Molecular Docking Cytochrome P450 lsoform 2C9 with Phenytoin and Cimetidine (Poster Presentations) - Bandung International Conference on Medicinal Chemistry, 6-8 Agustus 2009

Arry Yanuar, author

Abstrak

ABSTRACT

Cytochrome P450 isoform 2C9 (CYP2C9) is a main enzyme which metabolizes phenytoin [I]. The inhibition of this enzyme will increase plasma level of phenytoin. Cimetidine is known as drug that inhibits this enzyme, resulting an increased plasma level of phenytoin [2]. Recently, the three dimentional molecular basis of interaction between phenytoin and cimetidine toward CYP2C9 has not been described well yet. The present findings may represent an important advance for understanding interaction CYP2C9 with drugs to predict its toxicity an also metabolism based on structural interaction from docking results. A computational methodology, molecular docking can be used to analyze interaction which exist between ligand and macromolecule. AutoDock is one of the most commonly used methodology, shows the efficiency of scoring function ligand that bound to its active site [3]. So that, it can be used to understand about interaction between phenytoin and cimetidine in CYP2C9. Crystal structure of CYP2C9 complexed with flurbiprofen (PDB ID: 1R90) has resolution 2.00 A. This structure, used in this experiment, has the closed conformational structure and complexed with S-warfarin. Three dimensional structure of phenytoin and cimetidine were minimized, charge were added for docking preparation. Binding of substrate phenytoin in CYP2C9 is stabilized by hidrogen bonds, interaction with cationic residue Argl08, hydrophobic interaction particularly with Phel 14. On the other side, binding of cimetidine inhibitor in CYP2C9 is stabilized by hydrogen bonds with some amino acid residues, including Glu300 which has role as anionic residue, also the exist of hydrophobic interaction. Cimetidine being competitive inhibitor of CYP2C9 at the substrate recognition site of phenytoin.