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Research Article

In silico Study of Some Isolated Compound Present in *Aconitum Carmichaelii* against Diabetes

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Abstract

Hyperglycemia prompts disability of muscle development and advancement of diabetes mellitus (DM). It is a dynamic condition in which the body winds up impervious to the ordinary impacts of insulin and additionally step by step loses the ability to deliver enough insulin in the pancreas. It is also related with modifiable way of life hazard factors. While there is currently no cure for type 2 diabetes, the condition can be managed through some medications. Here we choose to review a paper NATURAL PRODUCTS AND PLANTS AS POTENTIAL ANTIDIABETIC DRUGS where different medicinal plants were suggested which gives good result against Type 2 Diabetes. We have selected the plant *Aconitum Carmichaelii* which gave remarkable anti-diabetic effects on mice. The glycans present in this plant exhibited pronounced hypoglycemic effects in normal mice. So, we selected this plant for in silico computational analysis to examine its effects on Alpha- amylase and 1,6 Fructose bi-phosphate protein enzyme. This two protein enzyme plays important role in controlling the blood glucose level. Also to analyses the effects of bio availabilities of these plant in human body.

INTRODUCTION

Diabetes has become a common disease nowadays. People of different ages can be affected by different type diabetes due to inability of pancreas to produce enough insulin or the resistant cells to insulin. This is called Diabetes mellitus. According to WHO Diabetes mellitus is a chronic disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. Such a deficiency results in increased concentrations of glucose in the blood, which in turn damage many of the body's systems, in particular the blood vessels and nerves. There are two principle forms of diabetes - Type 1 diabetes (formerly known as insulin-dependent) in which the pancreas fails to produce the insulin which is essential for survival. This form develops most frequently in children and adolescents, but is being increasingly noted later in life. Type 2 diabetes (formerly named non-insulin-dependent) which results from the body's inability to respond properly to the action of insulin produced by the pancreas. Type 2 diabetes is much more common and accounts for around 90% of all diabetes cases worldwide. It occurs most frequently in adults, but is being noted increasingly in adolescents as well. Recently compiled survey data of WHO shows that approximately 150 million people have diabetes mellitus worldwide, and that this number may well double by the year 2025. Much of this increase will occur in developing countries and will be due to population growth, ageing, unhealthy diets, obesity and sedentary lifestyles [1-5].

Molecular docking is a very important tool in the development of new drugs. Docking method allows characterizing the behavior of an experimental small molecule in the binding site of the receptor target of interest. A successful docking methodology must be able to correctly predict the native ligand pose the receptor binding site (i.e.to find the experimental ligand geometry within a certain tolerance limit) and the associated physical-chemical molecular interactions [6-10].

Aconitum Carmichaelii is a species of flowering plant of the genus *Aconitum* in the Ranunculaceae family. It is native to East Asia and found in Bangladesh, India, Bhutan, Chine, Malaysia, and Myanmar. It is commonly known as Chinese aconite; Carmichael's monkshood or Chinese wolfs bane. Growing to 1.2 meters (4 ft) tall by 30 centimeters (12 in) wide, it is an erect perennial, with 3- to 5-lobed ovate, leathery leaves. Dense panicles of blue flowers are produced in late summer and autumn [11-13].

Aconitum is an essential component in the formulations of Chinese and Japanese traditional medicine. They possess various pharmacological properties such as cardio tonic effect, blood pressure elevation, analgesic, anesthetics, and anti-inflammatory effect. In Chinese herbal medicine, the plants tubers and roots are generally preferred for the treatment of various diseases, such as collapse, syncope, rheumatic fever, painful joints, gastroenteritis, diarrhea, edema, bronchial asthma, various tumors, and some endocrinal disorders like irregular menstruation [14-20].

METHODS AND MATERIALS

Protein preparation

Three dimensional protein structure of Alpha-amylase (PDB

ID: amylase (PDB id: A (1PPI) and 1,6- Fructose bisphosphate PDB id:(F 2JJK)] was downloaded in pdb organize from the protein databank [21,22]. From that point onward, structure was arranged and refined utilizing the Protein Preparation Wizard of Schrödinger-Maestro v10.1. Charges and bond orders were allocated, hydrogens were added to the overwhelming molecules, selenomethionines were changed over to methionines and all waters were erased. Utilizing power field OPLS_2005, minimization was completed setting most extreme substantial iota RMSD (root-mean-square-deviation) to 0.30 Å.

Ligand preparation

Compounds were reprocessed from PubChem databases i.e **Salicylic acid** and **P-Hydroxy-cinnamic acid.**

Glide standard precision (SP) ligand docking

SP versatile ligand docking was done in glide of Schrödinger-Maestro v10.1 inside which punishments were associated with non-cis/trans amide bonds. Van der Waals scaling variable and fractional charge cutoff was being 0.80 and 0.15, exclusively for ligand molecules. Last scoring was performed on vitally restricted positions and appeared as Glide score. The best docked pose with most insignificant glide score regard was recorded for each ligand.

Ligand based ADME/Toxicity prediction

The QikProp module of Schrodinger (Maestro, form 10.1) is a rapid, exact, easy to-use absorption, distribution, metabolism, and excretion (ADME) anticipating setup to convey certain descriptors related to ADME. It predicts both physicochemical basic descriptors and pharmacokinetically critical properties. ADME properties choose sedate like action of ligand iotas in light of Lipinski's regulate of five.

