ИНСТИТУТ ПО ОРГАНИЧНА ХИМИЯ
С ЦЕНТЪР ПО ФИТОХИМИЯ
ГОДИШНА НАУЧНА СЕСИЯ

27–28 АПРИЛ 2023 г.

ПРОГРАМА

27.04.2023 г.

09.45 Откриване на сесията
10.00 Публична академична лекция на доц. д-р Явор Митрев
10.30 Публична академична лекция на доц. д-р Глория Исса
11.00 Публична академична лекция на проф. д-р Бойко Цинцарски

14.00 Постерна сесия

28.04.2023 г.

10.00 Публична академична лекция на доц. д-р Надежда Маркова-Петрова
10.30 Публична академична лекция на доц. д-р Атанас Курутос
11.00 Публична академична лекция на доц. д-р Иванка Стойчева

14.00 Постерна сесия

15.30 Награждаване на най-добрите постери

ГОДИШНАТА НАУЧНА СЕСИЯ, ПРОВЕДЕНА НА 27–28 АПРИЛ 2023 г. Е ОРГАНИЗИРАНА С ЛЮБЕЗНОТО СЪДЕЙСТВИЕ НА:

АСМ2 ЕООД

ШИМАДЗУ БЪЛГАРИЯ ЕООД

ТЕАМ ООД

ЛАБИМЕКС ООД

АКВАХИМ АД

ЛАБПРИМ ЕООД

ИНСТИТУТ ПО ОРГАНИЧНА ХИМИЯ С ЦЕНТЪР ПО ФИТОХИМИЯ

ГОДИШНА НАУЧНА СЕСИЯ

ПОСТЕРНА СЕСИЯ – РЕЗЮМЕТА

Съдържание:

FERROCENE MODIFIED ANALOGUES OF IMATINIB AND NILOTINIB AS POTENT ANTI-CANCER AGENTS

Irena Philipova[1], Rositsa Mihaylova[2], Georgi Momekov[2], Rostislava Angelova[2] and Georgi Stavrakov[1,2]

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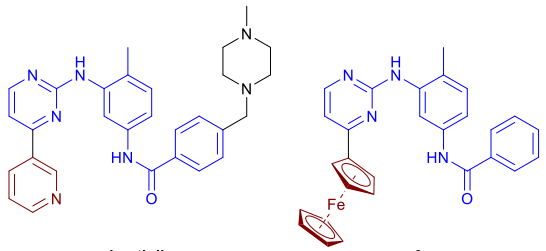
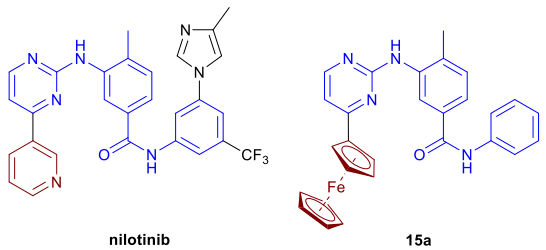
The discovery of the first bcr-abl targeted tyrosine kinase inhibitor imatinib revolutionized the treatment of patients with chronic myeloid leukemia and became a cornerstone in the further advancement of small molecular inhibitors directed toward the human kinome [1]. The unique features of ferrocene and the need for development of targeted anticancer drugs [2], inspired the design, synthesis and biological evaluation of ferrocenyl modified tyrosine kinase inhibitors by replacing the pyridyl moiety in imatinib and nilotinib generalized structures with ferrocenyl group. A series of seven new ferrocene analogues were synthesized and evaluated for their anticancer activity in a panel of bcr-abl positive human malignant cell lines using imatinib as a reference drug [3]. The metallocenes exhibited a dose-dependent inhibition on malignant cell growth with a varying antileukemic activity. The most potent analogues were compounds **9** and **15a** showing comparable or even superior efficacy to the referent in all leukemic models. Their cancer selectivity indices suggest a favorable selectivity profile, indicating a 250 times higher preferential activity of **15a** towards malignantly transformed K-562 cells and an even twice greater one (500) of **9** in the LAMA-84 leukemic model as compared to normal murine fibroblast cell line.





Acknowledgements
Financial support of National Science Fund, Bulgaria (Grant KP-06-N53/9, 11.11.2021) is gratefully acknowledged.

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NEW SOLVENT EXTRACTION PATHWAYS TO SUSTAINABLE PROCESSES FOR RARE EARTH METALS

Katrin Chavdarova[1], Ilina Todorova[1], Aleyna Chamdere[1], Maria Atanassova[1], Nina Todorova[1], Dessislava Gerginova[2], Stanislava Todorova[2], Svetlana Simova[2], Vanya Kurteva[2]

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Study of the liquid-liquid extraction of Eu(III) ion with a series of chelating ligands and determination of the process parameters are presented employing ionic liquids and typical organic diluents. Investigation of the extraction with a chelating compound, 4-benzoyl-3-methyl-1-phenyl-2-pyrazolin-5-one (HP), 4-benzoyl-3-phenyl-5-isoxazolone (HPBI) as well as by the β-diketone, 2-thenoyltrifluoroacetone (HTTA) alone and in combination with two synergistic agents d,l-hexamethylpropyleneamine oxime (HM-PAO) and its bis-imine precursor (pre-HM-PAO) and determination of the process parameters are presented. The interaction between the two extractants (acidic/neutral) in deuterochloroform has been studied by ^{1}H, ^{13}C, ^{19}F spectra and ^{1}H-^{1}H NOESY experiments. Several conclusions are given highlighting the role of the ionic diluent in complexation processes and selectivity with an employment of the chelating agent HL for various metal s-, p-, d- and f-cations in periodic table. The objective is to optimize a synergistic system for 4f-ions extraction, based on the HM-PAO and β-diketone/isoxazolone/pyrazolone partnership. As detailed above, a little enhancements of extraction efficiencies have been obtained either by use of basic synergistic agents, such as HM-PAO and/or by use of pre-HM-PAO. The competitive solvent extraction test of almost 25 metal ions as well as nearly 18 f-ions by ligands diluted in ILs or organic diluents has also been conducted in order to evaluate the switchable hydrophilic diluent, i.e. ethylene glycol as a more polar liquid phase instead of water. As the demand for critical metal increases, new types of resources are considered, both in nature and through the recycling. One difficulty with these less conventional resources is the significant dilution of the metals of interest among other components, often with similar chemical properties, which makes their separation difficult. There is hence an urgent and crucial need for the development of new processes and technology, among which solvent extraction has a major role to play.

Acknowledgments: The research leading to those results received funding from the Bulgarian National Science Fund: Grant Agreement № КП-06-Н69/5(2022), “Green twist to synergistic solvent extraction and separation of rare earth metals”.

