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ANTI-HYPERGLYCAEMIC PROPERTY OF *CINNAMON VERUM* USING AN *IN SILICO* APPROACH

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ABSTRACT

Food we eat is converted into glucose and transported to various cells with help of digestive enzymes, hormones and transporter. Hyperglycaemia means high blood sugar or glucose. Much research has been devoted to natural products that can modulate these mechanisms as they are considered safer and more economical than drugs. Cinnamon is a widely known culinary herb and usedas traditional medicine. The objective of this research, an in-silico approach is used to study inhibitionof enzymes leading to hyperglycaemic condition by phytochemicals from cinnamon. An approach was made to bind selected phytoligands with receptors and inhibiting glycation products.

KEYWORDS: *Cinnamomum verum, Hyperglycaemia, Enzyme Inhibition, Molecular docking.*

INTRODUCTION[1][2][4][6]

Starch from food is converted into glucose with help of digestive enzyme, α- amylase. Various enzymes, hormones and transporter helps moves glucose intoyour cells to give them energy. Hyperglycaemia means high blood sugar or glucose. It happens when your body doesn't make enough insulin or can't use it the right way. Various symptoms of hyperglycaemia include *seizures*, *fever* and *dyspnea*. Sustained hyperglycaemia also results in micro- and macrovascular complications occurring through a number of mechanisms of which oxidative stress (OS) and inflammatory changes via the innate immune system have increased in interest for medical diagnostics.

Hyperglycaemia is related to diabetes mellitus. Chronic hyperglycaemia is considered to be a

major causative factor in the establishment of microvascularand macrovascular complications observed in T2DM. Reactive oxygen species(ROS), as a result of hyperglycaemia, are known to damage nucleic acids, lipids, and proteins with the degree or extent of damage related to the duration of hyperglycaemia.

Dietary approaches for managing hyperglycaemia centre around regulating carbohydrate digestion, absorption and glucose uptake rates.

Much research has been devoted to natural products that can modulate these mechanisms as they are considered safer and more economical than drugs.[12]

Cinnamon is a widely known culinary herb and traditionally used in medicine applications. Cinnamon, is harvested in sheets found beneath the bark of tree, has been being widely used to treat cough and sore throat since medieval times. It also has a popular history as a commonly used spice and flavouring material for desserts, candies, chocolate, etc.[3][5][7][9]

Taxonomic Classification[8]

Table 1: Taxonomic Classification of Cinnamon.

Kingdom	Plantae
Subkingdom	Viridiplantae
Infrakingdom	Streptophyta
Super-division	Embryophyta
Division	Tracheophyta
Subdivision	Spermatophytina
Class	Magnoliopsida
Superorder	Magnolianae
Order	Laurales
Family	Lauraceae
Genus	Cinnamomum
Species	*Cinnamomum verum*

Pharmacological Activities[15]

- Anti-oxidant
- Lipid-lowering
- Anti-cancer
- Neuroprotective
- Anti-inflammatory
- Cardiovascular protective

- Anti-microbial Phytoconstituents:

Phytochemicals present are epicatechin, terpinenol, phenols, fibre, thiamine, tannins, protein, carbohydrate, fats, piperitone, cinnamic acid, cinnamaldehyde, proanthocyanidin and coumarin.

Table.2: Nutritional Composition of Cinnamon powder.

Carbohydrate	0.4g
Protein	0.1g
Fats	0.03g
Ash	2.5%
Moisture	0.5%
Fibre	1.0g
Calcium	26mg
Potassium	11mg
Ascorbic acid	30.9mg
Vitamin A	8IU
Beta-carotene	3µg

Fig.1: *Cinnamon.*

MATERIAL AND METHOD

- **Molecular Docking**

Proteins selected as target[11]

Sr. No.	Protein	PDB ID	Binding Site
1	Pancreatic alpha-amylase	3BAI	X= 8.376 Y= 28.730 Z= 50.227
2	GLUT1	4PYP	X= 583.669 Y= -30.811 Z= 202.910

Phytochemicals selected as ligand[9][10]

Sr. No	Phytochemical	Molecular Weight
1	Cinnamaldehyde	132.16
2	Cinnamic acid	148.16
3	Proanthocyanidin A	592.5

Protein preparation[14]

1. Proteins (target) were procured from RCSB PDB in the PDB format file(.pdb)
2. The targets were translated into receptor form by deleting water molecules, inserting polar hydrogens and by giving Kollman charges inAutodock Tools-1.5.6
3. Select grid for dimension of binding site and save it as grid file in textformat (.txt)
4. Save it in the PDBQT format (.pdbqt)

