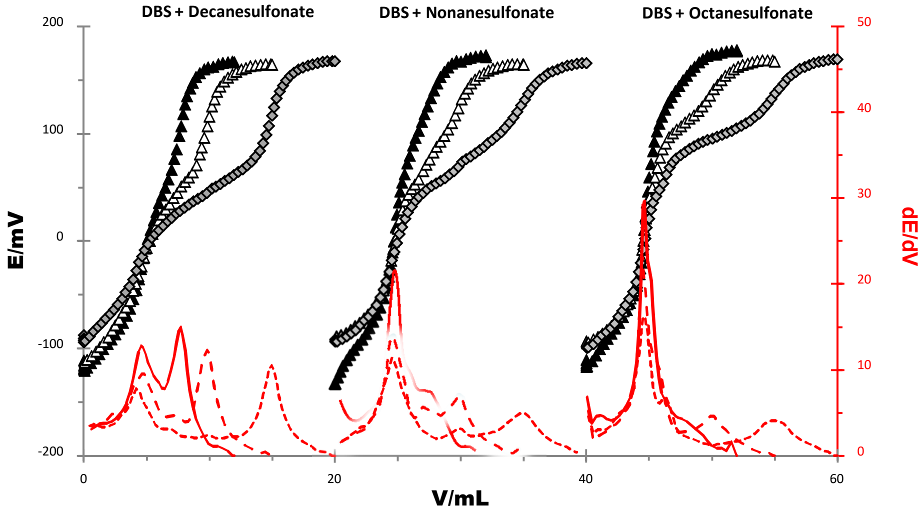

Figure 1. Titration curves and their first derivatives of model solutions containing NaDBS and homologous of sodium alcane sulphonates

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Changes of the geochemical parameters in water of the Plitvice Lakes over the past 30 years

Promjene geokemijskih parametara u vodama Plitvičkih jezera u posljednjih 30 godina

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Within this work we represent the results of analyses of water temperatures and chemical parameters (pH, c(Ca^{2+}), c(HCO_3^-), c(Mg^{2+}), c(CO_2), calcite saturation index (SI_{calc}), calcite dissolution ionic ratio (IR_{calc}) and Mg/Ca ratio) in period 1981-2014 on eight locations at the Plitvice Lakes (two springs, two rivers and four lakes).

Statistical analyses considered that the data was not collected systematically and evenly for all seasons by using a two principles: by observing changes in each calendar month over the whole period and by comparing the mean annual values in two end periods, 1981-1986 and 2010-2014.

In accordance with the trend of global and local air warming (recorded increase of air temperature in Gospić in 1981-2014 was ~2 °C), a warming of spring (~0.5 °C) and lake waters (~1.5 °C) is observed in the past 30 years. An increase is also observed for c(Ca^{2+}) and c(HCO_3^-), 7% and 15% respectively, but no change in c(Mg^{2+}), resulting in Mg/Ca decrease. This implies that the increase in water temperature caused an increase in geochemical dissolution of calcite, but not of dolomite, also making Mg/Ca useless as a temperature proxy. The temporal water warming could have caused increased degassing of CO_2, but this does not seem to be the case since the trend of downstream c(HCO_3^-) decrease has not changed for the observed period. SI_{calc} and IR_{calc} show an increase on dolomite based lake locations indicating a local increase of bioactivity in the last 30 years. There is no statistically significant changes observed for pH and $c(CO_2)$.

The work in detail has been described in A. Sironić, J. Barešić, N. Horvatinčić, A. Brozinčević, M. Vurnek, S. Kapelj *Applied Geochemistry* **78** (2017) 12-22.
doi: *10.1016/j.apgeochem.2016.11.013*

Seasonal variations of carbon mass concentrations in airborne particulate matters of western part of Zagreb

Sezonske varijacije masenih koncentracija ugljika u lebdećim česticama u zraku zapadnog dijela Zagreba

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Levels of elemental carbon (EC) and organic carbon (OC) in $PM_{2,5}$ particles (particles with aerodynamic diameter less than 2,5 µm) in air were determined in this study. Seasonal variations of carbon mass concentrations in $PM_{2,5}$ between seasons (spring, summer, autumn and winter) were studied and compared.

The monitoring site was situated in the western part of Zagreb and characterized as urban industrial site. $PM_{2,5}$ particle fraction samples were collected during 24-hour periods on working days. Small-volume air samples (≈55 m^3) of airborne particles were collected on quartz fiber filters pre-fired at 900°C for three hours. $PM_{2,5}$ mass concentrations were determined gravimetrically according to the HRN EN 12341 standard. Organic carbon, elemental carbon and total carbon (TC, a sum of EC and OC) in $PM_{2,5}$ fraction were determined by the thermal-optical transmittance method (TOT) using carbon analyzer with a flame ionization detector following a NIOSH-like protocol. Statistical analysis was performed using STATISTICA 13.0. statistical software.

Statistically significant seasonal variations between seasons were observed, except between winter/autumn and spring/summer period. The highest mass concentrations of $PM_{2,5}$, EC and OC in $PM_{2,5}$ were observed during the cold period (winter and autumn), while the lowest concentrations were observed in the summer and spring. Higher OC/EC mass ratios indicated the presence of secondary organic aerosols [1-3].

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Recycling copper slag to iron oxide and water glass (silica): part II

Recikliranje bakrene troske u željezov oksid i vodeno staklo (siliku): 2. dio

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A new approach is proposed for the recycling of copper slag to the iron oxide concentrate, and the solution of silicon in the alkali metal hydroxide, which can be used for the production of water glass and silica. The process is optimized in two parts, containing a total of 5 stages, namely:

Part I: a) air oxidation of copper slag; b) hydrothermal treatment of the slag with sodium hydroxide solution; c) separating the solid phase (iron oxide concentrate) from the liquid phase by hot filtration.

Part II: d) Formation of the gel by hydrolysis of a silicate liquid phase by changing the pH; e) Preparation of amorphous SiO_2 (silica gel).

The aim of this study was investigation and optimization of the processes of gel formation and preparation of the amorphous SiO_2 with low density, fine particle size and high surface area. For this purpose, the formation of the gel by neutralization of the alkaline silicate liquid phase with some mineral acids was studied, varying the type and concentration of the acids used and dilution of the initial solutions.

An initial silicon solution with 20 g/l Si and 140 g/l NaOH was used directly or diluted with water in different ratio alkali solution/water. HCl or H_2SO_4 solutions with concentration of 5 and 10 mol/l were added to the alkaline silicon solutions at intensive stirring and room temperature. The method of monotonic titration was applied and pH change of each step was followed. The obtained gel was filtrated, washed and dried at $80^{o}C$. The particle size and specific surface area of the gel were measured and residual concentration of silicon in the liquid phase, as well as the distribution of trace amounts of Al, Fe, Ca, Mg, Cu and Zn was analyzed.

Acknowledgements

The results were obtained with the financial support of the NSF of Bulgaria project No E 02/1/12.12.2014 entitled “Study of the interaction of complex composite-silicates of metallurgical slag with alkaline solutions” funded by the Fund “Scientific Research” of Bulgaria.

Performance evaluation of the polymeric and ceramic membranes in the treatment of textile dye processing wastewater

Ispitivanje radnih karakteristika polimernih i keramičkih membrana pri obradi otpadne vode iz procesa bojenja tekstila

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Textile wastewaters are rated as one of the most polluting among all industrial sectors [1, 2] and their treatment is regulated with strict regulations on the quality of wastewater discharged into the public drainage system. Advanced membrane processes are increasingly used in wastewater treatment, primarily due to separation efficiency and compliance with regulations [3-5]. Ceramic membranes have higher thermal, chemical and mechanical stability compared to polymeric membranes and since wastewater from textile process has high temperature and it is extremely alkaline, ceramic membranes could be appropriate choice for its treatment [1, 3, 6, 7].

This research represents the assessment of possibilities for textile wastewater treatment collected from the process of dye processing with polymer and ceramic membranes with the pores of same size (MWCO 1 kDa). The aim was to get a high quality permeate; to remove the color and presence of organic matter and to reduce the amount of wastewater. The experiments were conducted with a laboratory scale cross-flow membrane systems with full recirculation of the retentate equipped with pressure and temperature transducers connected to the PLC unit. The permeate flux recovery after chemical cleaning membrane was evaluated and the efficiency of wastewater treatment was estimated on the basis of the analysis of raw water and permeate. The effect of the cross flow velocity (CFV) on membrane fouling and normalized flux decline was investigated. Energy consumption has also been studied.

PES flat membrane has proven to be more effective in the treatment of wastewater from the textile dyeing process with the following achieved separation of TSS, TOC and color: 56%, 72% and 85%. Almost complete regeneration of PES membranes was achieved with chemical cleaning procedure. Unlike the ceramic membrane in the case of PES flat membrane ratio of energy consumption for permeate and retentate stream is less.

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Iron(III) complexation and extraction by aromatic hydrazones

Kompleksiranje i ekstrakcija željeza(III) aromatskim hidrazonima

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Aromatic hydrazones, such as salicylaldehyde isonicotinoyl hydrazone, 2’-hydroxyacetophenone isonicotinoyl hydrazone and 2’-hydroxypropiophenone isonicotinoyl hydrazone, have been shown as promising iron-chelating agents [1]. Three methoxy derivatives (**L1**–**L3**) of salicylaldehyde nicotinoyl hydrazone (Figure 1) were prepared in this work and their complexation and extraction properties toward iron(III) were studied by UV-Vis spectrophotometry.

Complexation of iron(III) was studied in acidic methanol/water 1/1 mixtures (0.01 mol dm^{-3} HNO_3). All hydrazones hydrolyze at these experimental conditions but the iron complexes are stable. The stoichiometries of the formed complexes determined by batch spectrophotometric titrations were 1 : 1 (Fe^{3+} : **L**).

The extraction of iron(III) from acidic aqueous solutions was performed with chloroform solutions of **L1**–**L3**. Optimal experimental conditions for extraction were determined, pH of aqueous phase was 3, concentration of ligand was 4×10^{-4} mol dm^{-3} and concentration of iron(III) was 4×10^{-5} mol dm^{-3}. Stoichiometries of extracted complexes were determined to be 1 : 2 (Fe^{3+} : **L**) based on the results obtained by Job’s method and equilibrium shift method. Number of protons released during complexation was three. Molar absorption coefficient of iron(III) complex of **L1** at 374 nm was 14091 mol^{-1} dm^3 cm^{-1}. The compound **L1** was the most suitable of investigated compounds for extraction of iron(III) from aqueous to chloroform phase due to the least overlapping of absorption maxima of complex and ligand.

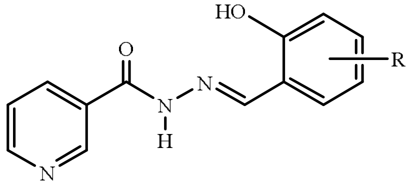

Figure 1: Molecular structure of the studied aromatic hydrazones; R = 3-OCH_3 (**L1**); 4-OCH_3 (**L2**); 5-OCH_3 (**L3**).

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Regio isomerisation in substitution reactions of cyclotriphosphazene derivatives with pyrrolidine

Regio izomerizacija u reakcijama supstitucije derivata ciklotrifosfazena s pirolidonom

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There is a wide range of nucleophilic substitution reactions in phosphazene chemistry and the formation of regio- and stereo-chemical isomers continues to attract attention. Therefore, to investigate the mechanism of nucleophilic substitution reaction at phosphorus (V) atoms is important for the prediction of regio isomers distribution [1-4].

The substitution reactions of mono-spiro and geminal di-substituted cyclotriphosphazene derivatives, $N_3P_3Cl_4R_2$ [R_2 = ($OCH_2(CF_2)_2CH_2O$) (**1a**); ($OCH_2CH_2CH_2O$) (**1b**); ($OCH_2CH_2CH_2NH$) (**1c**); SPh (**1d**); NHPh (**1e**) and $NHBu^t$ (**1f**)] with pyrrolidine were carried out under standard reaction conditions in order to investigate possible geminal or non-geminal directing effect in the di-substitution stage of the group already present on the cyclotriphosphazene ring (Figure 1).

Isolated compounds (non-geminal *cis* / *trans* and geminal) were analysed by the standard spectroscopic techniques such as elemental analysis, mass spectrometry, ^1H, and ^{31}P NMR spectroscopies and suitable single crystals were characterised by X-ray crystallography.

