The medicinal chemistry of novel iron chelators for the treatment of cancer.


Source
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Abstract
Cancer is one of the leading causes of death worldwide and there is an increasing need for novel anti-tumor therapeutics with greater selectivity and potency. A new strategy in the treatment of cancer has focused on targeting an essential cell metabolite, iron (Fe). Iron is vital for cell growth and metabolism, forming a crucial component of the active site of ribonucleotide reductase (RR), the rate-limiting enzyme in DNA synthesis. Cancer cells in particular require large amounts of Fe to proliferate, making them more susceptible to the Fe deficiency caused by Fe chelators. Beginning with primordial siderophores, Fe chelators have since evolved to a new generation of potent and efficient anti-cancer agents. Recently, investigations have led to the generation of novel di-2-pyridylketone thiosemicarbazone (DpT) and 2-benzoylpyridine thiosemicarbazone (BpT) ligands that demonstrate marked and selective anti-tumor activity both in vitro and in vivo against a wide spectrum of tumors. The mechanism of action of these novel ligands includes alterations in the expression of key regulatory molecules as well as the generation of redox active Fe complexes. Interestingly, non-synthetic Fe chelators including silybin and curcumin, both of which are derived from plants, also have vast potential in the treatment of cancer. This review explores the development of novel Fe chelators for the treatment of cancer and their mechanisms of action.

PMID:
21192781