vol. 11, issue 2, 2015 (suppl. 1) ISSN 1734-1922 eISSN 1896-9151 bimonthly www.archivesofmedicalscience.com

Archives of Medical Science

April 2015

AMS

11th Warsaw International Medical Congress for Young Scientists

May 7-10, 2015

11TH WIMC
11TH WARSAW INTERNATIONAL MEDICAL CONGRESS

Abstract book

Students' Scientific Association
of the Medical University of Warsaw

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25 mg/kg it can increase the resistance in experimental mice to exogenic hypoxia with hypercapnia by 128% and in dose 50 mg/kg the resistance increases up to 279% compared to those experimental animals that do receive the pharmacological protection.

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Pharmacological profile of a new xanthone derivative with antidepressant-like properties

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Introduction: Depression is nowadays a serious global illness among mental disorders. It is assumed that until 2020 year it will be the second most commonly diagnosed ailment in the world after ischemic heart disease only. Moreover limited efficacy and numerous side effects of current antidepressant drugs are the reasons for searching new chemical compounds as potential antidepressants.

Aim of the study: The aim of this study was to determine potential antidepressant-like activity, possible mechanism of action and the influence on cognitive and motor function of a new xanthone derivative HBK-7, which in previous studies showed a high affinity for serotonergic 5HT1A receptors.

Material and methods: The forced swim test (FST) in mice was conducted to determine potential antidepressant-like activity and locomotor activity test was performed to verify the obtained results. Step-through passive avoidance and rotarod tests were used to evaluate the influence on cognitive and motor function, respectively. The effects of joint administration of sub-effective doses of HBK-7 and fluoxetine, reboxetine or bupropion as well as pretreatment with p-chlorophenylalanine or WAY-100635 on antidepressant-like activity of HBK-7 in FST in mice were investigated to define the possible mechanism of action of the compound.

Results: HBK-7 at the dose of 10 mg/kg showed significant antidepressant-like activity in FST in mice, comparable to mianserin, and the observed effect was specific. Furthermore, at antidepressant-like dose HBK-7 did not influence cognitive and motor function. Combined treatment with sub-effective doses of HBK-7 and fluoxetine reduced immobility in FST, whereas combination with reboxetine and bupropion showed no effect. Pretreatment with p-chlorophenylalanine and WAY-100635 completely antagonized the antidepressant-like effect of HBK-7 in FST.

Conclusions: The obtained results confirm antidepressant-like activity of HBK-7, which is comparable to mianserin. Moreover, the tested compound did not impair long-term memory and motor coordination at the active dose. It is most likely that the compound mediates its effect through serotonergic system and especially serotonergic 5HT1A receptors. Given the promising results, HBK-7 may have potential in the treatment of depression, so studies on this compound should be continued.

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Heavy metals content in *Spirulina* and *Chlorella* supplements available on Polish market

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Introduction: *Spirulina* and *Chlorella* are the microalgae growing naturally in the sea waters of warm climates. Nowadays they are grown worldwide for the commercial purpose. These microscopic plant organisms are the unique source of nutrients like proteins, balanced fatty acids, minerals and antioxidant vitamins. Thus they are more and more commonly consumed as an alternative for the synthetic supplements. It has been proved that algae have ability to absorb metals direct form water. As a result of this fact algae reflect metal concentration in water, in some cases we can observe several thousand times higher metal concentration in algae than in the water. This phenomenon of bio-accumulation of heavy metals may cause long-term negative effects on human health. Since the algae are regarded as superfoods, almost no one is aware of the potential health hazard.

Aim of the study: This aim of the study was to estimate the safety of the algae supplementation regarding to heavy metals contents. The study concentrated on products available on Polish market.

Material and methods: Concentrations of heavy metals was determined in 20 organic and 12 non-organic *Spirulina* and *Chlorella* supplements in the

form of powder, tablets, flakes, which were bought at online shops and pharmacies. Each of products was digested prior the analyses. Concentration of metals were determined by Inductively Coupled Plasma Mass Spectroscopy (ICP-MS).

Results: The results shown that in the case of three organic supplements, the recommended dosages result in exceeding the acceptable daily intake of Pb up to 30%. Moreover, for three supplements we noted the relative high concentration of Cd responding to about 30-90% of the maximum level of the daily intake.

Conclusions: Considering the content of heavy metals in the studied supplements, we conclude that they cannot be recognized as generally safe. Moreover, the organic food also gives no guarantee of low levels of heavy metals. The high supplements consumption might results in exceeding the acceptable daily intake of heavy metals and health problems. Thus, our results are the further argument for the need of more strictly controlling of the supplements market.

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The MIC and sub MIC concentration of antibiotics interfere with biofilm formation by *Staphylococcus epidermidis*

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Introduction: *S. epidermidis* possess polysaccharides and adhesion protein factors which provide special ability to construct biofilms in the host tissues. Biofilm enabling bacteria attachment on biomaterial surfaces, immune avoidance of host defenses and survival to common medical antibiotic therapy.

Aim of the study: The aim of this investigation was to assess the effects of antibiotics at a MIC and sub MIC concentrations on the capability to form biofilm by *S. epidermidis* to polystyrene surface.

