In Silica Analysis of Inhibition CYP3A4 by Nelfinavir using Molecular Docking Technique (Poster Presentations) - Bandung International Conference on Medicinal Chemistry, 6-8 Agustus 2009

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Abstrak

Cytochrome P450 3A4 (CYP3A4) contributes to the metabolism of 50% of drugs used in therapy [l]. Nowadays, the structures of CYP3A4 are available through crystallography technique and these structures show that CYP3A4 has a flexible active site which allows many probabilities of ligand interaction [2]. Nelfinavir, one of the HIV-Protease inhibitors, is a substrate and also an inhibitor of CYP3A4. However, the CYP3A4-mediated metabolism of nelfinavir result in unknown reactive metabolites which then inactivate CYP3A4 [3]. In silica method through molecular docking is used in this research to study the inhibition of CYP3A4 by nelfinavir and to predict the reactive metabolites of nelfinavir that inactivate CYP3A4. The docking result show that nelfinavir fits the CYP3A4 active site with the conformation that coordinates to the forming of M8 metabolite of nelfinavir. The docking result for M8 gives positive binding energy and the docking result for the intermediate metabolite between nelfinavir and M8 indicates that this intermediate metabolite is responsible for the inhibition of CYP3A4 by nelfinavir through mechanism-based inactivation.