1. ABSTRACT

High performance liquid chromatography (HPLC) is a progressive analytic method which belongs among the most frequently used separation techniques.

Iron is an irreplaceable biogenous element, which is involved in many important biochemical processes in human body. However, under specific pathophysiological conditions its severe effects may occur.

Anthracycline cytostatics belong to the frequently used drugs for the treatment of various hematologic malignity and solid tumors. Their most important toxic effect is cardiotoxicity. Anthracyclines are able to form complexes with iron that are very redox active. They produce by the cyclic mechanism the high amount of cytotoxic hydroxyl radicals. This mechanism is believed together with own redox ability of anthracyclines molecule to be responsible for the drugs cardiotoxicity.

Dexrazoxane, bisdioxopiperazine derivative, is the only clinically used drug for the treatment of anthracycline induced cardiotoxicity. It is supposed, that dexrazoxane is bioactivated inside the cardiomyocytes to active metabolite - ADR-925. Iron chelating ability of ADR-925 is believed to be responsible for the cardioprotective effect of dexrazoxane.

This work is aimed at development of the optimal mass spectrometry compatible chromatographic conditions for the separation of dexrazoxane, its hydrolytic intermediates as well as the active metabolite - ADR-925. The best separation was achieved using the chromatographic column Discovery® HS F5 150×3mm, 5µm I.D., (Supelco, USA). The mobile phase was composed of water (component A) and methanol (component B). Following gradient profile was employed: 0 – 4 min. (5 % B); 4 – 8 min. (5 – 20 % B); 8 -15 min. (20 % B); 15 - 15,01 min. (20 – 5 % B); 15,01 – 25 min. (5 % B), (v/v).

A flow rate of 0.3 mL/min, a column temperature of 25 °C and detection at 205 and 215 nm were used for the analysis.

The results of this work will be utilized for further development of LC-MS method for determination of dexrazoxane in biological material.