Abstract

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Title of diploma thesis: Amaryllidaceae alkaloids as inspiration for preparation of selective butyrylcholinesterase inhibitors I

The Amaryllidaceae family is considered to be very important source of biologicaly active natural compounds, alkaloids. These compounds are intensively studied because of their antiviral, antifungal, antiparasitic, antioxidative and antiinflammatory properties and especially for their ability to inhibit cholinesterases. This source is still not entirely depleted, which is proved by recent isolation of utterly new structural type of Amaryllidaceae alkaloids, carltonines, isolated form *Narcissus pseudonarcissus* cv. Carlton. Carltonines have shown promissing inhibitory activity of BuChE.

Isolation of carltonines has become an inspiration for synthesis of highly selective BuChE inhibitors based on norbelladine structural type. This diploma thesis proceeds from pilot series of 20 compounds. During this study, another 21 compounds were prepared, expanding the portfolio and knowledge of structure-activity relationships within selective BuChE inhibitors group. Generated compounds were identified using NMR and ESI-HRMS. All compounds were studied for their inhibitory activity of AChE and BuChE, ability to cross BBB was calculated as BBB score. The most active compounds were FC020 (IC_{50} = 188,03 ± 23 nM, inhibition of BuChE 96,31 ± 0,26%), FC012 (IC_{50} = 193,2 ± 55,39 nM, inhibition of BuChE 96,38 ± 0,79%) and FC013 (IC_{50} = 353,13 ± 98,63 nM, inhibition of BuChE 94,09 ± 0,35%). These three compounds were subsequently tested for cytotoxicity against cell line SH-SY5Y. They did not show any toxicity in active concentrations.

Key words: Amaryllidaceae, alkaloids, carltonines, derivatives, cholinesterases