Summary

Human organism has always been exposed to a vast array of chemicals encountered in the environment. Chemical revolution has significantly influenced biological evolution of humans leading to serious unpredictable toxicities. In response to continual chemical stress they have developed a variety of enzymes to transform these xenobiotics. Xenobiotics are mostly highly lipophilic and cannot readily be excreted from the body without metabolism to more hydrophilic, water-soluble metabolites. Not only environmental chemicals represent xenobiotics but also drugs, dietary components etc.

Biotransformation studies play an important role in the drug discovery and development process. Usually data from drug metabolism is required before a new substance can advance towards the development stages of a new therapeutic agent. Data on metabolism is frequently used to optimize drug candidates, suggest more active compounds or support toxicology studies. The increased flux of new chemical entities into drug discovery has placed an increased need for fast and reliable information on the metabolism of these substances. Liquid chromatography coupled with mass spectrometry can meet demands for rapid drugs and metabolites analysis imposed by modern drug discovery strategies.

This dissertation thesis presents an evidence of versatile usability of liquid chromatography and mass spectrometry in drug metabolism study and brings new approaches to solve questions of drug metabolism. Metabolites of quinlukast and sibutramine were characterized using a direct infusion of samples into the ion trap mass spectrometer. Coupling of liquid chromatography and mass spectrometry enabled study of amlodipine metabolism in detail. Differences in amlodipine metabolism from the chiral point of view, i.e. differences in metabolism of *rac*-, R- and S-amlodipine were specified. Further the metabolic profile of amlodipine was investigated and metabolic pathways yielding twenty-one characterized metabolites suggested. Liquid chromatography coupled with mass spectrometry was utilized in combination with “cocktail strategy”, in which a mixture of substrates is incubated at once, and the metabolites of the substrates are determined within a single assay. This combination enabled to develop rapid and reliable quantitative method for determination of glucuronides and human recombinant UDP-glucuronosyltransferases *in vitro*.