UNIVERZITA PAVLA JOZEFA ŠAFÁRIKA V KOŠICIACH

BOOK OF ABSTRACTS
NEW TRENDS IN CHEMISTRY

Trends in chemistry, research and education at Faculty of Sciences of P. J. Šafárik University Košice

November 10, 2017, Faculty of Sciences,
Pavol Jozef Šafárik University, Košice, Slovakia

Renáta Oriňáková (ed.)

Faculty of Sciences

Košice 2017

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Organized by: Faculty of Sciences, Pavol Jozef Šafárik University in Košice

New trends in chemistry, research and education at Faculty of Sciences of P. J. Šafárik University, Košice 2017

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INVITED LECTURES ***Invited Lecture I***

Metal complexes with azamacrocycles for radiomedical applications

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Macrocycles are used as metal carriers in medicine due to high thermodynamic stability and kinetic inertness of the complexes. One of the promising radiometals is copper. Its complexes could be utilized as imaging agents in positron emission tomography or for radiotherapy. Several classes of ligands are used for Cu(II) radioizotope complexation, most of them are based on azamacrocycles. The most promising are those based on cyclam (1,4,8,11-tetraazacyclotetradecane) as they provide not only high stability and inertness of the complexes, but also very good selectivity for Cu(II) ions over Zn(II) and Ni(II) ions which are common impurities associated with preparation of the copper radioisotopes. However, application of cyclam-based ligands is generally limited by slow complexation. The medical radioisotopes show mostly rather short half-lives (minutes or hours). To reach a high activity of the radiopharmaceuticals, the isotope production and isolation, preparation and application of the pharmaceutical must be performed in the shortest possible time. Therefore, attention is focused on development of new ligand systems with improved complexation and labeling.

Complexation rate is significantly modified by introduction of pendant arms – coordinating groups attached to macrocycle nitrogen atoms. We have synthesized and studied series of cyclam-based ligands bearing phosphonate and phosphinate pendant arms (Figure 1). We have studied in detail not only stability, formation and dissociation of the complexes, but also their isomerisation that is typical for cyclam complexes. Further, we have modified the macrocycle by introduction of an additional ethylene bridge. This class of cross-bridged cyclam ligands is generally expected to show enhanced kinetic inertness.

All the studied ligands show good selectivity for Cu(II) and fast formation and stability of their Cu(II) complexes. Complexation is based on a two- or three-step mechanism. The first step is formation of the out-of-cage complex in which the metal ion is coordinated only through the pendant arms, whereas macrocycle remains protonated. The second step is a transfer of the metal ion to the macrocyclic cavity and formation of the in-cage complex in which all four nitrogen atoms are coordinated. This step is initiated by deprotonation of one of the macrocycle nitrogen atoms. Some of the complexes show also another step which is isomerisation of the in-cage complex.

In conclusion, the prepared ligands are promising Cu(II) carriers for further investigation towards radiomedical applications.

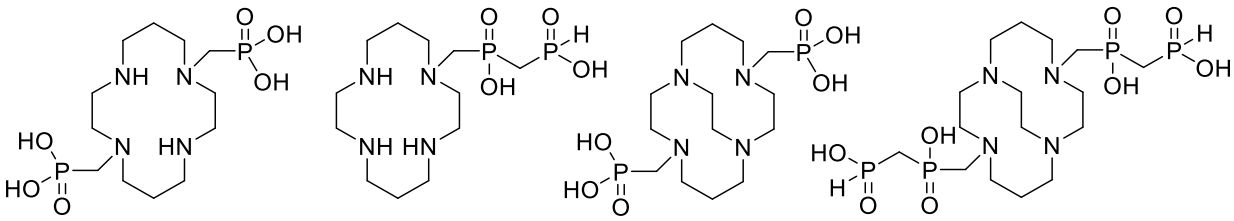

Figure 1. Studied cyclam-based phosphonate ligands.

INVITED LECTURES ***Invited Lecture II***

Theranostics for biomedical applications – CADD and CAND modeling

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Theranostics are complex molecules/nanosystems designated for dual therapeutic and diagnostic usage. Their invention and development started more than a decade ago. The world-wide R&D interest related to these systems exhibits exponential annual increase, as seen from current publication data (PubMed) related to the theranostics subject. Cancer diagnosis and treatment belongs to the most important areas of theranostics utilization [1, 2].
Theranostics are composed from metallic core, covered and functionalized with specific bioactive compounds. Different molecules can facilitate the monolayer covering, glutathion, chitosan or histidine among them. We were using "in silico" methodologies to built particular gold-core nanopartciles (AuNP), varying not only the assembly of the coverage, but also the particle size, starting from Au_{25} to clusters of larger articles having more than one hundred gold atoms. In addition to the above mentioned organic molecules, we were also interested in building of novel class of $Au_{25}(SR)_{18}$ theranostics covered with *closo*-dodecaborane thiols.
State-of-the-art computer-aided drug design (CADD) and nanodesign (CAND) methods were used to design and compute the properties of nanoparticles, belonging to the above-mentioned nanosystems.
The Au-S-Borane-based theranostics under study are supposed to be suitable not only for bioimaging, but exhibit simultaneous antiviral, antibacterial and cancerostatic features. The anticancer utilization relates to the so-called boron neutron capture therapy (BNCT). This anti-tumor therapy utilizes the generated alpha particles. Boron in such nanocluster arrangement can generate alpha particles very efficiently at the safe inner cellular distance approaching the cancer cells. The biological processes of the healthy cells should not be affected at such arrangements.
We were also interested in modeling the possible binding modes of the generated nanoparticles. We modelled the interactions of AuNP with very complex systems such as chromatin fragments. At first, models for AuNP and nucleoseome core particle (NCP) were generated. Different gold coverage was used in these steps. The results reflect the influence of the nanoparticle coverage on NCP binding efficiency.
Ongoing studies on further functionalization of the theranostics nanoparticles will target their better drug-delivery and binding efficiency.

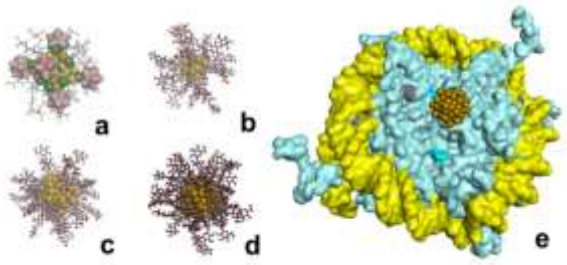

Figure 1. Selected examples of modeled nanoparticles. a) $Au_{25}Bor_6Glut_{12}$; b) $Au_{25}Chit_{18}$; c) $Au_{102}Chit_{25}$; d) $Au_{102}Chit_{30}$; e) "naked" Au_{102} in interaction with NCP.

Acknowledgements
This work was funded by the EU 7FP grant CELIM 316310. EU projects 26210120002, 26110230097, 26220120021, 26220120033, 26210120012 are acknowledged for generous funds for hardware and software resources.

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INVITED LECTURES ***Invited Lecture III***

Use of Glycosidases in the Synthesis of Phenylethanoid Synthons of Glycophenolics

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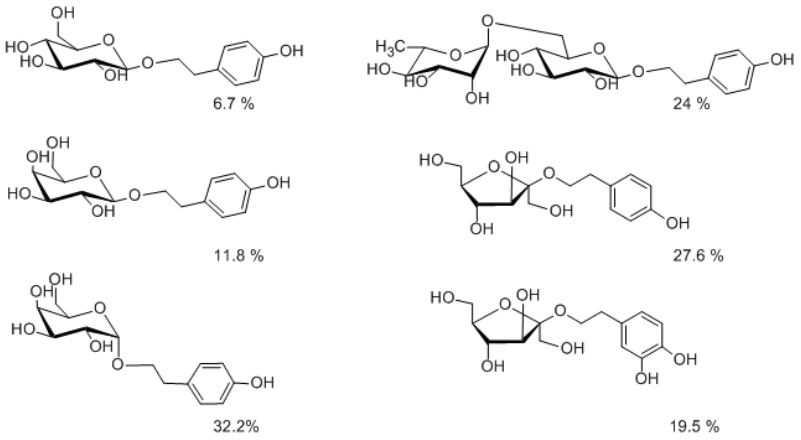
Tyrosol and hydroxytyrosol belong to the most active natural antioxidants. Their glycosides, themselves possessing several biological activities, may serve as structural fragments of numerous biologically active plant metabolites. The lecture will provide our experience with enzymatic preparation of salidroside and its glycosidic analogues. The optimized reactions provide salidroside, tyrosol α-D- and β-D-galactopyranosides, β-D-fructofuranosides of tyrosol and hydroxytyrosol as well as tyrosol rutinoside. The glycosylations were realized through transglycosylations starting from the corresponding disaccharides (cellobiose, lactose, melibiose, sucrose) or from rutin. The reactions were catalyzed by commercial glycosidases and plant materials (tartary buckwheat, dried sophora flower buds). All glycosylations proceeded selectively on the primary hydroxyls of tyrosol and hydroxytyrosol. Isolated yields ranged from 7 to 32 %. The study of mentioned reactions had also opened the way to interesting side-products. Among them, rutinose as economically very attractive item was produced on gram level.



INVITED LECTURES ***Invited Lecture IV***

Determination of Biogenic Amines in Biological Samples

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Biogenic amines (BAs) are basic nitrogenous compounds of various structures containing characteristic amino group. They are conveniently divided into aliphatic monoamines, aliphatic di- and polyamines, aromatic, or heterocyclic amines. Most of them have strong physiological effect and play an important biological role as sources of nitrogen and precursors for synthesis of hormones, alkaloids, nucleic acids and proteins. Small amounts of BAs are generally bio-synthesised in plant and animal cells and large quantities are found as a consequence of microbial metabolism in fermented foods such as sausage, fish products, cheese, fermented vegetables, and beverages (beer, ciders and wine). They can by markers for levels of microbiological food contamination as their concentrations increase during fermentation and spoilage.

Analysis of BAs is important because of their toxicity and their usage as indicators of the degree of freshness or spoilage of food. Histamine, putrescine, cadaverine, tyramine, tryptamine, phenylethylamine, spermine, and spermidine are considered to be the most important biogenic amines occurring in foods. That eight BAs are often analysed in food.

Spermine, spermidine, putrescine and cadaverine are aliphatic amines widely spread in the human body. Their concentrations together with their acetyl conjugate increase significantly in the biological fluids and in the affected tissues of cancer patients. Their concentrations decrease with the improvement in the patient's condition on multiple therapies.

The analytical methods used for quantification of BAs are mainly based on chromatographic methods: high-performance liquid chromatography (HPLC), thin layer chromatography (TLC), gas chromatography (GC). Sometime is used capillary electrophoresis (CE). HPLC is most often used for the analysis method of BAs. Due to low volatility and lack of chromophores of most BAs, direct UV-spectrometric detection cannot be used. Some work also describes the use of electrochemical detectors. The large majority of assays employ precolumn or postcolumn derivatization and UV or fluorescence detection. Some work also describes the use of electrochemical detectors. New trends in analysis of BAs combine HPLC, or GC separation and mass spectrometry detection. These methods are often used today. Prior to the analysis, samples are to be treated from biological matrices sing extraction methods. Liquid-liquid extraction, or microextraction, solid phase extraction, or solid phase microextraction are used nowadays.

High performance liquid chromatography is presented here for the simultaneous determination of eight BAs (histamine, putrescine, cadaverine, tyramine, tryptamine, phenylethylamine, spermine, and spermidine) with derivatization and UV detection. Samples of meat, meat products, fish and vegetables were extracted with trichloracetic acid and then filtered through a membrane filter. As a derivatizing reagent was used dansyl chloride. Then the samples were evaporated and dissolved in acetonitrile. HPLC analysis was performed on a reversed phase column C18 with the mobile phase of 0.02 M acetic acid, and acetonitrile. Samples were detected at 254 nm. Detection limits for individual biogenic amines were in the range of 0.01 μg/mL to 0.1 μg/mL.

Acknowledgements
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INVITED LECTURES ***Invited Lecture V***

Cyclodextrin Story: from Supramolecular Complex, through Micelle Double Confinement, to Surface Nanostructure

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Cyclodextrin, oligosaccharide, has been studied extensively as a host molecule for variety of guest molecules, forming together inclusive host/guest supramolecular complex. In our case, we use cyclodextrin molecule as an example of complex system, as a simple model of biosystem, and eventually as a tool to build surface nanostructures. A confinement of coumarin C153 within host/guest based on β-cyclodextrin (β-CD) and 6-deoxy-6-thio-β-cyclodextrin (β-CD-SH) in water are studied by fluorescence spectroscopy [1]. For β-CD/C153, the 1:1 complex is proposed, and for β-CD-SH/C153 both the 1:1 and 2:1 complexes are suggested. The 2:1 β-CD-SH/C153 complex has an association constant of $4.2\times10^5\ M^{-1}$ and a C153 population of 82 %, supportng the proposed β-CD-SH disulfidic dimers. The fluorescence relaxation is determined by the ultrafast components of time-resolved spectroscopy to be 3 and 7 ps for the 1:1 β-CD/C153 and 2:1 β-CD-SH/C153 complexes, respectively. Coumarin, C522, in cyclodextrin, CD, cavity is additionally placed into the reverse sodium dioctyl sulfosuccinate, AOT, micelle as the double confinement is compared [2]. The ultrafast decay in the case of w=3 ranges from 9.5 to 16 ps, with an average of 12.6 ps, in the case of the C522/micelle system and from 9.0 to 14.5 ps, with an average of 11.8 ps, in the case of the C522/CD/micelle system. Increasing the w values (from 10 to 40) result in a decrease of the ultrafast decay values in both cases to an average value of about 6.5 ps. The average ultrafast decay times are 12.6 ps and 6.5 ps for the micelle sizes of w = 3 and w = 40, respectively. The supramolecular complexe between cyclodextrin ($C_{42}H_{70}O_{35}$, 1134 u) and iron species are studied by using secondary ion mass spectrometry [3]. The iron species are prepared by pulsed-laser ablation of bulk iron in water, providing Fe^+ (56 m/z) and $FexOy^+$ (x, y=1–7) species. The relevant peak to supramolecular complex at 1210 m/z is observed and assigned as $C_{42}H_{67}O_{35}FeNa^+$. The complex combination of thiolated cyclodextrin, chemisorbed on gold surface, with deposited iron species is studied (Au-S-CD/Fe) [4]. Using laser ablation in water, the solution of iron species is dropped on Au-S-CD, where mass peaks at 1227 m/z, 1243 m/z, and 1260 m/z are observed and assigned to $C_{42}H_{68}O_{34}SNa\text{-}Fe^+$, $C_{42}H_{68}O_{34}SK\text{-}Fe^+$ together with $C_{42}H_{68}O_{34}SNa\text{-}FeO^+$, and $C_{42}H_{68}O_{34}SK\text{-}FeO^+$, respectively. These cyclodextrin based supramolecular complexes provide not only the fundamental information about the fluorescence dynamics and the complex structures, but also serve as building blocks of the surface nanostructure with potential applications in functional devices like digital memory medium.

