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Research Article

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Beneficial Binding Affinity of the Active Compound of Cyamopsis Tetragonoloba with the Receptors Responsible for Hepatotoxicity

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ABSTRACT

Cyamopsis tetragonoloba is a commercially available plant found all-over India, this plant is commonly called as kotthavarai in Tamil which is commercially available as guar gum powder, that is known to have properties like anti-inflammatory, anti-microbial and anti-tumour. It is used for treating diseases like cancer, diabetes and has weight loss property. Hepatotoxicity is caused by the adverse effect of synthetic drugs that mainly affects the liver. The aim of our research study is to know the potential binding activity of C.tetragonoloba through in silico study analysis. The analysis is done through Patch dock online server. 3D structure of the ligands of C.tetragonoloba was retrieved from PubChem online server followed by the molecular network called Corina. The receptors which are responsible for causing hepatotoxicity were obtained from RCBS protein data bank. Using Patch dock online server the docking of ligand and receptor was carried out and the binding site is visualized using PyMOL software. The ligands like alpha-Monostearin, Ethyl alpha-d-glycopyranoside, Hexopyranosyl hexopyranoside, 2-Hexadecanoyl glycerol, 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol, 3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one, Ethyl alpha-d-glycopyranoside, Mono(2-ethylhexyl) phthalate, 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol, and palmitic acid has shown high binding potential activity with corresponding receptors of C.tetragonoloba. Based on our in silico analysis, further in vivo study can by analysed to know the potential binding activity of C.tetragonoloba plant.

Keywords: *Cyamopsis tetragonoloba*; Patch dock; Hepatotoxicity; In silico docking; Hepatotoxicity

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INTRODUCTION

Cyamopsis tetragonoloba is a botanical name of cluster bean or guar. It is available in the form of gum powder or guar gum. It is an annual plant, belongs to the family *Fabaceae*. The origin of a plant is unknown and it is assumed and developed from the species of *Cyamopsis senegalensis* native regions of Africa. This is known to be grown in India and Pakistan for more than centuries [1]. It is a legume plant and has much value in crop rotation. Naturally guar gum is the symbioses in nitrogen-fixing bacteria like Rhizobium, azotobacterial [2]. The plant grows at the maximum height of 2-3m long. Guar gum has the weight losing property as it is rich in fiber content. It can be also used as the dietary supplement [3]. More than 900 drugs are responsible for causing liver damages which includes Non-Steroidal Anti-Inflammatory Drugs (NSAIDS), corticosteroids and colchicines [4]. The risk factors for drug-induced liver injury are due to age, sex, alcohol ingestion and genetic factors [5].

The mechanism behind the hepatotoxicity is the inhibition or over expressions of the gene such as CAR (Constitutive androstane receptor) in regulating the membrane transporters, transferase and metabolic enzymes which belong to ligand-activated nuclear receptors [6], FXR (Nuclear bile acid receptor) is known to maintain the liver and glucose haemostasis [7], PXR (Human Pregnane X Receptor) has the activity of maintaining the adaptive defence function of the body which acts against toxic substances during chemical reactions [8], Nf-kB (Nuclear factor kappa-light-chain-enhancer of activated B cells) on over expression is known to cause the diseases such as breast cancer, liver diseases and other forms of toxicity [9], LXR (Liver X receptors alpha) is known to play vital role in the formation of inflammation, lipid homeostasis, maintaining transcription program and macrophage functions [10].

MATERIALS AND METHODS

Designing of Receptor

The Receptor which is responsible for hepato toxicity is selected from the literature. The selected receptors and PDB structure were retrieved from RCSB (Research Collaborator for Structural Bioinformatics) (https://www.rcsb.org/) protein data bank. The PDB Id for each receptor is shown in (Table1). Each receptor was prepared for docking by removing the water molecule and hydrogen atom.

Table 1. Used receptors for molecular docking

S. No.	Receptor	PDB Id.
1	Apo Human Pregnane X Receptor	1ILG
2	Nuclear bile acid receptor FXR	1OSH
3	Constitutive androstane receptor	1XNX
4	LXR alpha	5AVI
5	Nf-kB	1NFK

Designing of Ligand

The active compounds of the plant *Cyamopsis tetragonoloba* were selected as ligand for docking analysis. The PubChem database is used to obtain the canonical smile of ligand which was submitted in Corina Molecular Network to get the PDB structure.

Table 2. Used Ligands for docking

Molecule Name	Molecule formula	Molecular weight (g/mol)	PubChem compound Id.
1,2-Cyclopentanedione	$C_5H_6O_2$	98.101	566657
Isopentyl acetate	$C_7H_{14}O_2$	130 .187	31276
3,5-Dihydroxy-6-methyl-	$C_6H_8O_4$	144.126	119838

