

РЕЗЮМЕ НА НАУЧНИТЕ ТРУДОВЕ

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УС „ФАРМАЦЕВТИЧНА ХИМИЯ“, ФАКУЛТЕТ ФАРМАЦИЯ, МУ- ВАРНА

Представени във връзка с участие в конкурс за заемане на академична длъжност „Доцент“ в област висше образование 4. Природни науки, математика и информатика, професионално направление 4.2. Химически науки по специалност „Биоорганична химия, химия на природните и физиологично активните вещества“ – един за нуждите на Факултета „Фармация“, катедрата „Фармацевтични науки и фармацевтичен мениджмънт“, ДВ бр. 36/27.04.2018 г.

I. РАВНОСТОЙНИ НА МОНОГРАФИЧЕН ТРУД ПУБЛИКАЦИИ:

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1. I. Kolev, G. Alexieva, V. Strashilov, I. B. Youssef, F. Sarry, H. Alem. „Layer thickness impact on the capacity of poly(urethaneimide) for sorbing toxic gases” Journal of Applied Polymer Science. 2016, 133(48) p. 44214. DOI:10.1002/app.44214 (IF 3,458)

ABSTRACT: The sensitivity of a thick layer (500 nm) of poly(urethaneimide) to toxic gases such as pyridine and hexamethyleneimine was studied by the quartz crystal microbalance method. The resonant frequency was registered by a spectrum analyzer. The successful overcoming of the unfavorable impact of the increased viscous damping, typical for the standard oscillator measurement method, allowed complete understanding of the behavior of a thick polymer layer toward highly pollutant gases. Quantitative information for polymer adsorption capacity and gas diffusivity was extracted. The comparison with our recent results for thinner layers revealed strong dependence on layer thickness for pyridine whereas the corresponding effect with hexamethyleneimine was found much less significant. Intermolecular interactions and the impact of the gas physical adsorption on the polymer matrix properties were shown as the driving parameters for the sensors response. The thickness dependence provides a tool for tuning the sensitivity of a potentially efficient poly(urethaneimide) sensor for pyridine.

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2. I. B. Youssef, F. Sarry, B. Nysten, G. Alexieva, V. Strashilov, I. Kolev, H. Alem. „Growth and toxic gas sensing properties of poly(urethaneimide) thin films” Talanta. 2016, 153, pp. 145-151. DOI: 10.1016/j.talanta.2016.03.021 (IF 1,860)

Abstract: In this work we present a study on the growth and the gas sensing properties of poly(urethaneimide) thin films. We first deeply characterized by atomic force microscopy (AFM) the nanostructuring of the poly(urethaneimide) holding different amine groups. We further studied the interaction between highly toxic gases such as hexamethyleneimine (HMI) and pyridine and the polymer by using an unconventional method based on Quartz Crystal Microbalance (QCM)

measurement. We showed for the first time that weak interactions, i.e. hydrogen bonding between the gas molecules and the polymer film allow the diffusion of the gas molecule deep in the polymeric film and the recovery of the film once the gas molecules leave the sensor. This first work paves a new way for the design of a completely recoverable sensor able to detect highly toxic gases for environmental concern.

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S. Petrova, **I. Kolev**, S. Miloshev, M. D. Apostolova, R. Mateva

„Synthesis of Amphiphilic [PEO(PCL)₂] Triarm Star-Shaped Block Copolymers: a Promising System for in cell Delivery”

Journal of Materials Science: Materials in Medicine. 2012, 23(5), pp. 1225-1234. DOI: 10.1007/s10856-012-4592-8; PMID: 22415360 (**IF 2,141**)

Abstract: Abstract The paper reports on a simple method of synthesizing [PEO(PCL)₂] triarm star-shaped copolymers by a combination of Michael-addition type reaction and ring-opening polymerization. A Michael-addition reaction yielded a PEO end-capped by two hydroxyl groups - a [PEO(OH)₂] macroinitiator - which was used for sequential building of PCL blocks. The macroinitiator and copolymers were analyzed by FTIR, ¹H NMR spectroscopy and SEC. The self-assembly behavior of the copolymers in aqueous media was studied by UV–Vis spectroscopy. The size and morphology of the obtained micelles were determined by TEM. None of the polymers had cytotoxic effects in vitro. Cellular uptake studies showed the accumulation of neutral red loaded micelles in the perinuclear area of human hepatocellular carcinoma cells revealing a cellular uptake associated with macropinocytosis and caveolae mediated endocytosis. The accumulation had a sustained effect over 3 days pointing at the potential application of the copolymers micelles as a drug delivery system.

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I. N. Kolev, S. P. Petrova, R. P. Nikolova, L. T. Dimowa, B. L. Shivachev

“Synthesis, characterization, and crystal structure of 2-iodo-3,4,5-trimethoxybenzoic acid”

Journal of Molecular Structure. 2013, 1034, pp. 318-324.
DOI:10.1016/j.molstruc.2012.10.039 (IF 1,599)

Abstract: This work describes the synthesis of 2-iodo-3,4,5-trimethoxybenzoic acid. The combination of iodine and silver trifluoroacetate (AgTFA) reagents was used successfully for the iodination of 3,4,5-trimethoxybenzoic acid. To improve the efficiency of the synthetic process a significant modification on the experimental design was also performed. The main structural features of the obtained aryl iodide were investigated by a single crystal X-ray diffraction analysis, FTIR, ¹H and ¹³C NMR spectroscopy.

