ABSTRACT

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Title of Doctoral Thesis: **Alkaloids of *Zephyranthes citrina* (Amaryllidaceae): isolation, structure identification, biological activity.**

Key words: Amaryllidaceae alkaloids, *Zephyranthes*, Alzheimer's disease, AChE, BuChE, POP, oncological diseases

Zephyranthes citrina Baker was chosen, based on result of previous screening study and literatury research, for detailed phytochemical work for the purpose of isolation of the widest range of AAs. From 35 kg of fresh bulbs was obtained 151 g of purified alkaloidal extract, which was processed using column chromatography to almost 700 fractions. These fractions were connected into 27 subfractions, which were processed by liquid-liquid extraction, flash chromatography, preparative TLC and crystallization. Finally, 27 pure alkaloids were isolated. All compounds were identified by MS (EI, ESI), HRMS, 1D- and 2D-NMR, CD, optical rotation and by comparison with literature data. Seven compounds were identified as new undescribed alkaloids (6α-ethoxyhippeastidine, 10-deoxy-6α-ethoxyhippeastidine, narcieliine, zephyjanine, zephycitrine I, 7-ethoxy-10-methoxy-1-methyllycorenane-9-ol a zephycitrin II). All alkaloids isolated in sufficient amount were tested for their biological activities associated with Alzheimer's disease (inhibition of *h*AChE, *h*BuChE, POP) and oncological diseases.

Inhibition of erytrocytic *h*AChE and serum *h*BuChE was determined by modified Ellman's method. Significant *h*AChE and *h*BuChE inhibitory activity was demonstrated by the newly described alkaloid narcieliine, with IC_{50} values of 18.7 ± 2.3 μM and 1.34 ± 0.31 μM, respectively. To evaluate the interactions of narcieliine with *h*AChE and *h*BuChE a kinetic study was conducted. This compound was also predicted to cross the blood-brain barrier through passive diffusion (PAMPA-BBB assay). The *in vitro* data were further supported by *in silico* studies of narcieliine in the active site of *h*AChE/*h*BuChE.

Determination of POP inhibition was performed by spectrophotometric method. Four compounds showed activity comparable to used standard berberine (IC_{50} = 142 ± 21 μM): narcieliine (IC_{50} = 163 ± 13 μM), zephyjanine (IC_{50} = 160 ± 10 μM), lycoramine (IC_{50} = 150 ± 10 μM) and 9-*O*-demethylgalanthine (IC_{50} = 146 ± 16 μM).

All isolated alkaloids went through the screening of cytotoxic activity on nine cancer cell lines (Jurkat, MOLT-4, A549, HT-29, PANC-1, A2780, HeLa, MCF-7 a SAOS-2) and one healthy cell line (MRC-5). Only haemanthamine, haemanthidine, lycorine and buphanisine showed cytotoxic activity.

Based on obtained results, *Z. citrina* can be recognized as a rich source of biologically active alkaloids with potential for further study.