

ABSTRACT

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Pharmaceutical Botany

Candidate: Adéla Potůčková

Supervisor: doc. Ing. Lucie Cahlíková, Ph.D.

Title of diploma thesis: Derivatives of Amaryllidaceae alkaloids and their biological activity

The plants of Amaryllidaceae family are source of a large amount of biologically active substances called Amaryllidaceae alkaloids. Their effects include cytotoxic, antifungal, antiviral, antibacterial or antimalaric activity and, last but not least, the inhibition of cholinesterases. The Amaryllidaceae alkaloids, galanthamine type also includes alkaloid chlidanthine, which is a positional isomer of the clinically practice used alkaloid galanthamine. The sources of chidanthine are *Chlidanthus fragrans*, *Haemanthus multiflorus* and *Hippeastrum aulicum*.

The object of this thesis was the preparation of chlidanthine derivatives, and the study of their biological activity connected to the therapy of Alzheimer's disease and cancer. Ten aromatic ester derivatives of chlidanthine were prepared. The chemical structures were elucidated by NMR, MS experiments and optical rotation. Most derivatives were screened for their AChE and BuChE inhibitory potential and their cytotoxic potential against a panel of tumor and non-tumor cell lines.

The most interesting activity was found with the 3-*O*-(2-methylbenzoyl)chlidanthine derivative, which showed selective inhibition against BuChE and was able to cross the BBB. Toxicity will be tested shortly. The substance could be used as a lead structure for further development.

Keywords: chlidanthine, Amaryllidaceae family, alkaloids, Alzheimer's disease, antitumor activity