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5. L. Ivanova, C. Popov, I. Kolev, B. Shivachev, J. Karadjov, M. Tarassov, W. Kulisch, J. P. Reithmaier, M. D. Apostolova

„Nanocrystalline diamond containing hydrogels and coatings for acceleration of osteogenesis“

Diamond and Related Materials. 2011, 20 (2), pp. 165-169.
DOI:10.1016/j.diamond.2010.11.020 (IF 1,913)

Abstract: In the present study, we have compared the effects of ultrananocrystalline diamond/amorphous carbon composite films (UNCD/a-C) and nanocrystalline diamond (NCD) containing hydrogels to support the osteogenesis of endothelial progenitor cells (EPCs). The course of EPCs osteogenic differentiation was followed 21 days and assayed by measuring cell-associated alkaline phosphatase activity, calcium deposition, and expression of fibronectin. We found that EPCs were capable to adhere to both surfaces in flattened and elongated morphology. The attachment and spreading on the UNCD/a-C films were faster as compared to the hydrogels containing NCDs (by day 7), and this was connected with the release and adsorption of fibronectin to the surfaces. During the process of EPCs differentiation, the release of fibronectin was favored by hydrogels+NCD (day 21). The formation of calcium nodules, characteristic of osteoblastic mineralization, was detected by Alizarin Red S staining. Differentiation-induced calcium nodules were detected in EPCs growing on both surfaces. The EPCs cultured on hydrogels containing NCD deposited more extracellular calcium in comparison with those on UNCD/a-C films on day 21. These results were consistent with the data about the alkaline phosphatase activity on the same day and verified that an active EPC transformation to osteoblast phenotype occurred on both substrates. Our results could have direct implications in the use of biomaterials in tissue engineering strategies, and this work might be useful for the improvement of the methodologies for substrate preparation (including scaffolds). Thus both surfaces studied could be used for modification of bone implants (bone-anchoring parts of joint prostheses or bone replacements) in order to improve their integration with the surrounding bone tissue, for which improved cell–substrate adhesion is also needed.

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V. Mavrodinova, M. Popova, I. Kolev, S. Stavrev, Ch. Minchev

„Effect of the preparation conditions of Ni-supported shock-wave synthesized nanodiamond catalysts: FT-IR and catalytic considerations”

Applied Surface Science, 253 (17), 2007, pp. 7115-7123. (IF 1,406)

DOI:10.1016/j.apsusc.2007.02.090; ISSN(Print): 0169-4332

Abstract: On the basis of the results from the FT-IR, XRD and catalytic studies, a suggestion about the mechanism of surface transformations of Ni supported detonation-synthesized ultradispersed diamond and the influence of these transformations on the state of the loaded metal have been made. It was proposed that in dependence on the inert or oxidative atmosphere applied for the elimination of the Ni salt precursor, different interactions of the support with the NiO species have taken place that determined the way of their coordination and stability as well as the dispersion of the metal nickel phase formed upon their reduction. The catalytic activity of the latter has been tested in the reaction of toluene hydrogenation.

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M. D. Popova, Á. Szegedi, I. N. Kolev, J. Mihály, B. S. Tzankov, G. Tz. Momekov, K. P. Yoncheva, N. G. Lambov

„Carboxylic modified spherical mesoporous silicas as drug delivery carriers“

International Journal of Pharmaceutics. 2012, 436 (1-2), pp. 778–785. (IF 3,458)

DOI:10.1016/j.ijpharm.2012.07.061; PMID:22884833; ISSN(Print): 0378-5173

Abstract: The present study deals with the development and functionalization of mesoporous silica nanoparticles as drug delivery platforms. Spherical MCM-41 and SBA-15 silicas

with different pore sizes (2.7 nm and 5.5 nm, respectively) were post-synthesis modified applying a new, two step process. The initial step was the modification with 3-amino-propyltriethoxysilane, and the next was the reaction with succinic anhydride in toluene in order to obtain carboxylic modified mesoporous carriers. The carboxylicfunctionalized mesoporous materials were characterized by XRD, nitrogen physisorption, TEM, ATR FT-IR spectroscopy. The successful carboxylic functionalization was proved by the changes of the zeta potential of the mesoporous materials before and after modification. The parent and the carboxylic-modified MCM-41 and SBA-15 materials showed high adsorption capacity (approximately 50 wt.%, except for nonfunctionalized MCM-41) for sulfadiazine that possesses amino functional groups. Mesoporous structure peculiarities lead to different adsorption capacities on the carriers. In vitro release studies showed slower release rate of sulfadiazine from carboxylic modified MCM-41 and SBA-15 mesoporous particles compared to the non modified ones. Both non loaded and drug-loaded silica materials demonstrated no cytotoxicity on Caco-2 cell line. The functionalized mesoporous systems are appropriate drug delivery platforms due to their biocompatibility and the possibility to modify drug release.

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Iliyan Kolev, Lyudmila Ivanova, Leni Markova, Anelia Dimitrova, Cyril Popov, Margarita D. Apostolova

„Osteoporosis: A look at the future”

(book chapter № 33) in “Osteoporosis” (Dr. Yannis Dionyssiotis, MD, PhD, FEBPRM, ed.), (2012) pp. 667-694, InTech, Croatia, ISBN 978-953-51-0026-3.

Osteoporosis – the commonest age-related skeletal chronic disorder – is characterized by loss of bone mass, alterations of bone micro-architecture, and increased fracture risk. It has, however, received much less attention than most chronic diseases. Osteoporotic fractures are expensive to treat, and cause significant mortality, morbidity, and loss of independence in an ever broader population of patients. As we have said, osteoporosis is a disease in which the mineral density of the bone (BMD) is reduced, its microarchitecture disrupted, and the expression profile of non-collagenous proteins altered. All these factors predispose bones to fractures, particularly the hip, spine and wrist, and are a major cause of disability, severe back pain and deformity. The World Health Organization estimates that approximately 70 million people worldwide have osteoporosis (Penrod J. et al., 2008). The total cost of osteoporosis is difficult to calculate because it includes in-patient and outpatient medical care, loss of working days, chronic nursing-home costs, and medication. The direct costs of osteoporosis arise mainly from the management of patients with hip fractures. Hip fractures also account for 40% of all deaths from trauma in patients over 75, with 68% of all patients not returning to their former level of activity following an osteoporotic hip fractures. The annual worldwide incidence of hip fracture is 1.5 million, a number projected to grow to 2.6 million by 2025 and to 4.5 million by 2050. For these reasons, it is necessary to pay a special attention to these health problems which disturb the quality of life.

Extraordinary progress has been made in the last decade towards the design of implants and scaffolds with a suitable multi-scale hierarchical structure. The limitations of the design of current bone implants arise mainly from the lack of firm quantitative mechanical data of bones in different stages of osteoporosis. Whilst it is known that osteoporotic bone is generally not cancellous in nature and has thin walls, the essential design paradigm of implants does not reflect this application. A simple system for assisted bone repair proposed is the in bone injection of “intelligent” polymers combined with progenitor cells. It utilizes autologous stem cells transplantation in combination with supportive bioresorbable matrices and bioactive molecules for enhancing growth and repair.