2,3-dihydro-4H-pyran-4-one			
2,3-Dihydro-benzofuran	C_8H_8O	120.151	10329
Acetyl monoglyceride	$C_5H_{10}O_4$	134.131	33510
1-(p-methoxyphenyl)propene	$C_{10}H_{12}O$	148.205	7703
Ethyl alpha-d-glycopyranoside	$C_8H_{16}O_6$	208.21	9815668
Palmitic acid	$C_{16}H_{32}O_2$	256.43	985
Ethyl hexadecanoate	$C_{18}H_{36}O_2$	284.484	12366
Hexopyranosyl hexopyranoside	$C_{12}H_{22}O_{11}$	342.297	1143
Phytol	$C_{20}H_{40}O$	296.539	5280435
Ethyl (9Z,12Z)-9,12-octadecadienoate	$C_{20}H_{36}O_2$	308.506	5365672
Ethyl (9Z)-9-octadecenoate	$C_{20}H_{38}O_2$	310.522	8123
Ethyl n-octadecanoate	$C_{20}H_{40}O_2$	312.538	8122
2-Hexadecanoyl glycerol	$C_{19}H_{38}O_4$	330.509	123409
Mono(2-ethylhexyl) phthalate	$C_{16}H_{22}O_4$	278.348	20393
Ethyl nonadecanoate	$C_{21}H_{42}O_2$	326.565	29008
Aletamine	$C_{11}H_{15}N$	161.248	20254
Propyleneglycol monoleate	$C_{21}H_{40}O_3$	340.548	6433267
alpha-Monostearin	$C_{21}H_{42}O_4$	358.563	24699
Ethyl docosanoate	$C_{24}H_{48}O_2$	368.646	22199
3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol	$C_{17}H_{18}O_5$	302.326	602152
Nonacosane	$C_{29}H_{60}$	408.799	12409
beta-Tocopherol	$C_{28}H_{48}O_2$	416.69	6857447
Tetracontane	$C_{44}H_{82}$	563.096	20149

dl-alpha-Tocopherol	$C_{29}H_{50}O_2$	430.717	14985
Ergost-5-en-3-ol	$C_{28}H_{48}O$	400.691	5283637
Stigmasterol	$C_{29}H_{48}O$	412.702	5280794
gamma-Sitosterol	$C_{29}H_{50}O$	414.718	457801
Alpha-amyrin	$C_{30}H_{50}O$	426.729	73170
Lupeol	$C_{30}H_{50}O$	426.729	259846

***In silico* Docking**

Molecular docking procedure was carried out using Patch Dock online server which is based on complementary algorithm principle. The receptors and ligands were submitted in the server on PDB format and the results were received through email. Docked complex was visualised and analysed using PyMOL software. The docked complex was analysed for interacting residues and atoms along with bond length which was labelled and recorded using the software.

RESULTS

Docked Complex of 1ILG Receptor with Ligands

Tables 1-3 represents the score, area, and ACE and bond length of the docked complex of 1ILG with the ligands of plant *C.tetragonoloba*. Among the docked complex of ligands with 1ILG, the interaction were found in the following ligands like Ethyl alpha-d-glycopyranoside, Hexopyranosyl hexopyranoside, 2-Hexadecanoyl glycerol, alpha-Monostearin, Ethyl docosanoate, dl-alpha-Tocopherol. The bond length, residue names and atom names are mentioned in Tables 1-3.

Table 3. Score, Area, ACE and Bonds of 1ILG receptor with ligands

Ligand	**ACE**	**Area**	**Score**	**Bonds**		
				Residue	**Atom**	**Length**
1,2-Cyclopentanedione	-98.73	220.20	1936	NIL		
Isopentyl acetate	-82.23	327.30	2954	NIL		
,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one	-74.38	269.10	2054	NIL		
2,3-Dihydro-benzofuran	-85.75	289.20	2648	NIL		

Acetyl monoglyceride	-91.53	270.60	2554	NIL		
1-(p-methoxyphenyl)propene	-90.20	364.20	3310	NIL		
Ethyl alpha-d-glycopyranoside	-167.74	354.00	3462	SER-208	H28	1.9
				LEU-318	H30	1.4
Palmitic acid	-200.13	506.60	4146	NIL		
Ethyl hexadecanoate	-95.49	501.90	4522	NIL		
Hexopyranosyl hexopyranoside	-120.26	487.70	4444	SER-247	O22	1.1
				SER-247	O21	3.6
Phytol	-252.54	626.40	5118	NIL		
Ethyl (9Z,12Z)-9,12-octadecadienoate	-290.36	687.10	4698	NIL		
Ethyl (9Z)-9-octadecenoate	-237.86	664.00	4992	NIL		
Ethyl n-octadecanoate	-230	582.60	4956	NIL		
2-Hexadecanoyl glycerol	-219.77	632.50	5260	ALA-294	H61	2.5
Mono(2-ethylhexyl) phthalate	-155.69	522.30	4602	NIL		
Ethyl nonadecanoate	-254.08	614.40	5150	NIL		
Aletamine	-135.82	407.30	3514	NIL		
Propyleneglycol monoleate	-260.45	679.60	5188	NIL		
alpha-Monostearin	-245.01	701.20	5438	PHE-315	H67	2.7

				TYR-328	O24	1.9
Ethyl docosanoate	-289.45	653.10	5548	TYR-328	O24	3.3
3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol	-132.82	457.20	4450	NIL		
Nonacosane	-268.27	822.30	6064	NIL		
beta-Tocopherol	-325.66	693.00	5822	NIL		
Tetracontane	-171.20	785.50	6006	NIL		
dl-alpha-Tocopherol	-221.82	807.50	6202	SER247	O31	2.4
Ergost-5-en-3-ol	-261.61	731.00	6356	NIL		
Stigmasterol	-451.84	773.20	6158	NIL		
gamma-Sitosterol	-244.87	736.30	6256	NIL		
Alpha-amyrin	-245.72	689.40	6290	NIL		
Lupeol	-234.60	676.50	6006	NIL		

Among the other interacting ligands, the docked complex 1ILG of alpha-monostearin, Ethyl alpha-d-glycopyranoside and Hexopyranosyl hexopyranoside were found to have potential interactive residues (Figure 1). Each had two interactions with the active compounds of *C.tetragonoloba.* The residues name and bond length of the docked complex of alpha-monostearin with 1ILG is PHE-315:- 2.7, TYR-328:-1.9, Ethyl alpha-d-glycopyranoside with 1ILG is SER-208:-1.9, LEU-318:-1.4 and Hexopyranosyl hexopyranoside with 1ILG is SER-247:-1.1, SER-247:-3.6.

