The use of modern and high-standard analytical techniques in interdisciplinary studies contributed to a kind of revolution in the field of natural sciences. It allowed, among others, to monitor the processes as complex as biotransformation and distribution of compounds within living organisms. The methods were also used to confirm the relationships significant from the point of view of medical diagnosis and treatment. The enormous progress in understanding of the phenomena and mechanisms of biochemical reactions highly accelerated the development of applied sciences, especially medicine and pharmacy.

Further progress of basic sciences (e.g. systems biology) requires more thorough studies dedicated to the mechanisms of biochemical reactions. In recent years, there has been an increased interest in compiling and comparing results obtained using different research techniques in order to elucidate the mechanisms. The most common approach is based on the identification of the content of a cell (or tissue) and on defining the relationship between all proteins, nucleic acids and metabolites present in the sample. Mentioned classes of compounds are within the fields of interest of consequently proteomics, transcriptomics and metabolomics .

The proposed project covers one of the typical issues of the latter concept - metabolic profiling. This technique involves identification of the possibly broadest range of metabolites (compounds of lower molecular weight than assumed, usually 1 kDa) associated with the same metabolic pathway. In the case of the planned study the metabolic pathway is a consequence of ingestion of a xenobiotic (a substance naturally not occurring in the organism or food). In view of the fact that the primary organ responsible for the metabolism of foreign substances is liver, the experiments will focus on the reactions involving mainly the enzymes present in its cells (the hepatocytes). During the research two types of systems, *in vitro* and *in vivo*, will be applied. The first one will require the use of various elements from human liver cells that are responsible for different stages of metabolism. In the second, each drug will be given to a set of model organisms (rats) and their urine will undergo further analysis. All samples are to be analyzed using modern analytical techniques, allowing the separation of compounds of a very similar structure, even if they are present in trace amounts. Analysis of the results received for both systems should allow the identification of the main metabolites of tested substances. The information obtained during the realisation of the project can be used to propose metabolic pathways of particular compounds for which no data has been published yet. In addition, they can provide a basis for further research concerning the metabolism of structurally related compounds, drug-drug interactions or so-called reaction profiling (determination of the enzymes involved in the reaction judging on the ratio of metabolites).

The main objective of the project is to study the metabolism of three groups of drugs which remain in clinical (or pre-clinical) trials or were withdrawn at any stage prior to the official introduction to the market. These compounds were tested for the use in treatment of various diseases including osteoporosis, diabetes, metabolic syndrome, anaemia or cancer. A common feature of all selected substances is that they belong to the latest generation of drugs which are expected to interact only with the paticular receptor. Theoretically, it should lead to the reduction of the effective doses (doses causing expected therapeutic effect) and consequently minimalization of the risk of adverse effects. Nevertheless, it also resulted in an increased interest from athletes (including amateurs) and people trying to lose weight or improve muscles without increasing physical activity. As a result, there arose a threat to life or health which is associated with insufficient recognition of the potential adverse effects and the ingestion of drugs without consulting a physician. One should not forget that the use of drugs for non-medical reasons very often leads to application of much higher doses than those tested in clinical trials. The parallel use of several substances, which is also very typical in such cases, significantly increases the risk of adverse effects. Given the fact that these compounds are commercially available for several years before the completion of clinical trials, there is an urgent need to develop analytical procedures valid for diagnostics, anti-doping and toxicological analysis. The information gathered during the project, as well as developed analytical procedures may underpin the development of procedures useful in the above mentioned types of analysis.

The innovative aspects of the project are the outcomes of conducting research on substances for which there is very little information on metabolism available in the literature. The subject of the study is within the range of constantly emerging branch of science - metabolomics. In addition, the data collected during the project can be useful for further research. In particular, that relating to drug design, predictions of metabolic pathways, evaluation of the toxicity or study of the mechanisms of addiction. Comparative studies of metabolites obtained from the *in vitro* and *in vivo* synthesis will allow to indicate markers of ingestion of drugs of interest. Additionally, the procedures developed during the presented project can be of significant importance for the development of analytical procedures for the purpose of medical diagnostics as well as toxicological and antidoping analysis. However, neither adapting procedures to the requirements of a particular type of analysis nor their verification and documentation are intended to be performed at any stage of the project.