Abstract

Charles University Faculty of Pharmacy in Hradec Králové Department of Pharmacology and Toxicology Candidate: Karolína Skoupilová Supervisor: prof. Přemysl Mladěnka, Pharm.D., Ph.D. Title of diploma thesis: Are currently used chelators of heavy metals also chelators of calcium and magnesium?

Calcium and magnesium are important elements for the human body. Calcium plays an important role in blood clotting and intracellular signalling, thus participating in muscle contraction and platelet aggregation, among other processes. Magnesium is a cofactor for many enzymes. A significant deficiency of both ions can manifest as disorders of heart rhythm and increased neuromuscular excitability.

The aim of this study was to determine the chelating activity of currently used heavy metal chelators and to determine the stability of the indicator. First, the ideal pH for the experiment was determined. In the next step, the chelation rate of 21 known metal chelators was measured using an *in vitro* spectrophotometric method. Finally, the chelation of the most active calcium chelators was verified on platelet aggregation in a human blood sample. At the same time, the long-term stability of the indicator ocresolphthalein complexone (CC) was determined.

In the first step, pH 7.5 was chosen, which was the only one suitable for our measurements due to its good sensitivity. The most effective calcium-chelating substances were ADR-925, ethyleneglycol-bis(2-aminoethylether)tetraacetic acid tetrasodium salt (Na₄EGTA), disodium edetate (Na₂EDTA), and diethylenetriaminepentaacetic acid (DTPA). Chelators significantly binding magnesium were ADR-925, Na₂EDTA, DTPA, iodoquinol, clioquinol, chloroxine, 5,7dibromoquinoline-8-ol and 8-hydroxy-7-iodoquinoline-5-sulfonic acid. The formed complexes with both metal ions were stable. At higher concentrations of certain halogenated derivatives of 8-hydroxyquinoline, precipitates were observed, making it impossible to fully evaluate their chelating abilities. The stability of the indicator was at least 105 days when stored in the refrigerator. Na₂EDTA, ADR-925, and Na₄EGTA were

able to completely inhibit platelet aggregation due to calcium chelation, with Na₂EDTA being the most effective.

In conclusion, a number of clinically used chelators are capable of strongly binding both calcium and magnesium ions, and the CC indicator is stable for at least 105 days.