

## **ABSTRACT**

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology and Toxicology

Candidate: Tereza Morávková

Supervisor: Assoc. Prof. Přemysl Mladěnka, Pharm.D., Ph.D.

Title of Thesis: Assessment of the complex stoichiometry of the active dexrazoxane metabolite ADR-925 with iron and copper by the standard Job's method

Iron and copper are important trace elements which participate on many physiological processes in humans. Their kinetics in the organism is tightly regulated since both lack or excess of these elements are associated with pathological states. Free ions of iron and copper can catalyse reactive oxygen species (ROS) production and hence cause damage to proteins and DNA. Imbalance in these metals is linked with diabetes, cardiotoxicity, cirrhosis of the liver and neurodegenerative diseases as Alzheimer's disease or Parkinson's disease.

Dexrazoxane is a drug with documented protecting effect against cardiotoxicity of anthracyclines. A former theory associated its protective effects against these cytotoxic drugs with the iron-chelating properties of its active metabolite ADR-925.

The goal of this diploma thesis was to explore if ADR-925 is able to chelate  $\text{Fe}^{2+}$ ,  $\text{Fe}^{3+}$ ,  $\text{Cu}^+$  and  $\text{Cu}^{2+}$  ions at physiologically and pathophysiologically relevant pH values (4,5; 5,5; 6,8 and 7,5) and to determine the stoichiometry of the formed complexes by use of the standard Job's method.

It was found that ADR-925 is chelating iron and copper ions at all selected pH conditions. The complex 1:1 was found in most conditions, however, the method failed to establish the stoichiometry in certain cases.