ENGINEERING OF SILICA MESOPOROUS MATERIALS FOR CO_2 ADSORPTION

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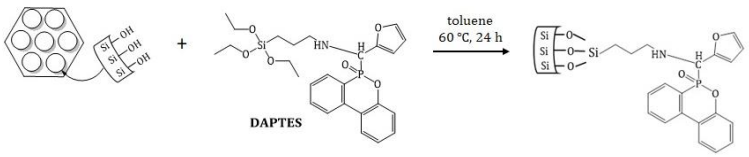
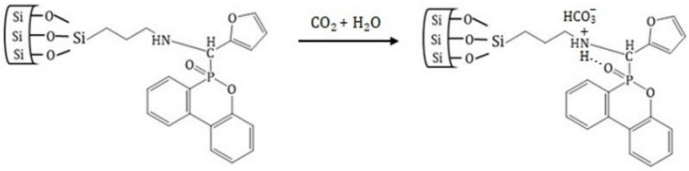
The adsorption methods for CO_2 capture are characterized by high selectivity and low energy consumption [1]. Therefore, engineering solid supports for efficient CO_2 adsorption attracts research attention [2]. Modification of mesoporous silica materials with tailor-made organic molecules can significantly improve silica performance in CO_2 capture and separation [3]. In that context, a new derivative of 9,10-Dihydro-9-oxa-10-phosphaphenanthrene-10-oxide, known for its anti-oxidative and flame-retarding properties, was synthesized and applied as a modifying agent of SBA-15, SBA-16, and KIT-6 silicates (Scheme 1). The physicochemical properties of the initial and modified materials were studied by nitrogen physisorption and temperature-gravimetric analysis. The adsorption capacity of CO_2 was measured in a dynamic CO_2 adsorption regime. The three modified materials displayed a higher capacity for CO_2 adsorption than the initial ones (Scheme 2). Among the studied sorbents, the modified mesoporous SBA-15 silica showed the highest adsorption capacity for CO_2 (3.9 mmol/g). In the presence of 1 vol.% water vapor, the adsorption capacities of the modified materials were enhanced. The total CO_2 desorption from the modified materials was achieved at 80°C. The obtained silica materials were stable in five CO_2 adsorption/desorption cycles.



Scheme 1. Modification of SBA-15, SBA-16, and KIT-6 by grafting of DAPTES



Scheme 2. CO_2 adsorption onto the DAPTES-modified silica adsorbents

Acknowledgments: This work was supported by the Bulgarian Ministry of Education and Science under the National Research Program "Young Scientists and postdoctoral students -2" approved by DCM 206 / 07.04.2022.

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IN SEARCH OF FORSYTHOSIDE B IN *VERBASCUM NIGRUM* L.

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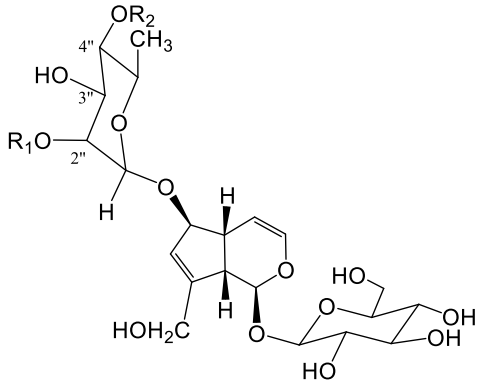
Verbascum nigrum L. (Scrophulariaceae) is one of the most widespread, widely used in traditional medicine and studied mullein species. The plant is well known as a source of valuable secondary metabolites as verbascoside and forsythoside B [1, 2] and the interest in their pharmaceutical potential is increasing in the last ten years. The aim of this study was survey of chemical composition of *V. nigrum* from Bulgarian origin (Mt. Vitosha), isolation and purification of forsythoside B and evaluation of its photoprotective activity. From the methanol extract of aerial parts of the plant typical for the species individual compounds were isolated - a large amount of verbascoside, aucubin and its acylated derivatives, saponins and flavonoid glycosides. It was established that Bulgarian sample of *V. nigrum* does not contain the target compound but during the process of identification of isolated iridoid glycosides, we found out that two of these were described in the literature with the same name – nigroside III, both sinuatol derivatives. Previously isolated from *V. nigrum* compound is *p*-coumaroyl derivative while the second one is an ester of cinnamic acid and until now it was isolated only from *Buddleja americana* [3].



R_1 = (*E*)-*p*-coumaroyl, R_2=H; Nigroside III from *V. nigrum*
R_1 = H, R_2 = (*E*)-cinnamoyl; Nigroside III from *B. americana*

Acknowledgments: This study is funded by the Ministry of Education and Science through the National Research Program "Young Scientists and Postdoctoral Students - 2", DCM 206/ 07.04.2022. For structural elucidation NMR equipment purchased by Project No BG05M2OP001-1.002-0012, "Sustainable utilization of bio-resources and waste from medicinal and aromatic plants for innovative bioactive products", funded by the OP "Science and Education for Smart Growth" 2014-2020, co-financed by the European Union through the European Regional Development Fund, was used.

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CHEMICAL COMPOSITION AND ANTIOXIDANT CAPACITY OF THE FRUIT SKINS OF EUROPEAN PLUM CULTIVAR "ČAČANSKA LEPOTICA" INFLUENCED BY DIFFERENT ROOTSTOCKS

Viktoria Ivanova[1], Boryana Trusheva[1], Mariana Kamenova-Nacheva[1,2], Sava Tabakov[3], Svetlana Simova[1] and Antoaneta Trendafilova[1]

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Plum fruits are valuable sources of nutrients, vitamins, minerals, dietary fibers and antioxidant compounds, accumulating predominately in their skins (peels). This study aimed to investigate the influence of the rootstocks on the content of sugars, organic acids and antioxidant phenolic compounds in the fruit skin of European plum cultivar "Čačanska Lepotica" grown on 'Wavit', 'Janka', 'Ishtara', 'GF-677' and 'GXN-15' rootstocks.^{1}H NMR of the methanol extracts led to the identification of sucrose, α- and β-glucose, sorbitol, fructose, malic and quinic acids, while LC-MS-DAD showed the presence of neochlorogenic and chlorogenic acids, cyanidin-3-O-glucoside, cyanidin-3-O-rutinoside, peonidin-3-O-glucoside, peonidin-3-O-rutinoside, hyperoside, isoquercitrin, rutin and an unidentified quercetin-3-diglycoside. The quantification of the individual compounds was performed by ^{1}H NMR (sugars and organic acids) and HPLC (phenolic compounds). A good correlation was observed between the content of total phenolics, flavonoids, anthocyanins and individual phenolic compounds in the extracts of the fruit skins and their antioxidant capacity (DPPH, ABTS and FRAP). The obtained results revealed that the content of the nutritional and bioactive compounds in the plum fruit skin was significantly influenced by the rootstock. The 'Wavit' rootstock appears to provide good fruit quality due to the highest content of sugars, organic acids and antioxidant compounds in the fruit skin.

Acknowledgments: The authors thank to The National Research Program "Healthy Foods for a Strong Bio-economy and Quality of Life" of the Ministry of Education and Science, Bulgaria for the financial support and the Centre of Competence: „Sustainable utilization of bio-resources and waste of medicinal and aromatic plants for innovative bioactive products" for the HPLC and NMR equipment used.

