Iron chelators in cancer chemotherapy.


Source

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Abstract

Iron chelators may be of value as therapeutic agents in the treatment of cancer. They may act by depleting iron, a necessary nutrient, and limiting tumor growth. Alternatively or additionally, they may form redox-active metal complexes that cause oxidative stress via production of reactive oxygen species, damaging critical intracellular targets and thereby eliciting a cytotoxic response. Studies in vitro have evaluated the structure-activity relationships and mechanism of action of many classes of iron chelators, including desferrioxamine (DFO), pyridoxal isonicotinoyl hydrazone (PIH) analogs, desferrithiocin (DFT) analogs, tachpyridine, the heterocyclic carboxaldehyde thiosemicarbazones, and O-Trensox. Animal studies have confirmed the antitumor activity of several chelators. Dexrazoxane has been approved for use in combination with doxorubicin, and its effectiveness in allowing higher doses of doxorubicin to be administered is, in part, based on the interactions of both drugs with iron. Clinical trials of the antitumor activity of chelators have been largely limited to DFO, which has been extensively studied as a consequence of its approved use for treatment of secondary iron overload. While the modest antitumor effects of DFO are encouraging, it is likely that more effective iron chelators may be identified.

PMID: 15579100