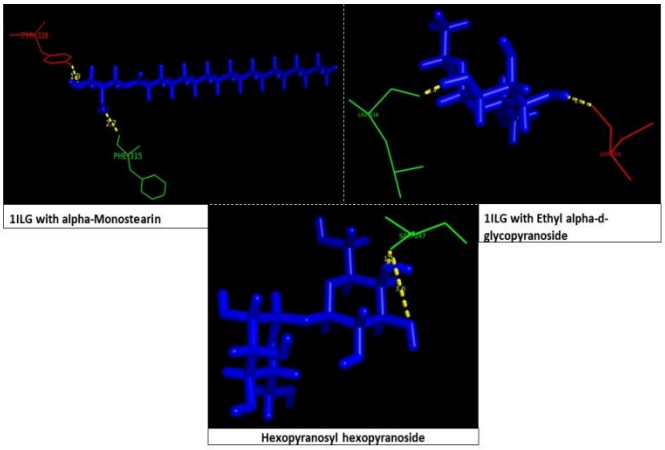


Figure 1. Docking of 1ILG with ligands

Figure 1 docked complex of Receptor (Blue) and Ligand (Green and red) with bonding (Yellow).

Docked Complex of 1XNX Receptor with Ligands

The docked complex of 1XNX receptor with ligands is represented in Table 4. The ligands like 3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one, Acetyl monoglyceride, 1-(p-methoxyphenyl)propene, Ethyl alpha-d-glycopyranoside, Ethyl hexadecanoate, Ethyl (9Z,12Z)-9,12-octadecadienoate, Ethyl n-octadecanoate, 2-Hexadecanoyl glycerol, Ethyl nonadecanoate, alpha-Monostearin, 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol, beta-Tocopherol, Ergost-5-en-3-ol and Lupeol were docked with 1XNX receptor.

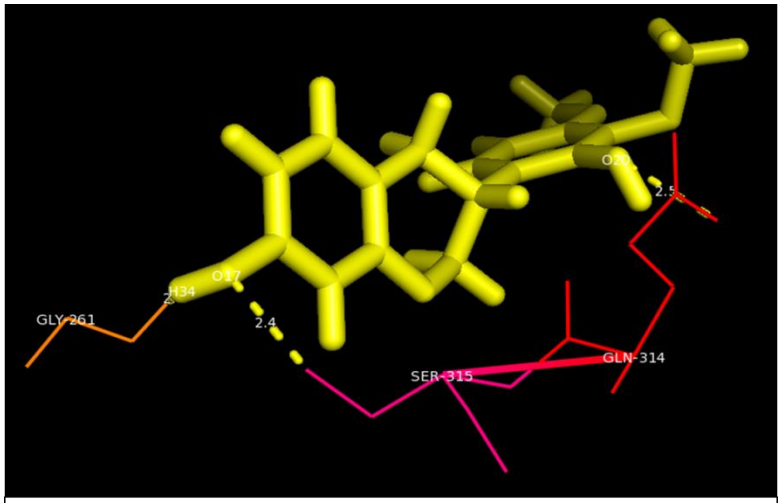
Table 4. Score, Area, ACE and Bonds of 1XNX receptor with ligands

Ligand	ACE	Area	Score	Bonds		
				Residue	Atom	Length
1,2-Cyclopentanedione	-65.84	244.20	2168	NIL		
Isopentyl acetate	-117.53	322.20	2942	NIL		
3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one	-67.21	286.80	2640	ARG-156	O5	3.0
				PRO-157	H18	2.4
2,3-Dihydro-benzofuran	-104.73	298.30	2716	NIL		
Acetyl monoglyceride	-56.27	299.50	2694	GLN-159	O4	3.2
				GLN-159	O9	3.5
1-(p-methoxyphenyl)propene	-124.35	336.30	3094	SER-315	O10	3.1

Ethyl alpha-d-glycopyranoside	-132.16	355.60	3322	HIS-213	H27	2.2
Palmitic acid	-195.76	475.90	4260	NIL		
Ethyl hexadecanoate	-176.54	584.30	5016	LEU-353	O18	3.2
				GLY-354	O18	3.1
Hexopyranosyl hexopyranoside	-196.17	481.20	4576	NIL		
Phytol	-136.68	556.60	5180	NIL		
Ethyl (9Z,12Z)-9,12-octadecadienoate	-179.06	592.20	5228	ASN-258	O20	2.4
Ethyl (9Z)-9-octadecenoate	-182.86	624.40	5406	NIL		
Ethyl n-octadecanoate	-197.00	626.90	5148	LEU-353	O20	2.6
				GLY-354	O20	2.3
2-Hexadecanoyl glycerol	-181.04	623.50	5234	GLY-354	O21	1.0
				LEU-353	O18	2.4
Mono(2-ethylhexyl) phthalate	-214.97	508.80	4454	NIL		
Ethyl nonadecanoate	-200.64	637.20	5414	GLY-354	O21	2.5
Aletamine	-130.76	394.50	3582	NIL		
Propyleneglycol monoleate	-208.08	667.70	5552	NIL		
alpha-Monostearin	-206.35	621.50	5340	GLY-354	O20	2.6
Ethyl docosanoate	-241.98	698.30	5520	NIL		
3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-	-153.21	484.20	4570	GLY-261	H34	2.6
				SER-315	O17	2.4

chromanol				GLN-314	O20	2.5
Nonacosane	-195.16	720.00	6232	NIL		
beta-Tocopherol	-259.18	693.90	6386	LYS-235	H78	2.8
Tetracontane	-136.17	693.60	5464	NIL		
dl-alpha-Tocopherol	-301.14	754.30	6330	NIL		
Ergost-5-en-3-ol	-347.19	710.50	5764	LEU-340	H71	2.5
Stigmasterol	-151.17	612.90	5400	NIL		
gamma-Sitosterol	-206.49	661.70	5190	NIL		
Alpha-amyrin	-329.72	714.80	5608	NIL		
Lupeol	-332.66	695.70	5584	ASN-175	O29	3.3

The docked complex of 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol with 1XNX was observed to have potential interaction (Figure 2). The docked complex of 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol with 1XNX has shown three interactions. The bond and residues of complex are GLY-261:-2.6, SER-315:- 2.4 and GLN-314:-2.5.