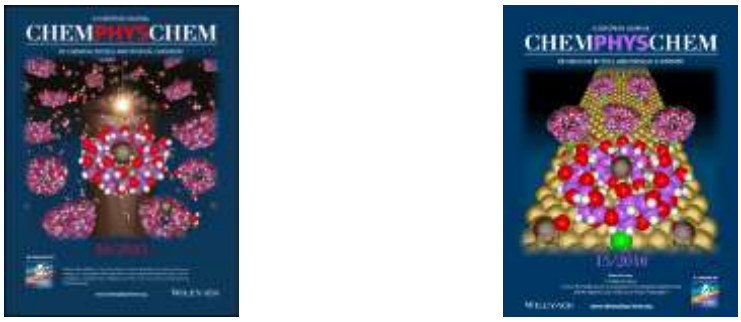

Figure 1. Cover pages of ChemPhysChem, the left one shows a preparation of the cyclodextrin/iron complex and the right one shows the supramolecular surface structure of iron/thiolated cyclodextrin/gold.

Acknowledgements
I appreciate the work of all my colleagues as listed in References and also APVV-15-0201 support.

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LECTURES ***Lecture I***

2´-Aminoanalogues of the cruciferous phytoalexins spirobrassinin, 1-methoxyspirobrassinin and 1-methoxyspirobrassinol methyl ether: Synthesis and anticancer properties

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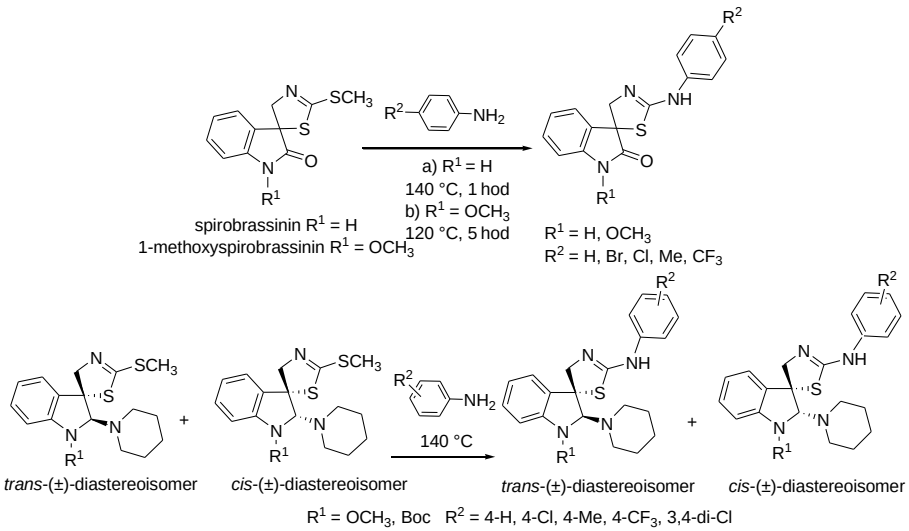
Indole-base group of naturally occurring compounds in vegetables of the family *Cruciferae* are cruciferous phytoalexins [1]. Cruciferous phytoalexins possess antibacterial, antifungal and antiprotozoal properties [2,3] and may also act as a chemopreventive or antiproliferative agents [4].

A method for the synthesis of new 2´-aminoanalogues of spiroindoline phytoalexins is reported. 2´-Aminonalogues of spirobrassinin, 1-methoxyspirobrassinin and 2,2´-diamino analogues of 1-methoxyspirobrassinol methyl ether were prepared by substitution of the methylsulphanyl group on the dihydrothiazole ring of corresponding phytoalexins. Final products were obtained by heating the phytoalexins with aniline or substituted aniline in the absence of solvent at 120 or 140 °C. By replacement of the SCH_3 moiety of (*S*)-(–)- or (*R*)-(+)-spirobrassinin, enantiomers of 2´-aminoanalogues of spirobrassinin were also synthesized. Determination of their enantiomeric compositions using HPLC with chiral stationary phase revealed partial enantiomeric enrichment. The occurence of a SIDA effect of our 2´-aminonalogue of spirobrassinin was evaluated by examination of a non-racemic mixture in non-polar C_6D_6. Complete enantioresolution and distinct signals for two enantiomers were observed for a number of ^1H and ^{13}C NMR resonances. New synthesized compounds were supplied for testing the antiproliferative effect on a panel of six human cancer cell lines. 2´-Aminoanalogue with CF_3 functionality exhibited more significant inhibitory effects than natural phytoalexins spirobrassinin.



Scheme 1. Synthesis of 2´-aminoanalogues of the cruciferous phytoalexins.

Acknowledgements

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LECTURES ***Lecture II***

Biodegradable Iron Based Biomaterials

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Recently biodegradable metallic materials are intensively studied as implants in orthopaedic surgery because of their biocompatibility, high strength and high elastic modulus [1, 2]. Degradable implants based on iron have a low degradation rate that is necessary to adjust because slow degradation can cause the same problems as permanent implant devices, such as chronic inflammation, creation of thrombus etc. [3]. Metallic implants are frequently covered with osteoconductive biomaterials, such as bioceramics or polymers, which possesses excellent biocompatibility and can help to improve bone growth and regeneration [4-6]. The biodegradable open cell material was produced by sintering of carbonyl iron powder and coated with hydroxyapatite (HAp) or polyethylene glycol (PEG) layer (Fig.1). The biocompatibility as well as electrochemical and static immersion corrosion behaviour of developed materials in Hank's solution was studied.

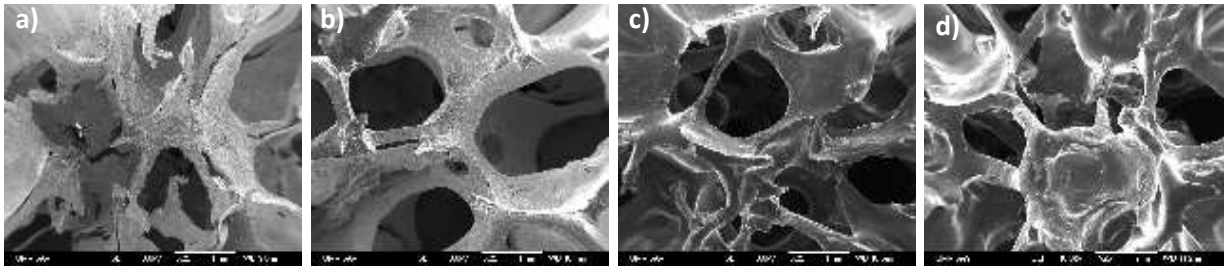

Figure 1. SEM micrographs of the surface of open cell iron samples: Fe sample (a); Fe-PEG1 (b); Fe-PEG2 (c); Fe-PEG3 (d).

Acknowledgements

This work was supported by the Projects APVV-0677-11 and VEGA 1/0074/17.

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LECTURES ***Lecture III***

Flow Systems in Green Analytical Chemistry

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For modern analytical chemistry, the development of new analytical methods covering the needs of green chemistry and analytical chemistry itself (high efficiency, yield, selectivity, sensitivity) is a major challenge. Flow systems, from their founding, have been predisposed to become an effective tool in green analytical chemistry. Their gradual development helped to develop from the original non-separation techniques new techniques, which allow to carry out rapid and automatized preconcentration, separation and detection of analyte and could be applied to samples with the complex matrix effect, having in the same time simple data evaluation [1-3]. Each of those steps could be considered as critical throughout the process and affecting on the reliability of the whole determination. Application of automated flow systems largely reduces the errors, in addition, the closed system for manipulation with samples is good compatible with various detection techniques and fully satisfied the requirements of modern green analytical chemistry.

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LECTURES ***Lecture IV***

G-Quadruplex: Why is this Non-canonic structural motif so attractive?

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G-quadruplexes are one of the most attractive structural motifs of nucleic acids. Guanine-rich (G-rich) DNA and RNA sequences have the propensity to form spontaneously stable G-quadruplex structures. However, such sequences are located non-randomly within various genomes in living organisms and viruses [1-3], but they frequently occur in important regions responsible for gene regulation and cell proliferation which are closely related with cancerogenesis. Recently, several G-quadruplex stabilizing drugs were discovered, and some of them were clinically applied for therapy of certain type of cancers. In addition, G-quadruplexes are highly polymorphic, depending on their sequence and condition. Their topology and driving force of folding sensitively depend on many factors. In addition, they can also form high-ordered multimeric structures. Multimeric forms obtain novel specific properties [4,5].
G-quadruplexes can show an extremely high affinity against various molecular targets including proteins. These structures show attributes which are typical for aptamers. The binding affinity of aptamers is comparable with antibodies. Therefore, these structures are considered as artificial antibodies. To date at least twenty different G-quadruplexes have been identified [6]. Nucleic acid aptamers are used not only in clinical medicine, but they are frequently applied in nanodevices, mainly as a recognition receptor element in various biosensors. The specific G-quadruplex aptamers together with nanoparticle conjugates represent a new strategy for molecular target visualization both in living organisms and *in vitro*.

Acknowledgements
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LECTURES ***Lecture V***

Periodic nanoporous materials – recent research trends

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Nanoporous materials, based on porous coordination polymers (Metal-organic frameworks, MOFs) or periodic nanoporous silicas (PNS) prepared by self-assembly of surfactant molecules have attracted considerable scientific interest in recent years. These materials are structurally well ordered with very well-defined pore sizes and exhibit unique physico-chemical properties determined by their high surface area, large pore volume, and the possibility of their modifications. These properties make MOFs and PNS suitable for applications in the fields of catalysis, adsorption, magnetism, or as drug delivery systems. The aim of the lecture is to give an overview of current trends and perspectives in the research of above mentioned classes of nanoporous materials.

The lecture will focus on four areas. In the first part, synthesis strategy and unique structural features of MOFs and PNS will be presented, including their topology and possibility of modification. The second part of the lecture will be dedicated to the use of nanoporous materials for sorption and separation technologically relevant gases. Very highly porous MOFs and PNS offer a variety of chemical compositions and structural architectures that are suitable for the adsorption and storage of gases like hydrogen and carbon dioxide [1]. Third part of the lecture will focus on the use of nanoporous materials as drug delivery systems. PNS materials possess favourable chemical properties, high porosity, stability and biocompatibility and thus are very promissing in drug delivery [2]. Final part of the lecture will be devoted to magnetic properties of MOFs and composite PNS, containing magnetic nanoparticles. The phenomena like magnetocaloric effect and superparamagnetism will be presented [3].

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SESSION I **Analytical Chemistry**

Antioxidant Activity of Extracts Selected Plants

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Biological activity of flavonoids is very broad, characterized by anti-inflammatory, antiallergic and antimicrobial effects. One of the most significant properties of flavonoids is their antioxidant activity, i.e. they can effectively eliminate free radicals.
Aim of the work was to evaluate the antioxidant activity of the extracts two different plants collected in Slovakia, *Mint Perpendicular* and *Wild Thyme*. The antioxidant action was determined using 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging and UV/VIS spectrophotometry.
The findings of the study confirmed that the plants extracts possesses strong antioxidant potential that was higher for natural growth plants compared with cultivated.

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SESSION I **Analytical Chemistry**

Application of Optical Probe for Automated Indirect Determination of Fluoride in Water Samples

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Fluoride is an important trace element, which enters into the organism with consumption of drinking water. The significance of fluoride control is that in the small amount fluoride could be a good the maintenance of bone health, but in the excessive intake makes worth carbohydrate metabolism thereby promoting different diseases [1,2]. Therefore, sensitive and automated methods for fluoride determination are still required.

In the current study, automated sequential injection procedure for indirect determination of fluoride, based on the bleaching the complex of aluminium (III) with 3-[4-(dimethylamino)cinnamoyl]-4-hydroxy-6-methyl-3,4-2H-pyran-2-one (ligand) [3] by fluoride using an optical probe for absorbance measurement was developed. The optimum conditions for determination of fluoride were achieved at pH 8 with concentrations of Al (III) and ligand 6.75 and 0.195 mg L^{-1}, respectively. Under optimized condition the calibration curve showed good linearity ($r = -0.9976$) in the range 0.01-1.9 mg L^{-1} of fluoride. The limit of quantification for fluoride was 0.01 mg L^{-1} (n=8). The relative standard deviation of eight blank tests was lower than 2.3%. The method was applied for determination of fluoride content in mineral water samples.

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SESSION I **Analytical Chemistry**

Study of Enantiomer Elution Order on a Cyclofructan Based Chiral HPLC Columns

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The enantiomer elution order (EEO) is one of the most important topics in the field of chiral separations. In most cases, it is desirable to detect the minor component in the front of the major one in analyzing the synthetic chiral compounds. For example, even an enantiomeric impurity as high as 1% was often impossible to detect when it is eluted as the second peak [1].

In this work, the study of HPLC enantioseparation of some spirobrassinin derivatives was performed on cyclofructan chiral columns under normal phase conditions with emphasis on differences in EEO and its dependence on the nature of the chiral selector and column temperature. Using the van't Hoff equation, the values of isoenantioselective temperature (T_{iso}) were established. Below T_{iso}, separation is enthalpy driven, and the selectivity decreases with increasing temperature. Above isoenantioselective temperature, enantioseparation is entropy driven, and a reversal of the elution order for a pair of enantiomers is expected. Unfortunately, the EEO reversal above calculated T_{iso} was not confirmed as it was out of allowed column temperature range. However, the reversal of enantiomer elution order was observed depending on the type of the cyclofructan chiral selector.