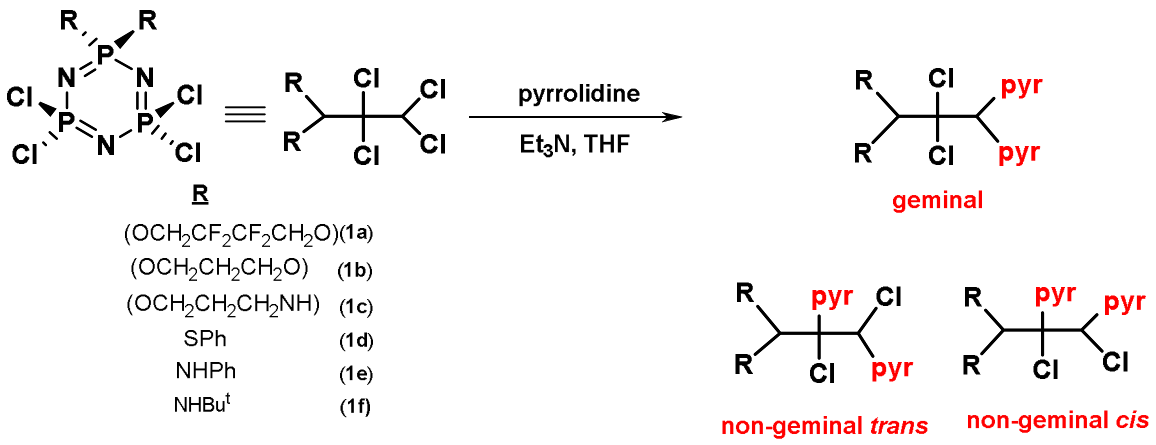

Figure 1: The reactions of compounds **1a**-**f** with pyrrolidine.

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Quantitative determination of flavonoids in the leaves of lemon balm - *Melissa officinalis* L.

Kvantitativna analiza flavonoida u listovima matičnjaka - *Melissa officinalis* L.

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Medicinal properties of lemon balm (*Melissa officinalis* L.) have been known for centuries in Europe and the wider Mediterranean area. In Croatia, use of lemon balm as a medicinal plant begun under the influence of German monasteries during the Middle Ages. Antidepressant, antidiabetic, cardioprotective and antimicrobial properties have been investigated in numerous studies. Polyphenols, including flavonoids, are considered to be the main components responsible for pharmacological activity.

The objective of this work was to determine the total content of flavonoids using spectrophotometric method by Christ and Müller [1]. In this method flavonoids are determined as aglycones after hydrolysis in a complex with Al^{3+}. Quantity of flavonoids in each sample was determined in triplicates and obtained results were expressed as mean value with standard deviation.

The highest flavonoid content of 0.42±0.01% was found in leaves collected from the Pharmaceutical Botanical Garden “Fran Kušan” (2016) while the lowest one of 0.14±0.01% was detected in leaves from Našice (2014).

These results correlate with content of rosmarinic acid and previously reported antiaggregatory effect *Melissa officinalis* leaf extracts [2]. Results vary between herbal drugs collected in different years and on different locations and are highly susceptible to weather conditions, heat, humidity, plant pathogens, air quality, etc.

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DRIFT spectroscopic investigation and quantification of acetylferrocene modified APS-silica gel

Istraživanje i kvantifikacija acetilferocenom modificiranog APS-silika gela DRIFT spektroskopijom

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The product 1-[ferrocenylethylidene]-3-aminopropylsilyl-silica gel, obtained by immobilizati-on of acetylferrocene (AcFe) on 3-aminopropylsilyl (APS) modified silica gel (Figure 1), was investigated using different spectroscopic techniques [1]. The immobilization reaction was carried out in different solvents using different acids as catalysts to obtain the immobilized ferrocene derivative (Figure 1). The results were supported by BET measurements and elemental analysis made on the immobilized and APS-functionalized products and on the activated silica gel, for comparison. In this case, the Diffuse Reflectance Infrared Fourier Transform (DRIFT) spectroscopy technique was proven to be the best choice to characterize the material and to determine the quantitative composition of the APS fragments and most importantly of the bonded AcFe. The possibility to follow the whole process with this IR technique was enabled by the presence of the bands arising from the $–NH_2$ groups in the APS-modified silica gel that diminish on immobilization of AcFe, but also through the appearance of new bands originating from the newly established imine (C=N) bond [2].

The attention was drawn not only to the way how to quantify the immobilized product, but also to optimize the synthesis of AcFe-modified aminopropylsilyl-silica gel (Figure 1) and to achieve greater yields. It was observed that it is highly difficult to obtain the imine from AcFe and APTMS. In order to find the best catalyst for obtaining the immobilized ferrocene derivative (Figure 1), a systematic investigation using many different acids as catalysts previously described in the literature was conducted. Eventually, the synthesis giving the highest yield proceeded by using the most common Lewis acid, $AlCl_3$.

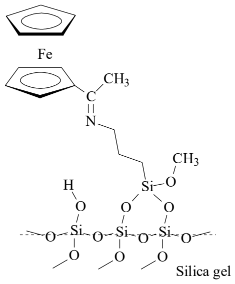

Figure 1: Schiff base obtained by the synthesis of acetylferrocene and APS-functionalized silica gel.

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A fluorescent probe for specific detection of hydrogen sulfide based on excited-state intramolecular proton transfer (ESIPT)

Fluorescentna proba za specifičnu detekciju sumporovodika temeljena na prijenosu protona između molekula u pobuđenom stanju (ESIPT)

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Hydrogen sulfide (H_2S) which has been known as a rotten eggs smell gas has been identified as the third gasotransmitter following nitric oxide (NO) and carbon monoxide (CO). In quite a long time, hydrogen sulfide was considered to be an absolute toxic gas and environmental pollutant. However, this view was modified as H_2S was first observed to present as a neuromodulator in the brain in 1996. As a matter of fact, hydrogen sulfide is also the smallest member among reactive sulfur species (RSS), making major contributions to the function of mammalian tissues. For example, the imbalance of hydrogen sulfide in living system may be harmful to peripheral and central nervous systems, leading to Down's syndrome, Huntington's, Parkinson's, and Alzheimer's diseases. Accompanied by the critical biological function of hydrogen sulfide, the chemical detection method of hydrogen sulfide in vivo has attracted considerable attention. Consequently, sustained research efforts have been devoted to the development of efficient strategies for detection of hydrogen sulfide. In contrast to the electro-chemical methods, gas chromatography, the fluorescent probes based on small molecules have been more attractive owing to its simplicity, high sensitivity, noninvasiveness, and real-time detection in living systems. Recently, a large number of fluorescent probes for H_2S have been developed. However, most of these probes are based on fluorophores which may suffer from small Stokes shift and/or undergo aggregation caused quenching (ACQ) in aqueous or physiological media. Hydrogen sulfide (H_2S) is a signaling gasotransmitter which fulfills various roles in modulating the functions of different systems. In this study, we developed a "turn-on" fluorescent probe for H_2S based on a familiar ESIPT fluorophore bearing AIE characteristic. The probe exhibited 80-fold fluorescent enhancement upon addition of H_2S with large Stokes shift. Furthermore, the probe has been successfully applied to detecting H_2S in HeLa cells.

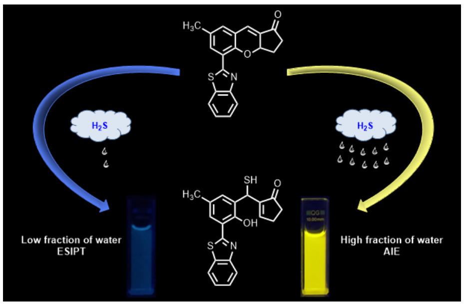

Figure 1: Probe for detection of H_2S based on ESIPT fluorophore bearing AIE characteristics.

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Lepidium spp. and *Allium* spp. as a source of volatile sulphur compounds

Lepidium spp. i *Allium* spp. kao izvori isparljivih sumporovih spojeva

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Sulphur-containing plant metabolites include a variety of chemical structures, varying from primary metabolites such as sulphur-containing amino acids to secondary metabolites like, thiosulfinates, glucosinolates and others. In recent years, volatile sulphur compounds (VSCs) have been assigned important biological properties, including antioxidant, cancer chemopreventive, blood lipid reducing, antibacterial, neuroprotective and immunomodulatory effects, as well as apoptosis induction activity [1]. The aim of the work was to uncover sulphur containing constituents by isolation of the volatiles using hydrodistillation in Clevenger type apparatus followed by GC-MS analyses.

Lepidium (Brassicaceae) is a genus that includes about 175 different plant species strikingly characterized by glucosinolates as molecular tags. The roots of three species, wild-growing *L. graminifolium* (grassleaf pepperweed), and cultivated *L. latifolium* (pepperwort, or peppergrass) and *L. meyenii* (maca) were investigated to uncover glucosinolates (GLs) by their degradation volatile products, mostly isothiocyanates and nitriles. The main GLs found in the roots of investigated *Lepidium* ssp. were: benzyl GL (glucotropaeolin) in *L. graminifolium* accompanied with 2-phenylethyl GL (gluconasturtiin) and 3-methoxybenzyl GL (glucolimnanthin) as a minor ones; allyl GL (sinigrin) in *L. latifolium* roots accompanied with the *sec*-butyl GL (glucocochlearin) and glucotropaeolin as the minor ones; glucotropaeolin in *L. meyenii* accompanied with minor glucolimnanthin.

Allium (Amaryllidaceae) is a large and very important genus which comprises of more than 500 species. Thiosulfinates and thiosulfonates are sulphuric compounds specifically found in this genus, where allicin an unsaturated thiosulfinate, has been found to possess striking biological properties [3]. The bulbs of wild-growing *A. commutatum* (Mediterranean onion), and cultivated *A. cepa* (onions, three varieties – red, white, yellow), and *A. sativum* (garlic) were investigated. The sulphur volatiles that constituted the major portion of the oil were: methyl (methylthio)methyl disulfide and dimethyltrisulfide in *A. commutatum*; dipropyl disulfide and dipropyl trisulfide in all *A. cepa* varieties; di-2-propenyldisulfide, along with 2-vinyl-1,3-dithiane and 3,3'-thiobis-1-propene in *A. sativum*.

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Acknowledgments

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Structural characterization of impurities in 3-bromo-5-(trifluoromethyl)aniline by LC-SPE/NMR

Strukturna karakterizacija onečišćenja 3-brom-5-(trifluormetil)anilina primjenom sustava LC-SPE/NMR

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Impurities define the quality of a chemical entity so their unambiguous structure determination is essential part of the pharmaceutical development. Liquid chromatography (LC) – solid-phase extraction (SPE) / nuclear magnetic resonance (NMR) methodology with cryoprobe was developed and applied for identification and structural characterization of unknown impurities in 3-bromo-5-(trifluoromethyl)aniline. The three main impurities were separated and isolated by LC-SPE system. After multiple trapping, isolated impurities were eluted from the SPE cartridges with deuterated acetonitrile and one- and two-dimensional homo- and heteronuclear NMR spectra were recorded. The structures of the unknown impurities were determined by detailed inspection of NMR spectra and by mass spectrometric (MS) analysis to show that the impurities in question are di-bromo derivatives of 3-(trifluoromethyl)aniline. The results demonstrated that LC-SPE / NMR can be used for rapid impurity profiling of 3-bromo-5-(trifluoromethyl)aniline.

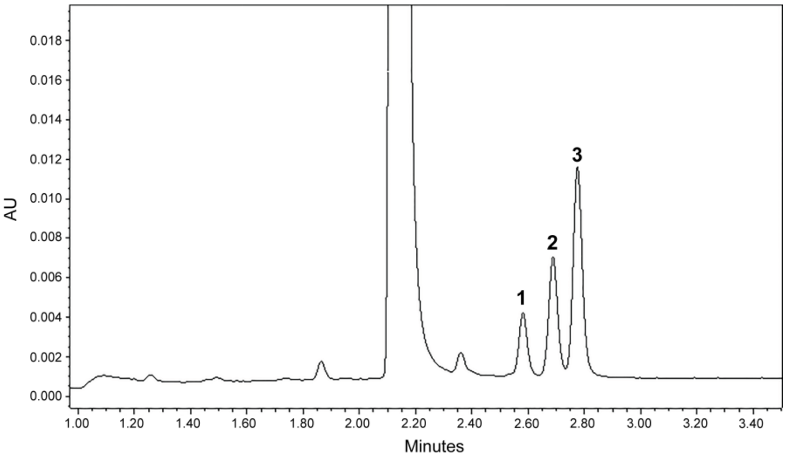

Figure 1: UHPLC-UV-DAD chromatogram of 3-bromo-5-(trifluoromethyl)aniline showing impurities **1**–**3** and the principal peak.