INFLUENCE OF SUBCRITICAL WATER EXTRACTION ON CELL WALL CONSTITUENTS OF LEMON BALM (*MELISSA OFFICINALIS* L.)

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The current study investigated the effect of subcritical water (SW) on the different cell wall constituents of lemon balm (*Melissa officinalis* L.) in connection with the extraction of rosmarinic acid. Different durations (10 and 20 min) and extraction temperatures (100 and 150 °C) were employed. It was found that a higher extraction time and temperature affect the components of cell walls. As a consequence, the yield of extracts increased. That was a direct result of the degradation of the primary cell wall constituents by SW as evidenced by the increased extraction and degradation of proteins and polysaccharides (PSs). The residues after extraction contained between 105% and 91% of the initial cellulose, suggesting that this PS was poorly affected. Only at the higher temperature and longer extraction duration began the destruction of the cellulose skeleton. In contrast, only 28% of the initial uronic acids were recovered in the residue indicating that 72% of them have passed into a soluble form. The yield of PS increased nearly 2 times with an increase in the extraction duration and temperature. Considering the data for the PS yield and recovery of uronic acids, it may be concluded that 54% and respectively 64% of the uronic acids are in such form – contained in the extract but do not build the corresponding PSs. Unlike PS components, lignin did not seem to change as a result of SW treatment. That was also evident from the recovery data of lignin in the residues after extraction (99% and 104% of the initial lignin). Free sugars remained unchanged at a lower temperature, but with an increase in temperature, even for a short time, their total amount was drastically decreased. These results reveal that SW enriches the obtained extracts with substances native to the herb, such as proteins, sugars, PSs, etc. These extracts could be used in the food industry as food antioxidants, or in the development of food supplements and functional foods.

Acknowledgments: Research equipment (Skalar San^{++} system) of distributed research infrastructure INFRAMAT (part of the Bulgarian National Roadmap for Research Infrastructures) supported by the Bulgarian Ministry of Education and Science under contract D01-155/28.08.2018, D01-284/17.12.2019, D01-382/2020 was used in this investigation. This research was funded by Operational Program "Science and Education for Smart Growth" 2014-2020, co-financed by European Union through the European Structural and Investment Funds, Grant BG05M2OP001-1.002-0012.

HYDRODEOXYGENATION OF LEVULINIC ACID TO γ-VALEROLACTONE OVER ZSM-5/MESOPOROUS SILICA SUPPORTED Cu-Ni COMPOSITE CATALYSTS

Manuela Oykova [1], Margarita Popova [1], Ivalina Trendafilova [2,3], Yavor Mitrev [1], Pavletta Shestakova [1], Magdolna Mihályi [4] and Ágnes Szegedi [4]

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Utilization of lignocellulosic biomass to produce valuable chemicals, materials, and fuels is emerging as a promising alternative to reduce dependence on fossil fuels [1, 2]. Lignocellulosic biomass can be hydrolyzed into a mixture of cellulose, hemicellulose and lignin. Hydrolysis of hemicellulose and cellulose leads to the formation of C5 and C6 monosaccharides. Levulinic acid can be produced from lignocellulose by acid-catalyzed hydrolysis and can be further used as a platform molecule for the production of valuable products, including biofuel precursors such as γ-valerolactone [3]. In the present study, we describe the application of Ni and/or Cu functionalized ZSM-5 mesoporous silica composites for vapor-phase hydrodeoxygenation of levulinic acid to γ-valerolactone. In ZSM-5 zeolite/mesoporous silica composite, used as a support for metallic nanoparticles, zeolite seeds provided acid sites, whereas larger pores of KIT-6 mesoporous silica facilitated the mass transfer of reagents and products.The catalytic behavior of the materials was investigated in a reaction for the gas-phase upgrading of lignocellulosic biomass-derived levulinic acid (LA) to γ-valerolactone (GVL) (Fig. 1). Among the studied catalysts, CuNi-ZSM-5/KIT-6 showed the highest LA conversion (100 %) and γ-valerolactone (GVL) yield (81 %) at 250 °C.

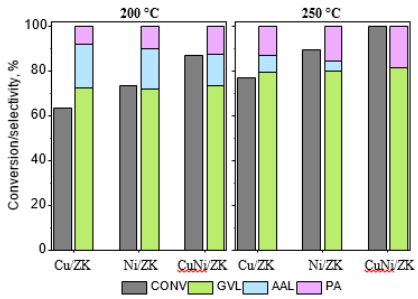

Figure 1: LA conversion and the products' selectivity on the Cu-ZSM-5/KIT-6, Ni-ZSM-5/KIT-6 and CuFe-ZSM5/KIT-6 catalysts.

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BIORENEWABLE ROUTES TO HUMAN METABOLITES

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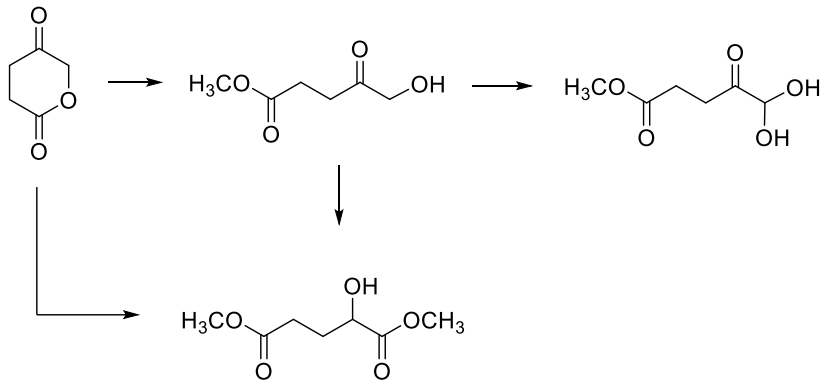
4-Keto-δ-valerolactone (KVL) is an important biorenewable compound, readily available from furfuryl alcohol [1]. It is used for the preparation of a recyclable and biodegradable polymer poly(4-ketovalerolactone) [2]. In the present study we aimed to diversify its use as a platform molecule for the production of some valuable plant and human metabolites. We achieved the high-yielding synthesis of 5-hydroxylevulinic acid methyl ester, a plant metabolite, via methanolysis of KVL. Furthermore, by applying a modified and optimized procedure for copper-catalyzed oxidation of α-hydroxyketones [3], we successfully obtained 5,5-dihydroxylevulinic acid methyl ester and dimethyl 2-hydroxyglutarate. The latter represents a dimethyl ester of 2-hydroxyglutaric acid, which in turn is an important plant and human metabolite. Noteworthy, dimethyl 2-hydroxyglutarate was prepared in high yield by a one-pot copper-catalyzed tandem reaction directly from KVL. To our knowledge, this is the first example of such transformation and a practical synthetic route toward valuable metabolites.