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SESSION I **Analytical Chemistry**

Application of Astraphloxine for Kinetic Spectrophotometric Determination of Dissolved Species of Chromium in Water Samples

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The aim of this work is the development, optimisation and validation of new spectrophotometric kinetic method for determination of dissolved species of chromium in water samples using polymethine dye (2Z)-1,3,3-trimethyl-2-[(E)-3-(1,3,3-trimethylindol-1-ium-2-yl) prop-2-enylidene] indole chloride also known as Astraphloxine (AP). The chemical reaction is research spectrophotometrically with immersion probe. This method is based on the catalytic effect of chromium (VI) on the rate of decline the astraphloxine concentration. The experimental data were evaluated using four methods specifically by the method of the average rate constant, by the method of the initial rate constant, by the method of constant time and by the method of change the volume of absorption peak in time. Two procedures were described during the development of the analytical method. The first procedure is for determination of chromium (VI) and under the optimal conditions the linear concentration range was 0.005 – 0.5 mg/L. The reaction mixture for first procedure contains sulphuric acid, chromium (VI) or sample and astraphloxine in this order. The second procedure is for the determination of total Cr(III) + Cr(VI) chromium and under the optimal conditions the linear concentration range was 0.005 – 0.1 mg/L. The reaction mixture for second procedure contains chromium (III) or sample, potassium periodate, sulphuric acid and astraphloxine in this order. For both procedures were optimalised the concentration of astraphloxine, the kind of acid, the acid concentration, the effect of temprature, the effect of ionic strength, the order of reactant addition, the concentration of potassium periodate and the time for quantitative oxidation of Cr(III). For the procedure of Cr(VI) determination were study the effect of interferents with oxidating features. The most interfering ions were nitrites and presulphates. The presented work was used for determination of chromium in model samples and in tap water with the method of calibration line and the method of standard additions. In the end of the work were calculated the limit of detections (LoD) for everyone method of evaluating the experimental data for both procedures. Under the optimal conditions by using the method of the average rate constant for evaulation of experimental data for the determination of Cr(VI) was found LoD = 1.87 ng/mL and for the determination of total Cr(III) + Cr(VI) was found LoD = 1.90 ng/mL.

Figure 1. Pictures of the reaction mixture at different times under the following conditions: c(AP) = 10 μmol/L; $c(H_2SO_4)$ = 0.9 mol/L; $c_m(Cr^{6+})$ = 0.5 mg/L; t = 60 °C.

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SESSION I **Analytical Chemistry**

Analysis of Oligosaccharides in Breast Milk

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Oligosaccharides are carbohydrates comprised of 2 to 10 monosaccharide units bound by O-glycosidic linkages. Due to the presence of β-glycosidic linkages, some of them are defined as non digestible oligosaccharides, thus being included among prebiotics. The most important are fructooligosaccharides (FOS), galactooligosaccharides, isomaltooligosaccharides, inulooligosaccharides and soybean oligosaccharides. These substances are added to the so-called functional foods that are defined as any foods that have a positive effect on human health [1,2].
The work was focused on the selection of a suitable chromatographic system for the analysis of oligosaccharides in breast milk as well as in other types of milk by means of thin-layer chromatography with chemical and densitometric detection. Experimental results include the selection of the stationary and mobile phases, the selection of a suitable detecting agent as well as the influence of multiple thin-layer development on the separation of complex carbohydrates in real samples.
For the analysis, silica gel thin-layer plates were used, developed in mobile phase: butanol-acetic acid-water (3: 3: 2, v /v). For the detection of the components, the detecting agent was a mixture of aniline, diphenylamine and phosphoric acid in acetone. The elaborated method was used for FOS analysis in real samples of: breast milk, goat's milk, cow's milk, two kinds of coconut milk, milk-free lactose milk and Nutridrink. Samples were detected based on the comparison of the R_f values of individual components in real samples with standards. In the sample of breast milk was confirmed the presence of prebiotic oligosaccharides identical to oligosaccharides in standard of raftilose, lactose and galactose.

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SESSION I **Analytical Chemistry**

Synthesis and Application of Carbon Nanotube Vanadium Sulphur (CNT-VS_2) for Solid-Phase Extraction of Trace Amount of Rhodamine B

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Vanadium sulphate nanoparticles were bound on multi-walled carbon nanotube, resulted in carbon nanotube vanadium sulphur CNT-VS_2. Synthetized material was used as a new sorbent for extraction of trace amount of rhodamine B before its spectrophotometric determination. Less than 1 mg of CNT-VS_2 was used for quantitative extraction of rhodamine B from sample solution. An acetic acid-ethanol (1:1, v/v) solution was found as ideal eluent for rhodamine B bound to the CNT-VS_2. Next the concentration of rhodamine B was determined by measurement of absorbance of solution at 557 nm. Calibration curve, included five concentration points was linear in a range 0.719 – 86.2 μg L^{-1} of rhodamine B with correlation coefficient 0.9996. The limit of detection calculated from blank test was 0.15 μg L^{-1} of rhodamine B. Preconcentration factor was 77, according to ratio of sample volume and final volume of measured solution (50mL/0.65mL). The ratio of slope of calibration curve obtained before and next after applying the method resulted enrichment factor 78. The method was applied for determination of rhodamine B in real samples as lip stick, nail polish remover and pepper. Synthetized CNT-VS_2 proved excellent absorption capacity of rhodamine B, 9 mg of rhodamine B per 1 mg of sorbent. It allows determination of trace amount of harmful dye rhodamine B.

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SESSION II **Biochemistry**

Analysis of Ebola virus putative G-quadruplexes

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G-quadruplex is the structural motif formed from nucleic acids which contains at least two guanine quartets. G-rich sequences able to form G-quadruplex were found in eukaryotic telomeres and in other important regions of human genome, e.g. gene promoters [1]. G-quadruplexes have long been a highly promising target for the development of new anti-cancer therapies [2].

The Ebola and Marburg viruses are some of the deadliest viruses in the world. The positive-sense RNA of Ebola and Marburg contain regions rich in G-residues which show a marked tendency to adopt G-quadruplex structures. G-quadruplexes have long been seen as a highly promising target for the development of new anti-cancer therapies. A recent study has also revealed the first evidence of G-rich sequences to be found in the negative-sense RNA of Zaire ebolavirus L [3]. Although this sequence is highly conservative among viral isolates, it is interesting to note that that it is located in the anticoding RNA strand; G-quadruplexes in this RNA can affect the viral transcription machinery influencing the formation of coding the (+) RNA strand. In this study, we analyze the complementary strands which are formed following the infection of the cell by the virus. G-quadruplexes formed in these strands can affect the viral and cellular processes of infected cells [4].

A series of G-rich DNA sequences derived from these types of viruses which possess the potential to form G-quadruplex structures are analyzed in this study. A set of DNA oligonucleotides derived from original viral isolates was used as a representative modeling sequence with which to demonstrate the influence of thiazole orange on circular dichroism (CD) spectral profiles. The results show the unique profile of the induced CD (ICD) signal in the visible region caused by interactions between the ligand and G-quadruplexes (Fig 1.). This ligand was found to stabilize the G-quadruplex structure and can also induce topological changes and facilitate G-quadruplex multimerization. Thus, the ICD signatures can be used to determine whether specific unknown sequences can form G-quadruplex motifs. The viral sequences were analyzed using standard spectral and electrophoretic methods. In addition, the ability to target G-quadruplexes located in filoviruses offers researchers attractive therapeutic targets which would be of particular use in the development of novel antiviral therapies.

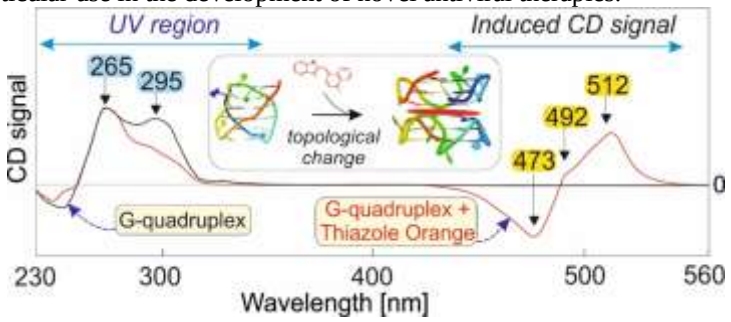

Figure 1. Schematic drawing of common features shared by all of G-quadruplex structures [4].

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SESSION II **Biochemistry**

Binding affinity of Thiazole Orange to G-quadruplex and triplex DNA

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DNA can form various structural forms that related to their physiological function, as well as their possible biological roles. One of such structural motifs are G-quadruplexes (G4) and triplexes. G4 are formed from guanine-rich sequences [1]. Potential G-quadruplex forming sequences have been identified in important regions of the genome, such as promoters of some oncogenes, telomeres, rDNA, and non-coding regions of mRNA. In recent years, the great attention has been paid to the G4, because they could play a key role in many fundamental biological processes, including uncontrolled differentiation, cell proliferation and senescence. These properties predetermine G4, as in the past triplexes, being a suitable target motif useful in the treatment of various diseases and cancer, including tumor-specific drugs with high affinity for these motifs. The cyanine dyes belong among these potential drugs [2].

Cyanine dyes interact with different types of nucleic acids. Thiazole Orange (TO) is one of the oldest synthetic cyanine dyes widely used in reticulocyte analysis. This dye penetrates via living cell membranes and efficiently stains residual RNA in reticulocytes. It also binds to dsDNA, one TO molecule on two base DNA pairs [3]. This binding to dsDNA results in a stock shift in the absorption spectrum, results in an induced CD signal, and leads to large increase in the fluorescence intensity of the dye. Binding of TO to dsDNA and ssDNA homopolymers is relatively weak and readily reversible [4-5]. A dimeric form of the TO has much higher affinity for dsDNA compared to that of the monomeric form. Although dsDNA is the most common form in cells, there is an increasing number of theoretical and *in vitro* evidences that G4 may coexist with dsDNA [5]. TO is one of the most used fluorescence probes in nucleic acid visualization due to its high fluorescence quantum yield, even higher than for G4 [2-3]. In this work, we have demonstrated by UV-Vis absorption and circular dichroism (CD) spectroscopy, that TO binds with much higher affinity to triplex and G-quadruplex DNA structures compared to dsDNA. The results confirmed that the affinity of TO with G4 is dependent on the presence of K^+ and Na^+ ions. TO can induce and stabilize G4 structures. [5].

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SESSION II **Biochemistry**

Biological activity and intracellular distribution of tacrine-cumarin hybrid molecules

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Coumarin and its derivatives are found widely throughout nature, and many of these compounds exhibit a broad range of useful biological activities. The naturally occurring coumarin ring system displays a number of interesting pharmacological properties and has intrigued chemists and pharmacologists for decades. It is therefore conceivable that these hybrid compounds could also be used as potential drug candidates for multifactorial diseases.

In this study, a series of novel coumarin-tacrine hybrids (**1a**–**1d**) were biologically evaluated for their potential inhibitory effect on topoisomerase I enzyme. The derivatives were analysed against A549 adherent lung adenocarcinoma cells. The presence of the particles was determined through observations of their fluorescence in the green channel. According to our results, the presence of derivatives was detectable predominantly in sample **1d**. In other samples, the fluorescence of the derivatives was not distinguishable from the autofluorescence of the cancer cells. In cells, the derivatives were distributed in cytoplasm and displayed no signs of interference with the cell nuclei. Based on mitochondrial staining and overall distribution of the signal, we were unable to confirm the accumulation of derivatives in mitochondria or in other organelles or membranes. Flow cytometric analysis of derivatives content in A549 cells revealed the cumulative fluorescence of derivatives **1a** -**1d** from the green (FL-1) to the red (FL-3) channel. Derivative **1c** was found to display the highest level of fluorescence. Moreover, the total cell number was sharply decreased (more than 50%) in the case of cells treated with compounds **1c** and **1d** but viability of the cells was only weaker reduced. The analysis of the cell cycle was determined that compounds **1c** and **1d** significantly increased the accumulation of the cell in phase G1, while cells in S and G2 phase was proportional divided. The obtained results could be of benefit in the design and development of new coumarin based agents.

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SESSION II **Biochemistry**

Anticancer Activity of BRACO-19 Inspired 3,6-Diamino-9-Substituted Acridine Derivatives and Their Interactions with DNA

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Acridine and its derivatives, with their heterocyclic aromatic structures, are interesting organic compounds which induce several biological effects. They possess promising anti-cancer and cytotoxic properties, moreover they display other forms of bioactivity and are used as biological fluorescent probes, antibacterial, antiprotozoal and antimalarial agents and also in the treatment of HIV and Alzheimer´s disease [1,2]. The interaction of acridine derivatives with DNA plays an essential role in their biological activity. Recent studies suggest, that trisubstituted acridine derivatives exhibit strong anti-tumor effect, which involves several parallel mechanisms like telomere uncapping, direct or indirect telomerase inhibition with the characteristic induction of senescence and apoptosis. Several structure-activity studies have led to the design of a new potent and selective telomerase inhibitor based on 3,6,9-trisubstituted acridine structure, named BRACO-19. Currently the subject of various synthetic methods is preparation of target acridine skeletons or modifications of even naturally occurring compounds, that exhibit promising anticancer activities [1,3,4].

Acridine derivatives represent an important class of drugs, which showed the ability to intercalate DNA and inhibit topoisomerase or telomerase enzymes. Topoisomerases are enzymes that can modify DNA topology by introducing breaks in DNA strands and play a critical role in DNA metabolism. Introduction of breaks in DNA strands serves to release the resulting topological stress during a critical cell processes [5]. Topoisomerase poisons transform the enzyme into a potential cellular toxin by stabilizing the covalent topoisomerase-DNA complexes that are intermediates during the enzyme's catalytic cycle. This results in creation of many breaks in the DNA, which the cell cannot repair, thus triggering an apoptotic signalling pathway. The main feature of the intercalation mechanism are π-stacking interactions with base pairs of double-stranded nucleic acids. Acridine moiety of the compound, with its flat, heterocyclic and polyaromatic structure intercalates into the gap between two chains of polynucleotides and disturbs their crucial role in cell division. The ability of these compounds to intercalate into DNA seems to be necessary for their anti-tumor activity and the strength and kinetics of binding acridine to DNA have a crucial impact on the activity of this type of anticancer agent.

