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Research Article

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Virtual screening of enzyme inhibitory activity of active components of *Spirulina fusiformis* against selected enzymes involved in glycemic control

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ABSTRACT

Diabetes mellitus (DM) has affected 7% of the world's adult population. Spirulina fusiformis is a rich nutritional supplement which is non-toxic and has antidiabetic, antioxidant and hypolipidaemic activity. Our study was aimed to investigate the in silico inhibitory effect of the chosen active compounds of Spirulina(3Z-phycocyanobilin, β-carotene and Vitamin B12) against human xanthine oxidoreductase, human glycogen synthase kinase 3-β, α-glucosidase, human aldose reductase and α-amylase. The docking experiments were carried out using Patch Dock server. PyMol molecular viewer was used for the analysis of patterns of interaction of the ligands against the chosen receptors. Vitamin B12 revealed significant interactions showing six hydrogen bonds each with human xanthine oxidoreductase and human glycogen synthase kinase 3-β.The potential of vitamin B12 in this regard needs to be studied further by appropriate in vivo models.

Keywords: *Spirulina*, Active components, Diabetes, *Insilico*

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder which cause defect in insulin secretion. This will affect the organs of nerves, blood vessels and also the increase the blood glucose level[1]. World Health Organism has reported that the diabetes mellitus would become the world's seventh deadly disease in 2030[2]. 7% of world's adult populations are suffering due to DM[3]. DM is one of the major health issues in developed and developing countries[4]. The International Diabetes Federation (ID) reported that 40.9 million of Indians are affected by DM which will increase to 69.9 million by the year 2025[5]. Recent report has showed that diabetes could cause vascular complication which is due to oxidative stress[3,6]. In younger age DM will lead to cataract problem. Due to diabetes mellitus lens of the eyes would be affected seriously, which may not be treated by insulin therapy. DM would lead to renal disease at the final stage[7].

Molecular docking helps the chemist to discover a new drug in lees time and less coast[8]. Docking studies is performed to analysis the active binding site of Spirulina which predicts its effectiveness. The active sites contain its highly conserved amino acid[9].

EXPERIMENTAL SECTION

RECEPTOR DESIGNING:

Structure of receptors Human glycogen synthase kinase 3-β (PDB id: 3SAY), Alpha-glucosidase (PDB id: 3WY1), Human Aldose Reductase(PDB id: 4PR4) and Alpha amylase (PDB id: 4PR4) were derived from RCSB (Research Collaborator for Structural Bioinformatics) protein data bank (http://www.rcsb.org/pdb/home/home.do). The structure of protein is prepared for docking by removing water molecule and adding hydrogen molecule[10].

Table 1: Used receptors for molecular docking

S. No.	Receptor	PDB Id.
1	Human xanthine oxidoreductase	2EIQ
2	Human glycogen synthase kinase 3-β	3SAY
3	Alpha-glucosidase	3WY1
4	Human Aldose Reductase	4PR4
5	Alpha amylase	4W93

LIGAND DESIGNING:

PubChem database (http://pubchem.ncbi.nlm.nih.gov) is used to retrieve the canonical smile of the active compound of spirulina like (3Z)-Phycocyanobilin, β-carotene and vitamin B12. PDB structure of each ligand is obtained from the Corina Molecular Network (https://www.molecular-networks.com/online_demos/corina_demo) by pasting its canonical smile.

Table 2: Characteristics of the active compound of Spirulina

Molecule Name	Molecule formula	Molecular weight (g/mol)	PubChem compound Id.
(3Z)-Phycocyanobilin	$C_{33}H_{38}N_4O_6$	586.67802	5280816
β-carotene	$C_{40}H_{56}$	536.87264	5280489
Vitamin B12	$C_{63}H_{88}CoN_{14}O_{14}P$	1355.365177	16212801