Ligand preparation[13][14]

1. Ligands were procured from PubChem in the 3D SDF format file
2. Convert 3D SDF format into PDB format using PyMol
3. Save it in the PDBQT format (.pdbqt)

Molecular docking[13][14]

1. Create a config file in text format (.txt) with reference to grid file
2. The docking was carried out by putting command in Command Prompt (cmd) using docking parameters
3. Docking parameters were kept constant for all the docking studies
4. The conformer with the lowest binding free energy was used for furtheranalysis
5. Results were analysed using PyMol

RESULTS

- Docking results

Binding Energy (Kcal/mol)	Cinnamaldehyde	Cinnamic acid	Proanthocyanidin A
Pancreatic alpha-amylase	-5.3	-5.8	-8.8
GLUT1	-5.6	-5.8	-9.4

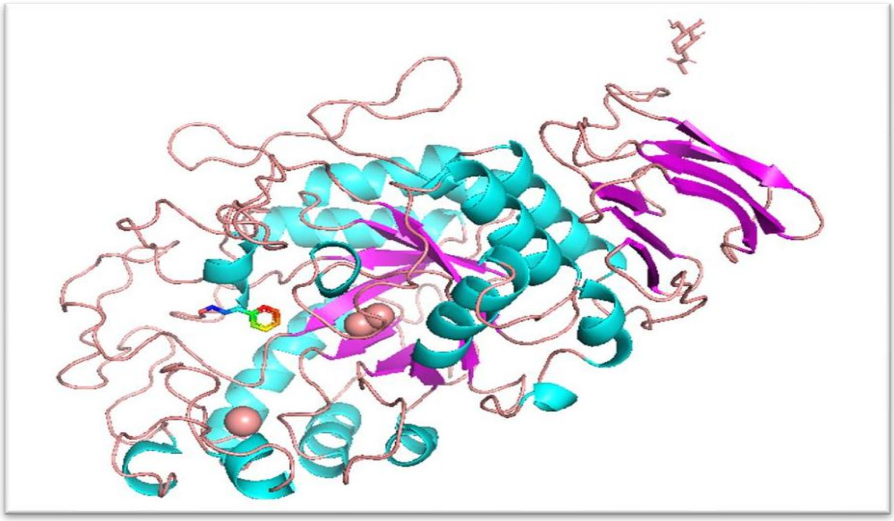

Fig.2: Docking of Pancreatic α-amylase with Cinnamaldehyde.

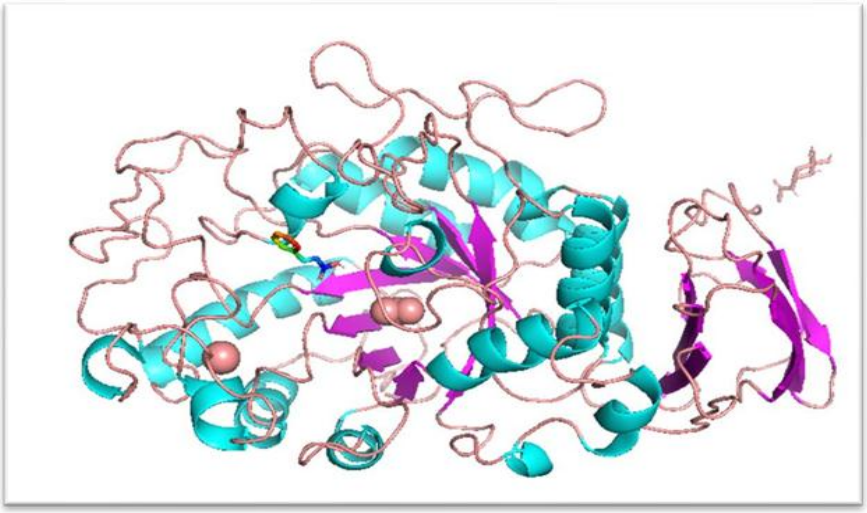

Fig.3: Docking of Pancreatic α-amylase with Cinnamic acid.