In order to find new anti-tumor agents and study of the ability to influence the activity of the enzymes topoisomerase I and II, new 3,6,9-trisubstituted acridine derivatives were synthetized at the department of organic chemistry [1,6]. Their biochemical, biophysical and biological properties were tested using spectroscopic techniques (UV-Vis absorption and fluorescence spectroscopy, circular and linear dichroism), viscometry and electrophoresis. Binding affinity of acridine derivatives with ctDNA (calf thymus DNA) was examined and their binding constants were determined. All of the measurements indicated that the investigated derivatives belong to DNA-interacting agents and also act as effective DNA intercalators.

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SESSION II **Biochemistry**

DNA binding and topoisomerase I inhibition activity of novel Zn(II) complexes

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Understanding the binding of small molecules to DNA is potentially useful in developing principles to guide the synthesis of new improved drugs which can recognize a specific site or conformation of DNA [1]. Generally, metal complexes upon binding to DNA are stabilized through a series of weak interactions such as the p-stacking interactions of aromatic heterocyclic groups between the base pairs (intercalation), hydrogen bonding and van der Waals interactions of functional groups bound along the groove of the DNA helix [2].

Toward this goal a series of new Zn(II) complexes with flufenamic acid (flu) has been synthesized, namely $[Zn_3(dmso)_2(flu)_6]$ (1), $[Zn_3(flu)_6(py)_2]$ (2), $[Zn(flu)_2(tmen)]$ (3), [ZnCl(flu)(neo)] (4), and $[Zn(cyclam)(flu)_2]$ (5), where py=pyridine, tmen =*N*,*N*,*N*′,*N*′-Tetramethylethylene diamine, neo =2,9-Dimethyl-1,10-phenanthroline and cyclam =1,4,8,11-Tetraazacyclotetradecane. These complexes have been characterized by infrared spectroscopy, single-crystal X-ray structure analysis, elemental and thermal analysis. Moreover, the DNA-binding properties of this new metal complexes were investigated by electronic absorption, fluorescence, and CD spectra. The observed trend in hypochromism of absorption bands, reflects strong DNA-binding properties of drugs. Additionally, competitive binding studies with ethidium bromide (EB) have revealed through the quenching of DNA-EB fluorescence. The ability of the complexes to displace EB from the EB-DNA system suggesting intercalation as a possible mode of their interaction with DNA, this assumption was confirmed also by CD measurements. All tested compounds exhibit good binding propensity to CT-DNA. From linear Stern-Volmer plot the K_{SV} binding constants were established in the range from 3.19×10^3 M^{-1} to 5.9×10^4 M^{-1}. Trinuclear complexes $[Zn_3(dmso)_2(flu)_6]$ (1) and $[Zn_3(flu)_6(py)_2]$ (2) show only partial intercalation hence suggesting other forms of interaction with the CT DNA including minor groove binding or covalent binding which could be possible upon release of the coordinated solvent molecules from terminal zinc atoms in a solution (dmso in 1; pyridine in 2). Furthermore, only these two trinuclear complexes can inhibit the catalytic activity of topoisomerase I at concentration of 60 μM.

Acknowledgements
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SESSION II **Biochemistry**

Hydrotropic Solubilization Driven by Disodium Cromoglicate

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Hydrotropy is defined as aqueous solubility enhancement of sparingly soluble substances by addition of small organic molecules – hydrotropes to the system. Hydrotropic properties have been observed in diverse classes of chemical substances since the last century, however, exact mechanism of hydrotropic solubilization is not known yet. The universal hypothesis of hydrotropic solubilization is discussed lately [1]. The possible applications of hydrotropes are e.g. solubilization enhancement of poorly soluble drugs, utilization as green solvents for organic synthesis or compounds helping in alternative biofuel production [2-4].

Disodium salt of cromoglicic acid (cromolyn, DSCG) is antiallergic drug derived from furanochromone khellin, which naturally occurs in plant *Ammi visnaga*. Cromolyn is effective in various hypersensitivity conditions and well-tolerated, although the exact mechanism of its action is not known. Cromolyn belong to class III of Biopharmaceutics Classification System, which means it is readily soluble in water environment, but is of low permeability and does not enter the cells. The therapeutic effect of cromolyn is therefore developed only locally. It is also investigated in many more possible medicinal applications, e.g. as anti-Alzheimer, antivirotic or antifibrotic agent [5-7]. However, papers on its possible utilization as hydrotrope are not frequent. Our reseach team has been studying hydrotropic properties of cromolyn. We are focused on solubilization of hydrophobic drugs hypericin, berberine and curcumin in water environment [8]. Such combination of drugs could also possibly attenuate the hydrophilic character of cromolyn and enable its entrance in cells.

Acknowledgements
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SESSION II **Biochemistry**

Interactions of cytochrome *c* with SDS:DDM mixed micelles

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Cytochrome c (cyt c) fulfills very different functions in cells: (i) transfer electrons between mitochondrial complexes in respiratory chain and (ii) participates in inducing apoptotic processes. The ability of cyt *c* to exhibit distinct functions is related to its cellular localization, the only peripheral protein that interacts with the external face of the inner mitochondrial membrane [1,2]. Taking this into account, nature and specificity of interaction of cyt *c* with lipid bilayers have been focus of numerous studies.

Interaction of cyt *c* with membrane surface is believed to be both electrostatic and hydrophobic, inducing methionine decoordination and the formation of non-native low-spin states and high-spin cyt *c* [3]. To better understand structural modifications of cyt *c* induced by interaction with membrane surface we utilized mixed micelles of dodecyl maltoside and sodium dodecyl sulphate as a model of the membrane surface. The utilization of the mixed micelles enabled us to assess a role of electrostatic interactions in conformational changes of cyt c on membrane surface. Effect mixed micelles (SDS:DDM) on structure, pK_a and T_m values and peroxidase-like activity of cyt *c* was measured by using absorption spectrometry (Soret, 620 nm and 695 nm), fluorimetry (Trp at 390 nm) and spectropolarimetry (Soret, aromatic and peptide region, 222 nm) in neutral pH. Modification of a charge of micelles was achieved by modification of ratio SDS:DDM (1:1, 5:1, 10:1 and 15:1) at three different concentrations of micelles: 0,5, 1,25 and 5 mM. In all ratios and all concentrations of mixed micelles there was no significant conformational changes of cyt *c*. Changes in the values of acidic pK_a and T_m of protein occurred only in the presence of micelles containing higher concentration of SDS, i.e. SDS:DDM 10:1 and 15:1 with significant changes at higher concentration of micelles. The rate constant of the peroxidase-like activity of cyt *c* increased with increasing proportion SDS in mixed micelles and with increasing of concentration of micelles.

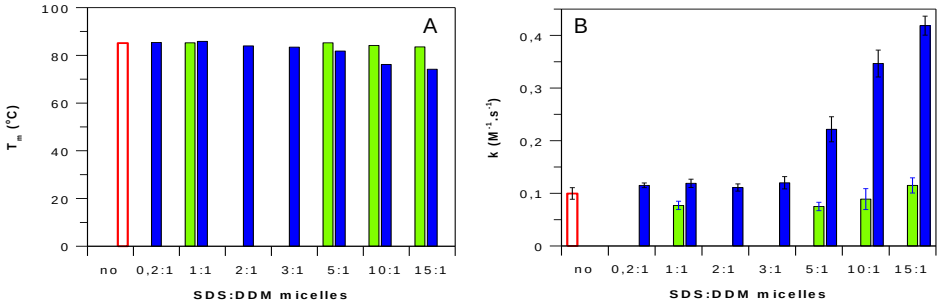

Figure 1. Temperature-induced confromational transitions (A) and dependence of bimolecular rate constant ($M^{-1}s^{-1}$) of peroxidase-like reaction on hydrogen peroxide concentration (B) of cyt *c* in the presence mixed micelles SDS:DDM: 1:1, 5:1, 10:1 and 15:1 with 0,5 mM DDM (green column) and mixed micelles SDS:DDM: 0,2:1, 1:1, 2:1, 3:1 5:1, 10:1, and 15:1 with 2,5 mM DDM (blue column) solutions and without micelles (red lined column) in 10 mM Na phosphate buffer in pH 7.0 at 20 °C.

Our results indicated that increasing of proportion SDS in micelles affected stability and rate of peroxidase-like activity of cyt *c* but had no effect on conformation of the protein in these conditions. This indicates that the surface charge density of mixed micelles affects dynamics properties of heme region of cyt *c*.

Acknowledgements

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SESSION II **Biochemistry**

Enzymatic Activity of Gluconolactonase Determined by Potentiometry

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Gluconolactonase (EC 3.1.1.17) is a hydrolytic enzyme that participates in pentose phosphate pathways, ascorbate and aldarate metabolism, and in a caprolactam degradation. The enzyme catalyzes hydrolysis of δ-gluconolactone to D-gluconic acid. Generally, when working with any enzyme, it is necessary to know its enzymatic activity, i.e. the amount of functional enzyme macromolecules. Up to date, only discontinuous (fixed-time) methods have been used to assay activity of gluconolactonase [1,2]. We have developed a continuous procedure that uses an electrochemical technique – potentiometry. The method is based on the fact that during the course of the reaction D-gluconic acid dissociates and released hydrogen ions are detected by a sensitive glass membrane pH electrode (Figure 1A). The original pH versus time plot has been transformed to $[H^+]$ on time dependence (Figure 1B) and the polynomial function has been used to fit the data. Finally, calculation of the first derivative of [H+] with respect to time give us information on the reaction rate at corresponding pH value (Figure 1C). The main advantages of the method are simplicity of the experiment, sensitivity of the technique and possibility to obtain data over a wide pH range. We have shown that the potentiometry is an effective technique in the study of enzyme kinetics and that it might be used in any enzyme-catalyzed reaction related to pH changes.

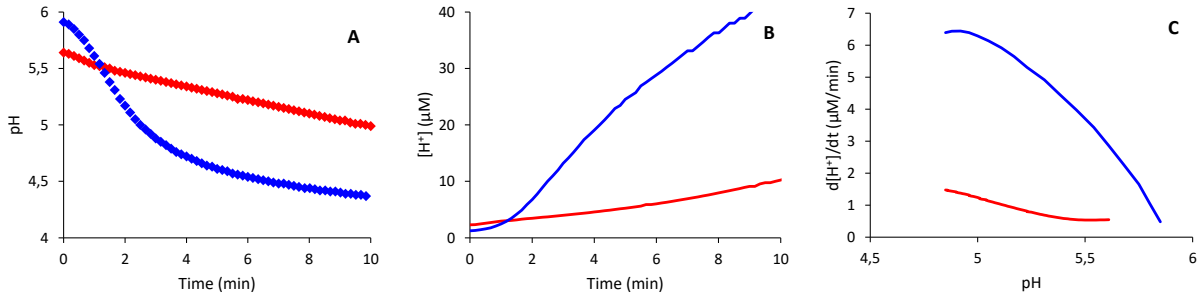

Figure 1. (A) Time-dependent pH change during δ-gluconolactone hydrolysis in the absence (red) and presence (blue) of 0.6 mg gluconolactonase at 25 °C. (B) Change of $[H^+]$ during the course of the reaction. (C) δ-gluconolactone hydrolysis rate (first derivative of $[H^+]$ with respect to the time) dependence on pH. The enzyme was isolated from baker's yeast and purified according to [1]. The temperature of the reaction mixture was controlled by a Peltier element. 5 mM glucose was used as a substrate for the pairing enzyme, glucose oxidase (0.1 µM), that produced δ-gluconolactone.

Acknowledgements
This work was supported by the research grants VEGA 1/0423/16, VEGA 2/0009/17 and APVV-15-0069.

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SESSION III **Inorganic Chemistry**

Complexing properties, solid-state study and antimicrobial evaluation of new silver complex with pyridine-2-sulfonate ligand

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Sulfonic acids (RSO_3H) are a class of organosulfur compounds and their amide derivatives are sulfonamides (RSO_2NH_2). Sulfonamides display a wide variety of pharmacological activities [1] and recently, the metal sulfonates have attracted attention because of their potential applications and structural topologies [2]. It is also well known that silver compounds show antibacterial, antifungal, antiseptic, anti-cancer and anti-inflammatory effects, thus the underlying idea is to connect silver ion as an antimicrobial metal with an efficient organic ligand into a new synergic drug [3].

The formation of silver complex species with pyridine-2-sulfonic acid in solution in dependence on pH was studied by the potentiometric titration method, on the basis of which the synthesis of the new silver complex with pyridine-2-sulfonate was performed. Silver pyridine-2-sulfonate was characterized by structural analysis, IR spectroscopy, elemental analysis and thermal analysis. The stability of the complex was also verified by ^{1}H and ^{13}C NMR measurements. The Ag(I) complex was tested for its interaction with CT DNA through UV-vis absorption measurements. The antibacterial activities of prepared complex, free ligand (pyridine-2-sulfonic acid) and silver sulfadiazine against *Staphylococcus aureus, Escherichia coli, Candida parapsilosis, Rhizopus oryzae, Alternaria alternata* and *Microsporum gypseum* were also evaluated.

The suitable reaction conditions for the synthesis of the new complex were observed by potentiometric measurements depending on pH. The new silver complex was prepared from aqueous solution and its crystal structure and composition were determined by X-ray structural analysis. NMR measurements confirmed the stability of the complex in DMSO for 96 h implying its stability during biological testing. Silver pyridine-2-sulfonate exhibits very good antibacterial and anti-yeast effects in comparison with the commercially-used drug, silver sulfadiazine. Moreover, UV-vis absorption measurements confirm the intercalative binding of silver complex into DNA and therefore, new silver pyridine-2-sulfonate is a suitable candidate for further biological studies and for subsequent use in pharmacy as an antimicrobial agent.

