Abstract

The Garcinia-derived biflavonoids GB1, GB2, kolaflavanone (together known as kolaviron) and morelloflavone have been reported for various bioactivities including protection of cellular tissues against damages from toxic compounds. In this study, computer-aided procedures were used to model the interaction of these naturally-occurring biflavonoids with aldehyde dehydrogenase (ALDH). This study sought to validate these compounds as potential inhibitors of the protein towards treatment/prevention of ALDH related pathophysiology-associated diseases. Detailed observation of the results obtained divulged that the Garcinia biflavonoids actually inserted only one of their monoflavonoid subunits into the putative substrate-binding pocket while the other subunit occupied the hydrophobic binding region in a manner that can prevent substrate access. Some amino acid residues found in the protein loop flanking the ligands within the putative binding pocket established interactions with the biflavonoids via hydrophilic bonds. Several hydrophobic interactions between the aromatic rings of the dimeric form of flavonoids and non-polar residues of the protein were observed to play crucial role in stabilizing the biflavonoids within the active site. Phe314 might further participate in π-π
stacking with the biflavonoids aromatic rings. The relatively large size of the biflavonoids enhances their occupation of the binding pocket, however having less interference with the solvent-exposed region. The compounds are therefore predicted as unique competitive inhibitors of ALDH.

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