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Sulfur- and nitrogen-containing volatile compounds from Capsella rubella Reut.

Sumporovi i/ili dušikovi hlapljivi spojevi sredozemne rusomače (*Capsella rubella* Reut.)

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This study represents the continuation of our research on chemistry of volatile compounds from Croatian wild-growing Brassicaceae plants [1-4]. Brassicaceae plants are known to contain sulfur-containing secondary metabolites, glucosinolates. During the extraction of these compounds their decomposition often occurs resulting with the isolation of volatile sulfur- and nitrogen-containing compounds. So, volatile sulfur- and nitrogen-containing compounds are not naturally present in intact plant but are formed mostly by enzymatic breakdown or thermal degradation of naturally occurring sulfur-containing glucosinolates [5]. These volatile compounds are interesting because they have been assigned for various biological activities.

Capsella rubella Reut. is a plant widespread throughout Mediterranean region of Croatia and often replaced by mistake with *C. bursa-pastoris*, the most widespread *Capsella* specie throughout the world. As far as we know, there are no reports on chemical composition of volatile compounds of this plant. In order to provide more complete insight of composition and content of *C. rubella* volatile constituents three different volatile isolates were prepared and analysed by GC-FID/MS.

The identification of volatile compounds revealed that sulfur- and nitrogen-containing compounds were quantiatively dominating constituents in all volatile isolates. Thus, *C. rubella* essential oil, that is volatile isolate obtained by hydrodistillation, was characterized by a high percentage of 3,4-epithiobutanenitrile (67.8%). The main compounds in autolysate, *i.e.* volatile isolate obtained by solvent extraction upon endogenous enzymatic hydrolysis, were 3,4-epithiobutanenitrile (44.1%) and ethyl isothiocyanate (29.4%). Same as in autolysate, the main constituents of hydrolysate, *i.e.* isolate obtained by solvent extraction upon exogenous enzymatic hydrolysis, were 3,4-epithiobutanenitrile and ethyl isothiocyanate, but with ethyl isothiocyanate as the dominating compound (57.8%) followed by 3,4-epithiobutanenitrile (15.6%).

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Optimization of microwave-assisted extraction of polyphenols from olive pomace

Optimizacija mikrovalno potpomognute ekstrakcije polifenola iz komine masline

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Olive pomace (OP) is a solid residue that is lagging behind in the production of olive oil. It contains various biologically active polyphenols (PP), primarily hydroxytyrosol (HTS), oleuropein (OLE), and tyrosol (TS) [1]. The potential of OP as the starting raw material for obtaining PP is not even close to fully utilized. The main reason is unavailability of adequate methods for the isolation of PP which leads to poor quality of obtained extracts being unsuitable for futher testing and processing. The aim of this study was to develop and optimize environmentally and economically acceptable ("green") microwave-assisted extraction (MAE) for obtaining high-quality extracts in terms of total phenolic content (TPC) and the content of hydroxytyrosol derivatives (the sum of tyrosol, hydroxytyrosol and oleuropein) representing the main bioactive fraction of OP.

Fast and simple MAE has been proposed as an alternative to conventional (solid-liquid) extraction in water-bath and ultrasound-assisted extraction (UAE). For MAE optimization Full Factorial (FF) design was used for studying the effects of three independent factors: 1) extraction solvent (20–96% ethanol); 2) microwave power (400–700 W); and 3) time of extraction (–10 min). TPC was determined using Folin-Ciocalteu method [2]. HPLC coupled with fluorescent detector was used for the separation and quantification of analytes, hydroxytyrosol derivatives.

Our results indicate that all analysed factors (microwave power, extraction time and concentration of ethanol) and their interactions had significant influence on TPC and the content of hydroxytyrosol derivatives. The highest yields of both, PP and hydroxytyrosol derivatives were obtained with the microwave power of 700 W, extraction time of 10 minutes, and 20% ethanol. In comparison to yields obtained under optimum conditions of UAE and conventional extraction [3], MAE was found to be superior method, requiring shorter extraction time and showing better efficiency.

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Heteropolynuclear compounds containing $[Cu(L)(\mu\text{-}C_2O_4)Cu(L)]^{2+}$ units bridged by $[Cr(C_2O_4)_3]^{3-}$ or $Cr_2O_7^{2-}$: a variety of unusual coordination modes

Heteropolinuklearni spojevi s jedinkama $[Cu(L)(\mu\text{-}C_2O_4)Cu(L)]^{2+}$ premoštenim s $[Cr(C_2O_4)_3]^{3-}$, odnosno $Cr_2O_7^{2-}$: niz neobičnih načina koordiniranja

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Heteropolynuclear metal complexes have been widely investigated for their ability to form different architectures and topologies, and also due to their interest for applications in catalysis, photoluminescence, gas storage and separation, magnetism and multifunctional molecular materials. In the last few decades, the chemistry of oxalate-containing complexes has become an active area of research – the oxalate moiety, $C_2O_4^{2-}$, acts as a linker between metal centres with various possibilities of bridiging modes. It is particularly interesting due to its ability to mediate electronic effects between paramagnetic metal ions. Stable mononuclear anionic oxalate complexes are often used as ligands toward another metal ion. The use of the $[Cr(C_2O_4)_3]^{3-}$ anion in the reactions with organic and inorganic cations results in different structure types, from discrete polynuclear metal compounds to polymeric one- (1D), two- (2D) or threedimensional (3D) assemblies, featuring a range of distinct magnetic properties.

Applying the layering technique i.e. slow liquid diffusion, the turquoise stick-like crystals of compounds $\{[ACrCu_2(C_2O_4)_4(bpy)_2]\cdot H_2O\}_n$ [A = K^+ (**1**) and NH_4^+ (**2**)] were grown from the reaction of an aqueous solution of $A_3[Cr(C_2O_4)_3]\cdot 3H_2O$ and methanol solution of $CuCl_2\cdot H_2O$ and 2,2'-bipyridine (bpy), in the molar ratio of 1 : 1 : 1. Structural analysis has showed that compounds **1** and **2** contain oxalate-bridged $[Cu(bpy)(\mu\text{-}C_2O_4)Cu(bpy)]^{2+}$ units mutually connected through oxalate groups from $[Cr(C_2O_4)_3]^{3-}$, forming ladder-like 1D chains (Figure 1a). Interestingly, in each of these complexes three different bridging modes of the oxalate ligand are observed. The change of *N*-donor aromatic ligand from bpy to 1,10-phenanthroline (phen) in the same reaction mixture influenced greatly the reaction outcome. Unusually, the $[Cr(C_2O_4)_3]^{3-}$ anions present in the starting solution have transformed to the $Cr_2O_7^{2-}$, accompanied by oxidation of Cr^{III} to Cr^{VI} in an almost neutral solution. The obtained compound, yellow polyhedra of formula $\{[Cu_2(C_2O_4)(phen)_2(Cr_2O_7)]\}_n$ (**3**), contains ladder-like 1D chains, in which copper(II) ions from $[Cu(phen)(\mu\text{-}C_2O_4)Cu(phen)]^{2+}$ units are bridged through four oxygen atoms of $Cr_2O_7^{2-}$ anions (Figure 1b). This is the first known example of such extraordinary bridging mode of $Cr_2O_7^{2-}$. In addition to the single crystal X-ray diffraction study, characterization of the new complexes has been accomplished by means of the IR spectroscopy and thermal analysis.

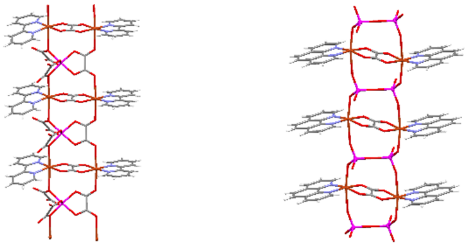
(a) (b)

Figure 1: Ladder-like 1D chains made of (a) $[CrCu_2(C_2O_4)_4(bpy)_2]^-$ (**1** and **2**) and (b) $[Cu_2(C_2O_4)(phen)_2(Cr_2O_7)]$ (**3**).

Determining structure of copper complexes with nicotinic acid aroylhydrazones using attenuated total reflectance (ATR)

Određivanje strukture kompleksa bakra s aroilhidrazonima nikotinske kiseline tehnikom prigušene totalne refleksije (ATR)

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Attenuated total reflectance (ATR) technique was used to study structure of copper complexes with aroylhydrazones derived from nicotinic acid hydrazide and salicylaldehide derivatives having different substituents on the benzene ring.

Aroylhydrazones can be involved in keto-enol tautomeric interconversion, when the hydrogen atom in keto form moves from amino to carbonyl group, forming an enol form [1]. In addition, if aldehyde moiety has a hydroxyl group situated in *ortho*-position with respect to the C=N double bond, the aldehyde part of the molecule can participate in keto-enol equilibrium. Considering different tautomeric forms, aroylhydrazones can act as neutral, monoanionic or dianionic *O*, *N*, *O* tridentate ligands [2]. Different tautomeric forms are characterized by distinctive spectral features and can be distinguished by means of various spectrometric methods, including vibrational spectroscopy.

In our previous studies it was found that in solid state and in solvents of different polarities aroylhydrazones appear in keto-amine form, which is generally the most stable one [1,3]. The ATR spectra of the complexes, formed due to complexation with copper(II) chloride in molar ratios hydrazone/Cu 1/1 and 2/1, pointed that the form of hydrazone was changed depending on substituents on the benzene ring. The spectra of the complexes in 1/1 ratio implied that hydrazones with hydroxyl group on the *ortho*-position alone or in combination with chloro or methoxy group on the *meta*-position according to the C=N bond, converted from keto-amine form to enol-imine form. If the two hydroxyl groups were positioned on the *ortho*- or *para*-position according to the C=N bond, the ligand retained in keto-amine form. It was also shown that the higher amount of the ligand (2/1 ratio) did not affect complexation, except in case of hydrazone with the methoxy group, for which different spectra were obtained, implying different tautomeric forms in 1/1 and 2/1 complexes.

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Amperometric determination of L-cysteine with an electrode based on ternary silver-copper sulfide

Amperometrijsko određivanje L-cisteina s elektrodom pripravljenom od ternarnog srebro-bakrovog sulfida

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A simple method for amperometric determination of L-cysteine using an electrode based on ternary silver-copper sulfide is presented. Electrochemical characterizations (by cyclic voltammetry) of three electrode materials, prepared under different condition, has revealed that the best electrocatalytical performance for L-cysteine oxidation showed electrode based on material that consists (proved by XRD pattern) of jalpaite (Ag_3CuS_2) doped with small amount of metallic silver [1,2]. For amperometric determination, electrocatalytical oxidation of thiol group at 0.04 V vs. Ag/AgCl has been chosen. Electrochemical impedance spectroscopy has revealed that oxidation takes place on electrode surface without fouling effect, which provides a wide linear working range between 0.5 μmol dm^{-3}–100 μmol dm^{-3}. The electrode could be operated at pH values between 4 and 8, although the best performance has been obtained under physiological conditions (pH 7-7.5). The calculated detection limit based on 3σ criterion was 0.025 μmol dm^{-3}, with sensitivity of 55 nA μmol^{-1} dm^3. In the presence of uric acid, folic acid, ascorbic acid and glucose no interference has been noticed. This amperometric sensor has shown remarkable stability and excellent reproducibility. The sensor was exploited for determination of L-cysteine in a dietary supplement with excellent recoveries.

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The persistence of dimeric $R^2_2(6)$ hydrogen bond motif in cadmium(II) acac-based complexes

Postojanost dimernog motiva $R^2_2(6)$ u kadmijevim(II) kompleksima s derivatima acetilacetona

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The self-assembly process with cobalt(II)/nickel(II) cations and dibenzoylmethanato (dbm)/hexafluoracetylacetonato (hfac) anions and multifunctional pyridine-oxime ligands (4-pyridinealdoxime, 4-Hoxpy; methyl 4-pyridyl ketoxime, 4-Meoxpy; 3-pyridinealdoxime, 3-Hoxpy; methyl 3-pyridyl ketoxime, 3-Meoxpy) was studied in order to target the desired supramolecular pattern - infinite 1-D chains based on O–H···N(oxime) hydrogen bonds (dimeric $R^2_2(6)$ motif) [1]. The self-assembly process produced the desired 1-D chains only in the case of [Co(dbm)$_2$(3-Meoxpy)$_2$], [Ni(dbm)$_2$(3-Meoxpy)$_2$] and all the hfac complexes prepared. The desired products were prepared by adjusting the reactants in an iterative manner to shift the magnitude of the electrostatic potential surfaces of competing hydrogen bond acceptor sites. Therefore, a robust synthetic protocol for the reproducible synthesis of the correct supramolecular products was obtained [1].