Acknowledgements

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SESSION IV **Organic Chemistry**

Stereoconvergent synthesis of the unusual sphingoid bases

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Sphingoid bases are class of the naturally occurring long-chain vicinal amino alcohols with the significant structural diversity [1]. These compounds show remarkable biological potential and are expected to be promising lead structures for novel therapeutic agents [1]. Clavaminols (A−N) [2,3] are relatively new group of 1-deoxysphingoid bases, with the unusual (2*R*,3*S*) configuration, which is opposite to that of the typical sphingosine such as D-*erythro*-sphingosine **1**[1]. The most potent member of the aforementioned family is clavaminol A **2** [2], which has demonstrated cytotoxic activity against several cancer cell lines [2,4] but also displayed antibacterial and antifungal properties [4].

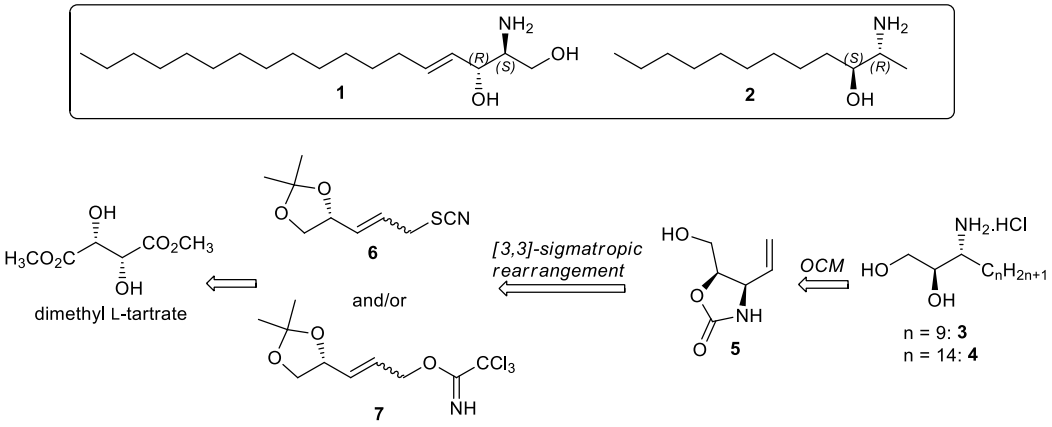

Figure 1. Structure of selected sphingoid bases and retrosynthetic plan towards targeted compounds **3**, **4**.

Due to mentioned potent biological properties we are attracted in creating of a new approach towards the unusual isomeric sphingoid bases **3** and **4**. Our approach utilizes dimethyl L-tartrate as the chiral template and the [3,3]-sigmatropic rearrangements of thiocyanate **6** and/or trichloroacetimidate **7** for the stereoselective instalment of the C-N bond. The required rearranged products with *erythro* configuration were modified to the common oxazolidinone **5** for both targeted compounds **3** and **4**. The corresponding long chain was incorporated via Grubbs' cross metathesis chemistry.

Acknowledgements
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SESSION IV **Organic Chemistry**

Synthesis of the advanced precursor to novel C-8a branched-chain pentahydroxyindolizidine

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Natural occurring polyhydroxylated indolizidine alkaloids such as swainsonine, lentiginosine and castanospermine isolated from various plants represent interesting class of compounds due to their promising biological activity as various glycosidases and glycosyltransferases inhibitors.[1] Although a number of members of this compound class have been studied at a clinical level, none of them have been approved as a drug. Attempts to improve the selectivity and efficiency of these inhibitors with minimal side effects have been made to develop several analogues of the naturally occurring heterocycles to meet the aforementioned challenges.[2]

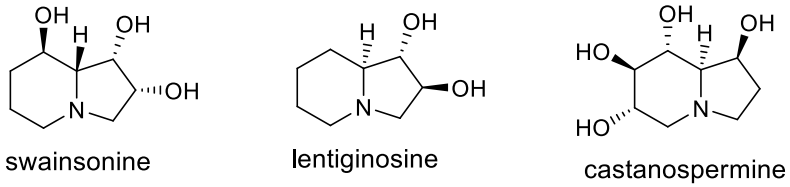

Figure 1. Some members of polyhydroxylated indolizidines family.

We present stereoselective synthesis of the advanced precursor to C-8a branched-chain indolizidine alkaloids bearing unusual structural pattern hard to find in the nature using isothiocyanate prepared by aza-Claisen rearrangement of appropriate D-glucose derived allylthiocyanates.[3] Six-membered ring was then formed by ring-closing metathesis and the new formed double bond was then dihydroxylated.

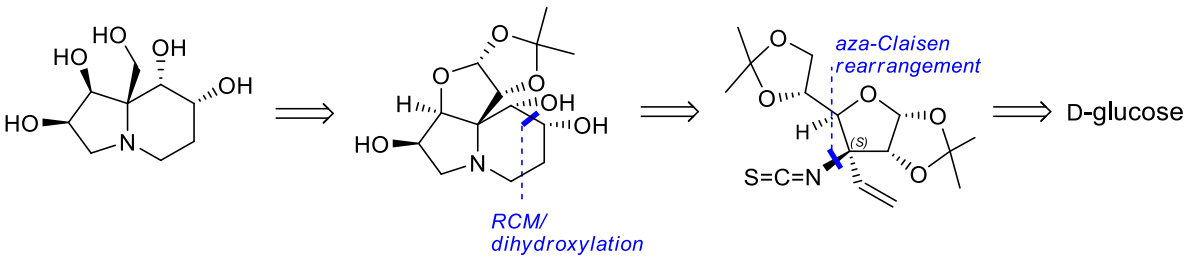

Figure 2. Retrosynthetic analysis of target compound.

Acknowledgements
The present work was supported by the Slovak Research and Development Agency (No. APVV-14-0883).

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Stereoconvergent access to spisulosine stereoisomers

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Introduction

1-Deoxysphingoid bases are vicinal long-chain amino alcohols, isolated mostly from marine organisms, whose common structural feature is the absence of the primary hydroxyl [1]. Among them, spisulosine **1**, isolated in 1999 from the marine clam *Spisula polynyma* displayed very strong cytotoxic activity on both leukaemia and solid cancer [2].

Synthesis

Retrosynthetic strategy illustrates our approach to the stereoisomers of spisulosine **1**, molecules **2** and *ent*-**1**, starting from D-isoascorbic acid. The *aza*-Claisen rearrangement of thiocyanate **3** created the desired vicinal amino alcohol motif. The obtained products **4** and **5** were converted to the corresponding carbamates **6** and **7**. The target spisulosine stereoisomers **2** and *ent*-**1** will be constructed by modification of **6** and **7**, respectively. Stereochemistry on the newly incorporated stereocentre was determined by chemical correlations, based on the comparison of ^{1}H and ^{13}C NMR spectra of the prepared derivative **9** and compound **10**[3] with the known configuration (Fig. 1).

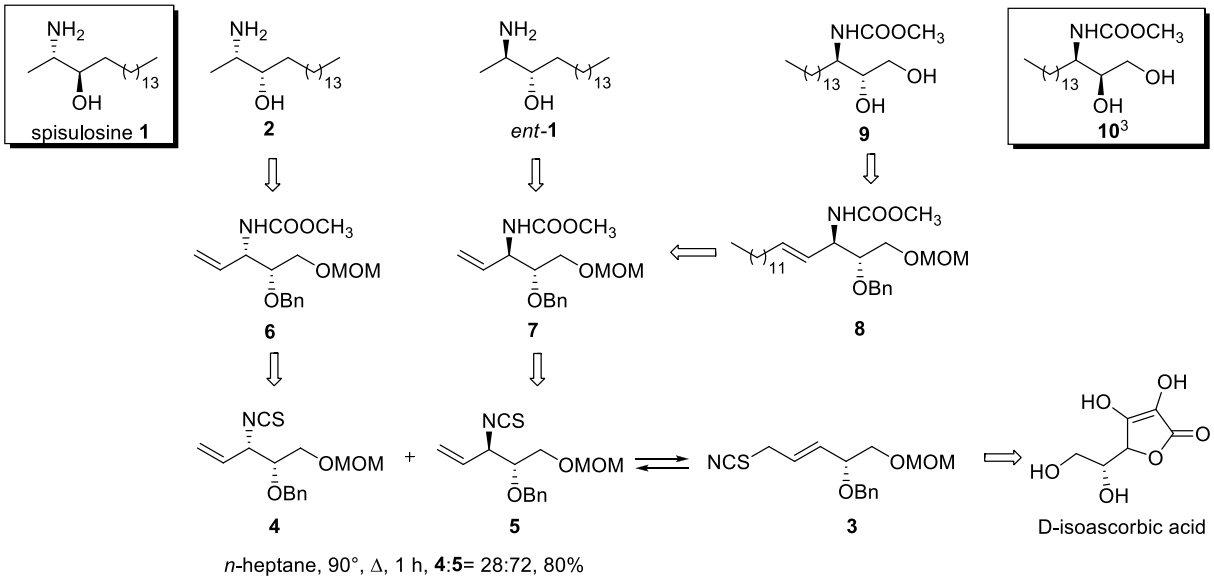

Figure 1. Retrosynthetic analysis.

Acknowledgements

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SESSION IV **Organic Chemistry**

Homo- and hetero- dimers of acridine derivatives as dual inhibitors of acetylcholinesterase and butyrylcholinesterase.

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In the last decade much attention has been paid to the development of homo- and hetero- dimers containing two identical or different structural units of known acetylcholinesterase inhibitors (AChEIs) linked by chain with a suitable length for simultaneous interaction with the active and the peripheral binding sites of AChE. A series of novel monotacrine, tacrine-tacrine, tacrine-acridine, tacrine-coumarin, acridine-coumarin and tacrine-quinoline ligands were designed, synthesized, and biologically evaluated as inhibitors of both acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) [1-7]. Among of monotacrine ligands, compound **7** in which tacrine is connected to an (benzylpiperazinyl)etyl unit exhibited excellent inhibitory activity against *h*BChE (IC_{50} = 0,4 nM) [3]. From tacrine-tacrine ligands, inhibitors **11b, c** showed a strong acetylcholinesterase activity, with an IC_{50} value of 2 nM and 8 nM resp [3]. The most effective inhibitors of *h*AChE within tacrine-acridine dimers were the derivatives **12**, **13** with an IC_{50} value of 3 nM and 6 nM [3]. The structure-activity relationship studies showed clear correlation between the structure of homo/heterodimers and their inhibition potential against *h*AChE.

Acknowledgements

Financial support from the Grant Agency for Science of the Slovak Ministry of Education (VEGA) (grant No. 1/0672/11, 1/0001/13), the Slovak State NMR Program (grant No. 2003SP200280203), and the Grant Agency of the Czech Republic (grant No. P303/11/1907) is gratefully acknowledged.

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SESSION IV **Organic Chemistry**

Synthesis of sphingoid base analogues with integrated molecular switches

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Introduction

Finding the efficient way of activity control of biologically potent molecules is a desirable, yet, challenging goal. However, an insertion of an azobenzene moiety into such molecule might become a powerful tool, since the azobenzene is well known for its ability to undergo a reversible *trans* to *cis* isomerisation when irradiated by UV-light of a proper wavelength. This conformational change is responsible for different physicochemical behaviour of both geometrical isomers, which is consequently reflected in the activity of biomolecules containing this azobenzene moiety. In our research we decided to investigate activity changes of differently substituted azobenzenes attached to the polar head of sphinganine (D-*erythro*-dihydrosphingosine), which is a precursor in biosynthesis of sphingolipids and plays an important role in diverse biological pathways [1,2].

Synthesis

For the synthesis of the sphinganine analogue (**1**) our strategy involved a modification of a D-isoascorbic acid into alcohol **2** following the strategy from literature [3]. The alcohol was then submitted to cyclisation reaction to obtain an oxazolidinone **3**, which was by series of reaction steps converted into aldehyde **4**, that represents the first building block subsequently used in a Wittig olefination with an ylide generated from an azobenzene salt **5**. By the saturation of a double bond of the Wittig reaction product **6** was prepared intermediate **7**, which after removal of protecting groups gave the desired product **1**.

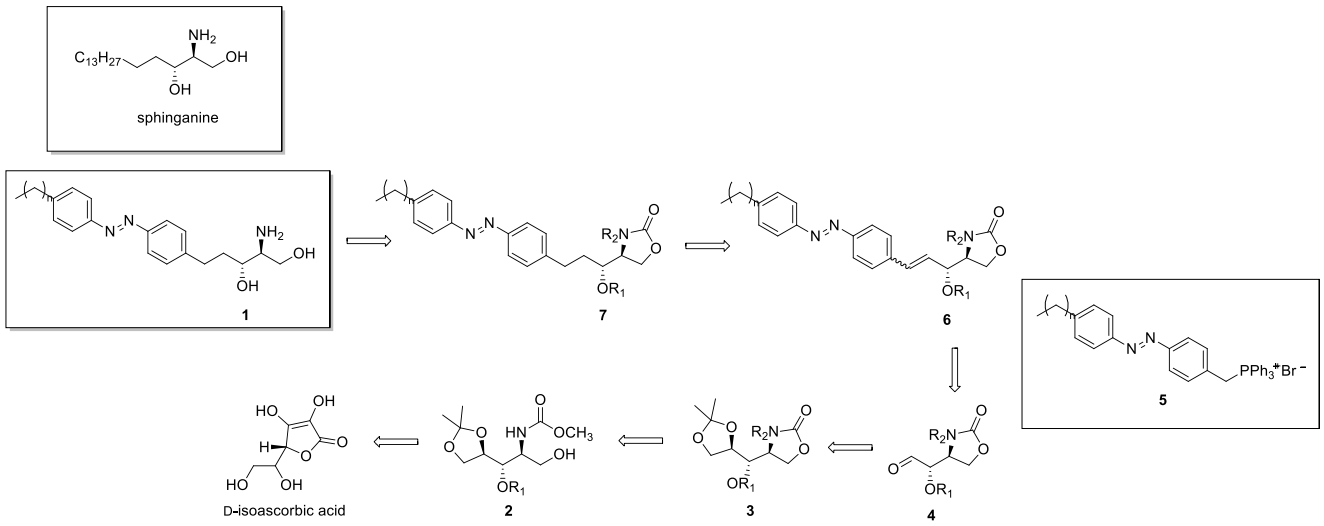

Figure 1. Retrosynthetic strategy of a sphinganine analogue with integrated azobenzene switch.