Ideally, endothelial progenitor cells obtained from peripheral blood of the same patient may be cultured in vitro in the presence of different stimuli and/or nanoparticles to undergo osteoblasts differentiation, prior to autologous transplantation.

This injectable therapy could also be used for: (1) modifying the bone interior morphology, porosity and interconnectivity, which are extremely important for cell adhesion, proliferation and differentiation; (2) prophylactic treatment for high risk patients to prevent fractures, especially the hip and vertebrae; (3) treatment to stabilize loose prostheses for patients who would soon require revision surgery; (4) providing exceptional repair of the osteoporotic bone by releasing pharmaceuticals to the specific sites with the purpose of accelerating healing, promoting angiogenesis, reducing the risk of infection, etc.

The pursuit of effective treatments for osteoporotic disease is an extremely challenging scientific frontier requiring the integration of multiple engineering, biological, chemical, surgical, and pathophysiology related disciplines. It is also necessary to have a better understanding of molecular and cellular mechanisms specific to osteoporosis. Studying genomics, proteomics and diseases biology in parallel is likely to yield transformative insights in this regard. Our results together with the continuously incoming new data could have direct implications in the use of biomaterials in tissue engineering and in combination with the rapid manufacturing techniques will offer great opportunities to generate different scaffolds for bone engineering in near future.

II. АВТОРЕФЕРАТ НА ДИСЕРТАЦИОНЕН ТРУД:

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Илиян Николов Колев (2011) „Модифициране на зеолит тип MCM-22 с оглед използването му като катализатор за превръщане на алкилароматни въглеводороди“ <http://94.26.42.220/ioh/documents/7/Avtoreferat.pdf>

Дисертационният труд засяга възможностите за контролиране на каталитичната активност, селективност и стабилност на един нов и перспективен материал, зеолит тип MCM-22, с потенциално приложение в основните каталитични реакции на превръщане на метилзаместени ароматни въглеводороди (толуен, ксилени и 1,2,4-триметилбензен). За целта е приложен широк набор от методи за модифициране на състава и структурата на този зеолит, като материалите, получени на негова основа, са изследвани в реакциите диспропорциониране, изомеризация, трансалкилиране и др.

Целта на дисертацията е, посредством прилагане на различни методи за синтез и модифициране на състава и структурните свойства на зеолит MCM-22, да се определят основните фактори, регулиращи каталитичните отнасяния на този тип катализатори в реакции на превръщане на метилзаместени ароматни въглеводороди.

За реализирането на тази цел са поставени следните задачи:

1. Получаване на зеолит тип MCM-22 с различен размер на кристалитите и различен изоморфен състав (съдържание на алуминий, бор и желязо) на кристалната решетка.
2. Синтез на деламинарани зеолити тип MCM-22 и въвеждането им в матрица на мезопорест силикат тип MCM-41 с цел получаване на хибридни микро-мезопорести композитни материали.

3. Оценка на ефекта от модифицирането върху киселинните и структурните свойства на зеолита чрез прилагане на комплекс от различни физикохимични методи.
4. Подбор на подходящи каталитични тест-реакции за превръщане на алкилароматни въглеводороди за оценка на ефекта от различните начини на модифициране на зеолита МСМ-22.
5. Избор на оптимални възможности за модифициране на зеолит тип МСМ-22 с оглед получаване на потенциални катализатори за реакциите диспропорциониране, изомеризация и трансалкилиране на алкилароматни въглеводороди.

Изводи:

1. Синтезът на зеолит тип МСМ-22 проведен в динамични или статични условия, при един и същ състав на реакционния синтез-гел, определя различията в размерите на неговите кристали. Големината на зеолитните кристали от своя страна, оказва значително влияние върху каталитичната активност, селективност и стабилност на този тип материали при превръщането на метил-заместени ароматни въглеводороди.
2. Модифицирането с амониеви катиони на зеолит тип МСМ-22 е необходим етап от получаването на неговата каталитично активна протонна форма. Този тип обработка води до стабилизиране на решетъчните алуминиеви атоми и съхранение на принадлежащите им кисели Брьонстедови центрове.
3. Използваните условия за синтез на частично изоморфно заместен с бор зеолит [Al,V]МСМ-22 осигуряват хомогенно разпределение на борните атоми в неговата кристална решетка. Въведените В атоми не притежават собствена каталитична активност, а основно оказват влияние върху структурните параметри на зеолитната кристална решетка. Намалението на размера и обема на микропорите на модифицирания зеолит предизвиква дифузионни ограничения и позволява да се регулира молекулно-ситовата селективност на получения катализатор по отношение на трите ксиленови изомера-продукти на реакцията диспропорциониране на толуен.
4. С помощта на комбинация от адсорбционни и каталитични методи се доказва, че по-високата дифузионна способност на пара-ксилен и улесненият му масопренос за сметка на другите два изомера в модифицирания с борни атоми зеолит, е причина за повишената селективност по отношение добива на този ценен продукт от реакцията диспропорциониране на толуен. Факторът киселинност не е от съществено значение при определянето на каталитичната активност, стабилност и селективност в този случай.
5. Установено е, че за разлика от немодифицирания и модифицирания с бор зеолит тип МСМ-22, структурният му аналог, съдържащ желязо е носител на значително по-слабо кисели протонни центрове. В сравнение с Al- и V- атоми, решетъчните железни атоми са нестабилни и лесно се трансформират в различни извънрешетъчни железни йони и/или частици. Модификация от този вид е неподходяща за получаване на катализатори за реакции от киселинен тип.
6. Размерът на кристалитите на зеолитния предшественик тип МСМ-22 определя ефективността на процеса деламинаране и структурирането на ламелите, както и способността за формиране на мезопореста силикатна компонента тип МСМ-41 в микро-мезопорести композитни материали. Процесът на деламинаране на предшественика, състоящ се от малки кристали, е по-ефикасен, а получените фини ламеларни частици осигуряват включването на по-малко количество мезопореста фаза в композита.
7. При процесите на деламинаране и синтез на композити тип МСМ-22/МСМ-41, част от локализираните в микропорите на зеолита МСМ-22 Брьонстедови кисели центрове се разрушават и върху повърхността на формираните ламеларни зеолитни модификации се

генерират слабо кисели силанолни групи. Загубата на тези Брьонстедови центрове е причина за понижената каталитична активност на тези материали по отношение на малки по размер алкилароматни молекули (толуен, ксилени). При взаимодействие с по-обемисти молекули (1,2,4-триметилбензен), обаче, увеличеният брой повърхностни силаноли при деламинираните образци и улесненият достъп до тях при композитите, компенсират загубата на каталитични центрове.