1XNX with 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol

Figure 2. Docking of 1XNX with ligands

Figure 2 docked complex of Receptor (yellow) and Ligand (orange, pink, and red) with bonding (Yellow)

Docked Complex of 1OSH Receptor with Ligands

The score, area and ACE of the docked complex were mentioned in Table 5. The interacting residues are 1,2-Cyclopentanedione, 3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one, Ethyl alpha-d-glycopyranoside, Hexopyranosyl hexopyranoside, Mono(2-ethylhexyl) phthalate, Ethyl docosanoate, 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol, beta-Tocopherol and gamma-Sitosterol.

Table 5. Score, Area, ACE and Bonds of 1OSH receptor with ligands

Ligand	ACE	Area	Score	Bonds		
				Residue	**Atom**	**Length**
1,2-Cyclopentanedione	-110.32	248.30	2248	THR-292	O4	3.5
Isopentyl acetate	-124.64	349.80	3224	NIL		
3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one	-93.95	276.70	2584	TYR-365	O8	3.5
2,3-Dihydro-benzofuran	-100.39	297.60	2764	NIL		
Acetyl monoglyceride	-106.88	289.00	2800	NIL		
1-(p-methoxyphenyl)propene	=139.51	386.00	3600	NIL		
Ethyl alpha-d-glycopyranoside	-102.74	352.60	3338	SER-336	H29	2.7
				SER-336	O14	3.5
				HIS-298	O14	2.4
Palmitic acid	-217.71	550.80	4586	NIL		
Ethyl hexadecanoate	-119.42	558.80	4868	NIL		
Hexopyranosyl hexopyranoside	-192.07	506.10	4656	HIS-298	O20	3.3
				HIS-298	H4	3.3
				SER-336	O21	2.3
				TYR-365	O18	2.5

				TYR-373	O22	3.0
				LEU-291	H38	1.3
				ALA-295	O16	2.8
Phytol	-254.00	681.50	5656	NIL		
Ethyl (9Z,12Z)-9,12-octadecadienoate	-242.42	665.90	5784	NIL		
Ethyl (9Z)-9-octadecenoate	-245.73	662.70	5578	NIL		
Ethyl n-octadecanoate	-8.22	602.20	4858	NIL		
2-Hexadecanoyl glycerol	-210.78	609.50	5182	NIL		
Mono(2-ethylhexyl) phthalate	-191.99	551.00	4806	SER-336	O11	2.9
				SER-336	O19	3.1
				SER-336	H42	2.4
Ethyl nonadecanoate	0.33	585.70	4856	LYS-266	O21	3.1
Aletamine	-170.34	400.10	3724	NIL		
Propyleneglycol monoleate	-225.79	678.20	6092	NIL		
alpha-Monostearin	-118.58	581.80	5028	NIIL		
Ethyl docosanoate	-20.78	676.80	5388	LYS-266	O24	3.1
				LYS-308	O23	3.0
3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol	-210.95	557.20	4818	SER-336	O18	1.9
				HIS-298	O18	3.2
Nonacosane	-93.90	784.00	6090	NIL		
beta-Tocopherol	-111.14	675.40	5814	LYS-403	030	1.9
Tetracontane	-105.31	650.60	4852	NIL		

dl-alpha-Tocopherol	-318.17	741.90	5938	NIL		
Ergost-5-en-3-ol	-382.72	742.50	5950	NIL		
Stigmasterol	-336.62	778.10	6282	NIL		
gamma-Sitosterol	-273.51	714.70	5862	TYR-365	O25	3.5
Alpha-amyrin	-340.57	711.10	5898	NIL		
Lupeol	-299.46	688.00	5580	NIL		

In Figure 3, The docked complex of ligands such as Ethyl alpha-d-glycopyranoside, Hexopyranosyl hexopyranoside and Mono (2-ethylhexyl) phthalate (Figure 3) has potential interaction with the receptor 1OSH. There were seven interaction were observed between the docked complex of Hexopyranosyl hexopyranoside with 1OSH. Ethyl alpha-d-glycopyranoside and Mono (2-ethylhexyl) with 1OSH has three bond of interaction. The residues and bond length of Ethyl alpha-d-glycopyranoside SER-336:-2.7, SER-336:-3.5, HIS-298:-2.4 and Mono (2-ethylhexyl) phthalate are SER-336:-2.9, SER-336:-3.1 and SER-336:-2.4. The residues and bond length of Hexopyranosyl hexopyranoside are HIS-298:-3.3, HIS-298:-3.3, SER-336:-2.3, TYR-365:-2.5, TYR-373:-3.0, LEU-291:-1.3 and ALA-295:-2.8.