Material and methods: The research was done into *S. epidermidis* strains isolated from 51 materials taken from hospitalized patients (UDSK, Białystok). Bacteria were identified on the basis of: inoculation on Blood Agar, Chapman Agar (OXOID), catalase test, coagulase test, API Staph (bioMerieux) biochemical test. To further steps of experience isolates characterized by good adhesion and biofilm formation to polystyrene surface were qualified (6 strains of *S. epidermidis*). The quantitative method of micro-dilution in liquid medium Mueller-Hinton were used to establish of MIC and subMIC concentrations of antibiotics. The following antibiotics were used: β-lactams – amoxicillin with clavulanic acid and cefuroxime (OXOID). Evaluation of the adhesion of *S. epidermidis* to the surface and the effects of antibiotics on biofilm formation was determined by microcalorimetric reduction of TTC method (by Richards et al., in our own modification). The assessment was done visually and quantitatively by measuring the absorbance.

Results: The MIC values of amoxycillin and clavulanic acid against *S. epidermidis* were in the range 0.12 to 32 mg/l and MIC values of cefuroxime were from 0.25 to 128 mg/l. The both of the tested antibiotics at concentrations of subMIC and MIC added to a suspension of planktonic inhibited biofilm formation. Amoxicillin with clavulanic acid at a concentration of subMIC are able to modify biofilm in 40.6%, while at a MIC concentration in 21.1%, whereas cefuroxime respectively 12.2% and 48.1%. Among used antibiotics no significant difference was noted in reduction of biofilm compared to control samples.

Conclusions:

1. β-lactam antibiotics (amoxycillin with clavulanic acid, cefuroxime) at a concentration of subMIC and MIC inhibited the process of the formation of biofilm by *S. epidermidis* to polystyrene surface.
2. β-lactam antibiotics (amoxycillin with clavulanic acid, cefuroxime) at a concentration of subMIC and MIC have not caused a reduction of biofilm produced by *S. epidermidis*.

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An NMR study of leflunomide and the interactions of teriflunomide within the receptor cavity – energy calculations

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Introduction: Leflunomide is a drug with anti-inflammatory and immunosuppressive properties, currently used for the treatment of rheumatoid arthritis. Its active metabolite, teriflunomide, is responsible for the biological activity of lefluno-

properties and SERT, NET and DAT inhibition affinity. Selection of compounds best suited for synthesis.

Material and methods: The study included sertraline derivatives containing secondary amine group in position 3' toward 4-(1,2,3,4-tetrahydronaphthalen-1-yl)-1,2-dichlorobenzene. These type of compounds bind to monoamine transporters in protonated form, therefore proton affinity was calculated by quantum methods, using Density Functional Theory (DFT), B3LYP functional and 6-31G* basis set, in Spartan '10. Physiochemical properties, such as logP, were calculated in Discovery Studio 2.5. In order to choose compounds best inhibiting SERT, NET and DAT, molecular docking was performed in the same programme, with Flexible Docking protocol and CHARMm force field. Models of the transporters were based on *Drosophila melanogaster* DAT template, the most related protein with known tertiary structure.

Results: The study concluded with appointing stable protonated compounds with lowest energy. Docking of chosen derivatives allowed to obtain most privileged complexes of protonated compounds with transporters and their binding energies. Calculating physiochemical properties gave insight in bioavailability.

Conclusions: All the results gathered led to selection of derivatives best suitable for synthesis due to their properties. Computational studies allow to evaluate designed structures and their affinity towards target proteins before synthesis. It reduces costs, time and simplifies process of searching new drugs.

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Development and validation of LC-MS/MS method for quantitative analyses of p-cresol sulfate and indoxyl sulfate in human saliva

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Introduction: p-Cresol sulfate (pCS) and indoxyl sulfate (IS) are uremic toxins, which in 90% occur in blood plasma in form bound to proteins. These substances are biologically active. Furthermore physiologically almost completely eliminate by kidneys. However in case of chronic kidney disease, accumulation of these compounds result in metabolic disorders and lead to condition called "ureamia". Concentration of these substances in serum correlate with the stage of renal failure and is related to increased risk of e.g., cardiovascular diseases. Saliva as a diagnostic material has huge advantages like accessibility and ease collection. Saliva examination could be an alternative to blood test, which are commonly burden to patients. Moreover collecting of the saliva may be performed in whereabouts of patient and next deliver to laboratory. Currently there are no method of determination of pCS and IS in human saliva.

Aim of the study: p-Cresol sulfate (pCS) and indoxyl sulfate (IS) are uremic toxins, which in 90% occur in blood plasma in form bound to proteins. These substances are biologically active. Furthermore physiologically almost completely eliminate by kidneys. However in case of chronic kidney disease, accumulation of these compounds result in metabolic disorders and lead to condition called "ureamia". Concentration of these substances in serum correlate with the stage of renal failure and is related to increased risk of e.g., cardiovascular diseases. Saliva as a diagnostic material has huge advantages like accessibility and ease collection. Saliva examination could be an alternative to blood test, which are commonly burden to patients. Moreover collecting of the saliva may be performed in whereabouts of patient and next deliver to laboratory. Currently there are no method of determination of pCS and IS in human saliva.

Material and methods: Material used in this study was saliva, which was collected from healthy people and next pooled into one sample. After sample cleanup, concentrations of uremic toxins were determined using the mass spectrometer QTRAP®4000 (AB SCIEX, Framingham, Massachusetts, U.S.). The validated procedure was used for determination of p-CS and IS in the real samples.

Results: Full validation (according to European Medicines Agency (EMA)) based on e.g.: determination of linearity, precision (repeatability), accuracy, stability of analyzed substances, lower limit of quantification and limit of determination, and matrix effect was performed. The method meets all criteria of validation and was tested on the real samples with the satisfactory results.

Conclusions: This researches and analysis of results show, that our new, accurate and sensitive LC-MS/MS method for determining concentration of p-cresol sulfate and indoxyl sulfate in human saliva is proper for this purpose.
