Abstract

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Title of diploma thesis: *In vitro* characterization of novel potential modulators of cholinesterases

This thesis focuses on investigating the interaction of newly synthesized potential drugs with human cholinesterases (ChE), particularly acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). The main objective is to assess the inhibitory potential of these molecules against recombinant human forms of AChE and BChE. Furthermore, the cytotoxicity of selected compounds is examined using a colorimetric method on the SH-SY5Y cell line employing MTT tetrazolium salt.

The theoretical part of the thesis delves into the structure and functions of cholinesterases, especially AChE and BChE, as well as the cognitive aspects of neurodegenerative diseases such as Alzheimer disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), and multiple system atrophy (MSA). Additionally, it addresses the toxic effects of organophosphates, which can inhibit the AChE enzyme, along with methods for determining cholinesterase activity.

The practical part focuses on experimentally determining the inhibitory potential of 58 compounds on AChE and BChE. The cytotoxicity of selected compounds was determined using human neuroblastoma cells SH-SY5Y. The lipophilicity of substances was also estimated using web tool SwissADME. The highest inhibitory effects on AChE were observed with compounds K2241, K2137, and K2125, while on BChE with compounds K2140, K2137, and K2124. The lowest cytotoxicity was recorded with compound K2134. These results provide valuable insights for further research into ChE inhibition and potential therapeutic applications of these compounds in the treatment of neurodegenerative diseases.