Abstract

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Title of Diploma thesis: Synthesis of haemanthamine derivatives

Based on previous studies, the haemanthamine alkaloid showing remarkable antitumorous activity was chosen as the subject of this thesis. The purpose of the thesis was preparation of its more active derivatives, namely esters. Preparation concerns the following derivatives: 11-*O*-butanoylhaemanthamine, 11-*O*-(3,4-dimethoxybenzoyl)-haemanthamine, 11-*O*-(4-trifluoromethoxybenzoyl)-haemanthamine, 11-*O*-isobutanoyhaemanthamine. These were created by the reaction of haemanthamine and the relevant acilating agent (acylchloride, anhydride) in the environment of anhydrous pyridine or tetrahydrofuran with adding dimethylaminopyridine as a catalyst. Most of the products were obtained in the form of colourless oil, one of the substances crystallized into white amorphous crystals. However, during an attempt of dioxolane ring opening, the preparation of 3-demethylhaemanthamine derivative proved unsuccessful. Prepared derivatives were mostly identified by EI-MS and NMR. All the substances were gained in sufficient outcomes in the scale of 43 – 81 %. All the compounds were prepared successfully at the first attempt, with the exception of 11-*O*-isobutanoylhaemanthamine. These derivatives (concentration 10 μM) were tested for cytotoxic activity against gastrointestinal cancer cells Caco-2, HT-29 and healthy fibroblasts FHs-74. Unfortunately, none of the substances tested showed the toxicity required (IC_{50} >10 μM) at this concentracion. Inhibitive activity against AChE and BuChE was also tested. Unfortunately, the results proved that none of the derivatives has an adequate inhibitive activity (IC_{50} >100 μM) and therefore has no perspective in future experiments.

Key words: Amaryllidaceae, AChE, BuChE, antitumorous activity, haemanthamine