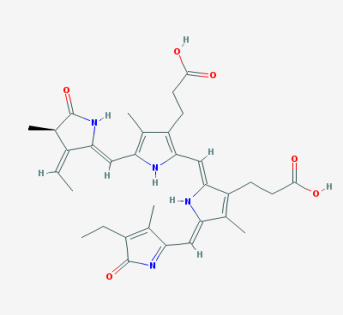

Figure 1: (3Z)-Phycocyanobilin

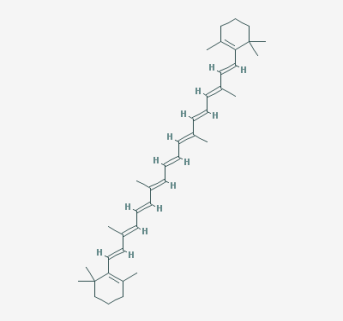

Figure 2: β-carotene

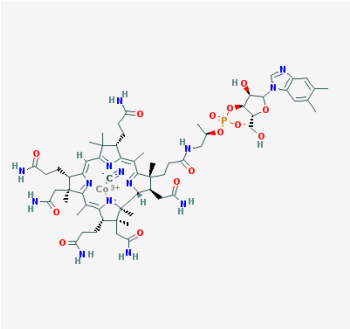

Figure 3: Vitamin B12

ANALYSES OF DOCKED COMPLEX:

Structure of docked complex is analyzed using PyMOL software which describe about its intermolecular interaction[8].Length of the hydrogen bond and the active site is been labeled.

RESULTS AND DISCUSSION

Table 3: Score, ACE and interacting residues of docked complexes

Ligand	Receptor	Score	Area	ACE	No of Bonds	Residue
3Z-Phycocyanobilin	2E1Q	6796	878.90	-323.14	4	ASP-59,LYS-57,ASN-288,ALA-302
		6446	840.70	-322.51	4	VAL-259,SER-347,ARG-394,ILE-353
β-carotene		7884	964.90	-149.58	Nil	
		7316	980.80	-392.60		
Vitamin B12		10104	1340.50	-379.74	6	GLU-23,ARG-394,SER-1126,ARG-508,GLY-502
		9060	1296.60	-487.08	6	TRP- 1329,ALA-432,ASP-360,GLU-263, SER-1226
3Z-Phycocyanobilin	3SAY	6420	794.50	-224.71	2	ASN-64,ARG-223
		6164	775.90	-367.68	Nil	
β-carotene		7336	902.30	-213.41	Nil	
		6820	794.90	-340.43		
Vitamin B12		10224	1329.70	-410.99	6	TYR-71, TYR-288, THR-59, LYS-36, GLU-290, THR-43
		10044	1350.10	-463.28	Nil	
3Z-Phycocyanobilin	3WY1	7184	881.60	-129.47	1	ARG-450
		6204	847.30	-193.38	2	ASN-447, ASN-46
β-carotene		7310	793.90	-140.21	Nil	
		6690	972.90	-368.26		
Vitamin B12		8938	1106.70	-158.37	3	ASN-447, GLN-439, ALA- 343
		8390	1205.30	-446.50	4	ASP-485, GLN-536, THR-410, GLY-416
3Z-Phycocyanobilin	4PR4	5532	734.40	-357.61	Nil	
		5012	716.50	-438.18		
β-carotene		7552	976.00	-238.50	Nil	
		5876	850.90	-424.63		
Vitamin B12		7914	1007.90	-325.20	1	ASP-98
		7058	1241.30	-694.40	2	PHE-121, SER-302
3Z-Phycocyanobilin	4W93	5750	710.10	-142.68	2	HIS-299,TYR-62
		5372	699.70	-365.71	2	SER-113,THR-71
β-carotene		6458	836.80	-233.22	NIL	
		6452	789.70	-338.68		
Vitamin B12		7524	876.90	-273.65	3	ASP-197,THR-163,ARG-161
		6650	868.50	-177.96	2	THR-114,GLU233