We further wanted to examine if the same trend of persistence of the dimeric $R^2_2(6)$ hydrogen bond motif could be observed in the analogous cadmium(II) acac-based complexes. Indeed, our preliminary results showed the presence of $R^2_2(6)$ motif in the crystal structure of [Cd(hfac)$_2$(4-Meoxpy)$_2$] (**1**) (Figure 1) and its absence in the crystal structure of [Cd(dbm)$_2$(4-Meoxpy)$_2$] (**2**) ($R^2_2(20)$ motif based on O–H···O(acac) hydrogen bonds was formed instead). In order to make the oxime N atom as good proton acceptor as possible and enable formation of the dimeric oxime motifs, it is not enough only to introduce an electron-donating methyl group in the vicinity of the oxime nitrogen atom, as it leads to the formation of $R^2_2(20)$ motif in **2**. The hydrogen-bond accepting power of the oxygen atom can be reduced by introducing electron-withdrawing substituents (fluorine atoms) at the acac-based ligand. This approach resulted with the desired $R^2_2(6)$ motif in **1**. The substitution of cobalt(II) or nickel(II) cations with larger cadmium(II) cation in the studied acac-based complexes results with the same general trend of $R^2_2(6)$ motif appearance, as established previously [1].

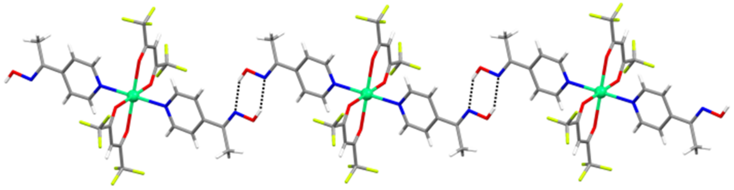

Figure 1: A dimeric $R^2_2(6)$ motif in the crystal structure of [Cd(hfac)$_2$(4-Meoxpy)$_2$] (**1**).

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Study of matrix effects of functionalized zero-valent iron nanoparticles on ICP-OES emission lines

Ispitivanje utjecaja matrice funkcionaliziranih neutralnih nanočestica željeza na emisijske signale u metodi ICP-OES

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Analytical performances of inductively plasma optical emission spectrometry (ICP-OES) are characterized by sensitive simultaneous measurements of numerous elements at different emission lines of the particular element. Interference effects in direct measurements of sample solutions depend on spectra complexity which is usually caused by complex matrix of solutions [1]. Recently, exploiting of nanomaterials in analytical sample preparation and procedures is often studied. The majority of works are focused to utilize synthesized or commercially available nanomaterials in extraction procedures [2]. Zero-valent iron nanoparticles (nZVI) are of great potential in removing of specific hazardous substances such as heavy metals and polychlorinated hydrocarbons form water solutions [3]. Their properties to adsorb metals of interest were often improved by suitable coatings on particle surface. However, studies which concern effects on measuring signals of extracted metals are mostly denoted to efficiency of their removal from solutions, and not to effects of coexisted iron released from nanoparticles [2].

In this work we used synthesis according to Zhang and Wang procedure for the preparation of nZVI particles, along with subsequent functionalization by dipicolinic acid [4]. Matrix effects of prepared solutions in inductively coupled plasma-optical emission spectrometry (ICP-OES) were studied using multielemental spectral solution which consists of Al. Ag, Ba, Ca, Cd, Cr, Co, Cu, Mg, Mn, Ni, Pb, V, Sr, and Zn. Intensities of chosen spectral lines were observed at different RF power (1.1-1.3 kW) and in concentration range from 0.1 to 10 $\mu g\ g^{-1}$ of added standard. The effects of bare and coated nZVI particles were studied using fixed amount of 10 mg and with variation of solvents. The influence of iron from nZVI particles in plasma was found to be complex. The effects are mostly dependent on sensitivity of elements line, excitation potential of line and on degree of organic ligand loading.

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Potentiometric determination copolymers of acrylic/maleic acid in detergents and cleaning products

Potenciometrijsko određivanje kopolimera akrilne/maleinske kiseline u detergentima i sredstvima za pranje

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Polycarboxylates are used in household cleaning products, and a variety of technical applications as dispersing agents for avoiding incrustation and soil redeposition. They are generally used in neutralised form (pH 6-8) as their sodium salts [1]. Major polycarboxylates used in detergent products are homopolymers of acrylic acid and copolymers of acrylic/maleic acid. Mean molecular weight of the homopolymers and copolymers of acrylic/maleic acid ranges from approximately 1000 to 78000 (most commonly in liquid detergents 4500), and 12000 to 100000 (most commonly in powder detergents 70000), respectively.

In alkaline medium (molecules of polycarboxylates behave as anions) anionic surfactant and polycarboxylate were titrated differentially at pH 10.5 in same titration. The first slightly distorted inflection corresponds to the anionic surfactant titration, whereas the diference beetwen first and second significantly weaker inflection relates to the carboxylate titration [2]. Due to the fact that the reaction betwen polycarboxylate and a titrant is not stehiometric, for quantitative determination of polycarboxylate equimolar mass should be determined experimentally. Method is new in literature, simple to perform, cost effective and environmentally friendly.

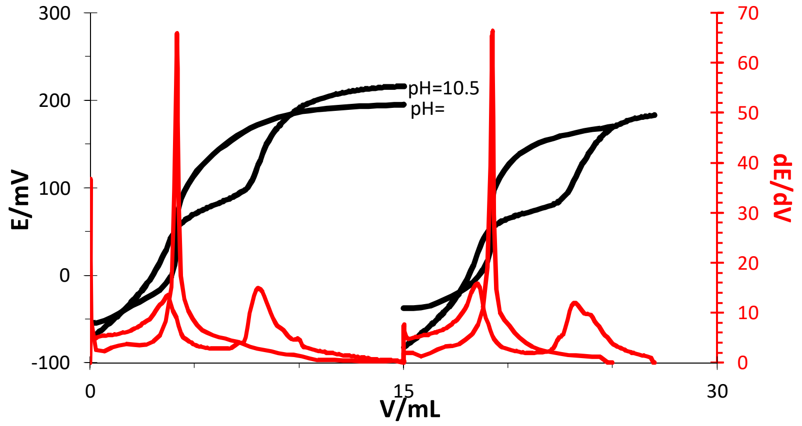

Figure 1: Titration curves and their corresponding first derivatives of two cleaning products containing anionic surfactant and polycarboxylate, using self-made surfactant-sensitive potentiometric sensor [3] for end-point detection.

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Novel method for detection of contrast agents and structural elucidation of their potential degradation products

Razvoj nove metoda za detekciju kontrastnih sredstava i utvrđivanje strukture njihovih potencijalnih produkata razgradnje

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Contrast agents are the most widely applied pharmaceuticals during radiographic procedures in hospitals. These bioactive compounds exhibit high polarity and are chemically inert drugs which are designed to be very stable in human metabolism as well as very persistent against environmental degradation [1-3]. Municipal wastewater treatment plants are not able to remove the contrast agents and they accumulate in drinking water and freshwater ecosystems [4].

There is a clear need for new rapid cost-effective analytical methods for environmental application, with an emphasis on reduced cost when compared to existing techniques. To contribute to the progress in this field we based our research on the development of novel method for detection of four iodine-based contrast agents (i.e. Iohexol, Iomeprol, Iodixanol and Diatrizoate) by combining thermal lens microscope (TLM) with microfluidic devices.

For detection of contrast media the development of a new method was based on the release of iodine from parent molecule by chemical reaction, and its extraction into an organic solvent such as chloroform which could be performed *on-line* in a microfluidic chip with TLM detection. Proposed degradation products and pathway was explained by the use of high resolution mass spectrometry (2D-LC-qTOF MS).

The developed µFIA-TLM method for determination of contrast agents based on detection of iodine provides about 60 times lower limit of detection (LOD) in comparison to common spectrophotometric methods. At the same time the new method enables shorter time of analysis and higher sample throughput for the purpose of fast screening method for bioactive compounds.

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ICP-OES analysis of silver in tobacco seedlings (*Nicotiana tabacum*) treated with silver nanoparticles

Analiza srebra metodom ICP-OES u klijancima duhana (*Nicotiana tabacum*) nakon izlaganja srebrovim nanočesticama

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In the last few years a remarkable progress has been made in the domain of nanotechnology. This discovery led to many commercial applications that involve the use of variety of nanoparticles [1]. Most widely commercially used are silver nanoparticles (AgNPs). Although there are benefits that come with their applicability, there is an increasing concern about their impact on the environment, especially plants. In order to better understand the interactions between AgNPs and plants and to differentiate between ionic and particle specific silver, morphological and proteomic changes were studied [2].

In this work we used inductively coupled plasma-optical emission spectrometry (ICP-OES) for quantitative determination of silver content in *Nicotiana tabacum* seedlings which were exposed to AgNPs stress. Working parameters of instrument were adjusted using the most sensitive silver emission line of 328.068 nm. Detection limit (1.5 ng g^{-1}) at higher RF power of 1.3 kW was determined using method blank which consisted of growth medium matrix. The analytical method required conversion of a dried plant sample into aqueous solution. Digestion of plant samples was performed using acid digestion (HNO_3, *Spectrapure* 70 % *v*/*v*; H_2O_2, ultrapure 30 % *v*/*v*) assisted by microwave irradiation.

Concentrations of Ag in plant seedlings, growth medium and residual precipitate were successfully determined in the concentration range of Ag 2.5 -18 µg g^{-1}. Precision (RSD < 1.0 %) and accuracy were determined using certified reference material (NIST-1573a CRM Tomato Leaves).

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pH and metal sensing properties of benzimidazole based Schiff bases

Schiffove baze temeljene na benzimidazolu kao senzori za pH i metalne ione

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Intramolecular charge-transfer (ICT) organic systems based on electron donor-π-electron acceptor structures (D-π-A) are widely used as fluorescent chemosensors. Benzimidazole moiety is an attractive building block of such molecular structures due to multifunctionality of its heteroaromatic conjugated planar structure. Schiff bases are one of the most investigated classes of organic compounds as a result of their excellent chelating ability. They are frequently described as optical chemical sensors [1] or chemodosimeters [2] due to their desirable optical properties, where benzimidazole is often incorporated as a functional or electron accepting unit in a respective D-π-A system [3]. Benzimidazole based Schiff bases exhibit structural similarity with biomolecules which offers an interesting platform for development of novel optically responsive sensor molecules.

The interactions of benzimdazole based Schiff bases **1**-**3** with different metal ions and effects of solvents and pH on their response have been studied by absorption and fluorescence spectroscopies. Basic photophysical properties are described in different solvents. Schiff bases exhibited naked-eye visible colour change upon protonation and pK_a values around 4. The pK_a is significantly increased upon immobilisation in bulk membrane (apparent pK_a = 6.7). All compounds indicated good sensing properties for metal ions. Compound **2** is presented as colourimetric sensor for Al^{3+} and fluorimetric sensor for Cu^{2+} ion (Figure 1).

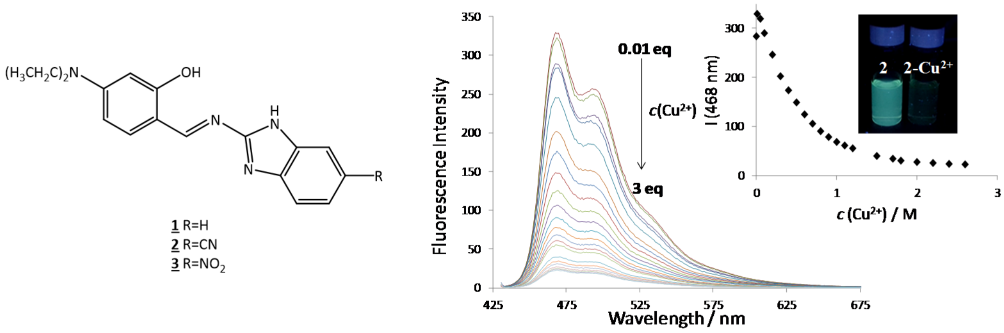

Figure 1: Emission properties of **2** (c = 10 µM) upon titration with Cu^{2+}.

