

ABSTRACT

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Title of diploma thesis: Ability of copper chelators to interact with iron and zinc

Copper plays in the human organism a role of an element with indispensable significance, whose biological influence and effects depend on its quantity. With elevated concentrations in the human body, copper becomes toxic, resulting in pathological conditions. The most well-known disease is the Wilson's disease, whose treatment consists of oral administration of chelators, i.e. chemical compounds, which are capable of binding copper ions in various proportions and eliminating them from the organism. Chelation therapy is currently the first choice after confirmation of the diagnosis. Chelation toxicity results from several factors, e.g. inhibition of copper dependent enzymes or low selectivity to metals. And precisely the selectivity of chelators is being discussed in this diploma thesis. An ideal chelator should not interact with any of the other physiological ions, that are necessary for the proper functioning of the organism. Five of the most frequently therapeutically or experimentally used substances /trientine, D-penicillamine, bathocuproine (or more precisely, its sodium disulfonate salt, BCS), ammonium tetrathiomolybdate (ATM) and dimerkaprol/ were chosen for the study. The ability to interact with two other, in the body naturally occurring ions iron and zinc, was monitored. Interactions include not only the chelation of ferrous, ferric and zinc ions, but also their reductive activity toward ferric cations. The spectrophotometric method was used. All tests were conducted in four different pH settings, defined as physiological or pathological. All investigated compounds exhibited chelating ability, which means insufficient selectivity. ATM and dimerkaprol chelated iron and zinc most efficiently. The measured data also pointed to the fact that BCS and trientine do not have reductive capacity. From this study of interactions of copper chelators with iron and zinc, it ensued that none of the tested substances was sufficiently selective.