ABSTRACT

Víchová Barbora: Biological activity of *Peganum harmala* L. alkaloids and their semi-synthetic derivatives I. Diploma thesis 2022. Charles University, Faculty of Pharmacy in Hradec Králové Department of Pharmacognosy and Pharmaceutical Botany

β-Carboline alkaloids are natural substances with potential use in tumor therapy. In particular harmine, which acts cytotoxically by several mechanisms. The aim of the diploma thesis was to prepare *N9*-derivatives of harmine derivatives, to clarify their structure based on common spectrometric and spectroscopic methods (ESI, ESI-MS, NMR) and subsequently to study their biological activity (cytotoxicity, AChE, BchE and GSk-3beta inhibition).

These tests resulted in several active derivatives, suitable candidates for further study. 9-*N*-(2-nitrobenzyl)harmine (HMA-22) was significantly cytotoxic to the Jurkat cell line (16% cell viability after 48 hours, compared to the control, with better cytotoxicity than the standard doxorubicin at a concentration of 1 μM). Another very active derivative was found 9-*N*-(5-bromopentyl)harmine (HMA-30), which was more cytotoxic to most tested cell lines than doxorubicin (1 μM), similarly as most of other derivatives. HMA-30 was also found as a potent BChE inhibitor ($IC_{50}$ 4.06 ± 0.48 μM). 9-*N*-(4-nitrobenzyl)harmine (HMA-20) showed a significant and selective AChE inhibitory activity and 9-*N*-(pentyl)harmine (HMA-29) was able to inhibit GSK-3β ($IC_{50}$ 15.10 ± 0.43 μM). In conclusion, harmine is a very promising compound for preparation of derivatives that can be useful in the therapy of tumors and Alzheimer's disease.

Keywords: β-carboline alkaloids, *Peganum harmala*, isolation, *N9*-substituted derivatives, cytotoxicity, Alzheimer's disease, acetylcholinesterase, butyrylcholinesterase