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Acknowledgements

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Functionalized carbon nanotubes as new sensor material for anionic surfactant sensing

Funkcionalizirane ugljikove nanocjevčice kao novi senzorski materijal za anionske tenzide

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Anionic surfactants (ASs) are commercially mostly used group of surfactants. In 2014 their annual production was 7686 KT [1]. ASs are used in detergent, pharmaceutical and cosmetic industry, biotechnology, etc. Considering their great consumption, it is necessary to monitor ASs concentrations in the environment, as well as in quality control of commercial products. Standard methods for their determination are two-phase titration [2] (for samples with high concentration of ASs) and Methylene Blue Active Substances method [3] (MBAS, for samples with low concentration of ASs). These methods have many disadvantages so there is necessity to find alternatives. Potentiometric determination of ASs using ASs selective electrodes is increasingly replacing standard methods [4]. Incorporating nanomaterials as membrane component improves ASs selective electrodes characteristic [5].

The new sensor material for ASs sensing was prepared by noncovalent functionalization of multiwalled carbon nanotubes (MWCNT) with tetraoctadecylammonium ion. As plasticizer, *o*-nitrophenyl octyl ether was used. The sensing membrane was incorporated in Philips electrode body IS-561. New sensor material was characterized and tested as a sensor for ASs detection using cetylpyridinium chloride (CPC) as titrant. Response characteristics were examined for dodecyl sulfate and dodecylbenzenesulfonate ions and both showed sub-Nernstian response. The new sensor material exhibited excellent selectivity for dodecyl sulfate over anions usually presented in commercial products.

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Crystallization and structural studies of cobalt and nickel bromo-derivatives of human insulin

Kristalizacija i strukturno istraživanje kobaltovog i niklovog bromo-derivata ljudskog inzulina

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Insulin is structured as a two polypeptide chains, chain A consists of 21 and chain B of 30 amino acids. In the absence of metal ions native insulin crystallizes as a dimer but in the presence of zinc ions and some other cations three insulin dimers assemble into a hexamer. There are three forms of insulin hexamers: T_6, $T_3R_3^f$ and R_6 [1]. These forms of insulin are used in therapeutc preparations for the control of type 1 diabetes mellitus.

Due to its big medical importance structural data for more than two hundred human insulin derivatives can be found in the *Protein Data Bank* [2].

As a part of our ongoing research on the crystallization and structural studies on human insulin derivatives [3] in the present study cobalt and nickel were crystallized in high bromide concentration. Single crystals of the cobalt and nickel bromo-derivative of human insulin were grown by the hanging drop vapour diffusion method using Zn-free insulin (Figure 1). Diffraction data were collected at the ELETTRA Synchrotron, beam line XRD-1. The cobalt insulin derivative belongs to the trigonal crystal system while nickel derivative belongs to the tetragonal crystal system. Optimal crystallization conditions, coordination of cobalt and nickel ions in hexamer and conformation of the insulin molecule will be discussed.

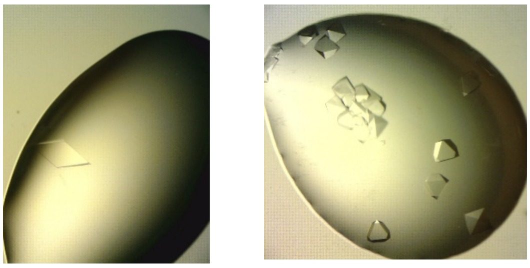

Figure 1: Single crystal of the human cobalt bromo-derivative of human insulin (left), single crystals of the nickel bromo-derivative of human insulin (right).

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Acknowledgment

This work has been supported by the Foundation of the Croatian Academy of Sciences and Arts under the project Crystallization and structural studies of human insulin derivatives and protein HP1026 from *Helicobacter pylori*.

Antioxidant activity and L-amino acids profile of wild and grown mushrooms from Bosnia

Antioksidativna ativnost i profil L-amino kiselina divljih i uzgojenih gljiva sa područja Bosne

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Several metabolic diseases and age-related degenerative disorders are closely associated with oxidative processes in the body, the use of mushrooms as a source of antioxidants to combat oxidation warrants further attention. Total phenols, antioxidant activity and total content of L-amino acids: tryptophan, arginine, cysteine, methionine, alanine, phenylalanine, lysine, valine, glycine and leucine were determined in the wild mushrooms: Peppery Milk-Cap (*Lactarius Piperatus),* Caesar's Mushroom (*Amanita Caesarea*), Saffron Milk Cap (*Lactarius Deliciosus*), Pear-Shaped Puffball (*Lycoperdon Pyriforme*), Parasol Mushroom (*Macrolepiota Procera*) and grown mushrooms: Champignon White (*Agaricus Bisporus*), Boletus (*Boletus Aestivalis*), Chanterelle (*Cantharellus Cibarius*), Oyster Mushroom (*Pleurotus Ostreatus*) and Champignon Brown (*Agaricus Bisporus var.Avellaneus*). All mushrooms were collected from Bosnian market. Total phenolic content was determined spectrophotometrically with Folin-Ciocalteu reagent. Free Radical Scavenging Activity Assay was done by using DPPH reagent. L-amino acids quantification was performed by high performance thin layer chromatography (HPTLC) method. Total content of phenols (mg GAE/g) was in the range from 2.20 to 35.56. The radical scavenging activity (%) was in the range from 43.88 to 192.57. The highest content of cysteine was detected in *Agaricus Bisporus var. Avellaneus*. The highest content of alanine, glycine phenylalanine, lysine, valine and leucine were found in *Pleurotus Ostreatus*. This study support the consumption of foods rich in bioactive components, such as mushrooms. Further investigation of the benefits of mushrooms in the overall maintenance of health and protection from age –related diseases are necessary.

Potentiometric determination of cationic surfactants using chemically functionalized carbon nanotubes based electrode

Potenciometrijsko određivanje kationskih tenzida elektrodom na bazi kemijski funkcionaliziranih ugljikovih nanocjevčica

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Cationic surfactants (CSs) are widely used in bactericidical, algaecidical, fungicidical, disinfection and anticorrosive products, as cosmetic and pharmaceutical components, etc. The reference method for their determination is two-phase titration [1]. The method have many disadvantages, the largest of which is the use of toxic organic solvents. Considering that, it is of great importance to find alternative method for CSs determination. CSs selective electrodes proved to be a good sensors for CS determination [2]. Their membrane usually consists of sensor material, plasticizer and PVC [3]. Nanomaterials, as component of the membrane can significantly improve sensor properties [4]. Using solid-contact electrodes without an inner electrolyte, additionally improve sensors, solving problems as leaching of the sensor material, signal stability and sensor life-time [5].

The sensor material of the electrode was prepared by chemically functionalization of multiwalled carbon nanotubes (MWCNT) with $-OSO_3^-CP^+$ group. Developed sensor was used as detector in potentiometric titrations of CSs. Hyamine, cetylpyridinium chloride (CPC), hexadecyltrimethylammonium bromide (CTAB) and 1,3-didecyl-2-methylimidazolium chloride (DMIC) were used as the analytes during the potentiometric titrations, and sodium dodecyl sulfate (NaDDS) was used as the titrant. The applicability of the sensor was tested in three commercial products with different concentrations of CSs. The results of CSs determination in commercial products were compared with those obtained by the reference method and showed the excellent correlation between the methods.

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Determination of elemental impurities in platinum enriched active pharmaceutical ingredient

Određivanje elementarnih onečišćenja u platinom obogaćenoj aktivnoj farmaceutskoj supstanci

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Inductively coupled plasma mass spectrometry is a sensitive and precise technique for the determination of metals in active pharmaceutical ingredients. Method development for use of inductively coupled plasma mass spectrometry (ICP MS) in determination of metals which are included by „International Conference of Harmonization“ directive. Elements which are covered by this directive are usually used as process catalysts, reagents or as equipment in technological operations of some process. Development of method on active pharmaceutical ingredient, a chemotherapy medication used to treat a number of cancers is conducted according to suggested tests and limits which are specified in United States pharmacopeia chapters <232> and <233>, Elemental impurities – limits and Elemental impurities – procedures. Method development is carried out with tests linearity and quantification limit. The sample was prepared by digesting in microwave reactor in acidic matrix composed of concentrated nitric and perchloric acid. Internal standards used in ICP MS analysis are of great importance for determining drift and problems with instrument or method but their use in this work is to recover losses caused by high concentrations of platinum in samples. Research of difficulties caused by platinum interference in determination of traces of gold and silver with single quadrupole mass analyzer is discussed. Use of the system with triple quadrupole mass spectrometer for enhanced removal of interference and comparison of results with single mass filter.

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Cobalt, nickel and copper complexes with *N*-alkylglycines: preparation, structural, spectroscopic and thermal characterization

Kompleksi kobalta, nikla i bakra s *N*-alkilglicinima: priprava, strukturna, spektroskopska i termička karakterizacija

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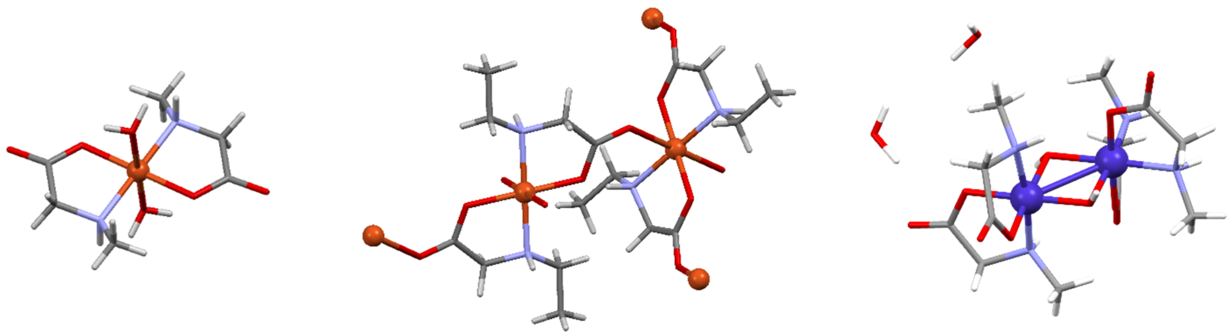
The most simple standard amino acid glycine, H_2NCH_2COOH (GlyH), is one of the most common chelating ligands [1]. Structural data for several hundred metal complexes with this ligand can be found in the *Cambridge Structural Database* [2], while complexes with *N*-methylglycine (sarcosine, CH_3NHCH_2COOH; SarH) appear to be quite rare. Metal complexes with higher *N*-alkylglycine derivatives were not known before this work. We have performed the reactions of copper(II), nickel(II) and cobalt(II) acetate with sarcosine and *N*-ethylglycine in aqueous solutions, and characterized the obtained complexes by X-ray crystallography, IR spectroscopy and thermoanalytical methods (TG/DTA and DSC).

Both amino acid derivatives in their anionic form act as *N,O*-bidentate ligands, forming three types of complexes. Complexes of the type **I** are monomeric species of the formula *trans*-$[M(Sar)_2(H_2O)_2]$ (M = Cu, Ni) or *trans*-$[M(Etgly)_2(H_2O)_2]$ (M = Co, Ni). Copper(II) complex with *N*-ethylglycine (type **II**) is a coordination polymer of the formula $[Cu(Etgly)_2]_n$ where the axial coordination sites are occupied by the carboxylate oxygen atoms from the neighbouring $[Cu(Etgly)_2]$ units. Cobalt(III) complex with sarcosine, $[Co(Sar)_2(\mu\text{-}OH)]_2 \cdot 2H_2O$ (type **III**), is a dimer containing the Co-Co bond. Details on the synthesis and structures of the complexes will be provided in the presentation.



I **II** **III**

Figure 1: Coordination environments around metal ions in the complexes $[Cu(Sar)_2(H_2O)_2]$ (**I**), $[Cu(Etgly)_2]_n$ (**II**) and $[Co(Sar)_2(\mu\text{-}OH)_2] \cdot 2H_2O$ (**III**).

