ABSTRACT

The topic of this thesis is the synthesis of rhodanine derivatives and evaluation of their biological activity, particularly as potential cholinesterases inhibitors. This group of compounds is important for treatment of many diseases, e.g., Alzheimer's disease or myasthenia gravis.

All synthetized compounds are based on structure of rhodanine (2-thioxothiazolidine-4-one), which is an important heterocyclic compound with a wide spectrum of biological properties. Its structure can be modified in many ways, which can be used in the development of new drugs. Its derivatives have been shown to have, for example, anti-inflammatory, anticancer, antibacterial and antifungal activities, as well as inhibitory activity against several enzymes, e.g., cholinesterases.

Seventeen compounds were synthesized in sufficient amount for characterisation and assessment of biological activity (7-93 %). Most of them are amides based on the structure of 2-thioxothiazolidine-4-one and thiazolidine-2,4-dione, that were prepared by carbodiimide-mediated coupling, other derivatives are based on the structure of 2-thioxothiazolidine-4-one and from 2,4-dioxothiazolidine-3-acetic acid. These compounds were prepared by *Knoevenagel condensation* in glacial acetic acid.

All compounds were tested for their inhibitory activity against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) using the Ellman's method (results are expressed as IC50 values); for the most active compound, the type of inhibition was also determined. Furthermore, antibacterial (G+ and G- strains), antifungal and antimycobacterial activities were evaluated by microdilution broth method (results are expressed as minimum inhibitory concentration, MIC, values). The lowest values of IC50 were found for 2-(4-oxo-2-thioxothiazolidin-3-yl)-N-(3,4,5-trichlorophenyl)acetamide with IC50 values of 34.42 µmol/L for AChE and 2.91 µmol/L for BChE; type of inhibition was found as a reversible competitive. The lowest MIC values against bacteria, fungi as well as mycobacteria were found for (Z)-5-(5-bromo-2-hydroxybenzylidene)-3-methyl-2-thioxothiazolidine-4-one, (Z)-2-[5-(5-bromo-2-hydroxybenzylidene)-2,4-dioxothiazolidine-3-yl]acetic acid and (Z)-5-(5-bromo-2-hydroxybenzylidene)-2-thioxothiazolidine-4-one: 125 µmol/L for bacteria, 62.5 µmol/L for fungi and 15.625 µg/mL for mycobacteria.

Keywords

Acetylcholin esterase, Alzheimer disease, myasthenia gravis, butyrylcholinesterase, cholinesterase inhibitors, rhodanine