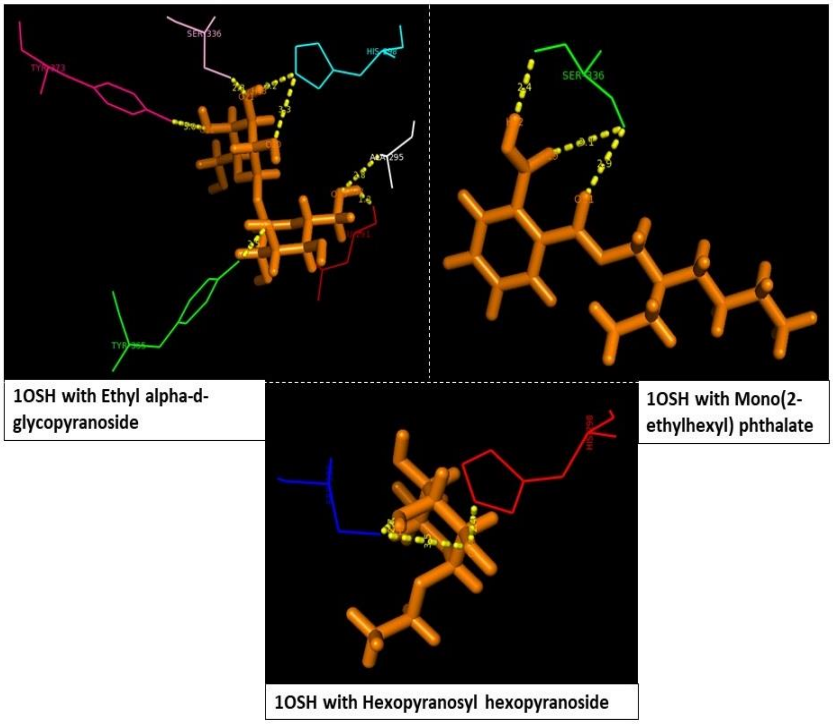


Figure 3. Docking of 1OSH with ligands

Figure 3 docked complex of Receptor (orange) and Ligand (Light blue, violet, green, red, white) with bonding (Yellow)

Table 6 represents the score, area, ACE of the docked complex of ligand with 5AVI. Interacting residues of 5AVI with the ligands such as 1,2-Cyclopentanedione, 3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one, Acetyl monoglyceride, 1-(p-methoxyphenyl)propene, 1-(p-methoxyphenyl) propene, Ethyl alpha-d-glycopyranoside, Palmitic acid, Ethyl hexadecanoate, Hexopyranosyl hexopyranoside, 2-Hexadecanoyl glycerol, Ethyl docosanoate, Ethyl docosanoate and 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol were observed.

Table 6. Score, Area, ACE and Bonds of 5AVI receptor with ligands

Ligand	Score	Area	ACE	Bonds		
				Residue	**Atom**	**Length**
1,2-Cyclopentanedione	-26.56	232.30	2246	SER-413	O4	2.0
				SER-413	O6	3.4
Isopentyl acetate	-19.26	366.30	3402	NIL		
3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one	-110.86	271.50	2700	HIS-421	O10	2.7
				PHE-257	H17	2.5
2,3-Dihydro-benzofuran	-120.99	284.70	2776	NIL		
Acetyl monoglyceride	27.38	324.50	2974	ARG-344	O9	2.9
1-(p-methoxyphenyl)propene	-5.93	420.90	3536	ARG-344	O10	3.4
Ethyl alpha-d-glycopyranoside	-56.67	363.90	3438	LEU-260	H29	2.4
				GLU-267	H28	2.8
Palmitic acid	-135.40	591.00	5362	LYS-317	O17	3.4
				LYS-317	O17	3.2
				ARG-	O18	1.5

				305		
Ethyl hexadecanoate	-181.35	645.40	5672	ARG-305	O17	1.6
				ARG-305	O17	2.0
Hexopyranosyl hexopyranoside	-221.37	505.60	4754	THR-302	O17	2.9
Phytol	-182.69	684.40	6416	NIL		
Ethyl (9Z,12Z)-9,12-octadecadienoate	-180.16	674.70	5674	NIL		
Ethyl (9Z)-9-octadecenoate	-172.58	656.60	5704	NIL		
Ethyl n-octadecanoate	-135.36	690.60	5926	NIL		
2-Hexadecanoyl glycerol	-78.20	731.90	5962	ARG-344	O17	2.5
Mono(2-ethylhexyl) phthalate	-217.24	532.60	5046	NIL		
Ethyl nonadecanoate	-135.16	718.70	6210	NIL		
Aletamine	-163.49	412.40	3788	NIL		
Propyleneglycol monoleate	-208.24	704.90	6132	NIL		
alpha-Monostearin	-79.90	705.20	5964	NIL		
Ethyl docosanoate	-127.40	746.30	6592	GLN-222	O24	2.5
3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol	-204.47	518.20	4892	THR-302	O20	2.5
Nonacosane	-167.76	922.80	7130	NIL		

beta-Tocopherol	-212.46	837.10	7236	NIL
Tetracontane	-113.84	868.20	6288	NIL
dl-alpha-Tocopherol	-212.66	806.10	7308	NIL
Ergost-5-en-3-ol	-376.96	724.00	6274	NIL
Stigmasterol	-347.11	783.20	6790	NIL
gamma-Sitosterol	-371.17	758.30	6216	NIL
Alpha-amyrin	-327.01	728.60	6014	NIL
Lupeol	-360.12	705.90	6244	NIL

Palmitic acid has shown three bonds of potential interactions with 5AVI. The residues and bond length of the docked complex of palmitic acid with 5AVI are LYS-317:-3.4, LYS-317:-3.2 and ARG-305:-1.5.