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Synthesis and structural characterization of Cd(II) coordination polymers: Supramolecular architectures stabilized by noncovalent interactions

Priprava i strukturna karakterizacija koordinacijskih polimera kadmija(II): Nekovalentnim interakcijama stabilizirane supramolekulske arhitekture

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Crystal engineering generally involves the design and synthesis of crystalline materials with desired properties and functions. Properties of crystalline solids are related not only to their composition but also to the manner in which building units are aligned and linked together in the solid state. Investigations of supramolecular interactions on metal-containing systems can therefore be divided into two pathways, (*i*) the study of assemblies primarily composed of 0D building units which are mutually linked *via* non-covalent interactions (in particular hydrogen and/or halogen bonds as the main crystal engineering tools), and (*ii*) the study of assemblies that rely on both coordination bond (1D- or 2D-coordination polymers) and much weaker and relatively reversible non-covalent interactions [1,2].

In order to investigate supramolecular assembles of solids composed of coordination polymers here we synthesized a series of halide complexes of Cd(II) with halogen substituted pyridine and pyrimidine ligands. Single crystal X-ray structure determination revealed 1D-coordination polymers comprised of halide-bridged Cd(II) octahedra (Figure 1a). The building units are assembled into supramolecular 3D frameworks *via* a combination of hydrogen and halogen bonds (Figure 1b). Structure-property correlations, particularly thermal stability and elasticity, were investigated. Spectroscopic, thermal and structural data were accompanied by detailed data mining.

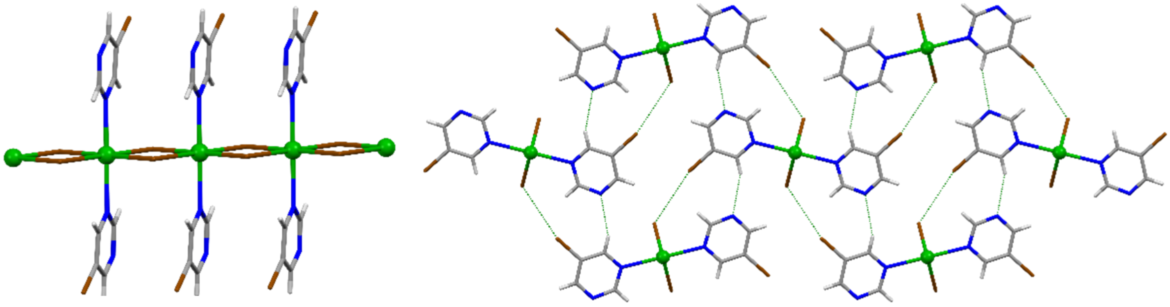

Figure 1: $CdBr_2(5\text{-}Brpm)_2$ (5-Brpm = 5-bromopyrimidine): (a) 1D-coordination polymer; (b) supramolecular structure formed by C–H···N hydrogen bonds and Br···Br halogen bonds.

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Development of method for determination of impurities in Entacapone by supercritical fluid chromatography

Razvoj metode za određivanje onečišćenja u djelatnoj farmaceutskoj tvari Entacapone kromatografijom superkritičnih fluida

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Entacapone is chemically described as (2E)-2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethyl prop-2-enamide. It is a selective, reversible catechol-O-methyl transferase (COMT) inhibitor for the treatment of Parkinson's disease and it belongs to a group of nitrocatechols [1].

A novel, simple, fast and efficient supercritical fluid chromatography (SFC) method was developed for the separation and determination of six impurities in Entacapone. Overall satisfactory resolutions and peak shapes for Entacapone and six impurities were obtained by optimization of the chromatography system. With the gradient elution of mobile phase, all of the impurities and the active ingredient were separated. Taking full advantage of features of SFC (such as particular selectivity, non-sloping baseline in gradient elution, and without solvent injection effects), the method was successfully used for determination of impurities in Entacapone.

The developed SFC method meets validation parameters with respect to specificity, LOD, LOQ, linearity, precision, accuracy and robustness. The method could be used in routine analysis of Entacapone chromatographic purity.

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Volatile compounds in wine from *Babić* grape variety

Isparljivi spojevi vina sorte *Babić*

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Babić is an autochthonous Croatian grape variety, originally from Šibenik region, the most widespread in Primošten area where is grown in varietal vineyards [1]. In past few years the vineyards of *Babić* are spreading on Litosols of the coastal area, where it can achieve high quality wines. Aroma is one of the most important quality factors of wine and is one of the key determinants of consumer acceptance [2].

In this paper, the headspace volatiles of *Babić* wine were isolated by headspace solid phase microextraction (HS-SPME) using a fiber coated with the layer of Divinylbenzene/Carboxen/Polydimethylsiloxane (DVB/CAR/PDMS) and liquid-liquid extraction using the solvent pentane: diethyl ether (1:2 v/v). Obtained sampels were analyzed by gas chromatography-mass spectrometry (GC-MS) using HP-5MS column. Using HS-SPME we identified 8 compounds, while using liquid-liquid extraction of volatile compounds we identified 23 compounds. The most common compounds of the detected HS-SPME method were: isoamyl alcohol (55.1%), ethyl acetate (13.6%) and ethyl octanoate (11.9%). Liquid-liquid extraction showed: ethyl hydrogen succinate (22.4%), diethyl phthalate (15.0%), 2-phenylethanol (6.8%), (*Z*)-octadec-9-en-1-ol (5.6%), sorbic acid (5.2%) and hexadecanoic acid (5.1%). Higher alcohols are secondary products of yeast metabolism and have been associated with pungent, sweet and fruity odors [3]. Esters are very important components of wine aroma, making positive contribution to the general quality of wine providing delicate ʻʻfruityʼʼ and ʻʻfloralʼʼ odours, affecting the sensory properties and aromatic finesse of wines [4]. Higher alcohols and esters, produced during alcoholic fermentation, play an important role in the flavour of the wines, depending on the types of compounds and their concentrations [5].

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Quantitative monitoring of an API synthesis reaction by in-line Raman spectroscopy

Kvantitativno praćenje reakcije sinteze aktivne farmaceutske supstance Ramanovom spektroskopijom *in-line*

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Over the past few decades, process analytical technology (PAT) has become one of the key tools to entirely implement accurate, versatile and reliable in-line sensors for monitoring and understanding of production processes in the pharmaceutical industry [1]. With respect to monitoring of chemical reactions, in-line vibrational spectroscopy is becoming a standard PAT technique [2]. Raman spectroscopy in particular was shown to be a very useful tool to gain valuable process understanding about the rate and extent of chemical reactions during scale-up [3,4].

The development of a quantitative in-line Raman spectroscopic method for the monitoring of an active pharmaceutical ingredient synthesis reaction is described. The spectroscopic measurements and the complimentary HPLC analyses, used in the calibration development, were gathered from a set of experiments, performed at a 1 L scale. Based on the data set obtained from the calibration experiments, a predictive partial least square (PLS) regression model was developed for all three reaction components, enabling an accurate determination of the percentage of each component present in the reaction mixture, at any time after the point when 25 % of the starting material has been consumed. The model was successfully used to monitor the reaction progress in a kilo-lab scale experiment and can further be used as a fast response analytical tool in process optimization. It also has potential to be used as part of a feed-back control loop in the production plant.

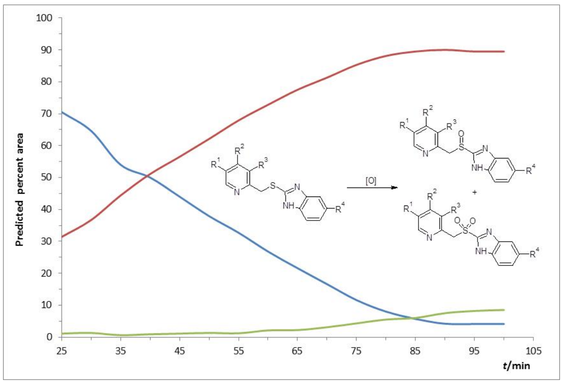

Figure 1: Oxidation reaction progress with PLS predicted % area values for all three reaction components.

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Preparation and characterization complexes Zn(II) with imidazole and 2-methylimidazole

Priprava i karakterizacija kompleksa Zn(II) s imidazolom i 2-metilimidazolom

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Complexes of imidazole and its derivatives with essential metal ions such as Zn(II), Cu(II) and Mn(II) have attracted much attention in recent years due to their antibacterial and antitumour properties [1]. They are also often used as structural models for certain metaloenzymes [2,3]. The biological role of complexes that contain an imidazole ring can be correlated with the two nitrogen atoms which have different properties; the deprotonated nitrogen atom can coordinate a transition metal atom, whereas the protonated nitrogen atom participates in hydrogen bonding [4].

Two novel zinc complexes with imidazole [$ZnX_2(Him)_2$] (X = Cl, Br, Him = imidazole) were prepared by direct mixing of solid reactants without addition of liquid. Completion of the reaction was confirmed by powder X-ray diffraction. Single crystals were obtained by recrystallization from a methanol solution. Complex of zinc(II) with 2-methylimidazole, [$ZnCl_2(2\text{-}Meim)_2$], was prepared by heating the reaction mixture under reflux. In all of these complexes the Zn(II) atom is tetrahedrally coordinated by two nitrogen atoms from imidazole ligands and by two halide atoms. The complexes were characterized by IR spectroscopy, powder and single crystal X-ray diffraction methods.

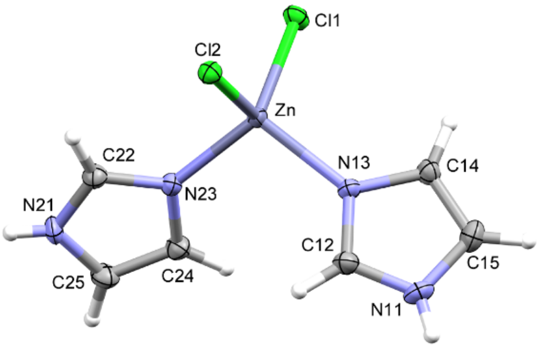

Figure 1: Molecular structure of [$ZnCl_2(C_3H_4N_2)_2$].

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Structural studies of Zn(II) complexes of (1,3-thiazol-2-yl)hydrazones

Strukturna istraživanja Zn(II) kompleksa (1,3-tiazol-2-il)hidrazona

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Antimicrobial resistance is nowadays a serious public health threat. Therefore, there is an urgent need for development of new classes of antimicrobials [1]. Significant number of studies indicates promising antimicrobial activity of (1,3-thiazol-2-yl)hydrazones [2]. We recently reported structural and bioactivity studies on Co(III) complexes of 2-(2-(pyridine-2-ylmethylene)hydrazinyl)-4-(phenyl)-1,3-thiazole (HL^1), 2-(2-(pyridine-2-ylmethylene) hydrazinyl)-4-(4-metoxyphenyl)-1,3-thiazole (HL^2) and 2-(2-(pyridine-2-ylmethylene) hydrazinyl)-4-(4-tolyl)-1,3-thiazole (HL^3) [3].

Here we present the structural studies of a series of their zinc complexes, prepared by simple reactions of $ZnCl_2$ and $Zn(NO_3)_2$ with $HL^{1–3}$: $[ZnCl_2(HL^1)]$ (**1**), $[Zn(HL^1)_2](NO_3)_2 \times H_2O$ (**2**), $[Zn(HL^2)_2][ZnCl_4]$ (**3**), $[Zn(HL^2)_2](NO_3)_2 \times MeOH \times H_2O$ (**4**), $[Zn(HL^3)_2][ZnCl_4]$ (**5**) and $[Zn(HL^3)_2](NO_3)_2 \times 3H_2O$ (**6**). Complexes were characterized by elemental analysis, molar conductivity measurements, UV-Vis, IR and NMR spectroscopic analyses. Single crystal X-ray analyses of **1**–**5** were accomplished. Structure of **1** is characterized by 1:1, while all other complexes reveal 1:2 metal to ligand ratio. In all complexes, the tridentate *NNN* coordination is observed. In **1** zinc is located in a centre of a distorted trigonal bipyramid. In cationic complexes of **2**, **3**, **4** and **5**, distorted octahedral coordination cores are observed and the overall charge is balanced by the presence of two nitrate anions (**2** and **4**) or two $ZnCl_4^{2-}$ anions (**3** and **5**). Crystal structure of **1** is characterized by the H-bonded centrosymmetric dimers of a graph-set notation *R*(2,2)10. In **2** and **4**, two hydrazine nitrogen atoms act as donors in a bifurcated H-bonds, connecting ligand molecules to O atoms from the corresponding nitrates. H-bonding patterns in **3** and **5** are analogous. A single observed H-bond connects the hydrazine nitrogen to a chlorine from the $ZnCl_4^{2-}$ anion as an acceptor, hence an “endless” chain is formed parallel to the crystallographic *a* axis.

