

Newly Synthesised Fluorescence Iron Chelators with Cytotoxic Effects and *In Vitro*, *In Vivo* Imaging Possibilities

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ABSTRACT

Iron is an essential element for humans and most other organisms. It is crucial for processes such as oxygen transport, energetic metabolism (oxidative phosphorylation), detoxification of chemicals, synthesis of DNA and many others. On the other hand, the excess of free iron can participate in oxidative stress reactions with the production of free radicals (Fenton's chemistry) and may cause severe tissue damage. That is why both systemic and intracellular iron levels must be tightly regulated. Iron, not surprisingly, plays an important role in many pathological conditions like neurodegenerative diseases and cancer.

The project was focused on cancer study and was divided in two parts- chemical and biological. First step was concentrate on characterization of complexation possibilities newly synthesised chelators. The titrations with ferric and ferrous ions were performed. The chelators with highest affinity to irons ions were chosen for advanced studies. The project covers *in vitro* cytotoxic studies on different types of tumor cell lines (MiaPaca, Patu, Capan), MTT assay was used to establish IC 50. Cytotoxic effect of chelators on tumor cell lines was compared with cytotoxicity on human fibroblasts (healthy cell lines). Imaging possibilities of fluorescent chelators were studied as well. The fluorescent chelators were able to cross cellular membranes, in concentration of 1 μ M and thus provide us the image of their intracellular transport, subcellular localization and intracellular redistribution. For *in vivo* imaging *nu/nu* mice with suppressed immune system were used. The distribution of fluorescence chelators after administration was visualized by Xtreme device (Brucker).

Keywords: Iron, Chelators, Imaging, Tumor diseases, Cytotoxicity

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