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The effect of strontium ions fertilization on isoflavones content in Glycine max (L.) Merr.

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Soy (*Glycine max* (L.) Merr.) is an annual plant cultivated worldwide mostly for high-quality food. Moreover, due to its pharmacological properties it is widely used in pharmacy for alleviating the symptoms of osteoporosis. Numerous literature data suggest that isoflavones, the major phenolic compounds present in soy, protect against post-menopausal osteoporosis associated with endogenous estrogen deficiency [1]. On the other hand, strontium salts have shown unique pharmacological effects on bone resorption and formation [2, 3].

The aim of our paper was investigation the influence of strontium ions fertilization on isoflavones content in Glycine max. Our research can be useful to obtain herbal preparations containing both phytoestrogens and strontium to prevent postmenopausal osteoporosis.

The analysis of isoflavones was performed by HPLC-DAD method; the content of strontium in plant depending on its concentration in growth media was determined by flame atomic absorption spectrometry (High-Resolution Continuum Source atomic absorption spectrometer ContrAA 700).

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The biological activity of quinoline derivatives

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Compounds containing quinoline moiety are well known due to their broad biological activities. A number of them have been widely investigated and clinically used as antifungal or antibacterial agents [1, 2]. Quinoline derivatives have gained strong attention recently due to their activity as perspective HIV integrase inhibitors [3]. Recently, some quinoline-based compounds have been synthesized and reported as potent antitumor agents by our research team [4]. Antiproliferative activity of the synthesized compounds was tested by the MTS assay against the human colon adenocarcinoma cell lines with normal expression of p53 protein (Hct116 p53+/+) and mutants with disabled TP53 gene (Hct116 p53-/-). The compounds were also tested for their cytotoxicity against mouse melanoma cell line B16-F10 and nontumor cell line NHDF. Anti-proliferative activity of quinoline derivatives was determined. Compound (Figure 1) demonstrated the highest anti-proliferative activity (**IC_{50}=1,40μM**). The most active compound makes it promising for further development.

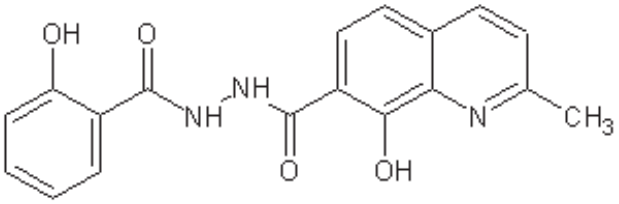

Figure 1. Chemical structure 8-hydroxy-*N*'-(2-hydroxybenzoyl)-2-methylquinoline-7-carbohydrazide.

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Rational design and synthesis of new 5-HT_6R ligands with the use of bioisosteric strategies. Crystal structures, biological evaluation and molecular modeling studies.

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The 5-HT_6 receptor, which is localized practically only in the brain [1] is a promising target for different new psychotropic drugs. 5-HT_6 receptors are supposed to be responsible mainly for motor control, memory and learning and its antagonists can be used to improve cognitive and memory functions in cognitive impairments [2, 3, 4] and also as an antiobesity drugs [5, 6]. Up to date several thousands of structurally diverse ligands have been synthesized but their binding mode has not been fully identified.

During virtual screening campaign for the search of novel 5-HT_6R

ligands, a 3-fold less active bioisostere of literature compound [7] was found. A series of its isosteres was synthesized in an attempt to increase affinity. One of this compounds proved to be 10-times more potent than the parent one. Crystal structures and molecular modeling studies justified structure-activity relationship.

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Development and validation of the GC method for quantitative determination of semi-volatile solvents in pharmaceutical substance Bosentan

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Bosentan is an active substance in the orphan drugs used to treat pulmonary artery hypertension (PAH). It is a dual endothelin receptor antagonist (ERA) with the affinity for both receptors of the A and B: endothelin-A (ETA) and endothelin-B (ETB). Under normal conditions, ETA or ETB receptors cause constriction of the pulmonary blood vessels. By blocking this interaction, bosentan decreases pulmonary vascular resistance [1].

The new gas chromatography method with direct-injection for quantitative determination of residual semi-volatile solvents such as acetic acid, dimethyl sulfoxide (DMSO) and ethylene glycol in bosentan - the pharmaceutical active substance has been developed and validated. The optimization of the method consisted in the selection of experimental conditions that allowed to meet the requirements for this procedure, including:

- The appropriate level of detection limit (LOD) of analytes, in particular for ethylene glycol,
- The stability of determination - decomposition peak of Bosentan were observed depending on the temperature of the injector,
- The appropriate specificity of the method between all solvents used in the synthesis of Bosentan
- The appropriate range of the determination which includes 10 - 120 % of specified limits of residual solvents. According to the Guideline Q3C (R5) 11 [2] acceptable limits (maximum allowable limit) of ethylene glycol is 620 ppm, acetic acid 5000 ppm and DMSO 5000 ppm in respect to sample preparation.

The developed method was validated according to the requirement of ICH (International Conference of Harmonization) validation guidelines Q2R1 [3]. Specificity, precision, accuracy, linearity, limits of detection and quantitation and robustness were determined and excellent results were obtained.

Acknowledgements:

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Synthesis of new piroxicam derivatives and their influence on lipid bilayers

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Modification of the surface properties of membranes by any ligand could lead to several phenomena like aggregation, leakage of trapped contents or permeabilization, fusion, etc. Such modulation of surface properties is a fundamental requirement for many biological processes [1]. In this work, we present the synthesis and interaction of new piroxicam derivatives with model lipid bilayers.

The starting material for the synthesis of the above mentioned compounds was 1,1-dioxo-1,2-benzothiazol-3-one (saccharin). It was condensed with 2-bromo-4'-fluoroacetophenone in dimethylformamide (DMF) in the presence of triethylamine giving 1,1-dioxo-2-(4-fluorophenyl)acetyl-1,2-benzothiazol-3-one, which was then rearranged to the corresponding 1,2-benzothiazine ring. The final compounds were prepared by alkylation of corresponding 1,2-benzothiazine with 4-aryl/heteroaryl-1-(2-chloroacetyl/3-chloropropyl)piperazine giving four new structures (PD 28-31). The separated products were purified by the crystallization from ethanol. The structures of the compounds obtained were confirmed by elemental and spectral (IR, H^1NMR) analyses.