Acknowledgements

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SESSION IV **Organic Chemistry**

The convergent synthesis of broussonetinines related analogues

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Introduction

Broussonetines, along with diastereomeric broussonetinines, the representative structures of which are illustrated by brousssonetine C (**1**) and broussonetinine A (**2**), were isolated by Kusano and co-workers [1] from the branches of the Asian deciduous tree *Broussonetia kazinoki* (Fig. 1). They represent a class of more than 30 well-identified and characterized polydroxylated pyrrolidine alkaloids, which possess variable side chains with the diverse types of functionalization. [1] Most of these *C*-alkyl iminosugars demonstrated significant glycosidase inhibitory activities with IC_{50} values in the micromolar to nanomolar range [1-3].

Synthesis

In our continuing studies based on the feasibility of the [3,3]-sigmatropic rearrangements in the total synthesis of sphingoid base-like natural products and their analogues [4] we were interested in investigating the use of such transformation as the key reaction for the construction of broussonetinines related congeners, which possess the simple C_{13} hydrocarbon fragment. Herein we would like to report the total synthesis and antiproliferative activity of two iminosugars **3** and **4**, starting from D-xylose. Our synthetic approach relies on *aza*-Claisen rearrangement of tiocyanate **9** and Overman rearrangement of imidate **10**, which are used for creation of a new C-N bond. The incorporation of C_{13} side chain is performed via OCM metathesis of aminoalcohols with tridec-1-ene and the pyrrolidine core is formed as a result of the intramolecular S_N reaction. [5]

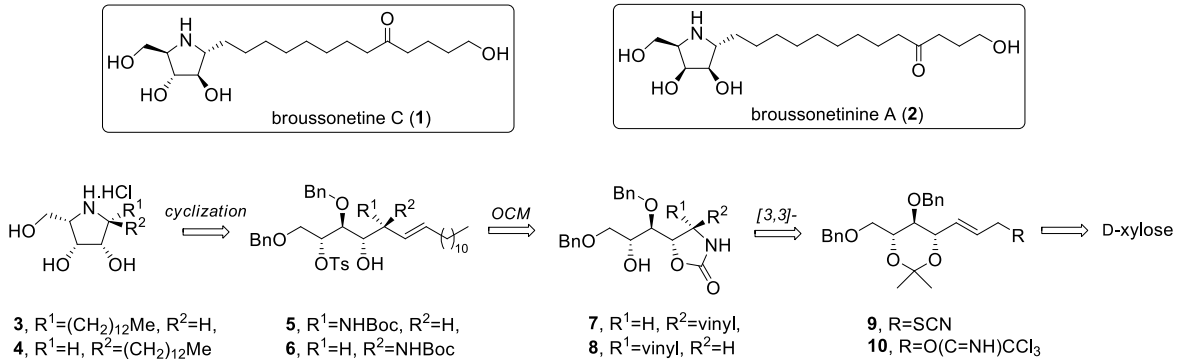

Figure 1. Retrosynthetic route towards broussonetinines related analogues **3** and **4.**

Acknowledgements

The present work was supported by the Scientific Grant Agency (No. 1/0168/15) of the Ministry of Education, Slovak Republic. It was also supported by the Slovak Research and Development Agency (SRDA Grant No. APVV-14-0883), Slovakia and by the project MediPark Košice: 26220220185 supported by Operational Programme Research and Development (OPVaV-2012/2.2/08-RO).

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SESSION IV **Organic Chemistry**

Cell proliferation inhibition and cytotoxic activities of novel diphenylamino derivatives

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Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most widely used drugs in the world. The cytotoxicity of diclofenac and tolfenamic acid has been attributed to diphenylamine contained in their structures. A novel series of diphenylamino derivatives were synthetised and evaluated for their cytotoxic activities and proliferation inhibition. The most active compounds in the cytotoxicity tests were derivative **6g** with an IC_{50} value of 2.5 ± 1.1×10^{-6} M and derivative **6f** with an IC_{50} value of 6.0 ± 3.0×10^{-6} M (L1210 cell line) after 48 h incubation. The results demonstrate that leukemic L1210 cells were much more sensitive to compound **6f** and **6g** than the HEK293T cells (IC_{50} = 35×10^{-6} M for **6f** and IC_{50} > 50×10^{-6} M for **6g**) and NIH-3T3 (IC_{50} > 50×10^{-6} M for both derivatives). The IC_{50} values show that these substances may selectively kill leukemic cells over non-cancer cells. Cell cycle analysis revealed that a primary trend of the diphenylamino derivatives was to arrest the cells in the G_1-phase of the cell cycle within the first 24 hours. UV-visible, fluorescence spectroscopy and circular dichroism were used in order to study the binding mode of the novel compounds with DNA. The binding constants determined by UV-visible spectroscopy were found to be in the range of $2.1–8.7\times10^{4}$ M^{-1}.

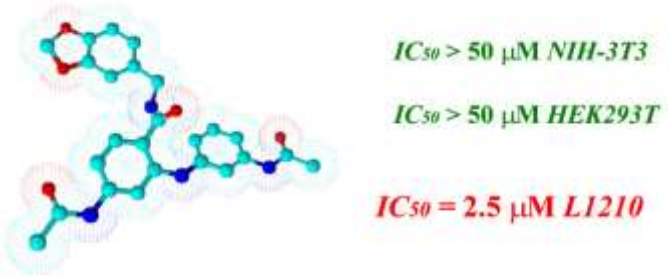

Figure 1. The structure of the derivate **6f** and its antiproliferative activities.

Acknowledgements
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SESSION IV **Organic Chemistry**

Synthesis of new 3-[(acridin-9-yl)-methylidene]-amino-2-thiohydantoin derivatives with potential biologic activity and their application as chiral Evans auxiliaries.

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2-Thiohydantoins are well-known compounds for their biological activity for many years [1]. Also acridines are important cytostatic compounds and dyes [2]. Starting material for our synthesis were commercially available hydrochlorides of aminoacids methylesters **1a-d** which were transformed to new acridine-2-thiohydantoins **2** in three steps. Prepared 5-substituted 3-[(acridin-9-yl)-methylidene]-amino-2-thiohydantoins were converted into corresponding *N*-acyl-5-substituted 3-[(acridin-9-yl)-methylidene]-amino-2-thiohydantoins **3**, which were used in asymmetric aldol condensation in various conditions due to structural similarity with Evans auxiliaries [3]. Stereoselectivity of aldol condensation **4** will be determined by ^{1}H NMR spectroscopy and using chiral shift reagents. The final step will be hydrolysis of **4** to obtain coresponding carboxylic acids **5** and alcohols **6**.

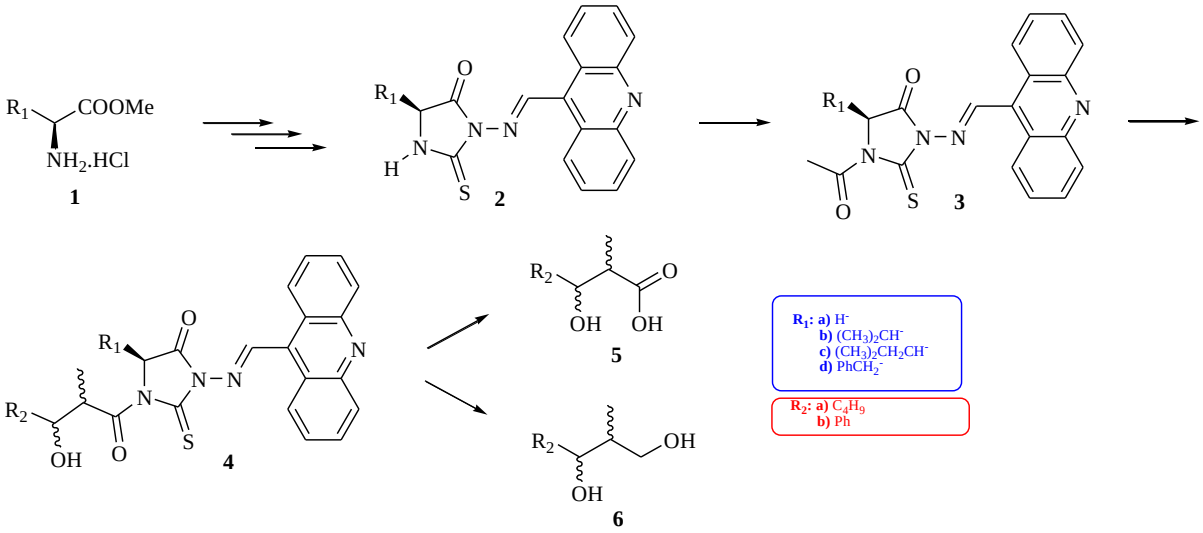

Figure. 1. General approach for prepare 5-substituted 3-[(acridin-9-yl)-methylidene]-amino-2-thiohydantoin and aldol reaction.

Acknowledgements

Doc. RNDr. Ján Imrich, CSc.

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SESSION IV **Organic Chemistry**

Stereoselective synthesis and biological activity of hydroxylated octahydroindoles from shikimic acid

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Octahydroindole scaffold, as a structural unit, appears in almost 1500 natural compounds, according to Dictionary of Natural Products database. As an expample, longanine is a highly active binder to the δ-opioid receptor[1]. Various nitrogen containing compounds were evaluated as inhibitors of several glycosidases[2]. Structurally related hydroxylated indolizidine alkaloids, for instance castanospermine, is a competitive inhibitor of α-D-glucosidase[3]. However, only a couple of pohyhydroxylated octahydroindole compounds, whose biological activity was evaluated, have been prepared yet.

The aim of this study was to prepare two diastereoizomers **1** and **2**, using shikimic acid as starting material, while as key steps of this synthesis were used [3,3]-sigmatropic Overman rearrangement and RCM metathesis. Prepared derivatives and intermediates were tested for inhibitory activity against several cancer cell lines or against glycosidases with good results.

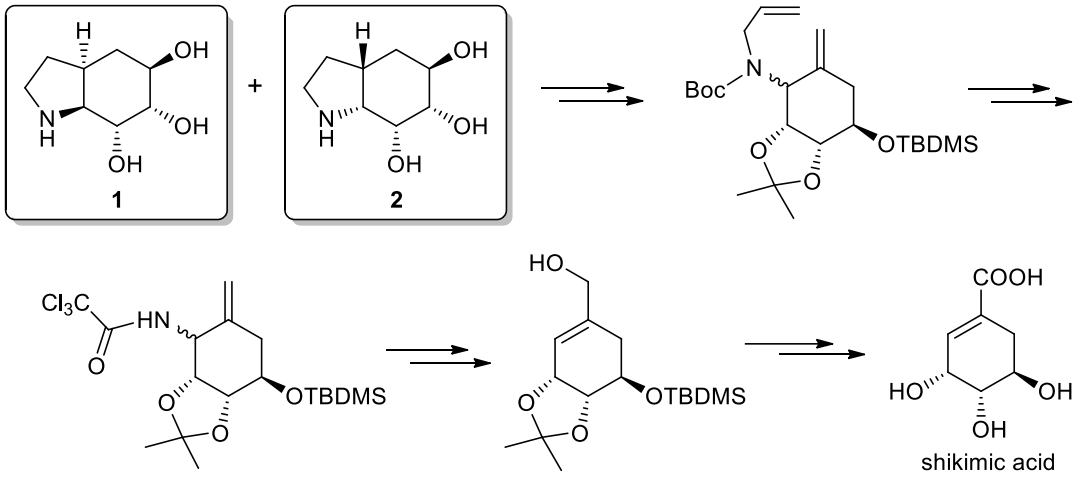

Figure 1. Retrosynthesis of final octahydroindoles **1** and **2.**

Acknowledgements
The present work was supported by the Grant Agency (Grant No. 1/0398/14) of the Ministry of Education, Slovak Republic. It was also supported by the Slovak Research and Development Agency (Grant No. APVV-14-0883).

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Studies on the Overman rearrangement of L-tartaric acid derived allylic trichloroacetimidates: the construction of sphingoid bases

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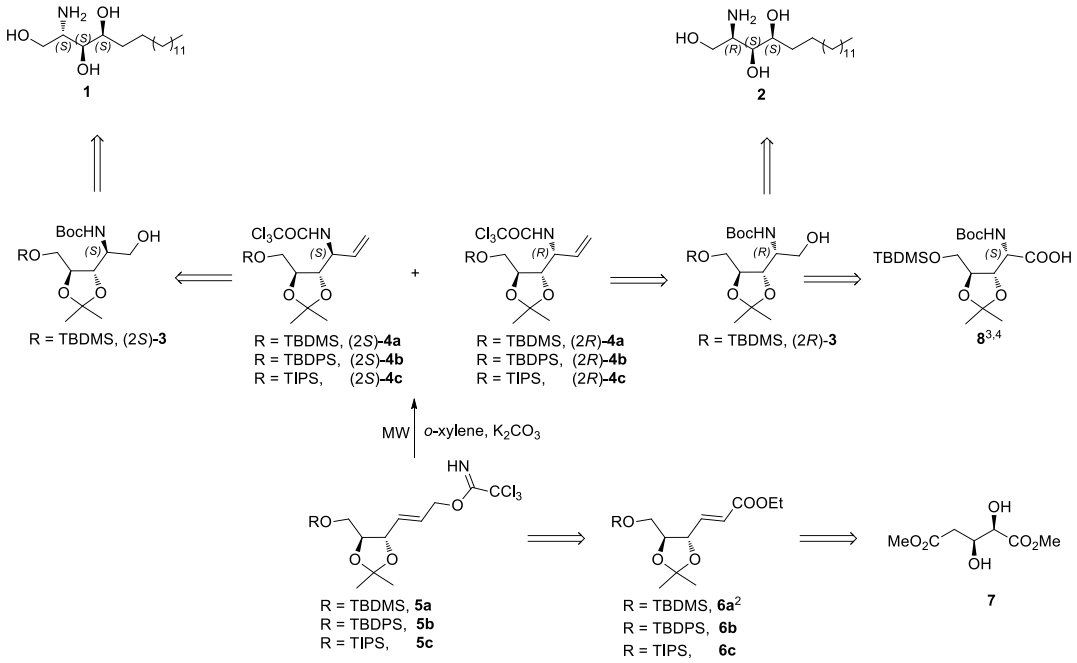
Introduction

Overman rearrangement (aza-Claisen) represents an effective tool for the stereoselective formation of a new C-N bond and thus afforded the corresponding amines as synthons for the construction of various natural products [1].

