ABSTRACT

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Title of Doctoral Thesis: Analysis of statins in biological samples

The doctoral thesis deals with analysis of statins in biological samples. Statins are the most widely used drugs for the treatment of Familiar hypercholesterolemia. Due to very low concentration of statins (ng/ml) in human plasma a choice of suitable analytical methods is limited. Liquid chromatography with mass spectrometry detection is the most suitable technique due to high selectivity and sensitivity. Sample preparation step has to be used before chromatographic determination of analytes in complex matrices, such as biological samples.

Primarily theoretical part of doctoral thesis summarizes individual pharmacological properties and effects of statins. Another part is devoted to theoretical knowledge of UHPLC-MS/MS. The widest section deals with description of the individual sample preparation techniques. The practical part contends with development of UHPLC-MS/MS methods for the determination of statins in biological samples and selection and development of suitable sample preparation techniques. Solid phase extraction (SPE) and microextraction by packed sorbent (MEPS) are used as the sample preparation step. The results of experiments are summarized in five original articles appended in the supplement I-V. Brief comments of articles are documented in part “results and discussion”. Doctoral thesis is divided into two sections with regard to use of sample preparation methods. The first part deals with use of solid phase extraction. Method for the determination of atorvastatin, simvastatin and their metabolites using SPE-UHPLC-MS/MS techniques in human serum was developed. Validated method was applied to patients with Familiar hypercholesterolemia. The second part of practical thesis is focused on application of MEPS which enables use of very small volume of sample. SPE procedure of determination of atorvastatin and their metabolites in human serum was transferred to microextraction by packed sorbent. MEPS-UHPLC-MS/MS method was validated and replaced earlier developed SPE extraction. Another method using MEPS as the sample preparation step was developed for determination of pravastatin and pravastatin lactones in rat plasma and urine