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A series of "turn-on" fluorescent probe for the selective detection of mercury(II) ions based on pyrene-modified phosphazenes

Serija "turn-on" fluorescentnih proba za selektivnu detekciju živa(II) iona temeljenih na pirenom modificiranim fosfazenima

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Nowadays, observation about releasing of metal residues in the environment is getting increased because of developing technology and expanding industrial applications [1]. Fluorescence sensors have many advantages such as high selectivity, sensitivity and instant monitoring, if compared to other instrumental methods [2]. Concentration levels of heavy metal ions such as mercury(II), in environmental and biological systems are generally expressed as mg/L or µg/L and complexity of this media makes the analysis difficult [3].

In this study, the design, synthesis and mercury(II) ion selectivity properties of a series of pyrene-modified cyclotriphosphazenes were investigated (Figure 1). The novel compounds were fully characterized by the standard spectroscopic methods, such as ^{1}H, ^{13}C and ^{31}P NMR spectroscopy and mass spectrometry (MALDI-TOF). The properties of compounds against mercury(II) ions were determined by UV and fluorescence spectrophotometry.

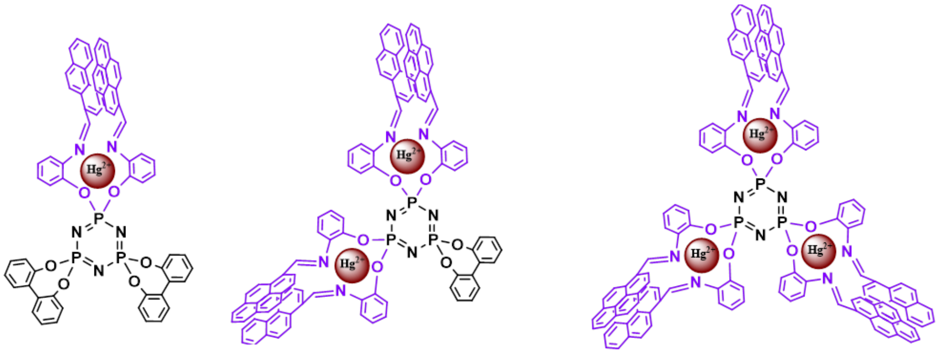

Figure 1: The structures and Hg(II) binding mechanisms of pyrene-modified phosphazenes.

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Acknowledgements

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Differentiated exploratory instruction in the chemistry classroom

Diferencirana istraživačka nastava u učionici kemije

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Nastavni sadržaji kemije u osnovnoj i srednjoj školi namijenjeni su učenicima u dobi od trinaest do osamnaest godina, različitih afiniteta, intelektualnih sposobnosti i interesa [1], što je uzrok različitih postignuća učenika tijekom učenja kemije. Na tragu inkluzivnog odgoja i obrazovanja uvedenog 90-tih godina 20. stoljeća (Salamanca sporazum) [2-3], može se govoriti o novijem pristupu odgoju i obrazovanju koji je učiteljima i nastavnicima kemije novi izazov: Kako isplanirati i provesti diferenciranu istraživački usmjerenu nastavu kemije?

Svrha provođenja radionice s učiteljima/nastavnicima kemije u osnovnim i srednjim školama bila je osmisliti i isplanirati nastavni proces i materijale (radom u skupinama) u ovisnosti o potrebama i sposobnostima učenika. [4] Uvodni dio radionice odnosio se na potrebu stručnog usavršavanja učitelja i nastavnika za izvedbu diferencirane nastave kemije s obzirom na sve veću pojavnost različitih potreba učenika u osnovnoj i srednjoj školi. U izvedbenom dijelu, budući da se radi o istraživački usmjerenoj nastavi [5-6], sudionici su samostalno bilježili opažanja temeljem izvedenog pokusa, a koja se s obzirom na konceptualni pristup obradi, mogu odnositi na kemijske sadržaje nastavnih tema: Makroskopske fizikalne i kemijske promjene tvari, Vrste tvari, Zrak i glavni sastojci zraka, Kemijske reakcije i očuvanje mase, Kemijske reakcije i energija, Soli i Karboksilne kiseline. U drugom dijelu radionice, sudionici su predlagali ishode poučavanja, aktivnosti učitelja i učenika te primjere provjere usvojenosti ishoda poučavanja ovisno o radnoj skupini u kojoj se nalaze (učenici s intelektualnim poteškoćama i poremećajima pažnje, nadareni učenici te prosječni učenici). U završnome dijelu sudionici su putem plakata izvijestili o zaključcima svake skupine. Nakon rasprave o iznesenim zaključcima, sudionici su dobili primjere razrade ishoda učenja i graduacije nastavnih aktivnosti te primjere razina usvojenosti za svaku skupinu prema zadanoj temi obrade. Na temelju iznesenog primjera diferenciranja nastavnih sadržaja, moguće je promišljati o pri(o)mjeni strategija i prilagodbi poučavanja u vlastitoj budućoj nastavi kemije ovisno o potrebama i sposobnostima učenika.

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''Lab escape'' – igra kao pedagoški alat u nastavi

''Lab escape'' – classroom tool

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Igre su interaktivni i interdisciplinarni koncepti koji nas nastoje naučiti utvrđivanju pravila, dostizanju ciljeva, adaptaciji, rješavanju problema, a sve kroz predstavljenu priču. Igre zadovoljavaju temeljnu potrebu za učenjem pružajući zadovoljstvo, strastveni angažman, strukturu, motivaciju, zadovoljstvo, kreativnost, socijalne interakcije i emocije u samom igranju dok se odvija – učenje. Istraživanjima provedenim među učenicima dolazi se do pozitivnih procjena koje se odnose na ulogu igre u edukacijskom procesu i na potencijal za poticanje učenika za sudjelovanje učenika u nastavi. [1,2,3]

''Room escape'' su aktivne, timski bazirane aktivnosti u kojoj igrači otkrivaju tragove, rješavaju zagonetke i ostvaruju zadatke u jednoj ili više prostorija, kako bi se ostvarili određeni ciljevi u ograničenom vremenskom razdoblju. Postavlja se pitanje može li se iz ovakve zabavne aktivnosti ostvariti i edukativni sadržaj?

Iako se u nekim obrazovnim kontekstima ne gleda pozitivno na uporabu edukativnih igara u nastavi i postavlja se pitanje umanjuje li uvođenje elemenata igre i zabave ozbiljnost i učinkovitost procesa učenja, osmislili smo igru u obrazovnom kontekstu kemije. Obrazovna igra ''Lab escape'' dizajnirana je kako bi sudionike podučili novim konceptima, proširili saznanja o određenim temama, sastavu i zdravstvenom učinku maslinovog ulja, te također kako bi igrajući je razvili pojedine vještine. Uvodna motivacijska priča kroz različite nivoe igre, rješavajući pojedine zadatke, izlaže sudionike učenju, novim znanjima, informacijama. Slažući koncepte koji se prožimaju kroz igru u ograničenom vremenskom periodu, potiču na razmišljanje i otkrivanje te dovode do rješenja zagonetke središnjom nastavnom aktivnosti - izvođenjem pokusa. Prema Bayiru [4] obrazovne igre su pedagoški alat kojim olakšavamo učenje na ugodan način.

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Integrated field course in natural sciences

Integrirana terenska nastava prirodoslovlja

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Korelacija predmeta u osnovnoškolskom obrazovanju podrazumijeva sagledavanje zadane problematike iz različitih perspektiva, što zahtijeva multidisciplinarnost [1, 2]. Međutim, podrazumijeva i spoznaju jednog predmetnog područja u drugi radi rješavanja određenih zadataka ili problema. Integrirano razmišljanje i znanje koje je isprepleteno interdisciplinarnim razmišljanjem, stvaranjem novih obrazaca i razvijanjem novih vještina odgovara učenju koje je u neposrednom doticanju sa svakodnevicom [1, 2]. Kao vrlo prikladan oblik takve nastave moguće je odabrati terensku nastavu. Ona obuhvaća učenje otkrivanjem, istraživanjem, ali i doživljavanjem tijekom kojeg se može obraditi novo gradivo ili sustavno ponoviti već naučeno [3]. Za učenike sedmih i osmih razreda vrlo je važna motivacija koja će biti inicirana od učitelja, tijekom kojih bi učenici trebali sami sustavno istraživati, zatim kritički promisliti, a tek na kraju pojedina zapažanja i naučene osnove stvaralački primijeniti na neke nove zadatke [3]. Tako učenici kemijske pojmove i promjene lakše pamte i razumiju ako su iste i sami radili, dakle učenje otkrivanjem temelj je za predmetnu nastavu kemije. Takav način učenja naša škola objedinjuje terenskom nastavom u Nacionalnom parku Paklenica, gdje se međusobno isprepliću predmetna nastava prirodoslovnih predmeta, te i ostala predmetna područja. Nizom interesantnih praktičnih radova na terenu učenicima su predočeni različiti pristupi zadacima na temu zajedničke dodirne točke - Nacionalni park Paklenica.

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The reflection – a story about water

Odraz – priča o vodi

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Polazeći od spoznaje da je voda izvor života dogovorili smo projekt o vodi "ODRAZ". Zajedničkim projektom pokušali smo prikazati jedan od mogućih načina obrade teme o vodi. [1-3] Izdvojili smo i probleme koji nas zanimaju: voda u prirodi, važnost vode u životu ljudi, fizikalna i kemijska svojstva vode te zaštita vode u prirodi.

Svrha projekta bila je povezati gradivo iz kemije, prirode, biologije sa svakodnevnim životom [4-5], te osvijestiti učenike o važnosti vode za zdravlje kao i o racionalnom odnosu prema pitkoj vodi. [6] Osim toga, učenike se željelo dodatno educirati o važnosti vode i očuvanju zaliha pitke vode. [6-7]

U izradi plana kako doći do odgovora učenici su istraživali udio vode u pojedinim namirnicama, analizirali različite uzorke vode, proučavali važnost vode za život svih živih bića. [4-5] Pokušali su odgovoriti na pitanje „Što ja mogu učiniti – promišljanja o očuvanju pitke vode“. [5,8] Učenici su izrađivali edukativne poruke, stripove s porukama o očuvanju vode. Traženje rješenja izveli smo na jednostavnim pokusima primjenom metoda koje smo prilagodili uzrastu uključujući učenike od trećih do viših razreda osnovne škole uz korelaciju s matematikom i doživljajnom stranom nastavnog procesa poput glazbenog, literarnog, likovnog doživljaja.

U tijeku projekta integrirano je praćenje grupnog rada (pružajući pomoć pri rješavanju zadataka i poučavanju suradničkim vještinama) i evaluacija učenika tijekom i nakon grupnog rada (kroz vrednovanje obrazovnih i socijalnih ciljeva). Primjenjivali smo strategiju KWL tablice (znam-želim saznati-naučio/la sam) kojoj je svrha aktivirati prethodno znanje (ili predrasude) o zadanoj temi, utvrditi očekivanja učenja, a na kraju utvrditi u kojoj su mjeri očekivanja ostvarena.

Učenici su upoznati s utjecajem vode na zdravlje [7-8], kao i s udjelom vode u namirnicama. Aktivnim učešćem i dijalogom učenici otkrivaju suradnički način učenja, vještinu važnu u široj društvenoj zajednici. U projektne zadatke uključili smo i učenike s poteškoćama u razvoju. Proveli smo različite oblike prilagođavanja i individualni pristup s ciljem osposobljavanja za samostalan rad i život prema osobnim sposobnostima učenika sukladno obrazovnoj inkluziji.

