IX.   ABSTRACT

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Title of thesis: Natural compounds and their biological activity X. Screening of selected alkaloids on inhibition of prolyloligopeptidase

Alzheimer´s disease is the most serious and incurable neurodegenerative disease, which incidence is increasing. For these reasons, the search for new therapeutic practices and especially medicines that would expand the portfolio of useful therapeutic agents. At the present time (based on EBM) two main groups of drugs come into consideration: cognitives (AChE, or BuChE inhibitors) and NMDA receptor antagonists. Although the causes of the disease are not known, partial pathophysiological processes that are applied in the development of the disease are known. The search for new drug candidates in other areas is subject of an emerging research. One of these areas is the search for inhibitors prolyl endopeptidase which can favorably be applied in processes related to memory and learning.

In this work, 41 alkaloidal substances (isoquinoline and quinolizidine alkaloids, alkaloids of plants from the family Amaryllidaceae), which were previously studied on the inhibition of AChE and BuChE, which were obtained from the working group ADINACO Research Group (Charles University in Prague, Faculty of Pharmacy Hradec Králové, Department of Pharmaceutical Botany and Ecology). Have been subjected to the study of POP inhibition. The IC_{50} value of reference substance baicalin is approaching most by reticulin, argemonine, hamayne and 8-O-demethylmaritidine. However, all substances except 8-O-demethylmaritidine are inactive (IC_{50}> 50 µM; 8-O-demethylmaritidine IC50 28,02 ± 2,42 µM (AChE)) from the inhibition of AChE and BuChE point of view. The study of their effect on other human brain enzyme systems (inhibition of BACE1, GSK-3β) shows to which extent these substances are suitable for futher work.

Key words: Alzheimer's disease, prolylendopeptidase, alkaloids