

istein for several days. Moreover, genistein was reported to cross the blood-brain barrier in rats with efficiency of several percent after intravenous administration. It is of our interest to find out if any other natural isoflavones (e.g. daidzein, kaempferol, apigenin, naringenin) or genistein synthetic derivatives reveal inhibitory effects on GAGs synthesis, combined with a relatively high potential in blood-brain barrier penetration, especially in mucopolysaccharidosis IIIA and IIIB fibroblasts, as severe neurological injury is observed in these MPS types. We tested 20 synthetic genistein derivatives with MPS III human fibroblast cultures and 5 of them, presenting the highest inhibitory effect on GAG synthesis (similar to genistein or even higher) were chosen for further experiments. In conclusion, it appears that gene expression targeted isoflavone therapy (GET IT), based on administration of specific natural isoflavones or genistein synthetic derivatives, may potentially be an effective treatment of MPS III patients.

17:40 Poster I-68

THE BIOLOGICAL TARGET DERIVED PHARMACOPHORIC MODEL FOR 5-HT₇ SEROTONIN RECEPTOR ANTAGONISM

Marcin Kołaczowski¹, Mateusz Nowak², Maciej Pawłowski¹, Andrzej J. Bojarski²

1. Jagiellonian University, Collegium Medicum, Department of Pharmaceutical Chemistry, Medyczna 9, Kraków 30-688, Poland **2.** Polish Academy of Sciences, Institute of Pharmacology, Department of Medicinal Chemistry, Śmętna 12, Kraków 31-343, Poland

E-mail: mkolacz@if-pan.krakow.pl

The biological target derived pharmacophoric model is presented for 5-HT₇ serotonin receptor antagonism. It was generated based on results of automated docking of examples of all known antagonists classes to the conformational ensemble of rhodopsin based receptor models. The methodology reflects conformational flexibility of both ligand and receptor. Current pharmacophoric model is divided into two sub-models: (1) "affinity" model - including features common for all (nonselective and selective) antagonists; (2) "selectivity" model - explaining which pharmacophoric features are responsible for selectivity toward 5-HT₇ receptor. Nonselective antagonists, described by the model (1), are situated along TM3, occupying the cavity formed by TMHs 4-6 and interacting specifically with Asp3.32, Phe6.61, Phe6.62, Ser5.42 and optionally Phe3.28, Tyr7.43. Selective antagonists form the network of interactions with the residues from TMHs 3 and 7: Asp3.32, Phe3.28, Tyr7.43 and Arg7.36 and optionally Phe6.61, Phe6.62. It is postulated that if the latter interaction pattern dominates over the former one, selectivity toward 5-HT₇ receptor is enhanced.

Acknowledgement

This study was partially supported by the research Grant no. 012/2002 from the Polish Pharmacy and Medicine Development Foundation, given by the POLPHARMA Pharmaceutical Works.

17:40 Poster I-69

SYNTHESIS AND SEROLOGICAL INTERACTIONS OF H.PYLORI UREASE FRAGMENT 321-339 IMMOBILIZED ON THE CELLULOSE SUPPORT

Beata Kolesińska¹, Sebastian Grabowski², Wiesław Kaca^{2,3}, Zbigniew J. Kamiński¹

1. Technical University of Łódź, Institute of Organic Chemistry (PL), Żeromskiego 116, Łódź 90-924, Poland **2.** University of Łódź, Department of Infectious Biology, Inst. of Microbiol. and Immunol., Łódź 90-237, Poland **3.** Akademia Świętokrzyska im. Jana Kochanowskiego, Świętokrzyska 15, Kielce 25-406, Poland

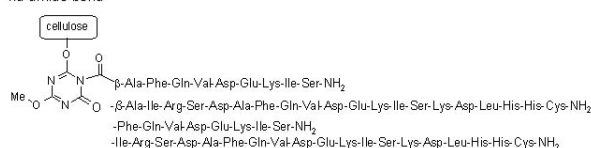
E-mail: kolesins@p.lodz.pl

H. pylori is a major etiological agent of gastroduodenal ulcer diseases. One of the significant pathogenic factor of *H. pylori* is urease production and anti-urease antibodies might be responsible for inflammatory reaction proceeding atherosclerosis [1,2].

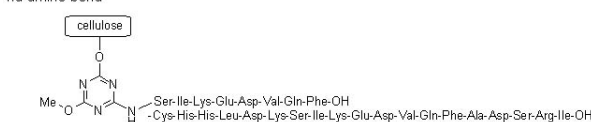
In order to study the recognitions of *H.pylori* UreB epitopes by sera of atherosclerosis patients we prepared 321-339 urease fragments attached to the cellulose plate with N-terminus as well as with C-terminus.

The F8 epitope: SIKEDVQF and UB-33 epitope: CHHLDK-SIKEDVQFADSRI [3] were synthesized directly on the cellulose plate by using triazine based condensing reagent [4].

via amide bond



via amine bond



via ester bond



The peptides were treated with sera of patients with medically confirmed arteriosclerosis and then with anti-human antibodies labelled by horse-radish peroxidase HRP, followed by ad-