Acknowledgments: The authors acknowledge the National Scientific Program "VIHREN" (grant КП-06-ДВ-1) for the financial support.

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ARTEMISIA ALBA TURRA (WHITE MUGWORT) – CELL, TISSUE AND ORGAN CULTURE FOR TARGETED SECONDARY METABOLITES PRODUCTION

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Artemisia alba Turra (white mugwort, Asteraceae) is an Euro-Mediterranean fragrant perennial shrub, widespread in Southern Europe with traditional utilization in the Mediterranean region as a stomach tonic. Scientific research has revealed a wide array of phytochemical activities of its essential oil (antimicrobial, antioxidant, etc.) and different types of extracted preparations (anti-inflammatory, pro-apoptotic, cytotoxic, etc.). Phytochemical research has evidenced a high variability in its essential oil profile [1] and its high morphological variability has placed it several times into different subgenera of the *Artemisia* genus [2]. The above has motivated an extended research to clarify the effect on secondary metabolites production caused by morphogenetic modification by means of different plant cell tissue and organ techniques. Production of essential oils with either monoterpenoid or sesquiterpenoid domination depending on the root formation in differentiated shoot cultures, as well as polyphenolics accumulation in non-differentiated cell aggregates as a result of different light and growth regulators treatments have been discussed in this work.

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COLLAGEN HYDROLYSATE EFFECTS ON PHOTO-PROPERTIES OF A PHOTOSENSITIZER

Vanya Mantareva [1], Inna Sulikovska [2] Ivan Iliev [2], Plamen Hristov[1] and Tsanislava Genova[3]

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Collagen has been well accepted for drug delivery structures due to its biocompatible chemical and physicochemical, and curative actions. The present study focuses on synthesis and investigation of novel gallium (III) phthalocyanine (GaPc) and the effects of a conjugate with hydrolyzed collagen used for human consumption (GaPc-Clg) on the main photophysical and photodynamic properties. The absorption of GaPc-Clg was evaluated with a decrease of the strong Q-band with a slight blue shift to 678 nm and a concentration-sensibly loss of Soret band at 353 nm in phosphate buffered solution (PBS, pH 7.2). The fluorescence spectra showed an intensive emission band at 704 nm in DMSO and 694 nm in PBS typical for monomolecular GaPc. The emission of conjugate was recorded more intensive at excitation 365 nm as compared to 615 nm due to collagen. Photodynamic efficacy of GaPc alone and the conjugate were studied on pigmented melanoma cell line (SH-4) vs. two normal cell lines (HaCaT and BJ) by the NRU-assay. It was shown a slight reduction of cytotoxicity for the conjugate as compared to GaPc which can be explained with singlet oxygen quenching by collagen macromolecules.

This study suggested that nevertheless, the promising drug delivery *in vivo* role of the native collagens, the used hydrolysate was observed to reduce *in vitro* PDT activity. However, there were determined some advantages for this conjugation such as the diminish of high cytotoxicity of GaPc and double increase selectivity.

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STRAWBERRY JAMS WITH DIFFERENT SUGAR SYRUPS – COMPARISON VIA NMR SPECTROSCOPY

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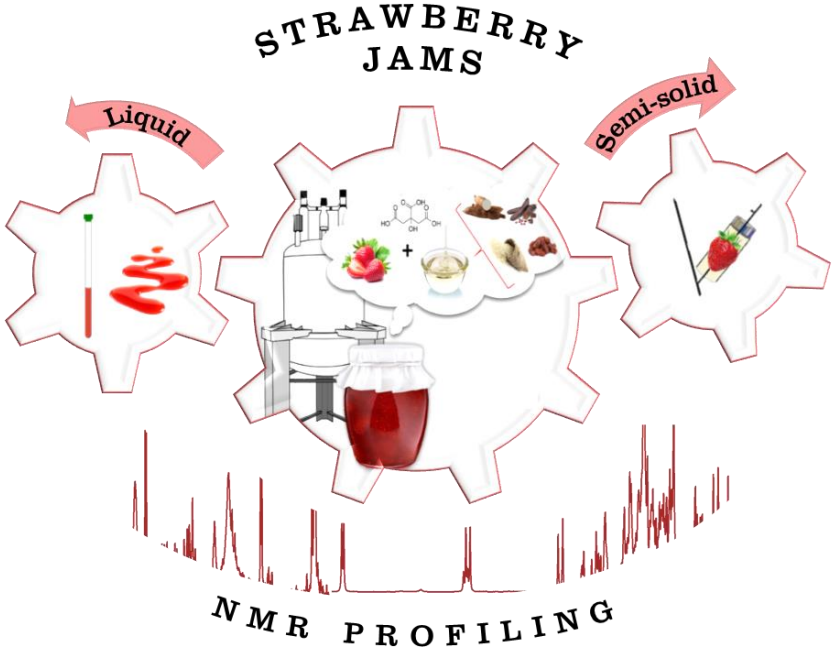
Strawberry jam is a delicious and widely consumed spread made by mixing and cooking strawberries and sugar. Despite its widespread consumption, the chemical composition of jams has received limited research attention so far. Recently, due to concerns surrounding traditional sugar, alternative sweetener sources such as tapioca, rice, dates and carob syrups have become more prevalent in jam production. These alternative sweeteners have a lower glycemic index and potential health benefits, but no studies have yet compared the impact of these syrups on the flavour and chemical composition of jams.

In this study we aim to investigate the effect of four different sugar syrups – from tapioca, rice, dates and carob – on the chemical profiles of strawberry jams. To achieve this, we analyse the syrups using ^{1}H NMR spectroscopy and put together the composition of the resulting jams via both ^{1}H liquid and HR-MAS NMR spectra. Statistical methods have been employed to compare the composition of the jams, the content of the syrups, and the ingredients of raw strawberries determined by HR-MAS. This investigation allows us to understand the chemical differences between jams made with various sugar syrups and to assess the impact of the manufacturing process on the jams.



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ANTI-INFLAMMATORY ACTIVITY OF ALKALOIDS FROM *PANDANUS AMARYLIFOILIUS*

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Pandanus amaryllifolius is a tropical evergreen tree with long, blade-like leaves. Its fragrantly-scented leaves are widely used as a popular culinary ingredient for flavoring various food products in Southeast Asia. The species is a medicinal herb used in traditional medicine for centuries in various ethnic societies in Vietnam, Taiwan, Thailand and Indonesia due to its purported health benefits for the treatment of rheumatism, hyperglycemia and epilepsy.

The phytochemical study of *P. amaryllifolius* revealed the presence a number of bioactive compounds as steroids, flavonoids, lignans, triterpenoids and alkaloids. *Pandanus* alkaloids are a specific class of organic compounds containing an unsaturated γ-lactone ring attached to a pyridine, piperidine, pyrrolidine or pyrrolidinone moiety [1]. The spiropiperidine units in these alkaloids received considerable attention, because they display interesting biological properties and can be used as potential anti-inflammatory agents [2]. To date, there are limited information of the biological activity of *Pandanus* plants that is directly associated with the alkaloids.

