Abstract

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Title of diploma thesis: Derivatives of Amaryllidaceae alkaloid haemanthamine as potential drugs

Modern research has shown that Amaryllidaceae alkaloids represent a rich reservoir of potential small molecules exhibiting several medicinal properties through various mechanisms. Among the many Amaryllidaceae alkaloids, galanthamine has been given a great amount of attention due the fact that it possesses potent acetylcholinesterase inhibition activity, and is distributed worldwide for the treatment of Alzheimer´s disease.

One of the interesting compounds is haemanthamine, β-crinine-type of Amaryllidaceae alkaloids, which displays significant *in vitro* cytotoxic activity against several different types of cancer cell lines.

The object of this diploma thesis was to prepare several derivatives of alkaloid haemanthamine, and try to find relationship between structure and biological effect. The present work deals with the preparation of haemanthamine derivatives, and their biological activity connected to the treatment of cancer and Alzheimer´s disease. Twelve aromatic ester of haemanthamine derivatives were prepared. The chemical structures were elucidated by MS, NMR experiments and optical rotation. Each all, prepared compounds were screened for their cytotoxic activity on a panel of selected cancerous and noncancerous cell lines. Unfortunately for their potential to inhibit, none of the derivatives showed interesting cytotoxic activity.

Substances were also tested to inhibition of hAChE and hBuChE. The most significant value for both enzymes was demonstrated by 11-*O*-(2-methylbenzoyl)haemanthamine (LC-90): hAChE: IC_{50} = 18.18 ± 1.30 µM; hBuChE: IC_{50} = 6.59 ± 1.19 µM. Selective inhibition of hBuChE, was showed by 11-*O*-(benzoyl)haemanthamine (LC-118) IC_{50} = 5.85 ± 0.31 µM.

Keywords: haemanthamine, derivatives, Amaryllidaceae family, alkaloids, antitumor activity