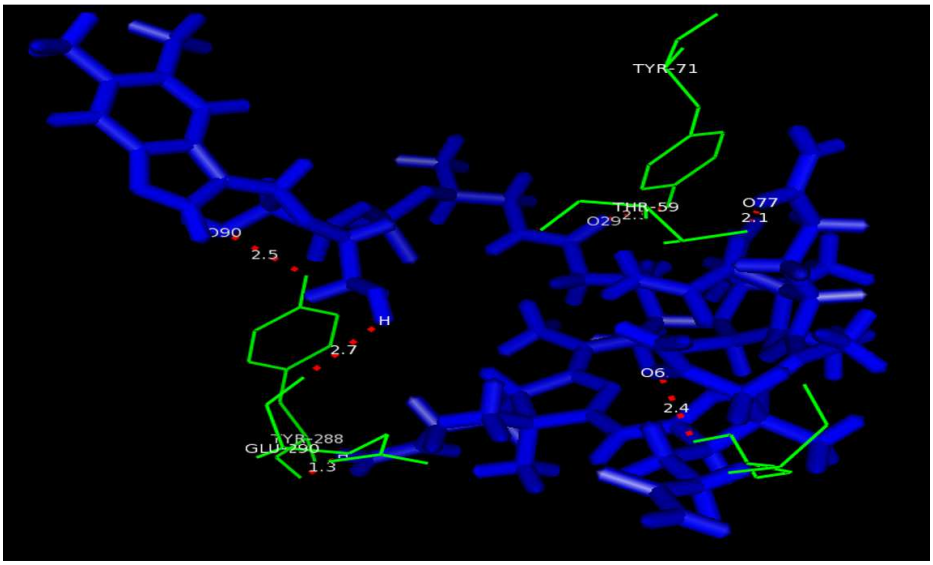

Figure 4: 3SAY docked with Vitamin B12

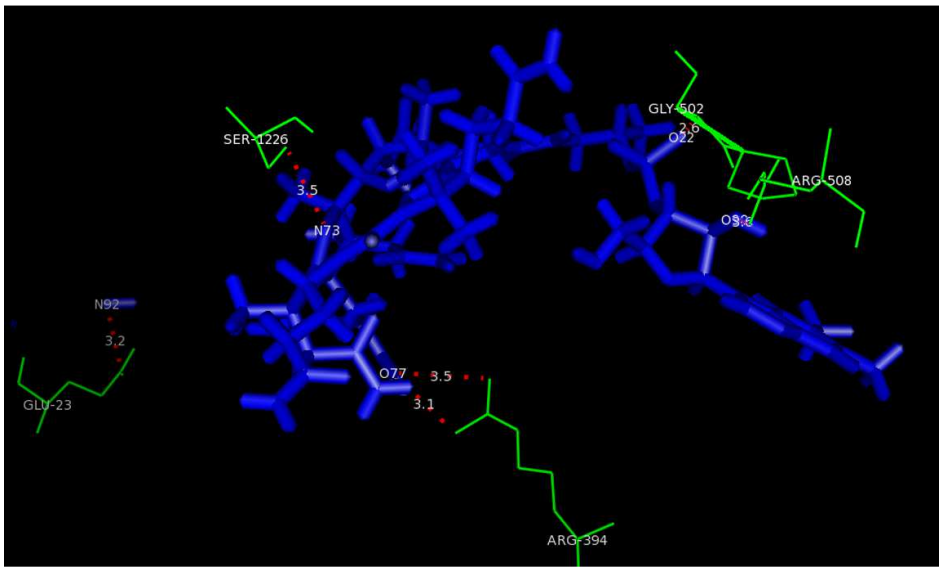

Figure 5: 2E1Q docked with Vitamin B12

High interacting residue and hydrogen bond was observed in the docked complex of 3SAY with Vitamin B12 (Figure 4) and 2E1Q with Vitamin B12 (Figure 5). The interacting residue and the bond length of 3SAY with Vitamin B12 (Figure 4) are TYR-71:- 2.3, TYR-288:-2.5, THR-59:-2.1, LYS-36:-2.4, GLU-290:- 2.7 and THR-43:-3.3 respectively. The interacting residue and the bond length of 2E1Q with Vitamin B12 (Figure 5) are GLU-23:-3.2,ARG-394:-3.1 and 3.5,SER-1126:-3.5,ARG-508:-3.6,GLY-502:-2.6 respectively. The interacting residue and the bond length of 3WY1 with Vitamin B12 (Figure 6) are ASP-485:-1.5, GLN-536:-2.9, THR-410:-3.2, GLY-416:-2.3 respectively. The biomass of Spirulina is reported to be used as Antidiabetic [11],[12]and antioxidant agent[13].Vitamin B12 is observed to show high significant effect which is followed by 3Z-Phycocyanobilin. There is no interaction found in the docked complex of different enzymes withβ-carotene.