The present work deals with investigation of the alkaloid composition of *P. amaryllifolius* Roxb. and nine pandane alkaloids were isolated and determined. The total alkaloid mixtures and alkaloid fractions of the species were evaluated for their anti-inflammatory activity using in vitro experimental models. The results suggest that they inhibit macrophage activation by reducing the proinflammatory cytokines TNF-α and IL-6. The total alkaloid mixture is more effective than the sub fractions. These positive outcomes are probably due to synergistic interactions between the alkaloids.

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[1,3]THIAZOLO[3,2-A]BENZIMIDAZOL-3(2H)-ONES CONTAINING ARYL AND HETEROARYL FRAGMENTS AT 2-POSITION: SYNTHESIS, STRUCTURAL CHARACTERIZATION, ANTIPROLIFERATIVE AND RADICAL SCAVENGING ACTIVITY

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Benzimidazole heterocycle system is very important pharmacophore and privileged structure in the medicinal chemistry. Its derivatives exert various biological activities such as antioxidant and anticancer. The benzimidazole ring system exists in the structure of many antiparasitic, anthelmintic, antifungal, antiviral and antitumor drugs [1]. 2-Substituted-[1,3]thiazolo[3,2-a]benzimidazol-3(2H)-ones have demonstrated previously promising anthelmintic, antimicrobial and radical scavenging activity [2,3].

This motivated us to further synthesize an extended series of 1,3]thiazolo[3,2-a]benzimidazol-3(2H)-ones containing aryl and heteroaryl fragments at 2-position and evaluate their radical scavenging ability and antiproliferative effect. The synthesis was carried out through 5 steps: the first step comprised the synthesis of benzimidazolethiol scaffold, from which at the next step benzimidazolethioacetic acid was obtained. Then the thioacetic acid was transformed into benzimidazolethiazoleone and finally in the last step the hydroxy- and methoxy-substituted aromatic and heteroaromatic rings were introduced and the target [1,3]thiazolo[3,2-a]benzimidazol-3(2H)-ones were afforded. The preferred structure of the compounds was established with theoretical computations. The more stable conformation of the exocyclic double bond is Z, and for compounds with a heterocyclic moiety in which rotation around the C-C bond to the aryl moiety results in different conformers, the s-cis isomer is more advantageous.

The radical scavenging activity was tested *in vitro* on lecithin, deoxyribose, ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) and DPPH (2,2-diphenyl-1-picrylhydrazyl) assays. The antiproliferative effect was studied on MCF-7 (ER-positive breast adenocarcinoma), AR-230 (chronic myeloid leukemia) and HeLa (cervical cancer) cell lines as well as 3T3 cells (mouse fibroblasts).

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DYNAMIC NMR STUDY AND DFT CALCULATIONS OF FLUXIONAL CARVACROLES

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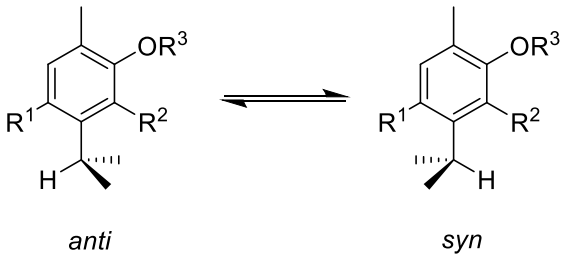
The synthesis and design of synthetic analogs of natural products that show valuable properties for medicine and biology are one of the main priorities of modern science, and their results can be a valuable source for the pharmaceutical industry. In the present study, the structure elucidation of eleven derivatives of 4,6-dihalogeno-3-isopropyl substituted synthetic analogues of the natural compound carvacrol was carried out by means of NMR experiments and DFT calculations. By comparing GIAO/B3LYP/6-311++G(d,p) calculated and experimentally measured vicinal $^{3}J_{CH}$ spin-spin constants, the individual conformers were assigned as *syn* and *anti*. The selective NOE experiments confirmed this assignment.
The conformational mobility of carvacrol analogues was studied by 1D and 2D NOESY and ROESY spectra. Application of homonuclear decoupling technique (HOBS experiment) in 1D and 2D NOESY spectra improves resolution without reducing the sensitivity. The rate constants of the isopropyl rotation between *syn* and *anti* conformers were determined and the corresponding energy barriers (14 – 17 kcal/mol) were calculated. The DFT calculations of the energy barriers in carvacrol derivatives allowed the determination of the steric origin of the restricted isopropyl rotation. The barrier of rotation mainly depends on the size of the substituents R^1 and R^2 and is insensitive to the electronic influence of the substituent R^3.



anti *syn*

$R^1 = R^2 =$ Cl, I, Br
R^3 = H, CH_3, Allyl, C(=O)i-Pr, C(=O)Et

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EFFECTS OF ASCORBYL PALMITATE CONCENTRATION ON THE STABILITY OF OMEGA 3-RICH *CAMELINA SATIVA* SEED OIL

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Camelina sativa oil can be utilized in the food industry if the erucic acid content meets the requirements of no more than 5%. Applications can be grouped depending on whether they relate to the camelina seeds, oil or pomace after oil extraction and include but are not limited to: functional food and diet supplements, cosmetic additives, animal feed, bio-lubricants, adhesives, polymers, biofuels and compost. Regardless of the application of the oil, it is necessary to ensure and increase as much as possible its oxidative stability. As a co-antioxidant regenerating native tocopherols (650-950 mg/kg), the effect of ascorbate or its lipid-soluble esters is highly concentration-dependent. The effect of ascorbyl palmitate addition in a wide concentration range (0.1 mM-2.0 mM) has been studied. A pro-oxidant activity observed at low concentrations, 0.1 mM and 0.2 mM, can probably be explained by the ratio between tocopherol(s) and the palmitate. Addition of 0.2 mM rosmarinic acid leads to an increase of oxidative stability of camelina oil and ensures an induction period comparable to that in the presence of ascorbyl palmitate at its maximal concentration in this study 2.0 mM, i.e. tenfold higher. On other hand the addition of 0.2 mM palmitate in an equimolar ratio (1:1) to rosmarinic acid significantly decreases the induction period.

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NMR PROFILING OF BULGARIAN COMMERCIAL AND CRAFT BEERS

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Beer is the most widespread alcoholic beverage around the world. It is made of grain, hops, yeast and water. In 1516 Duke Wilhelm IV of Bavaria introduced Reinheitsgebot – the German Beer Purity Law, with the aim to limit the ingredients in beer in Germany and the states of the former Holy Roman Empire. It is speculated that the production of commercial beer is made cheaper by replacing grain with rice and corn. In addition, identified insufficient control by the state authorities on food products in the country and increasing number of Bulgarian craft breweries being established, represent a potential threat to the consumers of this alcoholic beverage, as the actual composition of the beer is unknown.