Приноси:

- Проведено е системно изследване на основните закономерности определящи каталитичното поведение на зеолитни материали от типа MCM-22, подложени на различни подходи за синтезно и след-синтезно модифициране - вариране размера на зеолитните кристали, изоморфно заместване на решетъчните алуминиеви атоми с различни хетероатоми (бор и желязо), деламиниране и включването им като компонента на композитни материали, съдържащи йерархична порова структура.
- Чрез избор на подходящи по размер алкилароматни молекули е разграничено участието на каталитично активните центрове, разположени в индивидуалните канални системи на зеолита MCM-22 и неговите модификации.
- Конструирано е оригинално измервателно устройство и е разработен метод за определяне адсорбционните и дифузионни свойства на алкилароматни въглеродороди върху зеолитни материали. Прилагането на комбинация от адсорбционни и каталитични изследвания позволи да разграничим влиянието на структурните и киселинни характеристики на зеолитните материали от този тип и индивидуалното им участие в каталитичния процес.

III. НАУЧНИ ПУБЛИКАЦИИ, СВЪРЗАНИ С ПРИДОБИВАНЕ НА ОНС „ДОКТОР”

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M. R. Mihályi, **I. Kolev**, V. Mavrodinova, C. Minchev, M. Kollar, J. Valyon
„Activity and selectivity of zeolite MCM-22 catalysts in the disproportionation of toluene”

React. Kinet. Catal. Lett. 2007, 92 (2), pp. 345-354.

DOI: 10.1007/s11144-007-5209-y (IF 0,584)

Abstract: Zeolite precursor MCM-22 samples were prepared by hydrothermal synthesis. The H-zeolites, obtained from the precursors, were characterized by scanning electron microscopy (SEM), Fourier-transform infrared (FT-IR) spectroscopy, and by their activity in the title reaction. Despite of the lower Brönsted acid site concentration of the zeolite having smaller crystallites, showed higher activity, while the zeolite, having larger crystals were more selective for p-xylene formation.

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R. M. Mihályi, **I. Kolev**, M. Kollár, V. Mavrodinova, Ch. Minchev, T.I. Korányi
„Toluene and 1,2,4-trimethylbenzene conversion on [Al]MCM-22 zeolite partially substituted by boron”

Studies in Surface Science and Catalysis. 2008, 174 (2), pp. 1215-1218.

DOI: 10.1016/S0167-2991(08)80106-1

Abstract: Catalytic activity of [Al]MCM-22 and [Al,B]MCM-22 zeolites were compared in toluene and 1,2,4-trimethylbenzene (TMB) conversions. In both reactions activity was found to be proportional with the Al content of the catalyst. Results indicate homogeneous distribution of boron and/or aluminum in the MCM-22 framework. The [Al,B]MCM-22 zeolite showed higher selectivity for p-xylene formation in the disproportionation of toluene. The improved p-selectivity was attributed to the modified adsorption/diffusion properties affected by the presence of B in the MCM-22 framework.

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I. Kolev, V. Mavrodinova, M. R. Mihályi, M. Kollár

„Comparative catalytic studies on alkylaromatics transformations over [Al]MCM-22 and boron-substituted [Al, B]MCM-22”

Microporous and Mesoporous Materials. 2009, 118(1-3), pp. 258-266.

DOI: 10.1016/j.micromeso.2008.08.036 (IF 2,652)

Abstract: The catalytic performance of [Al]MCM-22 and boron-containing [Al,B]MCM-22 was compared in the conversion of four alkyl aromatic hydrocarbons in view of the impact of their cage/channel pore structure. The contribution of the pore geometry to the observed molecular-sieve effects is discussed on the basis of the XRD, thermal analysis (TGA) of template and coke removal, N₂ adsorption, 11B-MAS NMR and the catalytic test reactions. It was found that the reaction products distribution is thermodynamically or selectively controlled, depending on the type of the pores to which the different feed molecules and reaction intermediates have an access, and on the presence or absence of boron in the framework. The geometric constraints caused by the introduction of framework boron and the framework Al- and B-atoms positioning regulate the product selectivity in these transformations.

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I. Kolev, V. Mavrodinova, G. Alexieva, V. Strashilov

„Pore volume probing of boron-modified MCM-22 zeolite by quartz crystal microbalance assisted study of o- and p-xylene adsorption”

Sensors and Actuators B: Chemical. 2010, 149(2), pp. 389-394.

DOI: 10.1016/j.snb.2010.06.044 (IF 3,370)

Abstract: A quartz crystal microbalance device (QCM) has been developed and tested in the sorption kinetics of o- and p-xylenes over [Al]MCM-22 and boron-modified [Al,B]MCM-22 zeolites. The results have been compared to those obtained by the GC pulse method. The B-modified MCM-22 material exhibits lower rate and capacity towards adsorption of both isomers which is attributed to a decrease in its pore volume and narrowing of the pore openings as a result of the introduction of boron into the zeolite framework.

On the basis of these adsorption measurements suggestions have been made about the impact of the pore topology and the mass-transfer effects on the catalytic behavior of both studied materials. From this point of view the results obtained during transformations of different aromatic hydrocarbons used as test reactants have been discussed.

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M. Kollár, I. Kolev, M. R. Mihályi, V. Mavrodinova

„Transformations of alkyl aromatics over delaminated MCM-22 zeolites and their composites with mesoporous MCM-41 silicate”

Appl. Catal. A. Gen., 2011, 393 (1-2), pp. 59-70.