ADME/T properties of the compound (DIM) was examined utilizing Qikprop 3.2 module. This investigation is finished by following server,

- http://www.scfbioiitd.res.in/software/drug design/ lipinski. jsp#anchortag
- https://ilab.acdlabs.com/iLab2/index.php
- http://www.molinspiration.com/cgi-bin/propertiess

RESULT AND DISCUSSION

In silico analysis Molecular docking analysis

In this examination, the coupling method of α-amylase protein and 1,6-Fructose bi-phosphate was explored by doing computational investigation, skim docking. Both Glid standard (SP) and additional precision (XP) mode had been presented, where additional accuracy mode utilized for cross approval reason. The consequences of docking examination were depicted in Table 1 and the docking figure appeared in Figure 1.

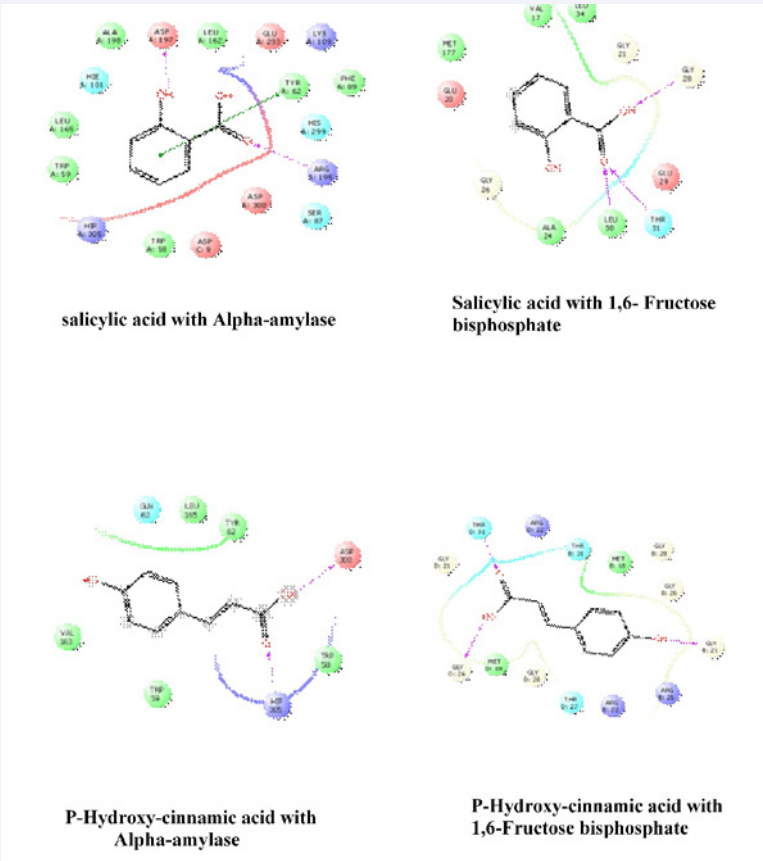


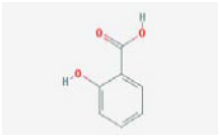
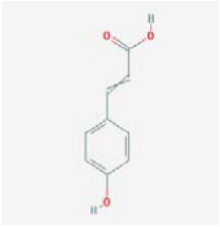
Figure 1 Docking results of Salicylic Acid and P-Hydroxy-cinnamic acid with Alpha amylase and 1,6-Fructose biphosphate.

Table 1: Docking results of Salicylic Acid and P-Hydroxy-cinnamic acid with Alpha-amylase PDB id: A (1PPI) and 1,6-Fructose biphosphate PDB id:(F 2JJK)]

Alpha Amylase: PDB id: A (1PPI)

Compound name	Pubchem ID	Docking score	Glide e model	Glide energy
Salicylic acid	338	-4.188	-32.819	-26.045
P-Hydroxy-cinnamic acid	637542	-4.452	-30.762	-22.835
1,6- Fructose Bi phosphate PDB id:(F 2JJK)]				
Compound name	**Pubchem ID**	**Docking score**	**Glide e model**	**Glide energy**
Salicylic Acid	338	-5.532	-35.527	-27.525
P-Hydroxy-cinnamic acid	637542	-6.003	-40.687	-29.477

Table 2: ADMET properties of Salicylic acid, P-Hydroxy-cinnamic acid, by QikProp module of Schrodinger.

Name of molecules	Pubchem CID	structure	MW	HB donor	HB acceptor	Log p	Molar refractivity
Salicylic acid	338		138.122 g/mol	**2**	**3**	1.87	35.42
P-Hydroxy-cinnamic acid	322		164.16 g/mol	**2**	**3**	1.43	45.13

ADME and toxicity analysis ligand based ADME prediction

The medication like action of the ligand molecule was orchestrated using ADME properties by QikProp module of Schrodinger. The ADME properties of the compound **Salicylic acid and P-Hydroxy-cinnamic acid** were assessed with QikProp module of Schrodinger, appeared in Table 2. The chose properties are known to impact metabolism, cell penetration, and bioavailability.

CONCLUSION

In experimenting the compound **Salicylic acid** and **P-Hydroxy-cinnamic acid** exhibit in the plant ***Aconitum Carmichaelii*** which was recommended by the author in their paper NATURAL PRODUCTS AND PLANTS AS POTENTIAL ANTIDIABETIC DRUGS, we got an amazing docking score. Additionally, in ADME investigation this mixes takes after the Lipinski's run which implies it might give better prominent bio availabilities. As it additionally gives hypoglycemic impacts in mice which we have found in the chose paper we can propose this compound for additionally tries.

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