Abstract

This bachelor thesis deals with the synthesis of novel acetylcholinesterase and butyrylcholinesterase inhibitors as potential inhibitors of both cholinesterases. All the prepared molecules contain propargylamine structural motif, i.e., a proved scaffold for drugs targeting central nervous system. Some of its derivatives are currently investigated for the treatment of neurodegenerative disorders including Alzheimer's disease.

The theoretical part summarizes facts about the Alzheimer's disease and its current treatment focused on cholinergic hypothesis and inhibitors of cholinesterases. The experimental part reports the synthesis and evaluation of potential inhibitors of acetylcholinesterase and butyrylcholinesterase. Seventeen compounds were synthesized in satisfactory yields, predominantly amides and imines of salicylic and cinnamic acid derivatives. All of them were investigated for their activities against both cholinesterases using Ellman's method. 5-Bromo-*N*-(prop-2-yn-1-yl)salicylamide and *N*-(prop-2-yn-1-yl)benzamide showed the lowest IC_{50} values for acetylcholinesterase (8.05 and 23.16 μM, respectively). 2,4-Dibromo-6-[(prop-2-yn-1-yl)carbamoyl]phenyl (*N*-ethyl-*N*-methyl)carbamate showed the best inhibition of butyrylcholinesterase (IC_{50} = 26.09 μM). Several of the prepared compounds were more active than a clinically used drug rivastigmine.

Keywords

Acetylcholinesterase; Alzheimer's disease; butyrycholinesterase; cholinesterases inhibitors; cinnamic acid; Ellman's method; enzyme inhibition; *in vitro* activity; propargylamine; salicylamides