

## **Abstract in English**

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Name of thesis: Comparison of iron-chelating effects of clinically used peroral iron chelators and 8-hydroxyquinolines

Iron is an essential element, which takes part in many vital processes. However, excessive iron can be toxic for the organism by catalyzing production of free radicals. Long-term administration of blood transfusions in the therapy of various anaemias is the most common cause of iron overload. Each transfusion represents an intake of 200-250 mg iron in the organism, which due to low daily elimination (only 1-2 mg) leads to iron overload. As a result, complications like cardiovascular impairment or liver fibrosis can emerge. The risk of these severe complications can be reduced by administration of iron chelators.

Deferoxamine has been traditionally used for the chelation therapy of chronic iron overload, but to his disadvantages belong frequent parenteral applications. In these days we can also use modern orally active chelators (deferipron, deferoxamin). Furthermore, there is a wide range of potentially new indications (inflammation, tumor, cardiovascular and neurodegenerative diseases). In all these conditions oxidative stress plays an important role. It is necessary to remind that the efficiency

of chelation therapy can differ in dependence on pH, and pH reduction is well documented in some of pathological conditions mentioned above.

The aim of this study was the comparison of chelation efficiency of registered orally active chelators (deferipron, deferasirox) and a group of 8-hydroxyquinolines (8-OH-Q, chloroxin, cliochinol) in pathophysiologically important pHs. Chelation efficiency was measured by spectrophotometric method using ferrozine. Statistical analysis was performed by comparison of 95% confidence intervals.

It was found out, that the activity of tested chelators rised with increasing pH. Although some of the chelators – cliochinol, cloroxin, deferipron - chelated ferrous ions with equal efficiency at pH 5.5-7.5, their chelation potencial was lower at pH 4.5. The most efficient ferrous chelator at pH 7.5 was deferasirox. At pH 4.5 all chelators were relatively less efficient. Chelation curves at pH 7.5 for ferrous ions were almost identical to chelation curves for chelation of total iron at pH 4.5, which suggests high affinity of chelators to ferric ions.

All chelators formed stable complexes with iron and ferric ions were not reduced to redox-active ferrous ions.

In conclusion, at neutral pH there are probably not big differences among tested efficient chelators, but in conditions connected with acidosis it is worth having a respect to different chelation activity of these substances.