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Abstract

The medicinal use of the spice turmeric has been documented in Ayurveda (the Indian system of medicine) for over 6000 years. It is commonly used as a spice, flavoring agent, food preservative, coloring agent, and for decoration. There are extensive literature and research reports that suggest that curcumins potential in the prevention and treatment of cancer. Turmeric, a spice consumed daily by millions of people all over the globe contains a mixture of curcuminoids, curcumin-(a) being the main component, while demethoxy curcumin and bis-demethoxy curcumin are minor components. Curcumin has shown multiple therapeutic activities, especially antiproliferation in several cancer cell lines. Curcumin inhibits thioredoxin reductase (TrxR) irreversibly and forms an adduct. In order to compare the potency of all three naturally occurring curcuminoids, docking has been carried out at both active site of TrxR. It is clear from the present study that active site of TrxR occurs at the junction of its E and F chains. Volume and area of both cavities has been simulated and also compared the binding of all three naturally occurring curcuminoids by docking. By distance mapping of the most active conformations we concluded that Se atom of catalytic residue SeCYS498 is at the distance of 3.56 Å from C-13 of demethoxy Curcumin at the E chain active site, where C-13 carbon atom forms adduct with Se atom of SeCys498. We also report that at least one methoxy group is necessary for interaction with catalytic residues. Pharmacophore of both active sites of the TrxR receptor for curcumin and demethoxy Curcumin molecule has been drawn and proposed for synthesis of more probable potent synthetic molecules. In order to validate these in silico results in vitro testing has to be carried out.