

Charles University

Faculty of Pharmacy in Hradec Králové

Department of pharmaceutical chemistry and drug analysis

Candidate: Libuše Klepalová

Supervisor: doc. PharmDr. Petra Kovaříková, Ph.D.

Title of the Master's Thesis: Analytical and bioanalytical study of selected drugs using UHPLC

Abstract

High-performance liquid chromatography coupled with mass spectrometry plays a crucial role in drug analysis from biological materials, mainly due to its sensitivity, specificity and ability to provide structural information on the analytes.

Multiple myeloma is a serious hematologic disease, accounting for about 1 % of all oncological diseases. New drugs from the group of proteasome inhibitors namely, carfilzomib and bortezomib represent a great promises for patients with relapsing multiple myeloma or in the case of the resistant to other anticancer drugs.

The aim of this work was to develop pilot chromatographic conditions for HPLC-MS analysis of carfilzomib and bortezomib and evaluate different extraction of these drugs from plasma. Separation was carried out on an Ascentis column C₁₈ 10 x 3 mm, 3 μm, (Supelco, Germany). Electrospray ionization with ion trap mass analyzer were used in both cases. The mobile phase consisting of water and acetonitrile (20:80) was the most appropriate for carfilzomib. The flow rate of the mobile phase was set to 0.3 ml/min. For bortezomib, a mixture of 0.1% HCOOH and acetonitrile (35: 65) was chosen as the most suitable mobile phase. The mobile phase flow rate was 0.3 ml / min. A protein precipitation using 250 μl of acetonitrile with 0,01 % HCOOH per 50 μl of plasma was selected for carfilzomib. The same sample preparation method was chosen for bortezomib. However, in this case, higher volume of precipitating agents had to be used, namely 500 μl of acetonitrile with the addition of 0.1 % HCOOH.