ABSTRACT

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Cobalt, as part of vitamin B_{12}, is an essential trace element for human organism. However, long-term exposure to high doses leads to toxicity. Chronic cobalt intoxication is currently most commonly observed after the implantation of cobalt-containing prostheses, which in some cases do not work properly and cobalt is released from them by mechanical friction or corrosion. That not only leads to a local reaction, but cobalt ions also enter the blood and lymphatic circulation and thus cause a systemic reaction. The intoxication is then manifested by neurological, cardiovascular and endocrine symptoms, which can lead to irreversible changes or even to the death. However, a chelator that would be able to effectively and selectively bind cobalt and thus effectively treat intoxication is not available in clinical practice.

The aim of this thesis was a search for an efficient cobalt chelator among known metal chelators. Chelation was measured *in vitro* by a method based on spectrophotometric detection of unchelated cobalt ions at different pH levels ranging from 4.5 to 7.5.

A total of 14 potential chelators were determined: ammonium tetrathiomolybdate (ATTM), bathocuproine, ciclopirox, deferiprone, deferoxamine, dexrazoxane and its metabolite ADR-925, dithizone, diethylenetriaminepentaacetic acid (DTPA), egtazic acid (EGTA), ferrozine, *o*-cresolphthalein complexone (CPC), pyridoxal isonicotinoyl hydrazone (PIH) and salicylaldehyde isonicotinoyl hydrazone (SIH). All substances have shown some level of chelation at least under some conditions. The most active substances in the whole pH range were DTPA and ADR-925, highly effective were also ATTM, SIH, PIH and except for pH 4.5 dithizone, as well. Moderately effective were ferrozine and CPC. At pH 4.5, EGTA was also well effective.

In conclusion, substances capable of efficiently binding cobalt ions and therefore potentially clinically administrable cobalt chelators have been discovered. DTPA and ADR-925 are most likely to have the highest potential for clinical use. It will be, however, necessary to verify their selectivity and safety in future experiments.