ABSTRACT

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Title of Diploma thesis: Synthesis of haemanthamine derivatives and their biological activity

Haemanthamine, an isoquinoline Amarillidaceae alkaloid, exhibits a wide and important range of biological activities, including antitumor, antiviral, antioxidant, antimalarial and anticonvulsant.

Biological activity of haemanthamine relatives closely with its structure. By modifying the different parts of the molecule, we can identify some structure-activity relationships. With this aim, the thirteen semisynthetic analogues of alkaloid haemathamine were prepared and purified using analytic and preparative TLC methods. The obtained substances were then subjected to structural analysis, specifically, there were used MS, HRMS, 1D and 2D NMR spectroscopic techniques.

Prepared compounds were tested on its possibility to inhibit human erythrocytic acetylcholinesterase (HuAChE) and human serum butyrylcholinesterase (HuBuChE).

The most promising biological activities have been shown by aromatic esters labelled as LC-70 ($IC_{50\ HuAChE}$ = 0,12 ± 0,01 μM) and LC-73 ($IC_{50\ HuAChE}$ = 0,17 ± 0,01 μM).

The cytotoxic activity of prepared compounds has been studied on panel of cancerous and noncancerous cells. Interesting activity have been shown by analogue LC-70. Four derivatives have been tested for its GSK-3β inhibitory activity. The best activity had 11-*O*-(2-methoxybenzoyl)-haemanthamine (IC_{50} = 26,2 ± 5,0 μM). The results suggest that some haemanthamine analogues can be used as a “lead structures” for potentional drugs.

Key words: alkaloid, haemanthamine, derivatives, Alzheimer desease, cytotoxicity