Synthesis

Our substrates for the study of Overman rearrangement, imidates **5a**-**5c**, were obtained via two reaction steps from the corresponding α,β-unsaturated esters **6a**-**6c** derived from the commercially available dimethyl L-tartrate **7** by the sequence of the functional group transformations (Scheme 1) [2]. Overman rearrangement of **5a**-**5c** carried out in *o*-xylene in the presence of K_2CO_3 in a focused microwave system at various temperatures (150 °C, 170 °C, 190 °C) furnished the corresponding amides (2*R*)-**4a**-(2*R*)-**4c** and (2*S*)-**4a**-(2*S*)-**4c** as chromatographically separable mixtures of diastereoisomers. Subsequently, the amides (2*R*)-**4a** and (2*S*)-**4a** will be modified to the targeted phytosphingosines **1** and **2** via the highly functionalized synthons (2*R*)-**3** and (2*S*)-**3**, respectively. The relative configuration of the newly created stereogenic centre in (2*R*)-**4a** was determined by chemical correlations based on the comparison of ^{1}H and ^{13}C NMR spectra of the known carboxylic acid **8** [3,4] and the same compound prepared from our synthon (2*R*)-**3**.



Scheme 1. Our synthetic plan toward phytosphingosines **1** and **2**.

Acknowledgements

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SESSION V **Physical Chemistry**

Non-enzymatic detection of glucose on gold-based microelectrodes

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Glucose electrochemical sensor has been widely used because of its excellent properties such as sensitivity, rapid current response and low cost. Among them gold-based electrodes are consider to be an eligible candidate for development of non-enzymatic glucose sensors, due to its excellent electrocatalytical properties [1]. Moreover, gold nanoparticles show enhanced current response, biocompatibility and ability to detect glucose in neutral and alkaline solution in comparison with another materials [2]. Gold microelectrodes (with diameter 1 mm) were used because of its application as non-enzymatic sensors. Miniaturisation of system could be achieved due to its small size. Mechanism of electrochemical oxidation of glucose on gold surface was studied with an effort to create optimal condition. The results were compared with literature. Effect of pH change was studied too and optimal condition was propounds. The electrode surface was modified by gold nanoparticles to achieve more active sites and better sensor properties. Modification by gold nanoparticle was simple and fast. Modified gold microelectrodes were able to detect glucose in linear range 0.5 – 40 mM. It meets commercialised glucose sensors requirements, where the linear range is 1 – 30 mM. Limit of detection was 0.4163 mM and sensitivity of modified electrode was $2.567.10^{-4}$ $\mu AmM^{-1}cm^{-2}$.

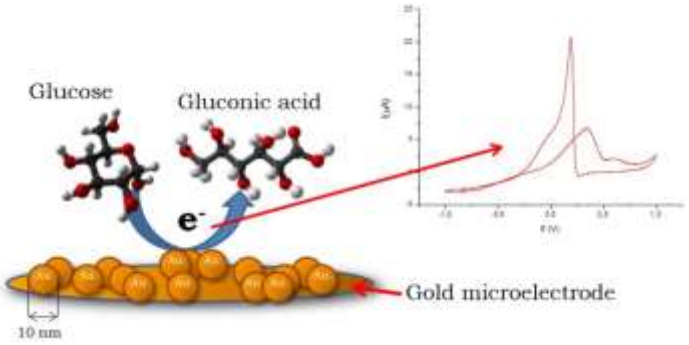

Figure 1. Schematic illustration of gold electrode modified with gold nanoparticles.

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SESSION V **Physical Chemistry**

Hydrophobic coatings in preparation of slow release fertilizers

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In recent decades, increasing attention has been poured into developing slow-release fertilizers throughout the world. This is mainly because the conventionally used chemical fertilizers have low efficiency and present serious source of ground water pollution [1]. The encapsulation of fertilizers using hydrophobic structured polymers slows down the release of fertilizer in aqueous media, and thus increases effectivity and prevents ground water contamination [2]. To decrease the usage of commonly used polymers made of petroleum-based PUs for controlled-release fertilizers, it is appropriate to consider the usage of renewable "green" coating materials [3]. There are relatively wide group well recognized eco-friendly biopolymers, including starch, chitosan, alginate, lignin and cellulose, vegetable oil, L-aspartic acid, and their counterparts to be widely studied to fabricate the biobased controlled-release fertilizer [1]. Wastes of starch-based materials, regardless of their origin, plasticized with urea and glycerol, if not composted or properly managed for that reason may be successfully used as a fertilizer in floriculture, horticulture or agriculture, supplying nutrients for the plants. Starch is a cheap, easily available and biodegradable natural polymer that arouses interest [4]. Experimental results showed that increase of the water-contact angle of the coating material and thus slowed the nutrient release from the PCUs [3]. Cassie and Baxter have developed following equation to describe this state of liquid on to solid surface by: $\cos \theta_{CB} = f_1 \cos\theta - f_2$. Where θ_{CB} is the Cassie-Baxter contact angle, f_i is the ratio of total area under the liquid to projected area, θ_Y is contact angle on to flat surface and $f_1 + f_2 = 1$. When a biobased slow release fertilizer with hydrophobic surface is being immersed in water its surface is still in gas phase and formed the atmosphere "outwear" at the interface [1]. The idea of using hydrophobic surface can provide new strategies for the development of novel slow release fertilizers.

Acknowledgements
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SESSION V **Physical Chemistry**

Electrochemical study of the biodegradable Fe materials modified by inorganic oxide nanoparticles

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New metallic biomaterials are very interesting for using in medicine applications. The properties of such material could be influenced by a various additives. The nano-inorganic metal oxides as MgO and ZnO added to pure iron material leads to control of corrosion resistance. These specific nanoparticles, however, provide a reduction in bacterial contamination [1, 2]. Materials of interest were manufactured by a powder metallurgy by mixing a carbonyl iron powder (CIP) with nanoparticles MgO or ZnO, pressing the mixtures and followed by sintering process. The research focused on the corrosion and selected mechanical properties of sintered alloys, as influenced by spatial variability in composition and microstructure. The distribution of microhardness values over the sample surface was examined and the effective Young's modulus of sample's material was determined. The biodegradability was studied by electrochemical methods.

The corrosion characteristics of these biodegradable materials were observed in contact with Hank's solution. Using the chronometrical potentiometry the open-circuit potential (OCP) was recorded. The corrosion potential of a freely corroding Fe sample and the Fe-ZnO and Fe-MgO samples decreased with time and exhibit a relatively constant course. The nanoparticles are uniformly distributed in the iron particles, therefore corrosion is largely uniform. Immediately after the determination of OCP, EIS and potentiodynamic measurements were performed. EIS results showed the dynamic development of the corrosion system. The several processes were obtained: the growth of corrosion products, corrosion cracking and peeling of the corrosion layer. Other identified processes can be dissolution of base material and pitting. The polarisation measurements show, that the addition of MgO or ZnO particles shift the corrosion potential to negative values, compared to the pure Fe sample. The negative shift causes an increased tendency to corrode these samples. It is probably caused the samples disorder. The corrosion rate is not influenced by the total porosity, rather the nature of pores, which can significantly accelerate the formation of pitting and crevice corrosion. Some samples were treated by spark plasma sintering. The corrosion rate of the mentioned samples is lower, because the material is more compact and the surface is more homogeneous. The samples were examined in more detail using a scanning electron microscope and EDX analysis. In the next research we studied the hemocompatibility of mentioned samples.

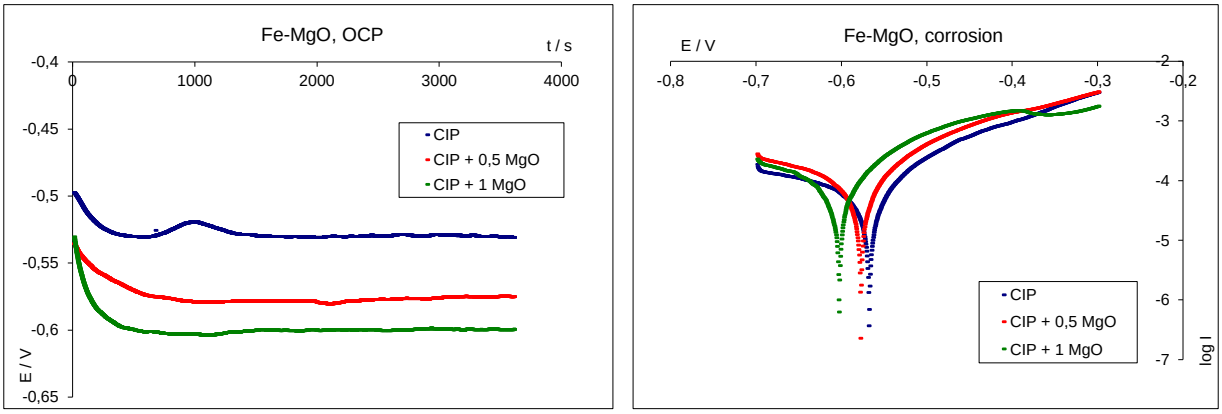

Figure 1. OCP and corrosion curves of the Fe-MgO samples.

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SESSION V **Physical Chemistry**

Silver substrates prepared by pulsed deposition for SERS applications in diagnostics

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Nowdays techniques such as fecal immunochemical test and colonoscopy are invasive, time consuming methods. Our work is presenting initial experiments for developing a new diagnostic test for early detection of colon cancer by SERS analysis of human blood plasma. Our electrochemically prepared silver surfaces are easily-made, low-cost and rapidly deposited SERS substrates, which can be used for direct diagnostic test in clinical practice. Silver layers were electrochemically deposited onto ITO glass (>7Ω) from solution containing 0.01M $AgNO_3$. For optimization of the most appropriate morphology of SERS substrate we prepared 16 samples by pulsed double potentiostatic method (E_1 = -0,4 V, E_2 = -0,1 V). We modified number of pulses from 10 to 70 and duration time of pulse E_2 from 0,5 s to 2 s. Experiments showed that pulsed deposited silver surface with 70 pulses with E_2= -0,1V for 0,5s had the highest enhanced factor ($2.1x10^9$) for molecule of Rhodamine 6G. Using this surface, we were able to detect all main components of human blood plasma. Based on the measured SERS spectra we will be able to find differences between these two observed groups and by principal component analysis (PCA) we will develop reliable diagnostic test for an early detection of colon cancer.

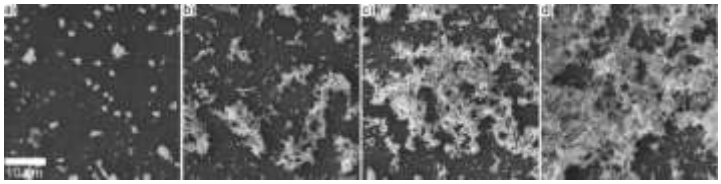

Figure 1. SEM images of silver dendrites electrodeposited on ITO glass by pulsed double potentiostatic method. Density of the surface coverage density is increasing with number of pulses and time of electrodeposition.

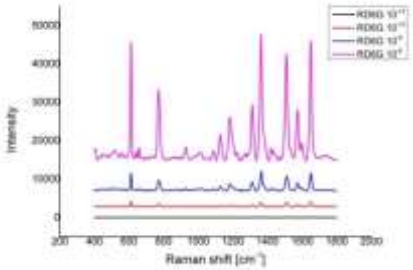

Figure 2. SERS spectra of Rhodamine 6G of concentration from 1.10^{-6} mol.dm^{-3} to 1.10^{-12} mol.dm^{-3}.

Acknowledgements
This research has been financially supported by grant VEGA 1/0074/17 of the Slovak Scientific Grant Agency and APVV-16-0029 of the Slovak Research and Development Agency.

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SESSION V **Physical Chemistry**

Ni/Ag nanocavities thin film for SERS applications

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The colloidal lithography is a simple technique to prepare nanostructured surfaces over a large area. This method used a colloidal polymer particles (polystyrene od PMMA) which are self-assembled into monolayer or multilayer on substrates [1]. Between colloidal particles is free space, which can be filled with required material. Due to this fact, the combination of colloidal lithography with electrochemical deposition of metal into the interspherical volume is suitable method to prepare nanocavities films [2]. Plasmonic properties of nanocavities films (wavelength of LSPR) can be easily modulate by changing height and diameter of nanocavities.

In our research, we prepared the Ni/Ag nanocavities films using different diameter of colloidal mask (100, 300, 500, 700 and 900 nm) and further, after SERS analysis the 500 nm nanocavities was tested with different normalized thickness of Ni and different time of Ag nanoparticles deposition. FDTD simulation of E field near to the nanocavities surfaces were calculated to the support experimental results. Colloidal masks were prepared by combination of drop coating and air/water interface method. Nickel films were electrochemically deposited from solution containing 0.6 mol dm^{-3} $NiSO_4$, 0.1 mol dm^{-3} $NiCl_2$, 0.3 mol dm^{-3} H_3BO_3 under -1 V. Ag nanoparticles films were deposited from 0.5mmol.dm^{-3} Ag_2SO_4 containing 1mol.dm^{-3} H_2SO_4.

The best SERS response using Rhodamin 6G as a analyte was observed for Ni/Ag nanocavities prepared from 500 nm polystyrene nanospheres, with normalized thickness of Ni ~0,5 and 200 s of Ag deposition. An important factor for SERS substrates is time stability and range of concentration which can be detected. In our case the concentration dependence was measured from 1.10^{-5} to 1.10^{-12} mol dm^{-3} with R^2=0.95 for peak at 770 cm^{-1}, standard deviation less than 18% and analytical enhancement factor was $1.078.10^{10}$. Time stability was measured for 13 weeks and was observed to decrease the intensity after first week with subsequent stabilization of intensity to the 50% of the original value. These results predict possibility of using Ni/Ag nanocavities as a SERS active substrate with high reproducibility, time stability and with low detection limit.