The aim of this study is to determine the chemical profile of Bulgarian commercial and craft beers. Using ^{1}H NMR spectroscopy, we have analyzed industrial and craft samples of each of the lagers and ales we have acquired from different parts of Bulgaria. Statistical methods have been used, in order to distinguish between craft and commercial beer, and to classify the beers in their respective style – lager or ale based on their chemical profile.

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NEW 5-METHOXY-INDOLE CARBOXYLIC ACID DERIVED HYDRAZONE HYBRIDS AS MULTIFUNCTIONAL NEUROPROTECTORS

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The underlying cause of neurodegenerative disorders such as Alzheimer's and Parkinson's disease still remains unknown. However, there is compelling evidence regarding the involvement of oxidative stress in early events preceding the dopaminergic degeneration and senile plaques formation. In light of the known neuroprotective properties of indole-3-propionic acid, melatonin and our previous studies on benzimidazole hydrazones with promising potential [1-3], a series of 5-methoxy indole-hybrids combining pharmacophores with proven activity were synthesized with special emphasis on antioxidant action. The majority of compounds possess an excellent safety profile with hemolytic effects < 5 % (200 μM), and IC50 > 150 μM in SH-SY5Y and b.End3 cells. The derivatives containing catecholic and vanilloid fragments exhibited the strongest neuroprotection in H2O2-induced oxidative stress on SH-SY5Y cells and 6-OHDA-induced neurotoxicity in rat brain synaptosomes. All compounds suppressed iron-induced lipid peroxidation. The hydroxy derivatives were also the most active in deoxyribose degradation inhibition and were able to decrease the superoxide anion generation. All of the compounds were able to inhibit hMAO-B. The in vitro blood-brain barrier (BBB) model with b.End3 cell line showed that some compounds increased the permeability of the endothelial monolayer whilst maintaining the tight junctions. The combined results demonstrated that most of the indole and benzimidazole derivatives as perspective multifunctional compounds for the treatment of neurodegenerative disorders.

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NEW 5(6)-METHYL-1*H*-BENZIMIDAZOL-2-YL HYDRAZONES: SYNTHESIS, COMBINED EVALUATION OF THE ANTHELMINTHIC AND ANTIOXIDANT ACTIVITY AND PERFORMED QUANTUM-CHEMICAL CALCULATIONS.

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Parasitic infections in humans, caused by parasites of the genus Trichinella play a significant role in human pathology [1] leading to tissue damages and immune system dysfunction that could be related to decrease of the antioxidant capacity of the organism and presence of oxidative stress [2]. The benzimidazoles are a large chemical family widely used in veterinary and human medicine to treat helminthic infections as well as an appropriate structural platform for antioxidant discovery efforts.
Herein, we present the design and synthesis of new benzimidazole derivatives that combine anthelmintic and antioxidant actions in one molecule. The synthesis of the 5(6)-methyl-1*H*-benzimidazol-2-yl hydrazones was achieved by a multi-step reaction pathway by using o-phenylenediamine, hydrazine hydrate and broad series of hydroxyl- and methoxyl-arylaldehydes as reagents.
The anthelmintic activity of the target hydrazones was evaluated *in vitro* on encapsulated *Trichinella spiralis larvae*. Compounds containing two or three hydroxyl groups demonstrated the strongest effect (100 % effectiveness) after 24 hours incubation period.
The radical scavenging properties of the hydrazones were studied *in vitro* towards stable free radicals – ABTS and DPPH as well as in model systems using as oxidisable substrate deoxyribose and lecithin. The tested compounds demonstrated potent radical scavenging activity (RSA%) in all systems.
Several mechanisms of radical scavenging activity were evaluated by DFT calculations. The ability of the studied compounds to deactivate different free radicals were modelled by transition states involving attack by •OCH_3, •OOH and •$OOCH_3$, at all reactive site.

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THEORETICAL AND EXPERIMENTAL STUDY OF NEW [6]-HELICENE DERIVATIVES FOR OPTOELECTRONIC APPLICATIONS

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Quantum chemical calculations were performed on a set of newly synthesized [6]-helicene derivatives armed with suitable functionalities. Electronic, optical and chirooptical properties were investigated employing a mixed theoretical-experimental approach. In order to choose a suitable theoretical method for characterizing structures and predicting their properties few DFT functionals - B3LYP, CAM-B3LYP, PBE0, BH&HLYP and wB97XD were used as B3LYP results best fit the experimental data. The focus of the study was the simulation of the UV/visible absorption spectra, the optical rotation (OR), as well as the electronic circular dichroism (ECD) spectra. The studied molecules showed a strong absorption in the UV region and significant ECD signals. High specific rotation values (+2500-3000 for the P-enantiomers) at λ=589 nm were determined both experimentally and theoretically which is close to the reported for similar helicenes [1]. In addition, the chemical reactivity of these molecules was obtained by mapping the electron density with the molecular electrostatic potential (MEP). Reduced Density Gradient (RDG) scatter plots and non-covalent interaction (NCI) plots were also performed in order to illustrate the type of internal non-covalent interactions and elucidate the structure-property relationship. The present DFT/TDDFT investigation demonstrates that theory is able to reproduce most of the experimental features and can help in interpreting the spectra [2].

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BIO-SYNTHESIS OF METAL NANOPARTICLES WITH WATER CHAMOMILE EXTRACT AND THEIR POTENTIAL ANTIBACTERIAL PROPERTIES

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Chamomile *(Matricaria chamomilla L.*) is a well-known medicinal plant species from the Asteraceae family often referred to as the “star among medicinal species.” Nowadays it is a highly favored and much used medicinal plant in folk and traditional medicine. Its multitherapeutic, cosmetic, and nutritional values have been established through years of traditional and scientific use and research. [1] It is commonly used for its antioxidant, antimicrobial, antidepressant, anti-inflammatory, antidiarrheal activities, angiogenesis activity, anticarcinogenic, hepatoprotective, and antidiabetic effects. Besides, it is beneficial for knee osteoarthritis, ulcerative colitis, premenstrual syndrome, and gastrointestinal disorders. [2] Metal nanoparticles (NPs) are the subject of a number of studies that prove their biomedical application. According to the World Health Organization, they show effectiveness against various microorganisms and pathogens using different mechanisms of action than traditional antibiotics. Plants are the "chemical factories" of nature. Obtaining NPs with their help is an example of a cost-effective and ecological alternative to chemical and physical methods. The green method for obtaining nanoparticles is easy and profitable. Regarding this, the aim of this study was to develop a "green" approach for obtaining metal NPs using *a Matricaria chamomilla L.* water extract as a reducer and to evaluate their antimicrobial properties.