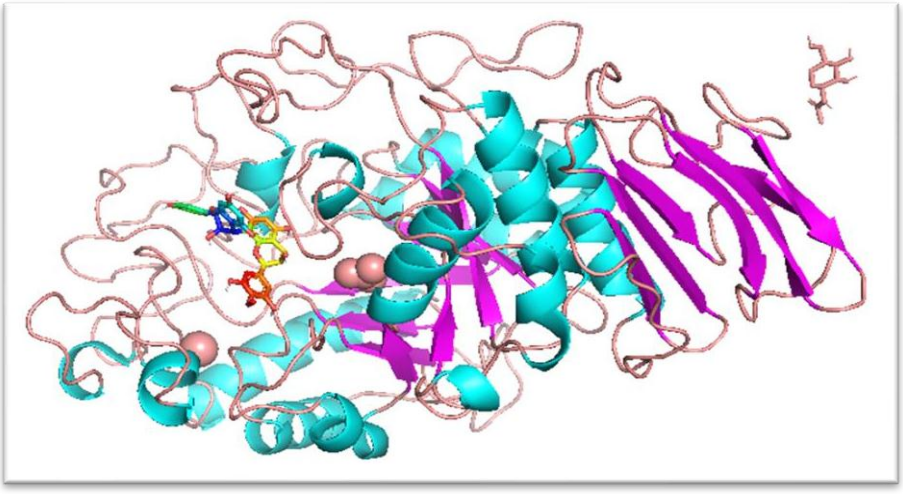

Fig.4: Docking of Pancreatic α-amylase with Proanthocyanidin A.

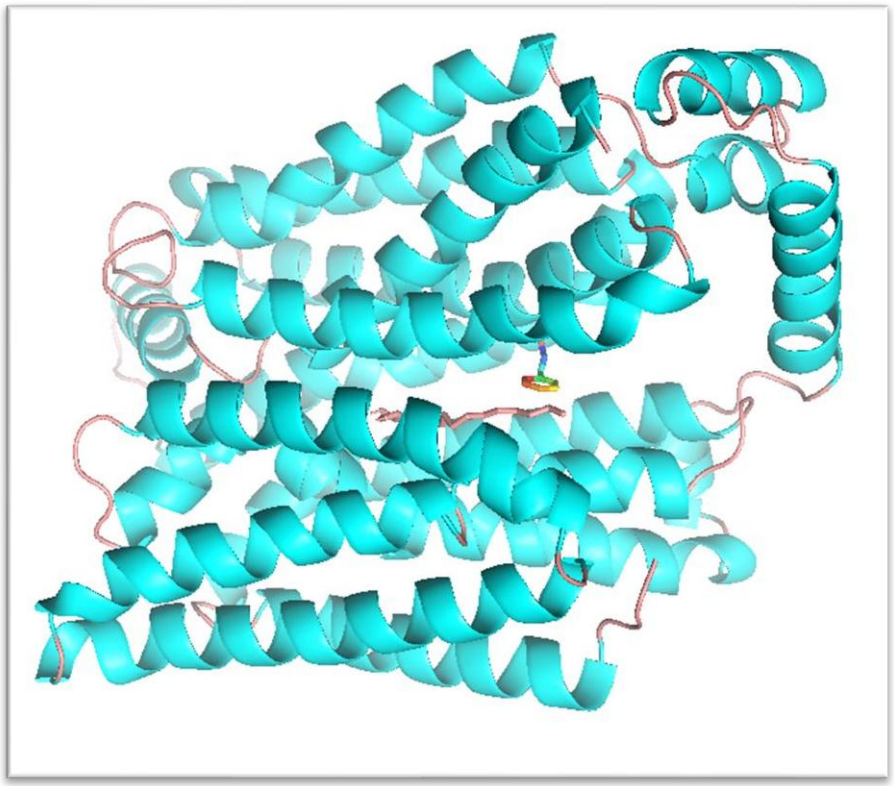

Fig.5: Docking of GLUT 1 with Cinnamaldehyde.

