Abstract

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Title of thesis: **Study and biological evaluation of new tacrine-tryptophan derivatives**

Alzheimer's disease (AD) is a chronic neurodegenerative disease with characteristic histopathological changes in the brain. It is the most common cause of dementia. There is about 7.4 million people affected by AD in Europe today. In connection with aging of the population a significant increase of patients affected by the disease can be expected in the coming years.

The cause of neural tissue damage is aggregated amyloid β (Aβ), which disrupts neurons by creating glial hem with consequent inflammatory processes. Hyperphosphorylated τ-protein causes neuronal damage intracellularly by forming so-called neurofibrillary tangles. This leads to macroscopically visible brain atrophy and loss of neurons.

Current AD pharmacotherapy is based on influencing the cholinergic system. Acetylcholinesterase inhibitors (AChEIs) - rivastigmine, donepezil and galanthamine are used for this purpose. Memantine, antagonist of *N*-methyl-D-aspartate receptors (NMDA) has been approved for the treatment of moderate to severe stages of AD. These drugs alleviate the symptoms of the disease but do not prevent its progression.

The aim of this thesis was to prepare compounds that are able to simultaneously affect multiple pathological processes of the disease. For this purpose derivatives of tacrine-tryptophan have been developed. This is a new series of heterodimers that represent new, in recent years intensively researched, approach to the treatment of AD in the form of so-called multi-target-directed ligands (MTDLs).