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ADVANCED CARBON MATERIALS WITH MAGNETIC PROPERTIES

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Magnetic properties in carbon materials are often due to the presence of impurities or minimal quantities of ferromagnetic metals – iron Fe, cobalt Co, nickel Ni, manganese Mn, chromium Cr, gadolinium Gd, etc. When the metal atoms are in very small content and uniformly distributed in the material, they cannot contribute to magnetization. The magnetic effect due to the presence of iron or other metals appears when the iron content is higher.
The mechanism of ferromagnetism in carbon structures that do not contain metal atoms is not well studied. Investigations of nitrogen-containing carbon ferromagnetic materials show that their structure is often amorphous. Carbon structures that contain nitrogen, boron, or phosphorus show different degrees of magnetization. Magnetic carbon structures usually contain ferromagnetic phases, due to the presence of π-delocalized spins caused by the presence of hetero-element impurities in the carbon matrix.
The main aims are synthesis and detailed characterization of new carbon materials with magnetic properties. Carbon composites are produced from polymers by thermo-oxidation treatment with nitric acid at 200^{o}C, pyrolysis at 600^{o}C, and further hydro-pyrolysis at 800^{o}C. The synthesized samples are characterized by BET, XRD, SEM, elemental analysis.
The obtained carbon materials are characterized by high surface area and high degree of graphitization. The samples also show well distinguished magnetic properties. The obtained materials have possible application in water purification, electronics and medicine.

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INVESTIGATION OF PURSLANE (*PORTULACA OLERACE*A L.) SEED OIL: NEUTRAL LIPID CLASSES AND THEIR FATTY ACIDS COMPOSITION

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Purslane (*Portulaca oleracea* L.) is a succulent plant growing in different geographic areas. It is consumed both as fresh and as cooking vegetable. In addition, it has been used for centuries as a medicinal herb because of its valuable healthy effects against inflammation, skin problems, hypercholesterolemia, etc.
Although the leaves and stems of purslane are the most popular plant parts, seeds focus attention too as a promising source of essential fatty acids as omega-3 18:3 (alpha-linolenic) and omega-6 18:2 (linoleic) fatty acids. For that reason we aimed to investigate purslane seed oil regarding its neutral lipid classes and their fatty acids composition. For the purpose, after extraction in Soxhlette apparatus the oil was subjected to Thin layer chromatography on silica gel G for separation, isolation and gravimetric determination of the following lipid classes: monoacylglycerols, diacylglycerols, free fatty acids, free sterols, unidentified zone, triacylglycerols, sterol esters and waxes. After trans-methylation of each lipid class its fatty acids composition was determined by Gas chromatography. Sixteen fatty acids with chain lengths of 12-26 carbon atoms and 0-3 double bonds were identified and quantified. The results revealed a very high content of the omega-6 18:2 (49 % in sterol esters) and omega-3 18:3 (40 % in triacylglycerols) essential fatty acids.

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GREEN SYNTHESIS OF METAL NANOPARTICLES WITH A REDUCER *PLANTAGO MAJOR L.* EXTRACT

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In recent years the danger antibiotic resistance poses forced medical related research towards finding alternative solutions, such as metal-based nanoparticles. However, using plants as precursors for the synthesis of such particles could reduce cost and toxicity of the final product, while increasing efficiency. This study aims to shed light on and fully optimize the green synthesis of metal-based nanoparticles with a *Plantago major L.* extract as a reducer. Firstly the most efficient method of extraction of the herb was determined using elemental analysis (ICP-MS) and comparing the results to a commercial product and antimicrobial tests (disk-diffusion and agar-well diffusion methods). For proving the successful formation of the nanoparticles Photocatalytic degradation, UV-Vis Spectroscopy and SEM with Surface Elemental Analysis were used, which also revealed their specific size and form. Different metal salts were used for the preparation of the nanoparticles as to determine formation efficiency and antimicrobial properties (antibacterial, antifungal, antiviral). Antibacterial properties were determined using disk-diffusion and agar-well diffusion methods. Successful formation of nanoparticles was observed in all samples. Some samples revealed a strong antibacterial effect, while others revealed no such effect. The specific compounds reducing the metal ions remain to be determining using HPLC and UHPLC Q-TOF MS analyses. If extended and successful, this research will lead to a new category of products having the potential of being used in pharmacy and cosmetics.

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EXPLORING AROMA PROFILE OF BULGARIAN RED WINES BY HS-SPME/GC/MS

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A headspace solid phase microextraction (HS-SPME) gas chromatography/mass spectrometry (GC/MS) method has been developed for the red wine aroma profile analysis. Two types SPME fibers (nonpolar polydimethylsiloxane (PDMS) and semi-polar divinylbenzene/carboxen/polydimethylsiloxane (DVB/CAR/PDMS)) were compared in respect of their applicability for the extraction of the volatile compounds, responsible for the wine aroma profile. The developed extraction procedure was applied to the analysis of 7 samples commercial Bulgarian Merlot wine, 3 samples commercial Bulgarian Cabernet Sauvignon wine and 2 samples of homemade wine. More than 50 individual volatile and semi-volatile compounds were identified, with the representatives of terpenes, esters, alcohols, acids, sulfur compounds, etc. Characteristic GC "fingerprint" allowed to distinguished between different varietal wines.

SYNTHESIS OF CAMPHOR-10 SULFONAMIDES WITH POTENTIAL BIOLOGICAL ACTIVITY

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Bacterial antimicrobial resistance (AMR) has emerged as one of the leading public health threats of the 21st century. Based on a study 4.95 million deaths were associated with bacterial AMR globally in 2019 [1]. Therefore, the preparation of new more effective agents with potential antibacterial activity is object of considerable synthetic efforts. The biological activity of sulfonamides drugs is notably used to treat a wide range of pathogenic microorganisms, such as *Escherichia coli*, *Pneumocystis carinii*, *Campylobacter*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Mycobacterium leprae* [2].

Therefore, based on the literature data regarding the activity of the various compounds, new series of structures will be designed [3]. The current study includes structural modifications of the camphor skeleton and introduction of pharmacophoric groups, which suggests obtaining derivatives with high biological activity, schematically shown in Figure. Our experience in recent years in the preparation of active camphane compounds leads us to assume that the proposed structures would be active against pathogenic bacteria, fungi and viral infections.

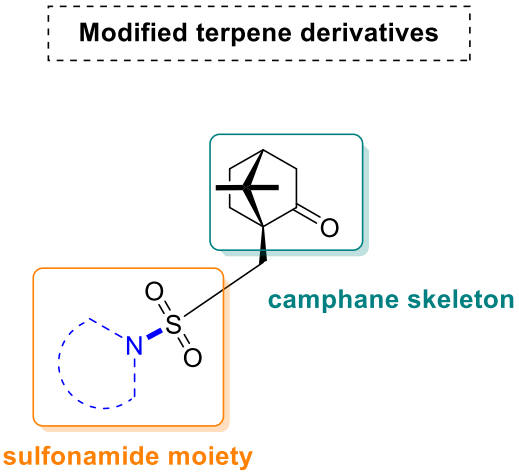

Figure. The design strategy for camphor-based derivatives with potential biological activity.