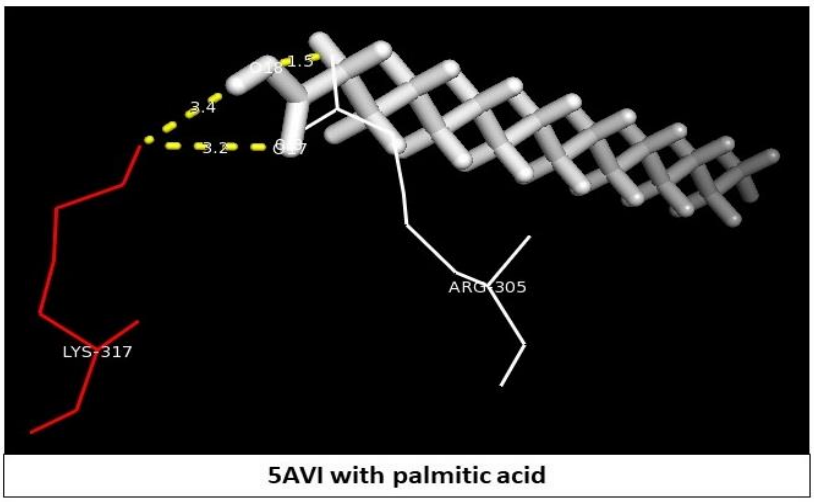


Figure 4. Docking of 5AVI with ligands

Figure 4 docked complex of Receptor (white) and Ligand (white and red) with bonding (Yellow)

Docked Complex of 1NFK Receptor with Ligands

1NFK was found to have interacting residue with the ligands like 3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one, Isopentyl acetate, Acetyl monoglyceride, Acetyl monoglyceride, Ethyl alpha-d-glycopyranoside, Palmitic acid, Hexopyranosyl hexopyranoside, Ethyl (9Z)-9-octadecenoate, Ethyl n-octadecanoate, 2-Hexadecanoyl glycerol,

Mono(2-ethylhexyl) phthalate, Ethyl nonadecanoate, Ethyl docosanoate, 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol, beta-Tocopherol, Ergost-5-en-3-ol and gamma-Sitosterol, Alpha-amyrin (Table 7).

Table 7. Score, Area, ACE and Bonds of 1NFK receptor with ligands

Ligand	ACE	Area	Score	Bonds		
				Residue	Atom	Length
1,2-Cyclopentanedione	-68.49	251.30	2254	NIL		
Isopentyl acetate	-64.89	338.00	3104	LEU-207	O8	1.9
3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one	-59.37	306.70	2808	DA-5	H17	2.0
				DA-6	O9	2.1
				DA-5	O9	2.7
				LYS-272	O8	2.8
2,3-Dihydro-benzofuran	-83.02	324.60	2950	NIL		
Acetyl monoglyceride	-52.00	319.90	2926	LYS-241	H18	2.5
				HIS-141	O9	2.3
1-(p-methoxyphenyl)propene	-137.61	402.60	3430	NIL		
Ethyl alpha-d-glycopyranoside	-94.91	397.50	3700	GLN-306	H28	1.5
				DA-5	O11	2.4
				DA-6	O9	2.3
				DA-6	O9	2.7
				LYS-272	H30	2.4
Palmitic acid	-76.73	602.50	5088	ARG-305	O18	2.7
				DA-5	O18	2.5
Ethyl hexadecanoate	-92.39	671.90	3734	NIL		
Hexopyranosyl hexopyranoside	-12.42	512.20	4620	ASN-247	O17	1.5
				ASN-247	H38	2.5
				ASP-271	H38	2.7
				DG-3	H41	2.6
				LYS-241	O22	1.3
Phytol	-298.86	694.00	5916	NIL		

Ethyl (9Z,12Z)-9,12-octadecadienoate	-130.35	696.00	5684	NIL		
Ethyl (9Z)-9-octadecenoate	-139.40	707.30	5822	LYS--272	O19	2.5
				ARG-305	O20	2.4
Ethyl n-octadecanoate	-93.26	735.80	6330	ARG-305	O19	2.1
				LYS-272	O20	2.7
2-Hexadecanoyl glycerol	-101.62	701.50	6104	DA-6	O18	2.6
				DT-7	H58	1.9
				DA-5	O21	2.5
				DA-6	O21	2.0
				DA-6	O23	2.2
Mono(2-ethylhexyl) phthalate	-155.69	606.90	5180	LYS-145	O20	1.2
Ethyl nonadecanoate	-104.78	737.00	6312	LYS-272	O21	2.5
				ARG-305	O20	2.4
Aletamine	-90.61	435.90	3648	NIL		
Propyleneglycol monoleate	-319.63	728.00	6092	NIL		
alpha-Monostearin	-86.80	755.60	6442	NIL		
Ethyl docosanoate	-119.74	826.20	7122	ASN-247	O23	2.4
3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol	-21.23	554.60	4924	DA-5	O21	2.6
				DG4	H37	2.0
				LYS-272	O2	2.1
Nonacosane	-136.05	980.30	8090	NIL		
beta-Tocopherol	-145.18	906.10	7260	DG-3	H78	1.3
Tetracontane	-246.86	1176.00	9536	NIL		

dl-alpha-Tocopherol	-152.96	925.20	7088	NIL		
Ergost-5-en-3-ol	-79.99	729.40	62668	LYS-241	O27	1.6
				DA-5	O27	2.7
Stigmasterol	-120.71	713.50	6108	NIL		
gamma-Sitosterol	-102.38	761.00	5956	DA-5	O25	2.4
				LYS-272	O25	1.2
Alpha-amyrin	-82.15	712.50	6130	LYS-272	O24	2.2
Lupeol	-100.70	748.20	6012	NIL		

In Figure 5a, 5b and 5c, the potential interaction was found in the docked complex of 1NFK with the ligands like 2-Hexadecanoyl glycerol, 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol, 3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one, Ethyl alpha-d-glycopyranoside and Hexopyranosyl hexopyranoside. The interacting residue and bond length of the 1NFK with 2-Hexadecanoyl glycerol are DA-6:-2.6, DT-7:-1.9, DA-5:-2.5, DA-6:-2.0 and DA-6:-2.2. The interacting residue and bond length of the 1NFK with 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol are DA-5:-2.6, DG4:-2.0 and LYS-272:-2.1. The interacting residue and bond length of the 1NFK with 3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one are DA-5:-2.0, DA-6:-2.1, DA-5:-2.7and LYS-272:-2.4. The interacting residue and bond length of the 1NFK with Ethyl alpha-d-glycopyranoside are GLN-306:-1.5, DA-5:-2.4, DA-6:-2.3, DA-6:-2.7 and LYS-272:-2.4. The interacting residue and bond length of the 1NFK with Hexopyranosyl hexopyranoside are ASN-247:-1.5, ASN-247:-2.5, ASP-271:-2.7, DG-3:-2.6 and LYS-241:-1.3.

