ABSTRACT

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology & Toxicology

Student: Karolína Pelnářová

Supervisor: Prof. Přemysl Mladěnka, PharmD., Ph.D.

Consultant: Václav Tvrdý, MSc.; Marcel Hrubša, MSc.

Title of diploma thesis: Searching of effective cobalt chelators – 8-hydroxyquinolines

Cobalt is one of the essential trace elements present in the human body. It forms a part of the organometallic complex of vitamin B_{12}, which is essential for many physiological functions. Both overload and lack of cobalt in the body is associated with pathological conditions. Manifestations of deficiency can lead up to pernicious anemia or hypofunction of the thyroid gland. Cobalt intoxication can occur in an industrial environment, such as by cobalt metal dust during heavy metal processing, or by its release due to corrosion from orthopedic prostheses. Systemic toxicity is manifested by a number of endocrine, cardiovascular and neurological symptoms.

The main aim of this diploma thesis was to find effective chelators of cobalt from the group of substances derived from 8-hydroxyquinoline. *In vitro* spectrophotometric measurement was used to determine the degree of chelation. The effect of chelation was also monitored *ex vivo* in rat erythrocytes.

All tested chelators – 8-hydroxyquinoline, nitroxoline, chloroxine, clioquinol and iodoquinol, were able to chelate cobalt in the ratio 1:1 (chelator: cobalt) at all tested pH. The only exception was iodoquinol, which was practically inactive at this ratio with an exception of pH 7.5. In general, chelating efficacies can be ranged as follows: chloroxine = clioquinol > nitroxoline > 8-hydroxyquinoline > iodoquinol. Cobalt alone did not increase the lysis of rat erythrocytes, but an addition of chloroxine to cobalt significantly increased it. Clioquinol also increases the lysis of erythrocytes, but its effect appears to be mainly independent of cobalt. Iodoquinol, again independently of cobalt, at least partially protected erythrocytes form lysis. The effect of other test substances on the lysis of red blood cells in the presence of cobalt was insignificant.

In conclusion, all 8-hydroxyquinolines chelate cobalt ions *in vitro*, but their properties also need to be verified under more relevant biological conditions, as some chelators may paradoxically induce lysis of erythrocytes in the presence of cobalt ions.