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SOLID STATE NMR INVESTIGATION OF THE EFFECT OF POLYBETAINE POLYMERS ON THE PHASE COMPOSITION OF BIOMIMETICALLY SYNTHESIZED CALCIUM PHOSPHATES

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Development of new materials for biomimetic remineralization of tooth enamel is a topic of great importance in the dental materials research as a new approach to the prevention, restoration and treatment of defective enamel. Recent studies demonstrated that polymers with betaine functionality can play a role in controlling mineralization reactions and lead to the desired calcium phosphate phase or mixture of phases.

In the present study novel Polymer/Calcium Phosphate (P/CaP) hybrid materials were synthesized and characterized by solid state NMR spectroscopy. The hybrid P/CaP systems were obtained by *in situ* precipitation of CaP in a physiological medium containing polymer with betaine functionality, either polycarboxybetaine (PCB) or polysulfobetaine (PSB) under different reaction conditions. For comparison pure CaP synthesized under identical conditions as for the preparation of hybrid systems were also investigated. ^{1}H, single pulse ^{31}P and $^{1}H \rightarrow ^{31}P$ cross-polarization (CP) MAS solid state NMR spectra provided insight to the structural characteristics and chemical composition of calcium phosphate phase formed in studied materials, as a function of sample preparation procedure, synthesis conditions and the type of the polymer. The NMR data revealed that the pure CaP phase formed under controlled conditions (pH, temperature, maturation time) represent a mixture of crystalline and poorly crystalline (nanocrystalline) hydroxyapatite (HAP). The ^{31}P NMR spectrum of CaP phase formed in the absence of polymer under identical conditions as for the synthesis of the hybrid materials, however, represented a complex pattern indicating the presence of mixture of orthophosphates and hydrogen phosphate species. The NMR spectra of the hybrid polymer/CaP sample obtained by in situ precipitation in a solution of PCB polymer demonstrate the formation of amorphous calcium phosphate, while in the presence of PSB a mixture of dicalcium phosphate dihydrate (CaHPO4.2H2O, DCPD) and poorly crystalline octa calcium phosphate (Ca8(HPO4)2(PO4)4.5H2O, OCP) was formed. The obtained results clearly evidencing the role of the polymer functionality on the composition and structural properties of the CaP phase.

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VARIATIONS IN THE FRAGMENTATION MECHANISM OF THE ETHYLENE GLYCOL CONVERSION OBSERVED ON SN AND/OR NI CATALYSTS IN THE AQUEOUS PHASE REFORMING REACTION

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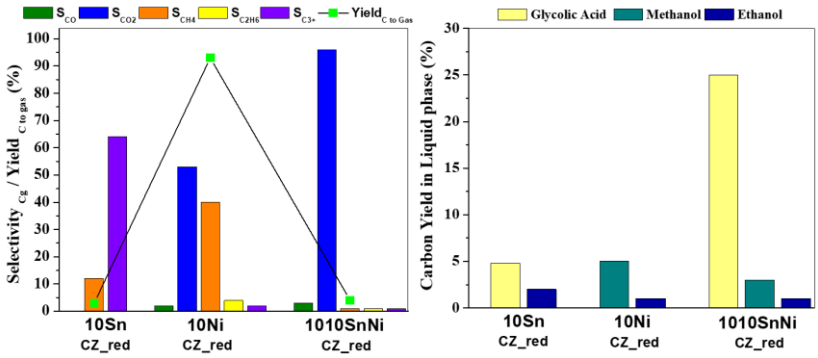
Introduction

The Aqueous Phase Polyols Reforming process is a well-known hydrogen production process starting from biomass, having the advantages of using relatively moderate pressure and temperature conditions [1]. As with most bio-refinery processes, the fate of the reaction products is dependent on the different interactions that the reactants have with the catalyst surface and the different mechanism of probable fragmentation of the reactants induced by the active sites. It has already been shown that the addition of small percentages of tin to a Ni-Raney catalyst (Ni content > 60%) drastically decreases the methanation reaction, thereby increasing the hydrogen yields in the gas phase products [2]. In addition to the gas phase, these intrinsic characteristics of the chosen active phase also influence the distribution of liquid phase products. The combined and well-directed use of this information, together with an extensive study of the spent catalyst, could lead to a deeper understanding of the chemical-physical mechanisms driving the process, enabling further improvements of the catalyst.

Experimental/methodology

The bimetallic catalysts and their corresponding monometallic references were obtained by impregnations of a $Ce(Zr)O_2$ support obtained hydrothermally by micellar-assisted synthesis, with different weight percentages of Sn and 10 wt.% of Ni. After the reduction pretreatment, the catalysts were processed for the APR reaction that was carried out in a batch "Parr" reactor, with an aqueous solution of ethylene glycol 6 % wt. at a screening temperature of 270 °C, an initial pressure of 20 bars of N_2 at alkaline initial pH. The catalytic products in the gas and liquid phase were analyzed by chromatographic tecniques while the spent catalysts where analyzed by a combination of characterization methods.

Results and discussion



The combined study of gas-phase and liquid-phase carbon products highlights how the choice of active metals and their quantitative combination, drastically affects the fragmentation pathway of ethylene glycol. The presence of a synergistically active support will also lead to of surprizingly good achievements in biomass valorization processes.

Acknowledgments

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PROPOLIS OF THE MEXICAN STINGLESS BEES *SCAPTOTRIGONA MEXICANA*: CHEMICAL COMPOSITION, VARIABILITY, PLANT ORIGIN

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Stingless bees (tribe Meliponini, Apidae), closely related to the common honey bees *Apis mellifera*, consist of over 600 species found in tropical regions. Like honey bees, they produce honey and collect plant resins to produce propolis and cerumen. Propolis is used by the bees as a construction material and to defend the colony from pathogens and predators; it has been also used for centuries in the traditional medicine of indigenous peoples. In Mexico, stingless bee products have important economic, social, and cultural impacts, and *Scaptotrigona mexicana* is extensively managed for the production of honey, pollen, and cerumen/propolis. Studies on stingless bee propolis have revealed enormous variability in chemical composition, depending on bee species, location and season. To investigate this variability, we studied 24 propolis samples from *S. mexicana* collected in two different locations, 12 from each location. GC-MS analysis of the ethanolic extracts after silylation revealed that one group of samples consisted almost entirely of *Mangifera indica* constituents. In the second group, mostly lignans and kaurene type diterpenes were detected, the most abundant of which were isolated and characterised as individual compounds. The latter originate from another, yet unidentified plant source. All propolis samples were tested for antioxidant activity. Further studies are needed in order to identify the new resin source, and determine the bioactivity of these propolis samples.

Acknowledgments: In this investigation GC-MS equipment purchased by Project No BG05M2OP001-1.002-0012, Center of Competence "Sustainable utilization of bio-resources and waste from medicinal and aromatic plants for innovative bioactive products", funded by the Operational Program "Science and Education for Smart Growth" 2014-2020, co-financed by the European Union through the European Regional Development Fund, was used.