DESCRIPTION FOR THE GENRAL PUBLIC

Recently, an increased incidence of cardiovascular disease has been observed. Poor eating habits, sedentary lifestyle, excessive stress or lack of physical activity are some of the factors that affect the development of the above mentioned diseases, which are the main cause of premature deaths in Poland and Europe. Platelet aggregation and thrombosis are the basic elements of the pathophysiology of myocardial infarction and angina. In turn, effective antiplatelet therapy reduces the risk of acute coronary syndromes in patients with chronic angina pectoris. Due to the above, antiplatelet drugs, including clopidogrel, belong to some of the most important in modern medicine.

In the case of many drugs, the total formula does not describe well the structure of the compound, because molecules with the same atomic composition may differ in the distribution of individual atoms in space, which will affect, among others, on the way drugs are combined with their specific molecular targets. The use of enantiomers in modern pharmacotherapy allows to optimize the clinical effect of racemic mixtures used up to now, and also allows to reduce the frequency and intensity of adverse effects that may be associated with the used pharmacotherapy. Enantiomers usually differ from each other in pharmacokinetic, pharmacodynamic and adverse effects profile. One of the methods to obtain a pure enantiomer is enzymatic kinetic resolution. For this purpose, a stereoselective biotransformation involving hydrolysis or esterification (transesterification) of the racemate is performed in the presence of an enzyme, which is an enantioselective biocatalyst. The enzyme may be present in the reaction mixture in free (native) or bound (immobilized) form, e.g. with the surface of magnetic nanoparticles. The immobilization process aims to increase the catalytic activity of the enzyme and to give the possibility of its easy isolation from the reaction mixture, by applying an external magnetic field, and to allow its reuse in the next reaction cycle, which significantly reduces the total biotransformation costs.

The scientific goal of this project is to conduct a stereoselective biotransformation of clopidogrel to obtain enantiomerically pure (*S*)-clopidogrel and its derivatives, which are responsible for the therapeutic effect. An additional goal is to assess the degree of drug-receptor interaction of the therapeutic agents with their specific molecular targets, i.e. platelet receptors, as well as the opportunity to investigate the antiaggregation effects of the obtained therapeutic agents.

In the process of stereoselective biotransformation with the use of lipases, the most common are organic solvents that are applied as the reaction medium. Nevertheless, most of these compounds are toxic and dangerous to the environment. In many cases, organic contamination of the final synthesis product may also occur. In the other hand, the use of ionic liquids as a reaction environment brings many advantages. These green solvents are environmentally friendly, and the transformations carried out in them often take place faster. In addition, ionic liquids can be recovered from the reaction mixture and reused in subsequent catalytic cycles.

The study of the mechanisms of drug interaction with its molecular target, e.g. the receptor, is currently very important issue of modern pharmacology. The drug-receptor interaction assessment is extremely important in predicting activity or side effects. Additionally, in the course of research tasks it is planned to monitor the antiaggregating effects of the active substances obtained. The tests will be performed using aggregometry based on visible light transmission (LTA) and impedance aggregometry (Multiplate - MEA). Both of the abovementioned methods allow for the *in vitro* assessment of platelet function and are commonly used in hospital diagnostic laboratories and in scientific and research facilities.

The proposed project is to be an attempt to combine nanotechnology and biotechnology with pharmaceutical sciences. The effect of the proposed tests would be to obtain a pure enantiomerically therapeutic agent that could be administered to patients with cardiovascular disorders, thus showing fewer side effects.