Abstract: Small (S)- and large (L)-crystalline zeolite MCM-22 precursors with the same Si/AlF ratio of 17, were synthesized and either converted to zeolites MCM-22(S/L) or delaminated. From the delaminated zeolite MCM-22 precursors delaminated zeolites MCM-22 (dl-MCM-22(S/L)) were prepared. Delaminated zeolite precursors were admixed to the synthesis mixture of mesoporous silica MCM-41 to obtain the respective dl-MCM-22/MCM-41(S/L) composite materials. The preparations were characterized by XRD, N₂ adsorption measurements, scanning electron microscopy. FT-IR spectroscopic studies of pyridine (Py) and 2,4-dimethylquinoline (2,4-DMQ) adsorption were used for determination of total (Brønsted and Lewis acidity) and external Brønsted acidity, respectively. It was found that the crystallite size of the MCM-22 precursors strongly influenced the structural, acidic and catalytic properties of the delaminated and composite materials. The effectiveness of the delamination procedure for the zeolite MCM-22(S) precursor having smaller and thinner particles is higher. At same synthesis gel compositions, the amount of mesoporous fraction in the composite materials was different. In dl-MCM-22/MCM-41(S) composite the formation of the mesoporous component was suppressed. Moreover, delamination resulted, for both delaminated and composite materials, in a similar decrease in the Brønsted acidity.

The reduction in toluene disproportionation activity confirmed the above structural and acidity changes. 2,4-DMQ adsorption results proved that both the dl-MCM-22 samples and the composites possess higher amount of external Brønsted acid sites than zeolite MCM-22. The enhanced external acidity and accessibility of the active sites of these preparations appeared favorable when more basic and bulkier reactant, such as 1,2,4-trimethylbenzene was transformed.

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R. M. Mihályi, I. Kolev, V. Mavrodinova, M. Kollár, T. Korányi, Ch. Minchev.

„Effect of the partial substitution of Al by B in MCM-22 zeolite on the selectivity and catalytic activity in toluene disproportionation“

Proc. Int. Conf. “Advanced Micro- and Mesoporous Materials”, (K. Hadjiivanov, V. Valtchev, S. Mintova, G. Vayssilov (Eds.), Heron Press, 2008, pp. 363-371.

ISBN: 978-954-580-239-3

Abstract: A comparative study of the acidity of [Al]-MCM-22 and [Al,B]-MCM-22 zeolites and their catalytic performance in toluene disproportionation has been performed. The acidity of the samples was studied by temperature-programmed ammonia evolution (TPAE) and by FT-IR spectroscopy using pyridine as a probe molecule. It was found that the acid strength of the sites associated with boron and aluminum are significantly different and boron generates weaker acidity. [Al,B]-MCM-22 is catalytically less active but more selective for p-xylene isomer formation than [Al]-MCM-22. Adsorption and mass-transfer effects were suggested to influence the catalytic performance of [Al,B]MCM-22 catalyst.

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I. N. Kolev, S. J. Ivanova

„The unusual behavior of the Gibbs' reagent versus Nitrofurazone”

Scripta Scientifica Pharmaceutica. 2018, 5 (1), pp. 14-19.

DOI: <http://dx.doi.org/10.14748/ssp.v1i1.4996>. ISSN 2367-6000 (print); ISSN 2367-5500 (online)

Abstract: The study covers a new qualitative analytic test (method) for detecting the semicarbazone chemotherapeutic Nitrofurazone. The combination of Gibbs' reagent and ammonia was successfully implemented for analyzing the drug. The main structural features of the obtained color products were determined by UV-VIS spectroscopy.

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Iliyan N Kolev, Nadezhda A Ivanova, Gergana E Alexieva, Gichka G Tsutsumanova, Vesselin L Strashilov

„Diltiazem-loaded Eudragit RS 100 microparticles for drug delivery: the challenge of viscosity”

Scripta Scientifica Pharmaceutica. 2018, Vol. 5 (1), pp. 20-24.

DOI: <http://dx.doi.org/10.14748/ssp.v1i1.5004>. ISSN 2367-6000 (print); ISSN 2367-5500 (online)

Abstract: Strongly shape-dependent viscosity has been found in drug-loaded and “empty” polymeric microspheres (drug delivery systems) made of pharmacopoeial Eudragit RS 100 representative. The dramatically increased viscosity of a layer of spherical particles deposited on the gold electrode surface of quartz resonators from water suspension leads to a large dynamic resistance and inability to sustain stable oscillations in a frequency measuring circuit. The viscosity is also affected by loading the polymer matrix with Diltiazem. Its adverse impact is removed by exposing the deposited layer to acetone vapor leading to “dissolving” the investigated spheres and changing their shape to a thin-layered one.

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V. Strashilov G. Alexieva, P. Petkova, I. Kolev, I. Ismailov, A. Amova, V. Vassilev

„Mid-infrared Optical Spectra of Chalcogenide Glasses from the System As₂Se₃-Ag₄SSe-PbTe”

Comptes rendus de l'Académie bulgare des Sciences 70 (11), 1501-1508, 2017. (IF 0,251) ISSN 1310-1331 (Print), ISSN 2367-5535 (Online)

Abstract: Four glasses from the new chalcogenide system As₂Se₃-Ag₄SSe-PbTe with appropriately chosen compositions are characterized optically by measurements of their mid-infrared absorbance in the range 7500-500 cm⁻¹. These glasses have a wide glass formation region permitting to increase the index of refraction by changing composition. A specific absorption band is found between 3600 and 2500 cm⁻¹ which is attributed to the electronic properties of the additives Ag₄SSe and PbTe. Phonon induced absorption is observed at small wave numbers. Thus a transparency window is established between 6600 and 3600 cm⁻¹ which combined with the considerably high index of refraction in this range is promising for photonic applications.

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V. Mavrodinova, I. Kolev, D. Mitev, S. Stavrev, Ch. Minchev

„Effect of the impregnation procedure for preparation of Ni-supported nanodiamond catalysts for toluene hydrogenation“

Proceedings of the 9th Workshop “Nanoscience & Nanotechnology”, Sofia, Bulgaria; Prof. Marin Drinov Publishing House, Issue 8, 2008, pp. 212-215.

