ABSTRACT

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Title of thesis: Zinc-chelating activity of selected novel chelators from 4-acylpyrazol-5-one group

Zinc plays a key role in many physiological functions in the human body. In case of increased concentrations of zinc in the body, a number of pathological manifestations may occur. In less severe cases, gastrointestinal discomfort and nausea can occur while in a worse case, cardiovascular failure can develop. After the diagnosis of zinc intoxication is confirmed, the chelation therapy is used. Its principle is based on the formation of complexes with excessive metal and their excretion. Substances from the group 4-acylpyrazol-5-ons were previously shown to be strong iron chelators. The aim of this thesis was to test the ability of these substances the chelate zinc and determine the structure-activity relationship. Based on the obtained results, it can be concluded that most of the tested 4-acylpyrazol-5-ons were almost inactive or showed ability to chelated zinc ions only at very high excess over Zn^{2+}. The most effective substances were H2QPyQ and H2Q4Q. However, each of them behaved very differently: chelation activity of H2QPyQ increased with increasing pH and reached 75 % of Zn^{2+} ions chelation at pH 7.5; while H2Q4Q reached about 50 % of Zn^{2+} ions at pH 5.5-7.5 at the highest ratio of 100:1 but reached 100 % at the most acidic condition of pH 4.5 even in a lower ratio of 10:1. Despite these results, these substances are unlikely to be used as zinc ion chelators, as their effectiveness in all conditions was lower than the experimentally used chelator TPEN.