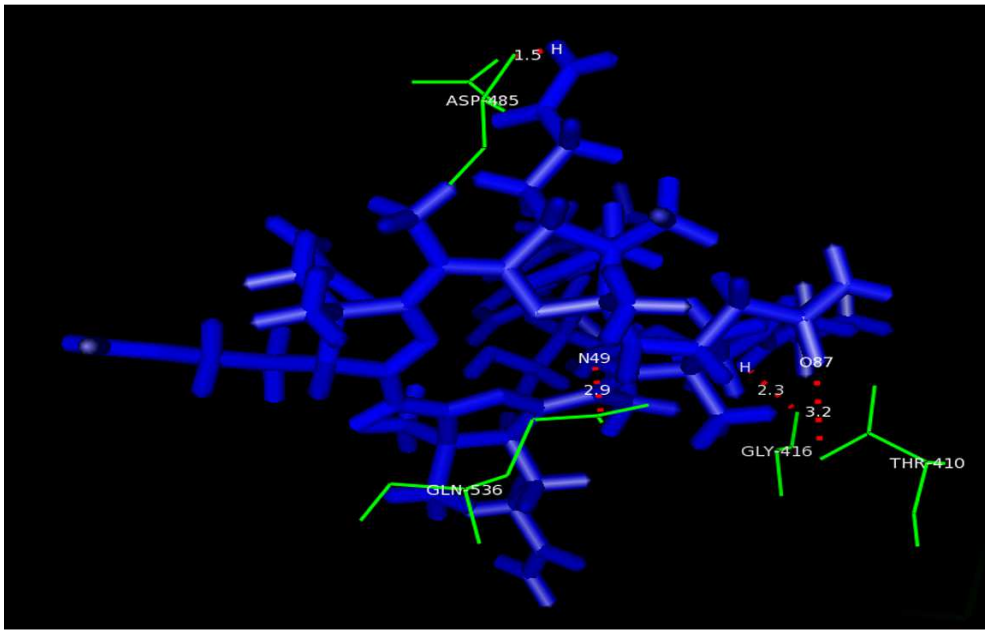

Figure 6: 3WY1 docked with Vitamin B12

CONCLUSION

In silico interaction of vitamin B12 is observed to possess high inhibitory effect compared to the other active compounds. The docked complex of vitamin B12 with human glycogen synthase kinase 3-β is predicted to possess high inhibitory effect. This could be futher studied by gene expression studies.

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REFERENCES

[1] Y-G Chen, P Li, P Li, R Yan, X-Q Zhang, Y Wang, *et al.Molecules*., **2013**, 18(4), 4221–4232.
[2] S Imran, M Taha, NH Ismail, SM Kashif, F Rahim, W Jamil, *et al.Eur. J. Med. Chem*.,**2015**, 105, 156–170.
[3] PVA Babu, D Liu, ER Gilbert. *J. Nutr. Biochem*., **2013**, 24(11), 1777–1789.
[4] A Hunyadi, A Martins, T-J Hsieh, A Seres, I Zupkó. Wagner B, ed. *PLoS ONE*., **2012**, 7(11), e50619.
[5] V Mohan, S Sandeep, R Deepa, B Shah, C Varghese. *Indian J. Med. Res*., **2007**, 125(3), 217–30.
[6] A Machha, FI Achike, AM Mustafa, MR Mustafa. *Nitric Oxide*., **2007**, 16(4), 442–447.
[7] M Stefek. *Interdiscip. Toxicol*., **2011**, 4(2).
[8] R Pingaew, A Saekee, P Mandi, C Nantasenamat, S Prachayasittikul, S Ruchirawat, *et al.Eur. J. Med. Chem.*, **2014**, 85, 65–76.
[9] M Yar, M Bajda, L Shahzadi, SA Shahzad, M Ahmed, M Ashraf, *et al.Bioorganic Chem*., **2014**, 54, 96–104.
[10] R Rodriguez, G Chinea, N Lopez, T Pons, G Vriend. *Bioinformatics*., **1998**, 14(6), 523–528.
[11] I Setyaningsih, M Bintang, N Madina. *Procedia Chem.*, **2015**, 14, 211–215.
[12] T-S Vo, D-H Ngo, S-K Kim. In: Kim S-K, ed. *Handbook of Marine Microalgae*. Boston: Academic Press; **2015**:299–308.
[13] E Rodríguez De Marco, ME Steffolani, CS Martínez, AE León. *LWT - Food Sci. Technol*., **2014**, 58(1), 102–108.