ABSTRACT

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Title of Doctoral Thesis: **Alkaloids of the genus *Hippeastrum* (Amaryllidaceae): isolation, identification, biological activity.**

Hippeastrum x *hybridum* cv. Ferrari was chosen based on results of previous screening studies for detailed phytochemical study for the purpose of isolation of the widest range of AAs. From 25 kg of fresh bulbs was obtained 29,46 g of purified alkaloidal extract, which was processed using column chromatography. Finally, 18 pure alkaloids were isolated including one new homolycorine-type alkaloid (9-*O*-demethyllycorenine). All compounds were identified by spectrometric techniques (GC-MS, ESI-MS, NMR, optical rotation) and by comparison with literature data.

All alkaloids, isolated in sufficient amount, were tested for their biological activities associated with Alzheimer's disease (inhibition of *h*AChE, *h*BuChE, and POP), and cytotoxic activity. The inhibitory activity against human cholinesterases was determined *in vitro* by a modified Ellman's spectrophotometric method. In the *h*AChE/*h*BuChE assay, except for 1,2-*O,O´*-diacetyl-dihydrolycorine which demonstrated a mild *h*BuChE inhibition potency with IC_{50} values of 68 ± 3 μM, the isolated alkaloids were considered as inactive (IC_{50} > 100 μM). POP inhibition activity was determined by spectrophotometric method, the most active alkaloids in the POP assay were zephyranthine (IC_{50} = 142 ± 10 μM) and homolycorine (IC_{50} = 173 ± 41 μM). These compounds displayed activity comparable to used standard berberine (IC_{50} = 142 ± 21 μM).

The majority of isolated alkaloids were screened for their cytotoxicity on a panel of human cancer cells of different histotypes (Jurkat, MOLT-4, A549, HT-29, PANC-1, A2780, HeLa, MCF-7 a SAOS-2). Among tested alkaloids, montanine has been considered as the most potent compound to inhibit Jurkat, MOLT-4, A549, HT-29, PANC-1, A2780, HeLa, MCF-7, and SAOS-2 cancer cells. Jurkat cells were the most sensitive cell line to montanine, with the value of IC_{50} of 1.04 ± 0.14 μM.

As a part of the continuation of this study, a pilot series of semisynthetic derivatives of haemanthamine-type alkaloid vittatine were developed. Vittatine derivatives were studied for their *h*AChE/*h*BuChE inhibition potential.

Keywords: *Hippeastrum* x *hybridum* cv. Ferrari, Amaryllidaceae, alkaloids, biological activity, acetylcholinesterase, butyrylcholinesterase, prolyl oligopeptidase, cytotoxicity.