

ABSTRACT

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Title: LC-HRMS analysis of selected antihypertensive drugs in biological material
for compliance assessment

About 40 % of Czech population between the ages of 25 and 64 suffer from arterial hypertension. Although an array of effective antihypertensives is available nowadays, optimal blood pressure during treatment is reached by mere 30 % of the patients. This is mainly due to the patients' poor adherence to the treatment, who use their medicaments incorrectly or not at all. The adherence of a patient to the treatment, as well as pharmacokinetics, represent the most significant source of variability of the answer to the treatment and notably influences its outcome. The monitoring of plasmatic levels of antihypertensives is one of the methods of modern medicine which enables both an effective supervision of the incorrectly compensated patients, and the adjustment of dosage scheme.

This diploma thesis focuses on development and optimisation of extraction procedures for selected antihypertensives (amiloride, amlodipine, betaxolol, bisoprolol, carvedilol, celiprolol, indapamide, metoprolol, moxonidine, nebivolol, nitrendipine, rilmenidine, urapidil). The method, subsequently validated in accordance with the Guidelines of European Medicines Agency (EMA), was used for determination of concentrations of antihypertensives in a serum by UHPLC-HRMS, assessment of compliance of patients and verification of correctness of the prescribed dosage.

The most suitable extraction method was the liquid-liquid extraction using ethyl acetate, where an optimal yield and repeatability were accomplished. All validation parameters met the required criteria, and the method was successfully put into practice. Within 12 months, 92 patients were examined (some even repeatedly) and the levels of a total of 173 samples were determined (mostly amlodipine, bisoprolol, and indapamide). Out of the total 92 patients, 17, 4 % were non-adherent.