ABSTRACT

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TITLE OF DIPLOMA THESIS: Amaryllidaceae alkaloids as inspiration of preparation of selective butyrylcholinesterase II

Plants of the family Amaryllidaceae are an important source of biologically active substances, which are labeled as Amaryllidaceae alkaloids (AAs). These natural products show a wide range of biological characteristics, for which they are also intensively studied. Their significant biological effects include antiviral, antibacterial, antifungal, anti-inflammatory, antiparasitic, and cytotoxic activity. Their other important characteristic is the ability to inhibit both cholinesterases: acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE). Inhibition of AChE is used in the therapy of Alzheimer´s disease (AD). Currently, in the treatment of the symptoms of this disease, one AA, galanthamine, is used. Recently a new structural type of AAs, carltonins, have been isolated from the plant *Narcissus pseudonarcissus cv. Carlton*. These substances showed a significant inhibitory effect against BuChE and became the inspiration for the synthesis of selective BuChE inhibitors. Within the current study, 20 substances were prepared that expand the portfolio of synthetic compounds structurally inspired by these minor natural compounds and deepen the knowledge of the relationship of structure and effect in the group of selective BuChE inhibitors. All newly synthesized compounds were determined for their inhibitory activity against AChE and BuChE, and their BBB score (ability to penetrate through HEB) was calculated. Substances **FC030** (IC50 = 0,171 ± 0,06 μM, inhibition of BuChE 96,66 ± 0,31%) and **FC030-1** (IC50 = 0,167 ± 0,02 μM, inhibition of BuChE 94,85 ± 1,05%) showed the highest activity. These two substances were tested for cytotoxicity against the neuroblastoma cell line SH-SY5Y and the hepatocellular cell line HepG2, where they showed no toxicity at effective concentrations.

Key words: Amaryllidaceae alkaloids, Alzheimer´s disease, carltonines, acetylcholinesterase, butyrylcholinesterase, synthesis