Abstract: Nanodispersed diamond powders isolated from shock-wave synthesized diamond blends by oxidative purification with $K_2Cr_2O_7 + H_2SO_4$ solution have been tested as supports for preparation of Ni-containing (7 wt.%) hydrogenation catalysts. Nickel was introduced by impregnation with different salt precursors, Ni-acetylacetonate (Ni(AcAc)), in chloroform and Ni(NO₃), from water solution. The deposition procedure was carried out either on a dry nanodiamond powder or on its sonicated suspension. The effect of the catalysts preparation on the formation of the active Ni metal phase is followed by XRD and FT-IR spectroscopy. The catalytic activity is tested in the reaction of toluene hydrogenation.

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M. Kollár, R.M. Mihályi, I. Kolev, V. Mavrodinova

„The effect of mesopore formation on the acidity and catalytic behavior of zeolite ZSM-5“

Current Issues in Organic Chemistry, Eds.: K. Hadjiivanov, V. Valtchev, S. Mintova, G. Vaysilov, Heron Press, Sofia, Bulgaria, 2010, pp. 200-210.

Abstract: Zeolite ZSM-5, having hierarchical porous structure, was synthesized applying amphiphilic organosilane as mesopore template. The structure, texture, morphology, and acidity of the obtained material were studied by X-ray powder diffractometric (XRD), scanning electron microscopic (SEM), Fourier transform infrared spectroscopic (FT-IR), N₂ adsorption isotherm, and temperature programmed ammonia evolution (TPAE) methods. The obtained sample was crystalline ZSM-5, having zeolite micropores and intracrystalline mesopores in the 3–10 nm diameter size range. Due to the presence of mesopores only about fifth of the framework Al had tetrahedral coordination. Most of the Al atoms were tricoordinated. The ZSM-5, having the hierarchical micro/mesoporous structure showed lower activity both in toluene disproportionation and in 1,2,4-trimethylbenzene (1,2,4-TMB) conversion than the microporous ZSM-5 reference catalyst. The activity was directly proportional to the concentration of the bridged hydroxyls associated with the tetracoordinated framework aluminum. The conditions that favored the generation bimodal hierarchical porosity were concluded to hinder the development of strong Brønsted acidity.

21

Svetlana Petrova, Iliyan Kolev, Stojan Miloshev, Rosa Mateva

„Amphiphilic PCL-b-PEO diblock copolymers: Synthesis and Characterization“

Journal of University of Chemical Technology and Metallurgy. 2012, 47 (2), pp. 139-146. ISSN 1311-7629 (print); ISSN 1314-3859 (on line)

Abstract: This work describes the synthesis of new biodegradable and biocompatible amphiphilic diblock copolymers based on poly(ϵ -caprolactone)(PCL) and poly(ethylene oxide)(PEO). A series of PCL-b-PEO diblock copolymers with different molecular masses and distribution between hydrophobic PCL and hydrophilic PEO blocks have been obtained via a three-step consecutive reaction. PhNHC(O)O-PCL-OH was first prepared via blocking of the hydroxyl

end group of the PCL chain with a highly reactive phenyl isocyanate (PhNCO). The kinetic behaviour of the reaction was monitored by FTIR spectroscopy. In a second step PhNHC(O)O-PCL-OH was functionalized by hexamethylene diisocyanate (HDI) as a chain extender, forming PhNHC (O) O-PCL-NCO. In the last stage PCL-b-PEO diblock copolymers were successfully synthesized by a reaction of coupling between PhNHC (O) O-PCL-NCO and PEO homopolymers. The course of the reaction was followed by FTIR spectroscopy. The composition and structure of the obtained series of diblock copolymers were assessed by FTIR and NMR spectroscopy, and their mass and dispersity index – by size exclusion chromatography (SEC).

22

Iliyan Nikolov Kolev, Sonya J Ivanova, Mihail K Marinov
„Electrochemical detection of Nitrofurantoin in the presence of sodium amminepentacyanoferrate (II)“

Scripta Scientifica Pharmaceutica 2018, vol5 (2) - Online first,
ISSN 2367-6000 (print); ISSN 2367-5500 (online)

Abstract: The present study deals with the development of a new qualitative electrochemical analytic test for detecting the chemotherapeutic agent Nitrofurantoin. The combination of sodium amminepentacyanoferrate(II) and electric power, provided by a 9V battery, was successfully implemented for the analysis of the medicine in question.

23

V. L. Strashilov, G. E. Alexieva, G. G. Tsutsumanova, I. N. Kolev, I. D. Avramov
„Gas adsorption on ZnO nanowires as studied by surface acoustic wave resonators“
Bulgarian Chemical Communications. 2016, 48 (1), pp. 134-140. ISSN: 0324-1130 (IF

0,238)

Abstract: The sensitivity of ZnO nanowires to gas adsorption has been studied by the surface acoustic wave resonance method. ZnO nanowire aggregates have been deposited on the surface of quartz two-port surface acoustic wave resonators with gold electrodes whose frequency output has been studied for gas sensing activity. High sensitivity combined with selectivity to specific analytes such as ammonia and acetic acid have been found. To exploit the maximum adsorption capacity of the wires, pretreatment with acetic acid has been found necessary. A considerable sensitivity to toxic pyridine and hexamethyleneimine has been separately established. The physical and chemical features of the adsorption processes have been discussed with focus on the inverse effect of gas adsorption on the nanowires sensing efficiency.

Научни публикации в български списания:

24

Sonya Ivanova, Iliyan Kolev
„Chirality through the eyes of a pharmacist“
Academic Journal “INDUSTRIAL TECHNOLOGIES” 2018 vol.5 (1) стр. 156-160.

ISSN 1314-9911

Abstract: Stereochemistry in pharmaceutical research and development is gaining increasing importance due to the fact that the 3D shape of drug molecules affects both their desired biological activity and clinical application.

More than 40 percent of the currently marketed and used medicines are mixtures of enantiomers and/or diastereoisomers. In most cases, single-enantiomer or diastereoisomer formulations can provide greater target selectivity and specificity, improved therapeutic responses and pharmacokinetic properties, and/or reduced side effects than a mixture of their enantiomers or diastereoisomers, respectively.

The current article reviews the nomenclature and chemistry of chiral drug compounds, emphasizing the differences between their biological, therapeutic, and pharmacological actions.

Acquirements in the stereochemistry of drug agents and their pharmacological manifestations will aid the practicing physician and pharmacist in assuring safe and effective drug therapy of his or her patients, and in providing optimal health outcomes.

