Qualitative and Quantitative Analysis of the Interaction of Antifungal Drugs and Albumin via Molecular Docking Method

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Introduction

Albumin is the prominent protein of plasma and drug-albumin interaction causes changes in pharmacokinetic s and toxicity of drugs(1). Studying drug-albumin interaction is an important and practical research field. No s ystematic computational study has been dedicated to the interaction of antifungals with albumin despite their significant role in pharmaceutical medications. In the present contribution, different antifungal drugs were e xamined by molecular docking to find possible binding sites with albumin and obtain structural information o f drug-albumin complexes.

Methods

Molecular docking calculations were performed by AutoDock 4.2 software(2). Interaction patterns were achie ved by Ligplot. 3D structures of albumin with warfarin and diazepam as representatives of active sites 1 & 2 were extracted from Brookhaven Protein Bank (2BXD & 2BXF).

Results and Discussion

Results revealed that antifungals made hydrophobic contacts and H-bonds with albumin. It was found that wi thin active site 2, Fenticonazole exhibited lowest free binding energy (-9.89 kcal.mol^{-1}) while Flucytosin show ed loosest binding to the albumin (-3.06 kcal.mol^{-1}). In the active site 1, Oxiconazole showed tightest binding (-9.01 kcal.mol^{-1}) while loosest contact was attributed to Fluconazole. However Fenticonazole could also achie ve high score (-8.70 kcal.mol^{-1}) within active site 1 but results indicated that polar interactions might be imp ortant in binding to active site 1 since oxiconazole possessed oxime moiety. Binding maps indicated that high er affinity of Fenticonazole might be related to possible hydrophobic contacts via additional aromatic rings at tached to sulfur atom.

Conclusion

Current computational results revealed that different antifungal drugs are important interfering agents since they may bind to human serum albumin with relatively high binding energies (< -6 kcal.mol^{-1}). Such studies m ight aid in developing novel antifungal scaffolds, comparing the mechanism and binding affinity of antifungal drugs with albumin and also obtaining structural information about drug-albumin complexes.

Keywords

Antifungal, Albumin, Pharmacokinetics, Docking, Binding

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