ABSTRACT

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Title of diploma thesis: Pharmacological evaluation of potencial drugs for Alzheimer's disease treatment

Alzheimer's disease (AD) is a neurodegenerative disease characterized by aggregates of beta-amyloid, neurofibrillary tangles of tau protein and by the loss of cholinergic neurons in the basal forebrain and hippocampus. Cause of AD is still unknown and only symptomatic treatment is available thanks to inhibitors of acetylcholinesterase (AChE) and memantine, inhibitor of glutamate receptors. M_1 muscarinic positive allosteric modulators (PAM) represent another variant of treatment that can improve cholinergic transmission. Thanks to their selectivity, they are able to decrease side effects.

The aim of the study was to measure novel compounds´ abilities to inhibit AChE and BChE and simultaneously act as PAM of M_1 receptors. Enzymes inhibition was measured according to Ellman's method and IC_{50} values were determined. For fluorescent measurement of compounds interaction with muscarinic receptor the CHO cell line stably expressing the M_1 receptor subtype was used. Statistical analysis of results was performed in GraphPad Prism 5.

None of the tested compounds acted as a PAM of M_1 receptors. All novel compounds acted as M_1 inhibitors. Moreover, AChE and BChE inhibition was comparable with standards.