25

Sonya Ivanova, **Iliyan Kolev**

“Carotenoids – chemistry, analysis, application”

Academic Journal “INDUSTRIAL TECHNOLOGIES” 2018, vol.5 (1) ctp. 161-165.
ISSN 1314-9911

Abstract: Carotenoids are naturally occurring organic pigments which are produced by plants and algae, as well as some bacteria and fungi. There are over 1000 known natural carotenoids with a different chemical composition and distribution. Carotenoids are commonly divided into two major classes - xanthophylls (oxygen-containing carotenoids) and hydrocarbon carotenoids or carotenes. In general, carotenoids absorb photons of green, blue, and violet wavelengths and reflect red, yellow, and orange ones.

In plants and algae, carotenoids serve commonly as compounds - photoabsorbers in the visible range with contribution to the photosynthetic act, and as (photo- and oxido)protectors of chlorophyll.

Today, carotenoids are mainly used in food industry and medicine. Approximately 10% of the carotenoids, consumed as food nutrients, can function as precursors of vitamin A or its functional derivatives. Carotenoids as well as retinoids exhibit a wide spectrum of biological activities. Usually they act as effective antioxidants, inhibitors of malignant tumour growth, inductors of apoptosis, effectors of cell growth, and as modulators of gene expression and immune response.

In this article, we briefly describe both the biological and immunological activities of the main carotenoids, and some of their key toxicological and pharmacopoeial features. A special attention is also paid to the physicochemical properties of some pharmacopoeial carotenoids and their analysis.

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Iliyan Kolev

“Alkenes – chemistry and analysis”

Academic Journal “INDUSTRIAL TECHNOLOGIES” 2018, vol.5 (1) ctp. 166-170.
ISSN 1314-9911

Abstract: Alkenes are unsaturated hydrocarbons containing at least one carbon–carbon double bond.

These compounds are also generically known as olefins or unsaturated hydrocarbons.

Being analytical subjects, alkenes should be put to undisputable qualitative control – a control, which is designed to give full confirmation of their structures in toto or, partially, of their peculiar unsaturated structural elements.

On the whole, the pharmaceutical qualitative analysis is intended to confirm the identity of pharmaceutical raw materials at the so-defined “acceptable” level of security. Thus, a wide variety of color reactions and some other types of identity tests are included in the scope of the so-called “second identification” pharmacopoeial analysis.

In this article, we briefly describe the qualitative analysis of a wide variety of olefins. Attention is also paid to the chemical reactivity of some pharmacopoeial representatives.

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Svetlana Georgieva, Nadya Agova, Pavlina Koseva, Silvia Stamov, Iliyan Kolev
“Alternative therapy for the treatment of Acne vulgaris”

Academic Journal Management and Education. 2018, Vol. XIV (5) “HEALTHCARE”,
стр. 132-137. ISSN 13126121

Abstract: Acne is one of the most common skin condition in the world. Acne is most prevalent during puberty, and it is often mild, tending not to last far beyond adolescence. In some cases, acne can last years beyond puberty; while untreated acne lasts around five years before dissipating, some deal with acne well into adulthood. Acne most often affects the face, but it may spread to involve the neck, chest and back, and sometimes even more extensively over the body. Treatment of acne vulgaris should be directed toward the known pathogenic factors, including follicular hyperproliferation, excess sebum, bacteria Cutibacterium (Propionibacterium) acnes, and inflammation. The most appropriate treatment is based on the grade and severity of the acne. More and more patients, however, are seeking alternative approaches to the treatment of acne. This is provoked both by the numerous side effects and prolonged intake of medications accompanying systemic acne therapy, as well as by the increasing resistance of P. acnes.

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Svetlana Georgieva, Iliyan Kolev, Sylvia Stamova, Nadya Agova, Pavlina Koseva
“Biological activity of nitroimidazoles: past and future”

Academic Journal Management and Education. 2018, Vol. XIV (5) “HEALTHCARE”,
стр. 138-147. ISSN 13126121

Abstract: Nitroimidazoles are class of the therapeutic drugs used mainly in the treatment of infections caused by susceptible organisms, particularly an aerobic bacteria and protozoa. Nitroimidazole are therefore important in the treatment of intra-abdominal and gynecologic sepsis, abscesses and tetanus. They are also an important component of prophylactic regimens for surgical procedures where contamination with anaerobic flora is likely. Nitroimidazoles are used to treat bacterial vaginosis (frequently associated with G. vaginalis) and dental infections, including acute necrotizing ulcerative gingivitis (Vincent's angina). Nitroimidazoles are also a component of modern triple eradication regimens for H. pylori. The large number nitroimidazole drugs are in use today. Some 5-nitroimidazole derivatives such as metronidazole, tinidazole, secnidazole and azomycin have been used long time for severe cases of infections. 2-nitroimidazoles play an important role as bioreductive markers for tumor hypoxia, as radiosensitizers and some are also known to demonstrate antiprotozoan activity. In this literature review, we will present new perspective of nitroimidazole derivatives in the future.

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Pavlina Koseva, Svetlana Georgieva, Nadya Agova, Silvia Stamova, Iliyan Kolev
“Graves' disease – symptoms, diagnosis, treatment and prognosis”

Abstract: Graves' disease is an immune system disorder that results in the overproduction of thyroid hormones (hyperthyroidism). Because thyroid hormones affect a number of different body systems, signs and symptoms associated with Graves' disease can be wide ranging and significantly influence overall well-being. Common signs and symptoms of Graves' disease include anxiety and irritability; a fine tremor of hands or fingers; heat sensitivity and an increase in perspiration or warm, moist skin; weight loss, despite normal eating habits; enlargement of thyroid gland (goiter); change in menstrual cycles; erectile dysfunction or reduced libido; bulging eyes (Graves' ophthalmopathy); thick, red skin usually on the shins or tops of the feet (Graves' dermopathy) and rapid or irregular heartbeat (palpitations). Although Graves' disease may affect anyone, it's more common among women and before the age of 40. The health care provider may suspect Graves' disease based on symptoms and findings during a physical exam. One or more blood tests can confirm hyperthyroidism and may point to Graves' disease as the cause. Other clues that hyperthyroidism is caused by Graves' disease are an enlarged thyroid; signs of Graves' eye disease, present in about one out of three people with Graves' disease and a history of other family members with thyroid or autoimmune problems. If the diagnosis is uncertain, the doctor may order further blood or imaging tests to confirm Graves' disease as the cause. To determine whether the thyroid is functioning properly, testing may begin with Thyroid-stimulating hormone (TSH) — typically low in Graves' disease; Free T4 — usually elevated and Free and Total T3 — often elevated. The above tests may also be ordered periodically to monitor thyroid function and hormone production. Laboratory tests used to help diagnose Graves' disease and distinguish it from other autoimmune conditions may include the presence of thyroid antibodies: Thyroid stimulating immunoglobulin (TSI) — presence of this antibody is diagnostic for Graves' disease; Thyroid stimulating hormone receptor antibody (TRAb) — less specific than TSI and Anti-thyroid peroxidase antibody (anti-TPO). There are three treatment options: medicine, radioiodine therapy, and thyroid surgery. Early diagnosis and treatment of Graves' Disease is essential, as it can have adverse effects on heart function, bone structure and the eyes.

