

DESCRIPTION FOR THE GENERAL PUBLIC

The problem of diabetes is extremely important. According to statistics the number of people treated pharmacologically due to diabetes in Poland is about 2 million (data provided by the Polish National Health Service, 2011), and this disease and related complications share about 2% in the causes of death in our country. According to World Health Organization (WHO) in 2014 the global prevalence of diabetes was estimated to be 9% among adults. WHO projects that diabetes will be the 7th leading cause of death in 2030. Despite the fact of enormous progress in medicine, the detailed mechanisms responsible for the development of diabetes have not been fully explained so far.

Currently available therapies for diabetes include insulin and various oral antidiabetic agents such as sulfonylureas, biguanides and glinides. Many of above mentioned agents have a number of serious side effects. Therefore, the search for more effective and safer hypoglycemic compounds is required. Since centuries plants have been the highly esteemed source of medicines. In this aspect, the very promising is the use of lupin seeds protein fraction - gamma-conglutin, as a natural compound exhibiting blood glucose lowering properties.

Lupin seed gamma-conglutin is a protein with a number of unusual properties. The unique properties of this protein include: binding of divalent metal cations, such as Zn^{2+} and Ni^{2+} , insensitivity to pancreatin and trypsin proteolysis, ability to bind insulin and native lupin seed flavonoids. The most interesting feature of this protein is its ability to reduce glycaemia in animal models and in humans, which makes this protein pharmaceutically interesting. Unfortunately, so far the detailed mechanisms of gamma-conglutin action in the treatment of diabetes have not been described. Difficulties associated with the explanation of molecular mechanisms responsible for unusual properties of gamma-conglutin are mainly due to the lack of information about the structure of this unique lupin seeds protein. Recently, our group determined the three-dimensional structure of gamma-conglutin and established its oligomerization state at pH 7.5. These findings provided progress in understanding of unique features of gamma-conglutin. However, the molecular basis of interactions between gamma-conglutin and various ligands are still not fully understood. It is highly probable that discovering mechanisms responsible for those unique gamma-conglutin features will help explain glucose-lowering action of this protein. Therefore, in-depth studies at the molecular level, planned in this project, are needed in order to fully reveal nutraceutical beauty of gamma-conglutin hidden inside the polypeptide chains.

A wide range of analyses planned in the project utilize modern methods based on state of the art scientific equipment dedicated to track even the smallest structural changes which take place during proteins-ligands interactions. In case crystallization screening and crystals soaking allow to obtain gamma-conglutinating crystals with various ligands measurements with the use of synchrotron radiation are planned.

The results of the research tasks which are planned in this project will provide clear evidence explaining the mechanisms responsible for the unique properties of gamma-conglutin. Based on these results it will be possible to set up applied technological studies. Thus, it certainly will help to optimize exploitation of lupin seeds potential for human nutrition as well as diabetes prevention and treatment. We assume that on the basis of the results obtained during this project it will be possible to assess direct mechanisms of gamma-conglutin action in reducing glycaemia. Therefore, sufficient evidence to start using specific health claims on lupin-based products will be provided.