In-silico study of binding interaction of a xanthone of *Hypericum mysorense* with aldose reductase

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In present, emphasis on plant research has vastly increased worldwide and a large body of evidence has been collected to show the immense potential of medicinal plants used in various traditional systems. *Hypericum mysorense*, is one such plant, a shrub with yellow flowers commonly found in central highlands of Sri Lanka. The timber of this plant has been reported to contain the xanthone, 3-hydroxy-2-methoxy xanthone, which has shown promising binding interactions with Aldose Reductase (AR), as a result inhibiting its action. AR is known to play a vital role in the secondary complications of diabetes, and therefore its inhibition proves to be an important drug target for the treatment of diabetes. For the *in-silico* studies, Tolrestat was used as reference. Docking and Binding energy calculations were performed using AutoDock Vina, and the active site of AR was defined using data from literature studies. Receptor and ligand complexes were subjected to Molecular Dynamic (MD) simulations using AMBER with GPU acceleration, where the dynamic behaviour of protein-ligand complex at different timescales was determined. MD simulations is applied in order to explore conformations of the protein receptor, optimize the structures of the final complexes, and calculate accurate energies. RMSD plots of the protein-ligand complexes within a 100 ns long trajectory were compared and it was prominent that 3-hydroxy-2-methoxy xanthone was well bound and stable within the active site of AR as compared to Tolrestat. This was further validated using the interaction diagrams of the ligands within the active site pocket. Followed by the MD studies, the absorption, distribution, metabolism, and excretion (ADME) properties, pharmacokinetic properties and the druglike nature of 3-hydroxy-2-methoxy xanthone was studied. 3-hydroxy-2-methoxy xanthone showed favourable physiochemical properties for oral bio availability with a very high gastrointestinal absorption and blood brain barrier permeation using the SwissADME web server.

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