

Type 2 diabetes is one of the most common metabolic disorders. The pathogenesis of this disease involves two basic metabolic defects: impaired insulin secretion and insulin resistance, which is defined as the reduction/lack of insulin sensitivity of the target tissues (e.g. adipose tissue, liver, but also the brain). The latest epidemiological studies have shown the relationship between obesity, insulin resistance and type 2 diabetes and cognitive disorders, dementia, depression, as well as an increased incidence of Alzheimer's disease. Therefore, numerous contemporary experimental and clinical studies are focused on insulin resistance pathogenesis (also at the brain level).

According to the current state of knowledge, a significant role in the etiology of brain complications of insulin resistance is attributed to oxidative stress. Oxidative stress is defined as the lack of balance between the formation of reactive oxygen species (ROS) and the efficiency of enzymatic and non-enzymatic antioxidant defence mechanisms. This condition results in oxidative damage to cell components (i.e. proteins, lipids and DNA) and thus the impairment of cell structure and biological functions. Therefore, it is not surprising that the scientific community is focused on finding new, effective therapeutic strategies to protect against oxidative brain damages. It is believed that the use of antioxidants can eliminate and prevent changes caused by oxidative stress.

In the proposed project we will determine the role of antioxidant α -lipoic acid in reducing the brain complications of insulin resistance. Despite the documented activity of ALA in the therapy of various diseases (including Alzheimer's disease, Parkinson's disease, Huntington's disease, schizophrenia, autism, bipolar disorder, hypertension and obesity), the exact mechanisms of this antioxidant action are still unknown. Moreover, there is no data on the effect of ALA on brain metabolism in the insulin resistance development. Therefore, **in the proposed project we will be the first to evaluate the influence of α -lipoic acid on cellular redox balance, oxidative stress, selected parameters of lipid and carbohydrate metabolism as well as selected markers of inflammation and apoptosis in the hypothalamus and cerebral cortex of the insulin-resistant rats' brains.** Bearing in mind the favourable properties of ALA in eliminating the peripheral effects of insulin resistance, we suppose that α -lipoic acid may improve brain functions under the conditions of reduced insulin sensitivity. **The proposed research will not only allow us to understand the mechanisms of therapeutic activity of α -lipoic acid in the brain but will also contribute to a more accurate understanding of the role of oxidative stress and disturbances of the lipid and carbohydrate metabolism in the development of brain complications of insulin resistance. Additionally, it should be noted that studies expanding our knowledge about antioxidant mechanisms of action are of outstanding meaning for the development of many fields of contemporary medicine and pharmacy.**