ABSTRACT

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Title of Diploma thesis: Synthesis and *in vitro* testing of tacrine-trolox derivatives as potential inhibitors of acetylcholinesterase

Alzheimer‘s disease (AD) is a complex neurodegenerative disorder, which involves gradual loss of episodic memory and impairment of cognitive functions. Characteristic histopathological hallmarks of AD are neuritic plaques and neurofibrillary tangles present in brain tissue as well as deterioration of cholinergic neurotransmission. Currently there are only two classes of drugs used for the treatment of AD. The first group represents inhibitors of acetylcholinesterase (AChEI), whereas the second only memantin, NMDA receptor antagonist. The aim of the thesis was to synthesize three series of tacrine - trolox derivatives. In particular derivatives of trolox with tacrine, 7-methoxytacrine and 6-chlorotacrine, which were connected by various linkers. To determine the therapeutical potential of new compounds Ellman method was used and results were compared with tacrine, 7-methoxytacrine and 6-chlorotacrine as standards. The antioxidant properties of new derivatives were evaluated using DPPH assay with trolox as reference compound. All of the newly synthesized derivatives showed inhibitory activity against cholinesterases from micromolar to submicromolar scale. Novel hybrids also exhibited antioxidant activity, which was however lower than that of trolox.