

IN-SILICO ANALYSIS AND DOCKING OF HUMAN SERUM PROTEIN WITH QUERCETIN IN T2DM

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Abstract - Quercetin acts on human serum protein. The human serum albumin in turn switches on the gene in the islet of Langerhans in the pancreas which induces the beta cells to produce insulin. This helps to lower the sugar levels in T2DM (type 2 Diabetes mellitus) patients. The interaction between Quercetin and human serum protein has been studied in detail using the Autodock (vina) software. Quercetin binds to the human serum protein and the docking energy for the process was recorded to be -9.2 kcal/mol.

Key Words: Quercetin, T2DM, Autodock (vina), Docking

1.INTRODUCTION

Diabetes has been one of the most prevalent conditions in Asian pacific region. There are two types of diabetes Type 1 and Type 2. Among these, type 2 has been considered as chronic progressive state. During this state the plasma glucose rises gradually in spite of the type of treatment [1].

Type 2 diabetes is one of the major public health concerns in both developing and developed countries in the Asian-Pacific region. It has become epidemic in a number of countries, particularly in newly industrialized nations. Healthcare budgets of many countries have been affected as a result of the direct and indirect social and economic costs of treating diabetes and its complications. Type 2 diabetes results in the following symptoms premature morbidity and mortality, particularly from cardiovascular disease (CVD), blindness, amputations and renal failure. Also it is a part of the metabolic syndrome, a cluster of major CVD risk factors previously also referred to as the insulin resistance syndrome, Syndrome X or the Deadly Quartet [2].

Quercetin (Pubchem CID: 5280343) is a polyphenolic flavonoid with potential chemopreventive activity. Quercetin, ubiquitous in plant food sources and a major bioflavonoid in the human diet [3]. Quercetin is rich in

capers, lovage, dock and raddish leaves and in red onions, higher concentrations of quercetin occur in the outermost rings and in the part closest to the root, the latter being the part of the plant with the highest concentration [4]. Quercetin, the most commonly found flavonoid in the human diet, has been shown to exert potent free radical scavenging and antioxidant actions, to cause vasodilatation in isolated vascular preparations, and to elicit blood glucose-lowering (anti-diabetic) effects in experimental diabetes [5]-[9].

Based on several in vitro, animal models and some human studies, dietary plant polyphenols and polyphenol-rich products modulate carbohydrate and lipid metabolism, attenuate hyperglycemia, dyslipidemia and insulin resistance, improve adipose tissue metabolism, and alleviate oxidative stress and stress-sensitive signaling pathways and inflammatory processes. Polyphenolic compounds can also prevent the development of long-term diabetes complications including cardiovascular disease, neuropathy, nephropathy and retinopathy. Further investigations as human clinical studies are needed to obtain the optimum dose and duration of supplementation with polyphenolic compounds in diabetic patients [10].

Significant evidence suggests that polyphenol-rich diets have the ability to protect against diabetes. The benefits of dietary polyphenols for type 2 diabetes can be summarized as: protection of pancreatic β -cells against glucose toxicity, anti-inflammatory and antioxidant effects, inhibition of α -amylases or α -glucosidases and thus decrease of starch digestion, and inhibition of advanced glycation end products formation [11]. Polyphenols, especially the large polymeric type or condensed tannins, appear to be responsible in part for the reduced glycemic response to carbohydrate foods [12]. In this paper we have made an attempt to study detailed interaction between human serum albumin and Quercetin.

2. MATERIALS AND METHODS

2.1. Pubchem

PubChem is an important public, web-based information source for chemical and bioactivity information. In order to provide convenient structure search methods on compounds stored in this database, one mandatory component is a web-based drawing tool for interactive sketching of chemical query structures [13]. PubChem is a database of chemical molecules and their activities against biological assays. In addition it could be used to calculate various physical properties of the molecule. The structure of Quercetin was retrieved from Pubchem in SDF format.

2.2. Protein Data Bank

Protein data bank (PDB) is a repository for 3-D structure of protein and which studies various proteins in detail. The 3-D file of human serum protein was obtained from PDB(Pdb ID 1N5U).

2.3. Autodock (vina)

Autodock is a docking and simulation software particularly used to study the interaction of ligand and receptor molecules. This docking and simulation software was used to load the ligand as well as the protein files and to study the interaction between Quercetin and human serum protein [14].

3. RESULT AND DISCUSSIONS

The ligand compound Quercetin structure was obtained from Pubchem (Fig-1).

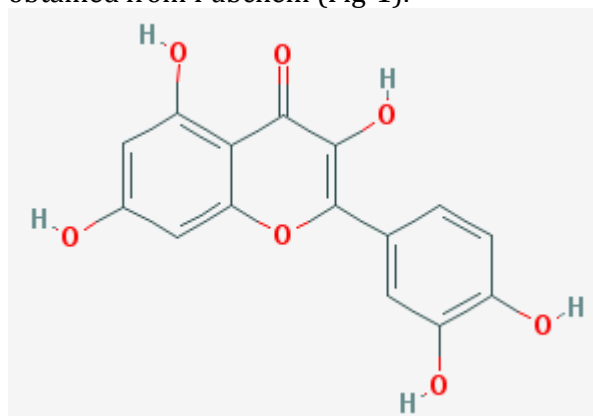


Fig -1: Quercetin 2D conformer from Pubchem

The human serum protein pdb file was obtained from PDB (Fig-2). Structural details of Human serum albumin was obtained from PDB and visualized in pymol.