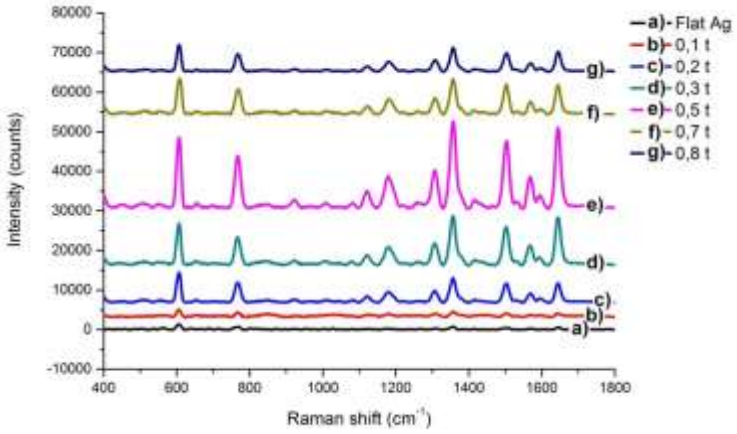

Figure 1. Representative SERS spectra of 1.10^{-6} mol.dm^{-3} Rhodamine 6G on 500 nm Ni/Ag nanocavities with different normalized thickness of Ni. SERS spectrum on flat Ag was measured with 1.10^{-3} mol.dm^{-3} Rhodamine 6G and multiplied 10 times for clarity.

Acknowledgements
This research has been financially supported by grant VEGA 1/0074/17 of the Slovak Scientific Grant Agency, APVV-16-0029 of the Slovak Research and Development Agency

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SESSION V **Physical Chemistry**

Sulfur-Carbon-Polypyrrole Composites as a New Cathode Material for Li-S Batteries

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Elemental sulfur represents the low-cost, environmentally friendly and safe cathode material for a lithium-ion rechargeable battery with theoretical capacity about 1672 mAh/g [1]. Recently, the work in progress concerning the improvement of conductivity, electrochemical stability and volume change of sulfur cathode. Electroactive conducting polymers (ECPs) are conjugated polymers that exhibit electronic conduction when partially oxidized or reduced and are capable of undergoing oxidation/reduction reactions [2]. Examples of ECPs include polypyrrole (PPy), polyaniline and polythiophene.

S-C-PPy cathode material was synthesized using a simple chemical oxidative polymerization of pyrrole monomer in acid media. Electrochemical measurements as cyclic voltammetry, galvanostatic charge/discharge measurements or electrochemical impedance spectroscopy were used for characterization of as prepared cathodes. Sample with 13 wt. % of PPy in composite shows the highest discharge capacity 1380 mAh/g-sulfur at a C-rate C/10. Fig. 1 shows the rate performance and discharge capacities of the S-C-PPy cathode material with 13 wt. % of PPy and 0.5 wt. % of PEG additive. As can be seen, it could deliver a discharge capacity of 1232, 1063 and 692 mAh/g at a rate of 0.5 C, 1 C and 2C respectively. The results of electrochemical testing proved that S-C-PPy composite is a promising cathode material for Li-ion batteries.

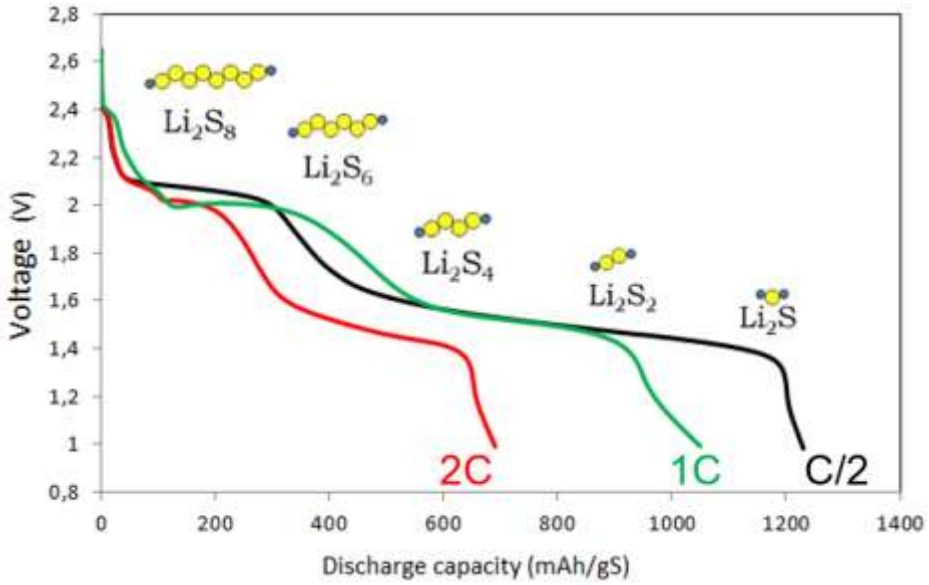

Figure 1. Discharge performance of S-C-PPy13wt.% with PEG additive at different C-rates between 1.0V and 2.8V.

Acknowledgements
This research was sponsored by the NATO Science for Peace and Security Programme under grant 985148.

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Electrochemical detection of insulin

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Diabetes mellitus (DM) is a heterogeneous metabolic disease characterized by chronic hyperglycemia [1]. Often, the symptoms are not sufficiently observable at early stages and so hyperglycemia causes that pathological and functional changes take place in advance, before the diagnosis of the disease [2]. Therefore, the development of sensors that are time saving, accurate, instrumentally undemanding are currently unavoidable.

This work deals with electrochemical determination of insulin on gold and carbon screen printed electrodes using cyclic voltammetry method. Mentioned electrodes have significantly smaller size compared to classic electrodes, achieving miniaturization of the system. The aim of the work was to find optimal conditions for insulin determination, while impact of pH and scan rate was observed. Based on the execution of measurements, correlation coeficient was determined, increase of which was obtained by modifying the electrodes with nanoparticles. In case of carbon screen printed electrode correlation coeficient was increased form -0,18 (unmodified electrode) to 0,87 (carbon electrode modified with CNTs and NiNPs). The active areas of the electrodes was also determined by the method of cyclic voltammetry. Modification with nanoparticles achieved a rapid increase of the active surfaces compared to the unmodified electrodes. In case of modification of gold screen printed electrode with the combination of CNTs and AuNPs, an increase of active area of the electrode was achieved by up to 183%.

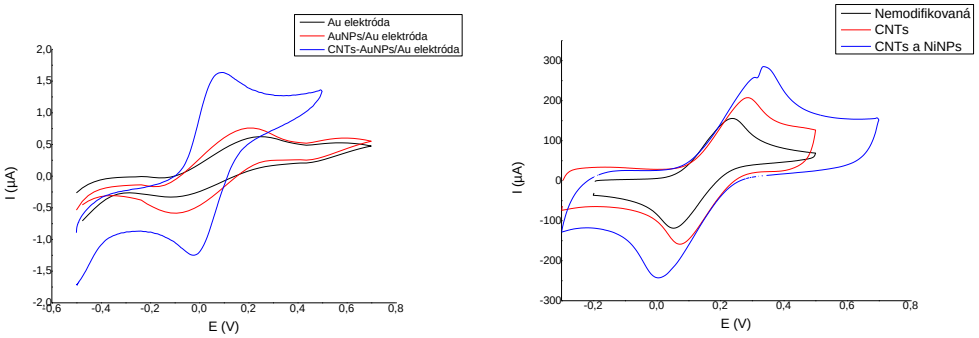

Figure 1. Determination the active area of unmodified and modified gold (left) and carbon (right) screen printed electrodes.

Acknowledgements

This work was supported by projects VEGA 1/0074/17 and APVV-16-0029

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SESSION VI **Division of Didactics of Chemistry**

Computer-Based Experiments in the Chemistry Teaching

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The school experimental activity of pupils should reflect the work of a "scientist" in a real laboratory so that natural sciences are not tearing away from reality for pupils. It is therefore necessary to include instrumental techniques in teaching. In school conditions, are therefore suitable School Measurement Systems (such as Vernier), which combine modern technology with the possibility to apply methods focused on inquiry of pupils. Methods focused on pupils include, for example, a computer-based experiment.
The aim of the pilot research was to identify the attitudes of students of teacher training to the computer-based experiment and its contribution to the cognitive development of pupils in theme *Physical-Chemical Properties of Water*. The research group was made up of 22 respondents - students of teacher training at the Faculty of Science UPJŠ in Košice. Students graduated the compulsory optional subject *Activating Methods of Chemistry Teaching* in the first year of Master's study. As a research tool, we used a custom-built questionnaire consisting of 9 items focused on inclusion of computer-based experiments in chemistry teaching. The research was conducted during the winter semester of the academic year 2016/2017. Students filled out the questionnaire before (pre-test) and after (post-test) implementation of computer-based experiments. Students performed the following computer-based experiments: *Determination of selected water-quality indicators in different samples of Water, Determination of pH, Measurement of conductivity, Exothermic and endothermic reactions* and *Acid-base titration with thermometric and potentiometric indication of equivalence point.*

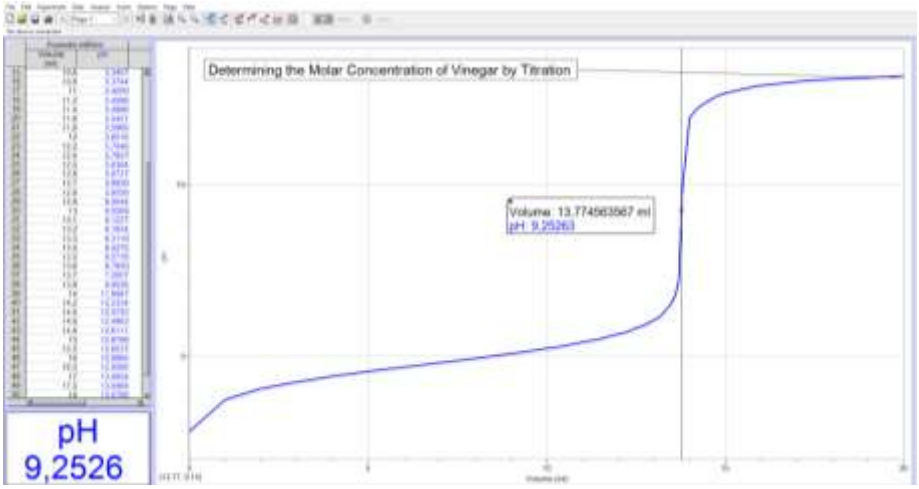

Figure 1. An example of a graph - Determination of the Concentration of Acetic Acid in Vinegar.

The results of our research indicate the differences in the attitudes of students' teacher training before and after learning with computer-based experiment. The analysis of the results revealed that the students were most interested work with modern technology, which is similar to the real work in the laboratories, that the devices can accelerate work in the lab, facilitate the work in lab work and help pupils to better understand the subject matter. The students' biggest concerns were the failure of the technique during the teaching.
The use of computer-based experiments in teaching shifts chemistry as a subject among subjects with more popularity and greater interest. Computer-based experiments help move the dimensions of activity in experiments from lower-level (watching the progress of the experiment) to higher level (ability to assess and correct of measurement errors).

Acknowledgements
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A. Diuzheva, J. Šandrejova, J. Balogh, V. Andruch, K. Gavazov

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P3 Binding affinity of Thiazole Orange to G-quadruplex and triplex DNA
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P4 Biological activity and intracellular distribution of tacrine-cumarin hybrid molecules.
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P7 Homo- and hetero- dimers of acridine derivatives as dual inhibitors of acetylcholinesterase and butyrylcholinesterase.
S. Hamuľáková, M. Hudáčová, M. Hrabinová, K. Kuca

P8 Synthesis of sphingoid base analogues with integrated molecular switches
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Physical chemistry

P9 Hydrophobic coatings in preparation of slow release fertilizers
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Division of Didactics of Chemistry

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E
Elečko Ján, Department of Organic Chemistry, *Abstract*

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Fabišíková Milica, Department of Organic Chemistry, *Abstract*

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Gonda Jozef, Department of Organic Chemistry, *Without contribution*
Gondová Taťána, Department of Analytical Chemistry, *Abstract*

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Hirková Simona, Department of Organic Chemistry, *Poster*
Hovancová Jana, Department of Physical Chemistry, *Abstract*
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I
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J
Jacková Dominika, Department of Organic Chemistry, *Abstract*
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K
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Kožár Tibor, Department of Biochemistry, *Invited Lecture*
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Kubíček Vojtěch, Department of Inorganic Chemistry, *Invited Lecture*

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Potočňák Ivan, Department of Inorganic Chemistry, *Without contribution*

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Reiffová Katarína, Department of Analytical Chemistry, *Abstract*
Rendošová Michaela, Department of Organic Chemistry, *Poster*
Rončák Róbert, Department of Organic Chemistry, *Without contribution*

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Slepčíková Paulína, Department of Organic Chemistry, *Abstract*
Sokol Jozef, Department of Natural Sciences, *Invited Lecture*
Sotáková Ivana, Division of Didactic of Chemistry, *Abstract*
Straková Fedorková Andrea, Department of Physical Chemistry, *Abstract*
Suváková Mária, Department of Biochemistry, *Abstract*

Š
Šandrejová Jana, Department of Analytical Chemistry, *Abstract*
Široký Michael, Department of Organic Chemistry, *Abstract*
Šišoláková Ivana, Department of Physical Chemistry, *Abstract*
Špaková Raschmanová Jana, Department of Organic Chemistry, *Abstract*

T
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Tóth Ján, Department of Analytical Chemistry, *Abstract*

V
Varhač Rastislav, Department of Biochemistry, *Abstract*
Vavra Martin, Department of Inorganic Chemistry, *Without contribution*
Velič Dušan, International Laser Centre, *Invited Lecture*
Víglaský Viktor, Department of Biochemistry, *Lecture*
Vilková Mária, Department of Organic Chemistry, *Without contribution*

Z
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New trends in chemistry, research and education at Faculty of Sciences of P. J. Šafárik University, Košice 2017
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