Description for the general public

Alzheimer's disease (AD – Alzheimer's disease) is a progressive disease that is the most common cause of dementia in patients over 60 years old. This disease belongs to neurodegenerative fatal disorders and affects mainly elderly people. It is characterized by progressive cognitive decline, memory loss and behavior changes. These symptoms can be referred to as stupor. It is estimated that annual incidence and prevalence of that disease increases dramatically with age being basic risk factor. Although AD is known for over a hundred years, there are only four acetylcholinesterase inhibitors approved by Food and Drug Administration so far. They are regarded to the one of the most important aims in AD treatment. First drug approved was tacrine (THA, 9-aminotetrahydroaminoacridine). It is the strongest and most effective acetylcholinesterase inhibitor, but it interacts with other many drugs and causes a lot of side effects. During the last decades scientists put a lot of effort in AChEIs (AChEIs - acetylcholinesterase inhibitors) modifications and attempts to find new structures. Unfortunately there is still no effective method in AD therapy. Moreover, nowadays we still don't know the exact cause of that disease. There are a few theories about the AD occurrence mechanisms but despite intensive studies it wasn't possible to develop effective drugs without serious side effects. Due to ever-growing number of AD patients, intensive research of the innovative therapies is highly recommended.

The main goal of described project is to develop tacrine derivatives as drugs with multidirectional activity. The main assumption is to project tetrahydroacridine and cyclopentanequinoline hybryd in such a way to not to reveal hard sides effects with their cholinergic properties. In result of conducted synthesis we can obtain new tetrahydroacridine and cyclopentanequinoline hybryds. Next level of studies will be complexation received derivatives with metals: copper and gallium. They are commonly used in nuclear medicine and therefore in further studies there will be chance to check i.a. biodistribution of the obtained derivatives and what is more their potential application as radiopharmaceuticals. Based on molecular modeling methods there will be made the analysis pharmacokinetic and pharmacodynamic properties of obtained derivatives and the simulation of the substance to enzyme docking. The analysis will also concern determining pharmacological properties of obtained derivatives based on *in vitro* studies and *in silico* computer calculations as innovative drugs in AD therapy. The new hybrids of biological properties will be evaluated based on biological studies of affinity to acetylcholinesterase and butyrylcholinesterase. The predisposition of beta-amyloid aggregation, cytotoxicity and oxidative stress will be thoroughly tested. For most promising derivatives there will be capacity of blood-brain barier penetration and affinity to aminoacids in three-hybrid system determined.