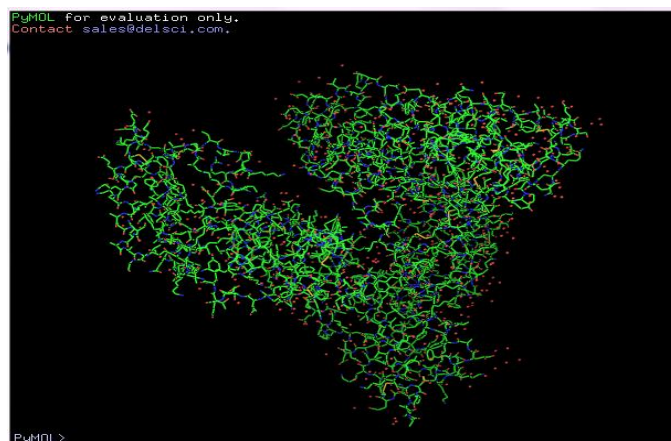


Fig-2: PDB file of human serum albumin

Docking of the ligand and the protein files was carried out by AutoDock (vina). It was observed that Quercetin compound binds to the A chain of human serum albumin at four different site with low binding energy. (Fig-3).

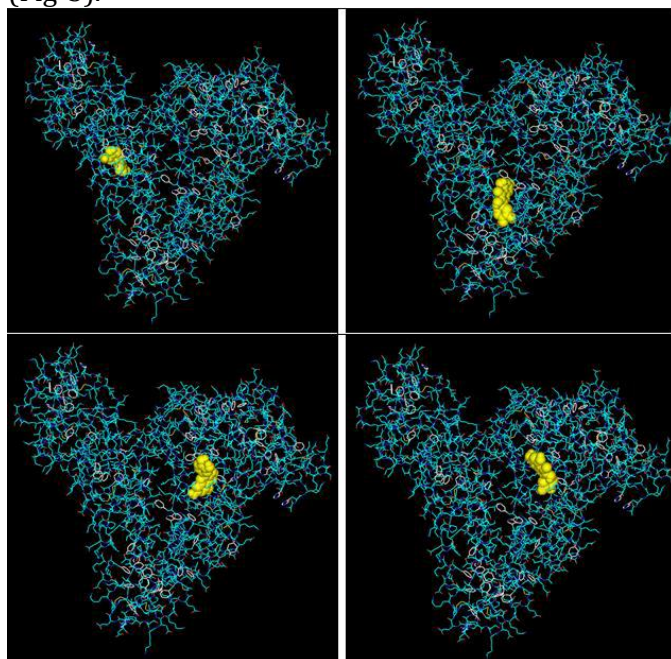


Fig-3: Quercetin displayed as spacefill model (in yellow) docked with human serum albumin (displayed as wireframe model)

Table 1: Results of Autodock (vina)

Mode	Affinity (kcal/mol)
1	-9.2
2	-8.4
3	-8.4
4	-8.4

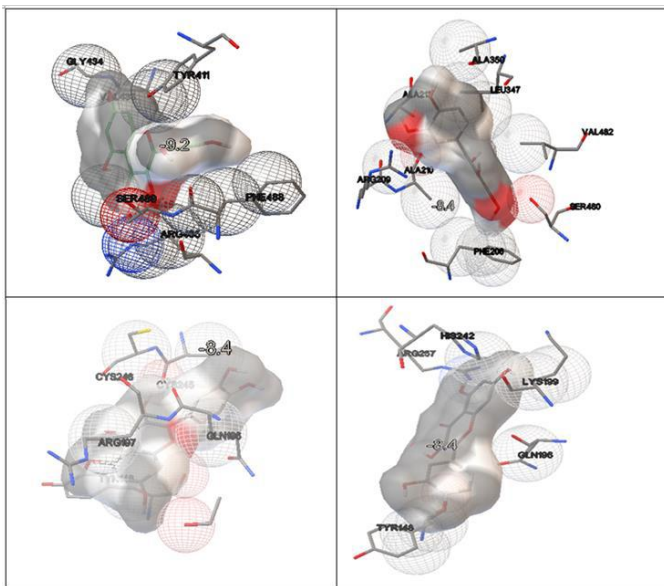


Fig-4: Atoms of amino acids interacting with the ligand molecule Quercetin at their respective binding energies.

The energy obtained after docking was -9.2 kcal/mol. This shows that Quercetin binds to human serum protein and the docked conformation has low energy and hence stable.

4. CONCLUSION

The insilico docking energy of -9.2 kcal/mol indicates that the interaction between Quercetin and human serum protein in the bound state is low. This shows stable conformation of Quercetin as well as the existence of interaction between Quercetin and chain A of human serum protein, this interaction may help in stimulating the Islets of Langerhan cells of the pancreas to produce insulin. Thus the intake of quercetin rich food in diets of patients with Type 2 diabetes may considerably lower the blood glucose level of Type 2 diabetic patients. Hence the inclusion of Quercetin in the diet of people with type 2 diabetes may reduce risk factors associated with diabetes.

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BIOGRAPHIES



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