Iron chelators as anti-neoplastic agents: current developments and promise of the PIH class of chelators.


Source

Children's Cancer Institute Australia for Medical Research, The Iron Metabolism and Chelation Program, PO Box 81, High St, Randwick, Sydney, New South Wales, Australia.

Abstract

The chelator currently used to treat iron (Fe) overload disease, desferrioxamine (DFO), has shown anti-proliferative activity against leukemia and neuroblastoma cells in vitro, in vivo and in clinical trials. Collectively, these studies suggest that Fe-deprivation may be a useful anti-cancer strategy. However, the efficacy of DFO is severely limited due to its poor ability to permeate cell membranes and bind intracellular Fe pools. These limitations have encouraged the development of other Fe chelators that are far more effective than DFO. One group of ligands that have been extensively investigated are those of the pyridoxal isonicotinoyl hydrazone (PIH) class. In this review the marked anti-proliferative effects of the PIH analogs are discussed with reference to their mechanisms of action and structure-activity relationships. In particular, we discuss the activity of a novel group of ligands that are "hybrid" chelators derived from our most effective PIH analogs and thiosemicarbazones. The anti-tumor activity of the PIH analogs and other chelators such as tachpyridine, O-trensox and the desferrithiocin analogs have been well characterized in vitro. However, further studies in animals are critical to evaluate their selective anti-tumor activity and potential as therapeutic agents.

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