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Bioinformatics analysis of human serum albumin for determination of herbal anti-diabetic compound binding site

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Background and Aims: Diabetes mellitus is known with increase in blood glucose concentration. According to WHO data, 346 million people worldwide suffering from diabetes. Unfortunately, most of anti-diabetic drugs have several side effects. Therefore, many studies have been focusing to discover new anti-diabetic compounds. Trigonella foenum-graecum (fenugreek), is an annual plant that has been used traditionally in treatment of both types of diabetes. Seeds of fenugreek contain an unusual amino acid, (2S,3R,4S) 4-hydroxyisoleucine (4OH-Ile), that had anti-diabetic effects through increasing insulin secretion and decreasing insulin resistance. It is necessary to know the interaction between 4OH-Ile and human serum albumin (HSA) as a carrier, in order to understand the mechanism of drug action at molecular level.
Methods: We applied Autodock 4 program to calculate possible interactions of 4OH-Ile and HSA. The docking parameter files were generated by adopting the Lamarckian genetic algorithm method. The grid parameter file was first set to the whole protein and then was restricted to the assumed active site. Finally, the best docking energy results were studied and assumed as the possible candidates for ligand-protein interaction.
Results: Our study indicated 4OH-Ile could bind to this site with the best inhibition constant and binding-energy of 77.87µM and -5.61Kcal/mol respectively. It is also have intermole-energy =-6.28 Kcal/mol, ligand-efficiency =-0.56Kcal/mol and electrostatic-energy =-2.97Kcal/mol. The interaction is supported mainly by hydrophobic interaction even though some hydrogen binding are involved too. There were hydrogen bonds between 4OH-Ile and amino acid residues of HSA such as LYS 190, ARG 428, LYS 432 and LYS 519.
Conclusions: 4OH-Ile is located in the sub-domain IIA close to Lys190 and LYS 519. The strength of this binding is well balanced and enables HSA for both carrying and releasing 4OH-Ile in blood. This study can supply insight into the mechanism of interaction between 4OH-Ile and HSA.

Keywords: Human serum albumin; *Trigonella foenum-graecum*; (2S, 3R, 4S) 4-hydroxyisoleucine; Molecular modeling; Diabetes mellitus