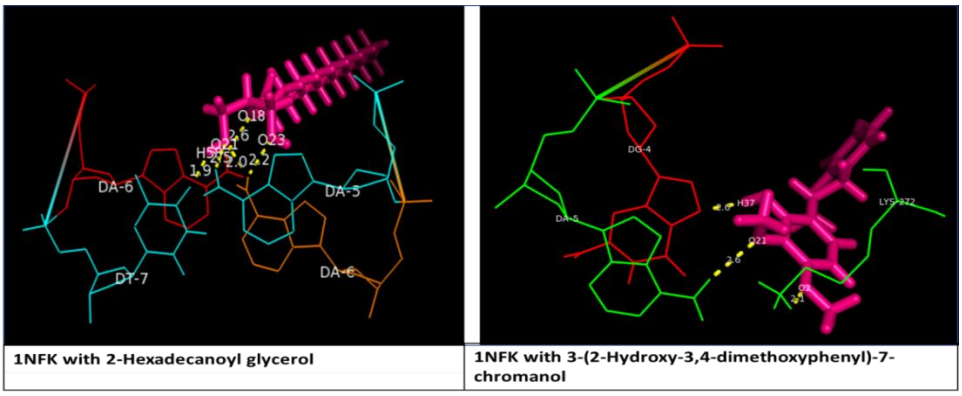


Figure 5a. Docking of 1NFK with ligands

Figure 5a docked complex of Receptor (pink) and Ligand (green, orange, blue, red, green) with bonding (Yellow).

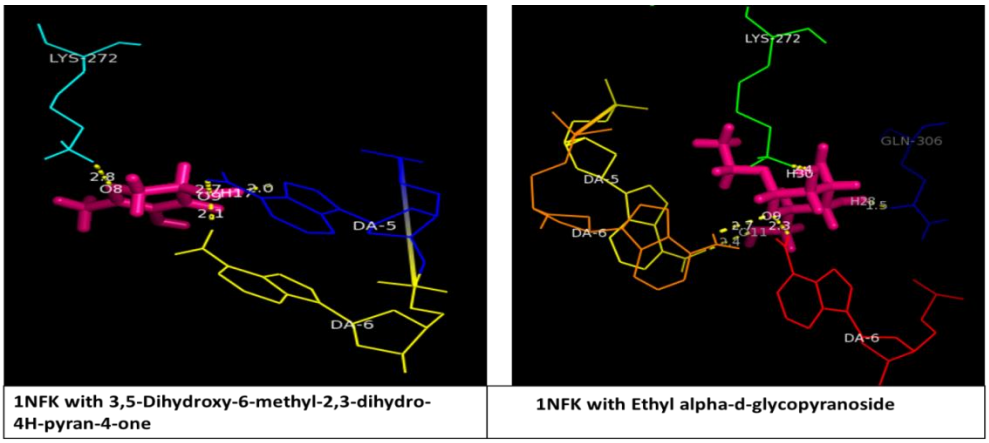


Figure 5b. Docking of 1NFK with ligands

Figure 5b docked complex of Receptor (pink) and Ligand (green, orange, light blue, red, green, yellow, violet,) with bonding (Yellow).

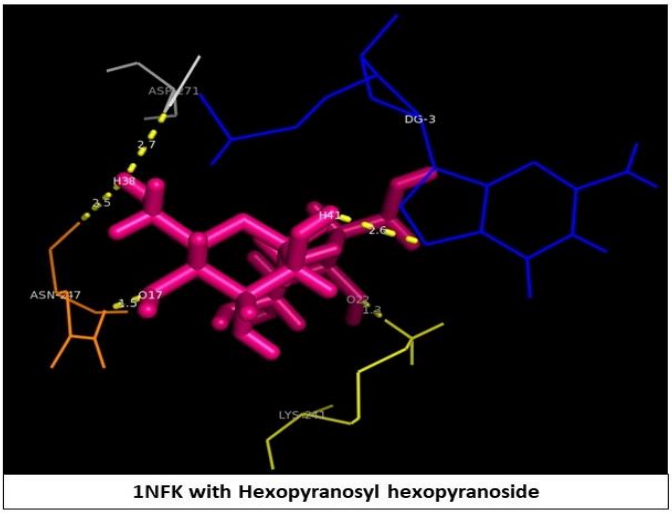


Figure 5c. Docking of 1NFK with ligands

Figure 5c docked complex of Receptor (pink) and Ligand (orange, yellow, violet, white) with bonding (Yellow).

