Chelators controlling metal metabolism and toxicity pathways: applications in cancer prevention, diagnosis and treatment.


Source
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Abstract
Chelating drugs and chelator metal complexes are used for the prevention, diagnosis and treatment of cancer. Cancer cells and normal cells require essential metal ions such as iron, copper and zinc for growth and proliferation. Chelators can target the metabolic pathways of cancer cells through the control of proteins involved in the regulation of these metals and also of other molecules involved in cell cycle control, angiogenesis and metastatic suppression. Other targets include the inhibition of specific proteins such as ribonucleotide reductase involved in DNA synthesis, the inhibition of free radical damage on DNA caused by iron and copper catalytic centers, the inhibition of microbial growth in immuno compromised cancer patients and the decorporation of radioactive and other toxic metals causing cancer. Chelating drugs and metal ions can affect the metabolism, efficacy and toxicity of anti-cancer drugs such as doxorubicin, mitozantrone, bleomycin and hydroxyurea (HU). Although many experimental chelators have been shown to be effective as anti-cancer agents, only a few, e.g., dexrazoxane, deferoxamine (DFO) and triapine, have reached the stage of clinical testing or application. In many experimental models, deferiprone (L1) has been shown to be effective in cancer prevention and treatment, and in the inhibition of doxorubicin-induced cardiotoxicity. New anti-cancer drugs could be developed using chelators and chelator complexes with platinum and other metals, and also new protocols of combinations of chelators with known anti-cancer drugs.

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