Alzheimer's disease is a chronic degenerative disorder of the central nervous system that leads to dementia and premature death. It is characterized by progressive disorders of memory, speech and motor coordination. Cognitive impairments often occur with depressive disorders. According to the World Health Organization, more than 30 million people worldwide suffer from Alzheimer's disease. It is predicted that this number will double over the next 20 years due to progressive aging of population. It is also predicted that Alzheimer's disease will be one of the most expensive civilization disorders. Generated costs include not only pharmacological treatment but also daily care and loss of patient productivity. Alzheimer's disease is a growing health, social and economic problem. Unfortunately, its cause is not fully known. There are several hypotheses that suggest the effect of impaired cholinergic transmission, neurofibrillary tangles formation or beta-amyloid accumulation at the base of the forebrain. One of the newest hypotheses combines cognitive disorders with insulin resistance of brain cells and hyperglycemia. Alzheimer's disease has even been termed type III diabetes, and clinical trials have examined the benefits of oral administration of hypoglycemic drugs in dementia of the Alzheimer type. However, at present we do not have effective drug to combat cognitive and depressive disorders that occur in the course of Alzheimer's disease.

The complex pathogenesis of Alzheimer's disease, the ineffectiveness of currently used drugs, as well as epidemiological data and epidemiology-based forecasting of the prevalence of dementia in the world make the search for new therapies for Alzheimer's disease one of the current research directions around the world. At the same time, the paradigm "one disease, one gene, one molecular target, one drug" has ceased to be dominant. Recently, it is believed that the effective anti-Alzheimer’s drugs should be simultaneously directed at various biological targets.

The new strategy for drug discovery in the treatment of disorders with complex etiology, especially neurodegenerative disorders, is the design of multifunctional ligands. Multifunctional ligands arise as a result of the combination of the pharmacophores of two or more active compounds. They are designed to provide a broader spectrum of action and therefore, greater pharmacological efficacy. The development of the multifunctional drug is associated with the compound that simultaneously interacts with several biological targets while maintaining an adequate activity ratio and selectivity for other molecular targets (so-called selective non-selectivity). Designing multifunctional ligands does not guarantee finding more effective and safer drugs, but it is an interesting alternative to other methods of drug discovery. Multifunctional ligands provide the chance to cure the patient and stop the disease, while reducing the risk of interactions, the risk of incorrect dosage and number of adverse events.

The aim of this project is to obtain a library of novel multifunctional ligands, anilide derivatives of long-chain cyclic amines, with potential ability to interact with 5-HT_{1A} and 5-HT_7 receptor and inhibit phosphodiesterase 7 (PDE7). It is assumed that simultaneous interaction with 5-HT_{1A} and 5-HT_7 receptors and PDE7 inhibition may enhance the efficacy of the treatment of cognitive and depressive disorders in Alzheimer's patients by modulation of glutamatergic, dopaminergic and/or cholinergic transmission and various intracellular signaling pathways.

Project research tasks will be carried out by relevant units of the Faculty of Pharmacy of the Jagiellonian University Medical College and the Institute of Pharmacology of the Polish Academy of Sciences. The research plan includes the design of potential 5-HT_{1A} and 5-HT_7 receptors ligands and PDE7 inhibitors using computer-assisted methods, synthesis of new compounds using microwave-assisted methods, *in vitro* and *in vivo* pharmacological evaluation of obtained compounds. Evaluation of affinity for 5-HT_{1A} and 5-HT_7 receptors and functional activity on 5-HT_{1A} and 5-HT_7 receptors as well as PDE7 inhibitory activity will enable selection of the most interesting compounds for behavioral studies to determine their potential procognitive and antidepressant activity in animal models of cognitive impairment and depression.

At the moment, there are no drug that effectively reduces cognitive and depressive disorders in Alzheimer's patients. For this reason, the search for new compounds with procognitive and antidepressant properties is an important direction for research from the point of view of society. The research project will allow to obtain the series of innovative compounds with ability to interact with 5-HT_{1A} and 5-HT_7 receptor and inhibit PDE7 as potential procognitive and antidepressant agents. The results may enhance our knowledge about the pathomechanism of Alzheimer's disease and indicate future directions for anti-Alzheimer’s drug research.