Abstract: В обзора са представени биоактивни материали като биоактивни стъкла и стъклоке-рамики при взаимодействието им с разтвори симулиращи телесна течност (SBF). Обърнато е по-специално внимание на факторите повлияващи разтварянето и на биологичните ефекти, до които водят отделените йонни продукти. Разглеждането на тези материали е свързано с бъдещи изследвания и установени специфични нужди в развиващото се поле на регенеративната медицина.

The main objective of this review is to present the reactions between sol-gel glasses and glass-ceramics with Simulated Body Fluid (SBF). Attention has been given to the factors influencing the ions release kinetics and the biological effects resulting in ions releasing products. The current review also presents the specific effect of the released ionic dissolution products on human cell behaviour. The review of these materials is presented with intention for future

investigations and identification for specific research needs to advance the field of regenerative medicine.

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Pavlina Koseva, Iliyan Kolev

„IODINE BASED RADIOLOGIC CONTRAST AGENTS IN IMAGING DIAGNOSTIC“

Academic Journal Management and Education. 2017. vol. 13. book 5 “HEALTHCARE”. стр. 160-167. ISSN 13126121

Abstract: Diagnosis is a crucial element of the therapeutic process. Medical diagnostic procedures are using different methods to define the diseases. Imaging diagnostic include procedures that use special x-ray equipment to create detailed pictures of difficult-access areas inside the body. X-rays are a form of electromagnetic radiation with wavelengths in the 0.01 nm and 10 nm range. Radiologic contrast materials, also called radiologic contrast agents or contrast media, are often used in medical imaging, especially in x-ray based imaging techniques, to enhance image contrast, therefore improve diagnosis quality. Radiologic contrast compounds are not dyes that permanently discolor internal organs, they are substances that change temporarily the way x-rays or other imaging tools interact with the body structures and their appearance on the images and help distinguish or “contrast” selected areas of the body from the surrounding tissue. Among other criteria, a good contrast media must have the highest attenuation coefficient (radiopacity). They can have a chemical structure that includes iodine, a naturally occurring chemical element. The four major classes of iodinated contrast agents are as follows: (i) ionic monomer - a single tri-iodinated benzene ring with a carboxylate containing benzene substituent; (ii) ionic dimer - two linked tri-iodinated benzene rings wherein at least one carboxylate-containing group in the benzene ring is substituted; (iii) nonionic monomer - a single tri-iodinated benzene ring without a carboxylate-containing benzene substituent and (iv) nonionic dimer – two linked tri-iodinated benzene rings that do not contain a carboxylate functional group within any benzene substituent. A wide variety of reagents has been reported as very efficient catalysts for synthesis of iodinating aromatic compounds. The most used are: $I_2 - CF_3CO_2Ag$ and $C_2F_3IO_2$. In these cases, the iodine or iodine-containing source is used in a combination with a strong activating agent in order to create an efficient iodinium donating system.

Научни публикации, публикувани в рецензирани сборници на научни звена или в сборници от проведени научни форуми в български списания

32

Илиян Н. Колев

“Получаване на метилови деривати на флавоноидни съединения”

Сборник научни трудове “Природни науки - 2003”, Университетско издателство „Епископ Константин Преславски“, Шумен, 81-84 (2003). ISBN 954-577-161-5

Abstract: Flavonoids compounds are important class phenolic compounds that are synthesized by plants of the so-called second synthesis. The flavonoid compounds play an important role in different biochemical pathways of living creatures. The explored of possible transformation

by means of different methods, for example methylation in artificial conditions when we have chemical synthetics. This explore creates possibilities for clarifying the probable transformations of these compounds in plants, animals and human being and their participation in important processes.

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Т. Д. Живкова, И. Колев, Д. Якимов, Й. Тачева

“Изследване на някои видове *Artemisia* за флавоноиди”

Сборник научни трудове “Природни науки - 2003”, Университетско издателство „Епископ Константин Преславски“, Шумен, 2003, pp. 117-120.

ISBN 954-577-161-5

Abstract: Flavonoids compounds are important class phenolic compounds that are synthesized by plants of the so-called second synthesis. In present work study quantity the flavonoid and spectrum in species *Artemisia*.

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Т. Д. Живкова, Д. Якимов, И. Колев

“Въздействие на фенолни вещества извлечени от род *Artemisia* върху началния темп на растеж на лен и салата”

Сборник. Доклади на национална конференция „Семеипроизводство, селекция и семеконтрол за качествен посевен материал“. София, 2004, pp. 187-195.

Abstract: In this paper was examined the influence of water extracts from 3 species of mugwort *Artemisia vulgaris*, *Artemisia absinthum*, *Artemisia pedemontana*, such as fenolic extracts taken from *Artemisia pedemontana*, into the first rate of growing. They are applied in different concentrations. The germination energy of seeds from *Linum sp.* is smaller, than the control, which the influences of water extracts. The germination energy of seeds from salad, the energy become bigger with 50%. The water extracts are getting smaller the seeds of salad and the fenolic extracts become her bigger with 50%. The germination energy become smaller from the water extract and the fenolic fractions doesn't make influence with them. The first growing of the column of *Linum sp.* Is stimulated from the eteric fraction. The growing of the racin of the seeds from salad is stimulated by etil-acetate fraction.