

In-silico approach towards identification of inhibitor for cholesteryl ester transfer protein (cetp): a novel strategi

Abstract

Atherosclerosis is a multifactorial disease which caused by a long term process of an accumulation of lipids combines with an inflammatory response which forms plaques or atheroma. The current focus in preventing atherosclerosis is by raising the HDL-C level. One novel approach is by inhibition of Cholesterol Ester Transfer Protein (CETP) function. Aim: The aim of this study is to see whether HCA does bind to the same active site in the CETP tunnel and to see the stability of the ligand-protein binding. Method: Docking studies are carried out by using X-ray crystallography structure (PDB ID: 20BD and 4EWS) by using Glides software from Schrodinger Inc and validated results using GOLD. The molecular dynamic simulation are being carried out by Desmond (Schrodinger inc) by using the ligand-protein complexes from the docking results. Results: Based on the molecular docking studies, HCA does bind to the active sites of torcetrapib is and based on the MD simulation analysis, the binding of the ligand-protein complexes are stable throughout the simulation. Further verification on in vitro experimentation of HCA does shows the potency against CETP activity and the results are in consonance with the in silico studies. Conclusion: This study prepares a solid foundation on how the binding mode of HCA against CETP and the study of mechanism of actions should be carry forward in order to see the real interaction between CETP protein residue and HCA in increasing the HDL-C level