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Microscale chemistry – an example of good teaching practice

Kemija na mikroskali – primjer dobre nastavne prakse

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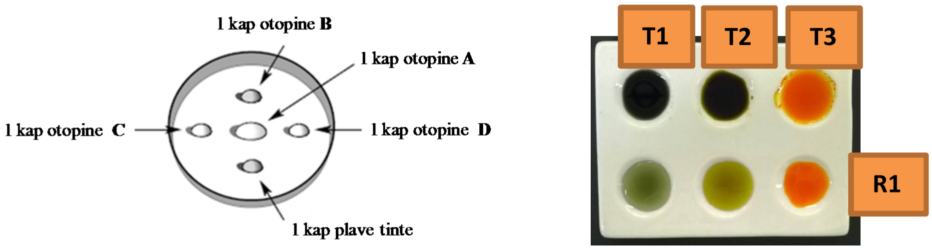
Pokusi na mikroskali odavno su našli mjesto u nastavnoj praksi kemije. Razvojem eksperimenata u mikroizvedbi bave se mnogi kemičari u stručnim i znanstvenim ustanovama. Metoda se od svojih početaka (1928. godine) do danas, vođena strategijom učenja otkrivanjem, a potaknuta lošim materijalnim uvjetima škola diljem svijeta, razvijala od prijedloga uporabe jednostavnog i priručnog pribora do industrijski načinjenih sofisticiranih setova za "mikrolaboratorije". U brojnoj i e-dostupnoj literaturi kroz sve razine obrazovanja, opisana su mnoga područja i teme gdje su pokusi na mikroskali pogodniji za uporabu od "klasične" eksperimentalne nastave. Pokusi na mikroskali u nastavne sadržaje integriraju i principe "zelene kemije" a imaju niz prednosti: uštedu vremena u pripremi pokusa, smanjenje otpadnih kemikalija, veću sigurnost, niže troškove i manji prostor skladištenja kemikalija i pribora, smanjenu ovisnost o ventilacijskim sustavima i ostalim instalacijama, ugodnu radnu atmosferu, kraće vrijeme reakcija, više vremena za neposrednu diskusiju i vrednovanje.[1] Međutim, često početna izrada mikrosetova i nerijetko njihova jednokratna uporaba mogu biti razlog odustajanja od složenijih pokusa i u ovoj izvedbi.

Uvažavajući navedeno, dan je prijedlog nastavnih jedinica *Halogeni elementi – klor* [2-3] i *Kemijska svojstva alkohola* [4] provedivih u redovitoj nastavi uporabom trajnog i jednostavnog pribora (slika 1) kao poticaj nastavnicima da pokusima na mikroskali unaprijede svoju praksu.



Slika 1: Pokusi na mikroskali: (lijevo) Halogeni elementi – klor [2-3]; (desno) Kemijska svojstva alkohola [4]

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Glow sticks as a teaching tool

Svjetleći štapići kao nastavno pomagalo

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Svjetleći štapići (engl. *glow sticks*) (Slika 1) jeftini su, jednokratni i kratkotrajni izvori "hladne svjetlosti" čiji se rad temelji na kemiluminiscentnoj reakciji aktiviranog estera oksalne kiseline s vodikovim peroksidom. Upotrebljavaju ih vojska, policija, spasilačke službe, izletnici, ribiči, ronioci itd., a posebno su omiljeni među mladima kao rekviziti na različitim zabavama, koncertima i u klubovima. Pokusi temeljeni na kemijskoj reakciji koja se zbiva u svjetlećim štapićima zbog svoje su velike atraktivnosti prepoznati kao vrijedno sredstvo za tumačenje mnogih temeljnih kemijskih pojmova i koncepata (kiseline i baze, oksidacija i redukcija, kemijska kinetika i termodinamika, katalizatori i inhibitori itd.). [1,2]

Slika 1: Shematski prikaz svjetlećeg štapića. Legenda: A – otopina vodikova peroksida u smjesi organskih otapala smještena u vanjskom valjkastom spremniku od savitljive plastike; B – otopina aktiviranog estera oksalne kiseline i fluorescentne boje u organskom otapalu smještena u staklenoj ampuli koja pluta u otopini A.

Imajući na umu te činjenice, svjetleće smo štapiće uveli kao nezaobilazno pomagalo u znanstveno-popularnim predavanjima, radionicama i aktivnostima namijenjenima najširem spektru publike, počevši od djece vrtićke dobi, preko učenika osnovnih škola, gimnazijalaca i studenata, pa sve do nastavnika kemije, biologije i fizike u osnovnim i srednjim školama.

U ovoj ćemo radionici polaznicima prenijeti dio svojih iskustava u primjeni svjetlećih štapića u nastavi kemije i popularizaciji znanosti koja smo stekli tijekom dosadašnjeg rada, a od kojega je veći dio izveden u okviru nedavno pokrenutog projekta „Kemijsko-inženjerske radionice HDKI-ja“. [3-5]

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Active learning styles in the function of developing basic chemical concepts

Oblici aktivnog učenja u funkciji izgradnje temeljnih kemijskih koncepata

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U prvom dijelu radionice, sudionici će, na temelju vlastite prosudbe i dosadašnjeg iskustva iz nastavne prakse identificirati temeljne kemijske koncepte koje bi učenici trebali usvojiti u određenoj školskoj dobi. U promišljanju o temeljnim konceptima važnim za daljnje uspješno učenje i poučavanje kemije trebalo bi se također rukovoditi idejama koje pomažu snalaženju u svakodnevnom životu, pridonose razumijevanju pojava koje nas okružuju u svakodnevnim situacijama ili pak očuvanju sigurnosti u izvanrednim okolnostima.

Nakon identificiranja temeljnih koncepata u nekoliko točaka odgojno-obrazovne vertikale, sudionici će prezentirati i analizirati postupke koje primjenjuju u učenju i poučavanju o tim temeljnim idejama. [1]

U drugom dijelu radionice, sudionici će na temelju provedbe jednostavnog pokusa [2], identificirati elemente istraživačkog učenja [3], i koncepte koji se pri tome razjašnjavaju te predložit način učenja i poučavanja [1], koji će najučinkovitije pridonijeti njihovoj izgradnji. Uslijedit će prezentacija te rasprava i kritički osvrt o predloženom.

U završnoj analizi rada, sudionici će navesti kompetencije koje se razvijaju istraživačkim učenjem, kao argumente za njegovu primjenu u redovitoj nastavi.

Tijekom izvedbe radionice bit će primijenjena temeljna načela suradničkog učenja. [4]

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The use of visualization in chemistry class

Primjena alata za vizualizaciju u nastavi kemije

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Kemija je jedna od temeljnih prirodoslovnih znanosti koja proučava sastav, građu, svojstva i pretvorbe tvari. Učenje i poučavanje kemije temelji se na stjecanju znanja i vještina putem složenih kognitivnih procesa percepcije, komunikacije te rasuđivanja. [1] Nastavni program kemije u osnovnoj školi prvenstveno je usmjeren na kemijska znanja potrebna za svakodnevni život, na zanimljivosti i doprinos kemije u izgradnji kvalitetnijega života. [2] Odgojno-obrazovni ciljevi učenja i poučavanja Kemije između ostalog su i razumijevanje i komuniciranje o temeljnim konceptima kemije, usvajanje i primjena kemijske terminologije i simbolike, razumijevanje principa znanstvenog pristupa istraživanja te rješavanju kemijskih problema. Većina kemijskih koncepata ima tri razine. Prva je makroskopska, druga je mikroskopska, dok je treća simbolička razina. [3] Vizualizacija u nastavi kemije predstavlja skup metoda, aplikacija, modela i analogija u 2D i 3D obliku prikazanih u tiskanom ili elektroničkom mediju. [4-5] Tijekom poučavanja kemije nužna je upotreba različitih alata za vizualizaciju, a koji omogućuju učenicima bolje razumijevanja kemijskih koncepata. Prirodne se pojave mogu prikazati pomoću fizikalnih modela koji najčešće nisu u mjerilu 1:1, ali su povećane ili smanjene vjerodostojne replike stvarnih objekata. Takvi su modeli često računalno animirani. Vizualizacije pomažu učiteljima da zornije objasne apstraktne prirodne pojave i procese koje učenici tada lakše pohranjuju u dugoročno pamćenje. [4]

Cilj je ove radionice dati pregled i analizu pojedinih alata i računalnih programa za postizanje visokog stupnja vizualizacije u nastavi kemije, a čija primjena u nastavi kemije ima pozitivan učinak na ishode učenja te omogućuju učenicima da budu uspješni u rješavanju zadataka koji uključuju elemente vizualizacije. Radionica će se provesti s nastavnicima kemije, kako bi stečena iskustva mogli primijeniti u svojoj svakodnevnoj nastavnoj praksi.

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It's time for something new – Labdisc

Vrijeme je za nešto novo – Labdisc

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Početak obrazovanja kemije, fizike i biologije započinju učenici u dobi kada su već iskustveno ovladali mnogim vještinama informacijske i komunikacijske tehnologije (IKT). To dragocjeno učeničko znanje gotovo se ne stavlja u kontekst ovladavanja nastavnih sadržaja prirodoslovnih predmeta, jer su još slabo i nesustavno razvijeni kvalitetni didaktički materijali, pribor i sredstva za njihovu primjenu. Primarno obrazovanje nastavnika (jer su obrazovani u drugačijem tehnološkom okruženju), materijalne mogućnosti obrazovnih ustanova i djelovanje u sustavu gdje integrirano poučavanje koncepata nije još dovoljno razvijeno, zapreke su za brže uvođenje i primjenu IKT−ih nastavnih pomagala. Treba napomenuti da ni mladi nastavnici nisu imali previše prilike upoznati niti koristiti takvu didaktičku tehnologiju tijekom studija. Sredstvima sve brojnijih projekata iz Europskog socijalnog fonda škole se opremaju suvremenijim nastavnim pomagalima, ali većina opreme i predloženih kurikula prirodoslovne skupine nastavnih predmeta namijenjena je izbornim sadržajima. Nove tehnologije ne smiju zaobilaziti redovito formalno obrazovanje prirodoslovlja, a napori u usvajanju novih nastavnih pomagala i materijalna potpora tim nastojanjima neminovno će se događati. [1-2] Prilog tome je i ova radionica gdje će nastavnici moći upoznati i neposredno raditi s interaktivnim mjernim uređajem Labdisc.

Labdisc mjerni uređaji su mali i prenosivi, te sadrže senzore prikladne za izvođenje većine mjerenja koja se provode u sklopu nastave kemije, fizike i biologije primjerene grupnom ili individualnom radu i učenju otkrivanjem. Postoji nekoliko različitih mjernih uređaja u paketu i svaki je prikladan za različite potrebe nastave ili prostora. GENSCI je uređaj koji obuhvaća senzore prikladne za nastavu fizike i kemije, dok su PHYSIO i ENVIRO prilagođeni nastavi fizike i biologije odnosno ekologije. [3] Predloženi didaktički materijali uz Labdisc mogu biti samo poticaj razvoju vlastitih pokusa i istraživanja u nastavi, a e-dostupna iskustava nastavnika diljem svijeta su mnogobrojna. Tijekom radionice predviđena je provedba/demonstracija sljedećih pokusa: temperatura zone plamena svijeće, vodljivost vodenih otopina različitih tvari i različitih koncentracija, uporaba pH-metra u različitom nastavnom kontekstu, uporaba kolorimetra, Boyle-Mariotteov zakon, slobodni pad i dr.

Primjena ovakvih mjernih uređaja u nastavi zajedno sa softverom koji omogućava detaljniju analizu podataka na računalu, ali i na učeničkim tabletima ili mobitelima, predstavlja učenicima dodatnu motivaciju a nastavniku ostavlja vrijeme za diskusiju i komunikaciju.

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Synthesis and kinetic analysis of novel imidazolium α-D-mannopiranosides

Priprava i kinetička analiza novih imidazolijevih α-D-manopiranozida

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It is well known from previously reported data that the adhesion in uropathogenic bacteria *Escherichia coli* is mediated by the FimH adhesin molecules located at the top of the *E. coli* type 1 *fimbriae* [1,2]. This specific interaction with mannose containing compounds enables bacteria to colonize various cell types and tissues causing illness [2]. The aim of this work was to find potential FimH ihnibitors and therefore bacterial anti-adhesion substances. A series of novel bicyclic imidazole α-D-manopyranoside derivatives was synthesised as potential FimH inhibitors. Synthesis of target molecules was conducted in four steps: protection of sugar hydroxyl groups by peracetylation, *O*-glycosylation of the anomeric C-atom with 2-bromoethanol leading to the introduction of two C-atoms spacer followed by condensation with bicyclic imidazole derivatives and the final removal of acetyls as protecting groups.

All compounds were prepared in good yields and were characterized by standard analytical methods (1D NMR, IR, MS) and optical rotation measurements. Additionally, simple computational methods (MM2 and conformational space searching) were used to optimize target molecules geometries which will be used in the study of FimH inhibitors interactions.

Furthermore, knowing the fact that many heterocyclic compounds inhibit the activity of butyrylcholinesterase (BChE) and are used as drugs for palliative treatment of Alzheimer's and Parkinson's disease, inhibitory properties of synthesized compounds towards BChE will be studied by applying Ellman's method [3]. Kinetic parameters and the inhibition constant (*K*i) will be determined for each compound.

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