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Quinolinesulfonamides as potential 5-HT$_7$ and 5-HT$_{1A}$ receptor ligands

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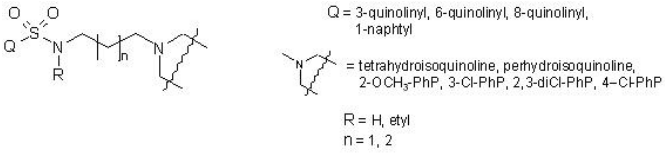
In the recent years a number of studies have been taken to evaluate the role of 5-HT$_7$ receptors. Of particular interests are the facts that several antidepressant and antipsychotic drugs show high affinity for the 5-HT$_7$ receptors.[1] Moreover, the blockade of these receptors potentiates the effect of antidepressants.[2] These observations placed 5-HT$_7$ receptors as potential target for the development of antidepressant agents.

Up to date a number of compounds have been found to bind to 5-HT7 receptors. One of the class of ligands are arylsulfonamides connected by the three or four methylene groups spacer with 4-substituted tetrahydropirydine, 1-arylpiperazine or tetrahydroisoquinoline fragments. Because these structural features are common with other G-coupled receptors ligands, mainly 5-HT$_{1A}$ ones, searching for the new 5-HT$_7$ ligands raises the problem of selectivity.

As a part of our ongoing project to identify new compounds with potential antidepressant activity, we designed series of azinesulfonamides containing different tertiary amines.



Herein, we disclose their synthesis and preliminary biological evaluation as 5-HT$_{1A}$ and 5-HT$_7$ receptor ligands. Starting azinesulfonylchlorides were synthesized according to the previously reported method.[3]

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Antiproliferative activity of novel synthetic genistein glycoside derivatives

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Genistein, a naturally occurring soy isoflavonoid, displays antitumor, antioxidant and antiinflammatory properties. It inhibits the activity of topoisomerases and several protein-tyrosine kinases. Genistein is capable of binding to the estrogen receptor. These activities, along with low toxicity, make genistein an important candidate for experimental anticancer therapy, as well as new lead-compound for anticancer drug design [1].

The principal aim of this study was the synthesis of glycoconjugates, which are the drug candidates in antitumor therapy research program. The sugar part is connected to isoflavonoid ring system through a carbonic chain. Our thesis is that the structure modification of glycoconjugates should enhance the bioavailability of these compounds. Therefore, we decided to carry out reactions of glycals with glycosyl acceptors - derivatives of genistein, and we obtained glycoconjugates with high α –stereoselectivity [2].

This new class of substances was shown to possess anticancer activity. Cytotoxic activity of genistein glycoconjugates was evaluated against the model cell lines. Active derivatives were processed for subsequent in vitro toxicitytest.Foreachactivederivative IC50valueswereobtained.Itwasfound,thatallnewcompoundsinhibitproliferation of various cancer cells.

Acknowledgementα

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Validation of a HPLC method for LI-S analysis

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A new liquid chromatography method has been developed and validated for the analysis of LI-S ((5R)-N-{[3-(3-fluoro-4 -morpholinylphenyl) -2-oxo-5-oxazolidynyl] methyl}acetamide)