

The aim of the proposal is to develop predictive models for prediction of metabolic properties of drug candidates, that in a consequence could lead to develop drug candidates with a greater chance for clinical success. The metabolism of xenobiotics is responsible for the processes leading to decrease or increase of the biological activity of the drug, and may result in drug-drug interaction, as well as some of observed adverse effects. The proposed procedures may become an element of rational design of new drugs, including their metabolic stability as an endpoint. The rationalization in a process of designing new drugs is extremely important and can contribute to reduction of a time needed to introduce innovative drug on the market and reduce its price.

The proposed project will examine the arylpiperazine derivatives - potential candidates for antidepressants and anxiolytics. Biochemical experiments will be performed *in vitro* and their interpretation will be based on chemometric tools and data obtained from the molecular modeling. Qualitative analysis of the experimental part is will be performed with the help of liquid chromatography-mass spectrometry technique. The developed models will enable the assessment of the relationship between chemical structure and metabolic stability, taking into account the first and second phase of metabolism, as well as the classification of the compounds according to the possibility to undergo glucuronidation.

Unique approach, which firstly does not ignore the importance and quality of experimental part, and secondly uses the latest advances in computational chemistry and chemometric modeling of biological phenomena, gives a chance for a real contribution to the rationalization of the design and synthesis steps, followed by the introduction of new, innovative drugs on the pharmaceutical market. The results of the project, which is worth noting, although directly focused on arylpiperazine derivatives, can be applied to assess the metabolic stability of other groups of drug candidates.