

ABSTRACT

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Title of Doctoral Thesis **Alkaloids from selected species of Amaryllidaceae family, their toxicity and biological activity (in vitro study) I.**

Zephyranthes robusta and Chlidanthus fragrans bulbs were chosen for phytochemical study as biologically active Amaryllidaceae alkaloids source, based on bio-guided study using spectrophotometric Ellman's method and GC-MS analysis of alkaloid extracts. Bulbs were extracted with ethanol and the summary extract was fractionated by column chromatography with the use of Al₂O₃ as a stationary phase and gradient elution chloroform – ethanol. Column chromatography, preparative TLC and crystallisation led to isolation of pure compounds the chemical structure of which was elucidated by MS and D1- and D2-NMR analyses. From fresh bulbs of Chlidanthus fragrans 11 alkaloids were isolated of which deoxypretazetidine, belladine, 3-epimakronine, ismine, undulatine, buphanisine and ambelline were reported for the first time from the genus Chlidanthus. Compounds were evaluated for their human AChE, BuChE and POP inhibitory activity. From Zephyranthes robusta bulbs 14 alkaloids of several structural types were isolated. Galanthamine, 3-epimakronine, hippeastidine, lykoramine, galanthine, tazettine, vittatine, 11-hydroxyvittatine, hammayne, 8-O-demethylmaritidine and 9-O-demethylgalanthine were reported for the first time from this species and alkaloids 3-epimakronine, hippeastidine, 8-O-demethylmaritidine and 9-O-demethylgalanthine were isolated for the first time from the genus Zephyranthes. All compounds were tested for their human AChE and BuChE inhibitory activity, with 9-O-demethylgalanthine there was also determined POP inhibitory activity. The cholinesterase inhibitory activity was determined by in vitro spectrophotometric modified Ellman's method. Inhibition of POP was determined with the use of Z-Gly-Pro-p-nitroanilide as a substrate. Besides galanthamine which is already used in therapy of AD undulatine, 8-O-demethylmaritidine, galanthine and 9-O-demethylgalanthine were considered as promising among the tested compounds. Undulatine – an crinine type alkaloid – inhibited AChE in concentration of $IC_{50} = 23.2 \pm 1.1 \mu M$, 8-O-demethylmaritidine – alkaloid of the same structural type – in concentration of $IC_{50} = 28.8 \pm 0.9 \mu M$. Unfortunately none of the tested alkaloids showed significant inhibition of BuChE. Promising activities were, however, achieved in the inhibition of POP study. The most active were undulatine ($IC_{50} = 1.96 \pm 0.12 mM$) together with two alkaloids of lycorine structural type: galanthine ($IC_{50} = 1.49 \pm 0.14 mM$) and 9-O-demethylgalanthine ($IC_{50} = 0.15 \pm 0.02 mM$), which showed 4 times higher activity compared to used standard baikaline ($IC_{50} = 0.61 \pm 0.021 mM$).