Designing and molecular docking studies of deferasirox and its derivatives

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Abstract: Cancer is one of main reason of death in the world. Drugs which could be able to act more selectively with higher potency are the basis of nowadays researches. [1] Iron is one of the essential metabolite for cell proliferation. Iron overload is accepted as one of the reason of cancer cause. Recently, iron chelators have been identified as a therapeutic approach to treat cancer by removing excess iron. [2] Furthermore, iron and Nickel are "Jmjd2 Histone Demethylases" cofactors. [3] This protein has an important role in cell proliferation in various cancers like bladder, colon, lung, prostate, and chest. [4] Hence, metal chelators could be a novel structure for both iron removal and Nickel-chelating in this field. For this purpose, the structures of deferasirox and its derivatives were considered.

We report herein design and molecular docking and structure-based deferasirox. The novel analogues containing some functional group or heterocyclic backbone such as tetrazole. The affinity of the designed compound was defined based on Autodock4 program. Due to Nickel role in JMJD2A; deferasirox and its derivatives were docked by JMJD2A to estimate chelation, interactions and inhibition constant. As a result, deferasirox and its derivatives can be considered as an appropriate candidate for the formation of an active-nickel complex in active site of protein. compound (6) which is the best structure for inhibiting JMJD2A with constant Inhibition 80 times lower than the natural inhibitor.

Keywords: Cancer; JMJD2A; Deferasirox; molecular docking

References

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