DISCUSSION

PXR is known to involved in the detoxification and clearance of the foreign toxic substances from the body which has response to up-regulate the expression of proteins [11]. The receptor gene PXR belongs to the nuclear receptor super family which is involved in the ligand and DNA binding domain characterized by transcription factors. This gene is also involved in the transcriptional regulator of the cytochrome P450 [8]. The gene PXR is activated by the exogenous and endogenous chemicals (e.g. steroids, antibiotics). The docking work shows high potential binding of PXR receptor with Ethyl alpha-d-glycopyranoside, Hexopyranosyl hexopyranoside, alpha-Monostearin and Ethyl alpha-d-glycopyranoside which is involved in the protection of the liver from alcohol toxicity. Alpha-Monostearin plays an important role in the liver preventing the breakdown of enzymes in various organs. Alpha-Monostearin is a protein made in the liver which is also called as Alpha-1 antitrypsin [12]. This protein helps in the curing of Alpha-1

disease, which is a rare liver disease which makes the defect in liver function. When the person is affected with the disease the protein Alpha-1 antitrypsin from liver transfer from the liver and protects other organs from the damage. The gene PXR which also helps in controlling the drug and cholesterol metabolism [13].

FXR gene is also known as the bile acid receptor which belongs to the nuclear subfamily. These genes are highly expressed in the intestine and the liver. This gene is also helping in the regulation of hepatic triglycerides. It also helps in reducing tumor growth factor [14]. The docking study shows potential binding of FXR gene with ligands such as Ethyl alpha-d-glycopyranoside, Hexopyranosyl hexopyranoside, Mono(2-ethylhexyl) phthalate, Ethyl docosanoate and 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol. When the bile is being overloaded with bile acid this gene helps in the regulation of bile which is released from the liver to remove the harmful effect of bile [15]. The ligand Hexopyranosyl hexopyranoside is responsible in the regulation of bile.

LXR gene is involved in the disruption of lipid homeostasis that affects the inflammatory response in the macrophages by the action of lipid import and it also indirectly regulates the immune system of the host [16]. In this in silico docking, the LXR gene has potential binding with ligand palmitic acid. Palmitic acid is most important in saturated fatty acids widely present in plants and it is involved in digestive properties in humans. These acids play an important role in the human body for the saturation of fatty liver acids [17].

Nf-kB is involved in the transcriptional process of different types of cells of androgen receptor [9]. This gene is also involved in the regulation of toxicological diseases like cancer and liver diseases. The gene is also playing a role in development of liver physiology and also helps in the regulation of embryonic liver homeostasis [18]. In our docking study this gene is high potential with the ligands such as 3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one, Ethyl alpha-d-glycopyranoside, Hexopyranosyl hexopyranoside, 2-Hexadecanoyl glycerol and 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol.

CAR gene is the metabolic enzymes, membrane transporters and transference which belong to the nuclear receptor with activated ligand [19]. This gene mostly involved in decreasing the effective activity of drugs which is taken by the humans [11]. CAR and PXR gene both have similar properties in decreasing toxicological activity of drugs. CAR gene has the high effective binding potential with the ligand 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol.

CONCLUSION

As a conclusion, our study has predicted the potential activity of the active compound of Cyamopsis tetragonoloba such as Ethyl alpha-d-glycopyranoside, Hexopyranosyl hexopyranoside and 3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol that shown higher binding affinity with the 1ILG, 1OSH, 1XNX, 5AVI and 1NFK receptors.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

ACKNOWLEDGMENT

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REFERENCES

[1] F Gresta; G Ceravolo; VL Presti; A D'Agata; R Rao; B Chiofalo. *Ind Crops Prod*. **2017,** 107, 122-129.

[2] RK Bhatt; AK Jukanti; MM Roy. *Legume Res Int J*. **2016,** 40(2), 207-214.

[3] D Mudgil; S Barak; BS Khatkar. *J Food Sci Technol*. **2014,** 51(3), 409-418.

[4] ES Björnsson. *Int J Mol Sci*. **2016,** 17(2).

[5] V Ramappa; GP Aithal. *J Clin Exp Hepatol*. **2013,** 3(1), 37-49.

[6] J Yan; B Chen; J Lu; W Xie. *Acta Pharmacol Sin*. **2015,** 36(1), 62-70.

[7] L Ding; L Yang; Z Wang; W Huang. *Acta Pharm Sin B*. **2015,** 5(2), 135-144.

[8] J Duintjer Tebbens; M Azar; E Friedmann; M Lanzendörfer; P Pávek. *Int J Mol Sci*. **2018,** 19(6).

[9] D Kumar; SK Singla; V Puri; S Puri. *PLoS ONE*. **2015,** 10(1).

[10] R Komati; D Spadoni; S Zheng; J Sridhar; KE Riley; G Wang. *Mol J Synth Chem Nat Prod Chem*. **2017,** 22(1).

[11] SC Chai; MT Cherian; Y-M Wang; T Chen. Biochim Biophys Acta. **2016,** 1859(9), 1141-1154.

[12] I Haq; JA Irving; AD Saleh; L Dron; GL Regan-Mochrie; N Motamedi-Shad. *Am J Respir Cell Mol Biol.* **2016,** 54(1), 71-80.

[13] T Smutny; S Mani; P Pavek. *Curr Drug Metab*. **2013,** 14(10), 1059-1069.

[14] U Deuschle; J Schüler; A Schulz; T Schlüter; O Kinzel; U Abel. *PLoS ONE*. **2012,** 7(10).

[15] S Byun; D-H Kim; D Ryerson; Y-C Kim; H Sun; B Kong. *Nat Commun*. **2018,** 9.

[16] H Korf; S Vander Beken; M Romano; KR Steffensen; B Stijlemans; J-A Gustafsson. *J Clin Invest*. **2009,** 119(6), 1626-1637.

[17] HY Kwan; X Fu; B Liu; X Chao; CL Chan; H Cao. *J Biol Chem*. **2014,** 289(44), 30525-30537.

[18] H Lu; X Lei,; Q Zhang. *BMC Gastroenterol*. **2015,** 15.

[19] J Tian; R Marino; C Johnson; J Locker. *IScience*. **2018,** 9, 209-228.