ABSTRACT

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

Haemanthamine type Amaryllidaceae alkaloids are characterized by interesting biological activity. This group also includes alkaloid vittatine with antitumor, antibacterial, antifungal and antimalarial effects. Although vittatine does not inhibit cholinesterases, its derivatives have shown promising activity against butyrylcholinesterase, which is one of the targets of potential drugs in the treatment of Alzheimer's disease.

Another series of semisynthetic vittatine derivatives was prepared in order to examine their biological activity. Reactions with acyl chlorides gave 11 aromatic esters. Identification of the prepared substances was performed by ESI HRMS, NMR and optical rotation measurements.

The derivatives were tested for inhibitory activity against human cholinesterases. The results show that the substances were not active against acetylcholinesterase, but almost all of them inhibited butyrylcholinesterase. The most active was 3-*O*-(6-chloro-2-fluoro-3-methylbenzoyl)vittatine with an IC_{50} value 0.29 ± 0.03 μM. According to the calculated value of logBB this derivative can be easily transmitted through HEB and has the potential to act in the CNS.

The cytotoxicity of the prepared substances was also determined. It was tested *in vitro* on 9 tumor and one non-tumor cell line. Only the 3-*O*-(3,5-dimethylbenzoyl)vittatine showed moderate cytotoxic activity against HT 29 colorectal adenocarcinoma cells. None of the tested derivatives reduced the viability of healthy cells (MRC-5).

Keywords: Amaryllidaceae alkaloids, vittatine, derivatives, Alzheimer’s disease, butyrylcholinesterase, cytotoxicity