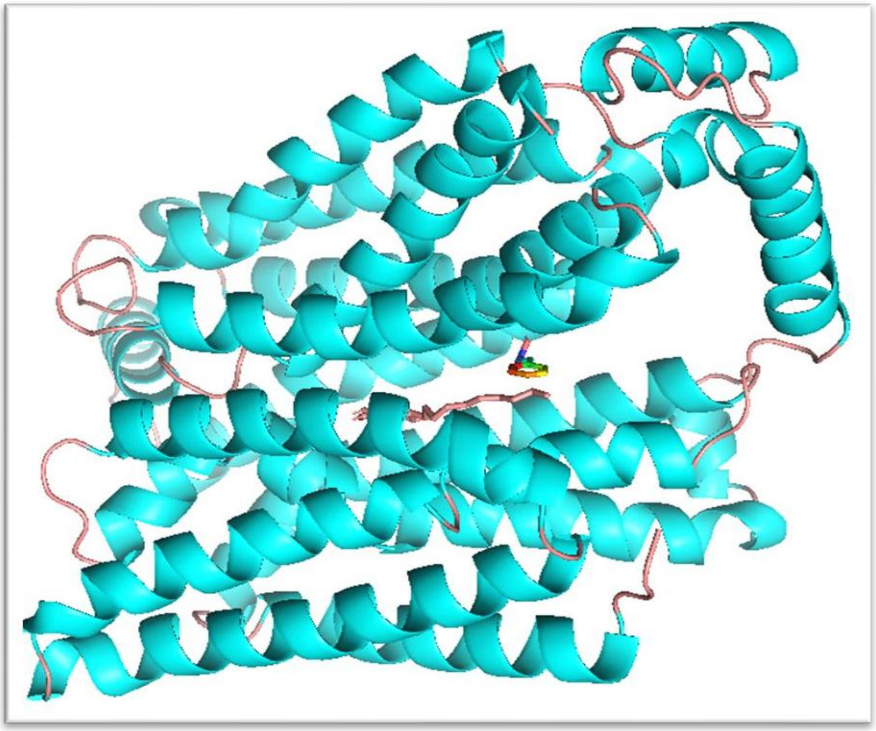

Fig.6 Docking of GLUT 1 with Cinnamic acid.

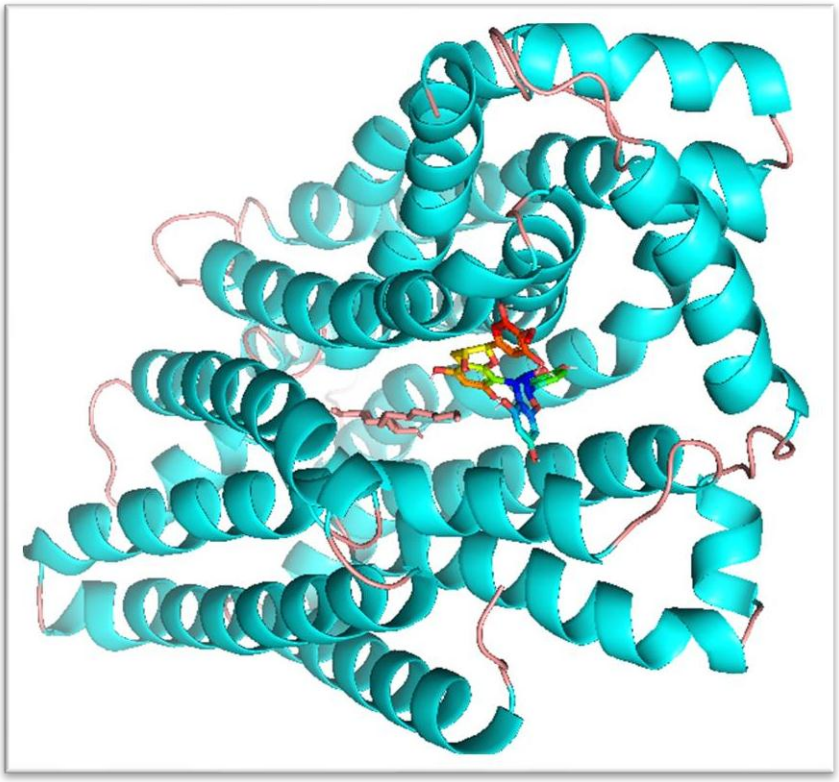

Fig.7 Docking of GLUT 1 with Proanthocyanidin A.

CONCLUSION

1. Molecular docking scores characterize energy of interactions when a ligand occupies binding site of receptor.
2. The conformation of the ligand in a particular pose is three-dimensionalarrangement of its pharmacophoric groups in which the energy of interactions can be calculated.
3. Interaction energy is the energy required for a ligand to enter into binding pockets and interact with the receptor.
4. The negative sign shows that the compounds can interact spontaneouslywith the receptor.
5. Negative molecular docking scores is preferred to be more attractive interactions over repulsive one.
6. Proanthocyanidin A have the strongest interaction with Pancreatic α-amylase and GLUT 1.
7. Proanthocyanidin A followed by Cinnamic acid shows the least bindingenergy score with all three of the target proteins.
8. Anti-hyperglycaemic property of selected phytoligands by binding stronglyto Pancreatic α-amylase and GLUT 1 which will inhibit glycation end products, can be concluded from *in silico* study.

DISCUSSION

1. Hyperglycaemia means high blood sugar or glucose. Dietary approaches for managing hyperglycaemia centre around regulating carbohydrate digestion, absorption and glucose uptake rates.
2. Much research has been devoted to natural products that can modulate thesemechanisms.
3. *In vivo and in vitro* studies of inhibition activity of phytoligands with selected proteins should be performed to evaluate this study.

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