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Molecular docking and drug design of phytoconstituents from *Couroupita guianensis* – An *in silico* perspective

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Abstract
The dependence of mankind for therapeutic applications on plants dates back to the start of the human race. Natural remedies from ethnobotanicals are found to be safe and cost effective. The early inclusion of pharmacokinetics consideration in the drug discovery process using *in silico* methods is becoming popular due to improved generation of software's. The aim of the present study was to identify the leads possessing strong antioxidant efficacy by *in silico* molecular docking studies. The present investigation deals with computational evaluation of compounds from *Couroupita guianensis*. These compounds were evaluated for molecular docking using ArgusLab and 1-click, drug likeness properties against selected protein receptors, drug likeness properties and pharmacological activity by using various *in silico* tools. Molecular docking analysis revealed that identification of lead with favorable binding energy, number of poses and hydrogen bond interactions confirmed the effective modulation of the receptor. Based on the dock score and number of hydrogen bond interactions, many compound observed to be the most potent compound. The result indicated that most of the compounds analyzed were having good drug-likeness properties. Pharmacological activities of these compounds were predicted individually using Prediction of Activity Spectra for Substances (PASS) server and results clearly depict that compounds were having good pharmacokinetic profiles with numerous biological efficacies. *In silico* molecular docking analysis predicted, that analysis drug can be used as a screening tool to choose appropriate final drug. Present study revealed strong binding affinity of compounds from *Couroupita guianensis* can be considered for the discovery of novel preventive and therapeutic drug.

Keywords: Molecular docking, ArgusLab, 1-click dock, Molinspiration, PAAS, *Couroupita guianensis*

Introduction
Couroupita guianensis Aubl., commonly known as Cannon ball tree, is found throughout India. Different parts of the plant are used for several medicinal purposes like, juice from leaves used for skin related diseases, toothache, malaria, and fruit pulp used to disinfect wounds. In the present study, 39 different compounds of *Couroupita guianensis* leaf reported by Kaneria *et al.* [1] were considered for the molecular docking using to different approaches. These compounds were identified from the most potent extract of the *C. guianensis* possess highest antioxidant efficacy, furthermore, in the present investigation three-protein targets, viz. Nitricoxide synthase (3NLE) [2], C-JUN N-Terminal Kinase (1JNK) and Glutathione S-transferase (18GS) [3], which has been used to predict antioxidant activity, were selected for molecular docking analysis. ArgusLab is offline software used by numerous researchers for the protein-ligand docking [4, 5], another one was 1-click docking, is web server based molecular docking tool also used by many researchers [6, 7]. This investigation involves the search of pharmacokinetic, drug-likeness, and bioactivity profile of reported compounds of *C. guianensis*on the basis of several physicochemical parameters by computational methods and *in silico* biological activity spectrum of the identified compounds for prediction of possible activity and inactivity. The main aim of the study was to identify potent lead by employing *in silico* molecular docking, can be further recommended for the drug discovery and development.

Methodology
Molecular Docking: Protein target were downloaded from database Protein Data Bank (PDB) (http://www.rcsb.org/pdb/home/home.do). 1JNK, 3NLE and 18GS are PDB id of the target protein. All water molecules were removed and on final stage hydrogen atoms were added to receptor molecule. SMILES was obtained from PubChem and was further translated to mol file using "Open babel" Translator A Molecular Mechanics (MM) method UFF was used for refining initial geometries, using the "Clean Geometry" option in the ArgusLab Software.

The active site was defined from the coordinates of the ligand in the original PDB files Protein for the receptor protein. Residues which lie within 5 Å unit area of ligand that interact with it through their side chain were identified and were considered as Active site residues. The docking between receptor and ligand was performed using the "Dock a ligand" option. A spacing of 0.4 Å between the grid points was used. Binding site box size was set to (15 × 15 × 15 Å) so as to encompass the entire active site. 1JNK, 3NLE and 18GS receptor protein was docked against ligands using Argus Lab 4.0.1 (Mark A. Thompson, Planaria Software LLC, Seattle, WA, USA, http://www.arguslab.com) to find the reasonable binding geometries and to explore the protein ligand interactions. Docking of the protein ligand complex was mainly targeted only on to the predicted active site. Docking simulations were performed by selecting "Argus Dock" as the docking engine. The selected residues of the receptor were defined to be a part of the binding site. 1-Click Docking web based server (http://mcule.com/apps/1-click-docking/) powered by AutoDock Vina docking algorithm [8]. It is online Desktop applications can't be simpler by definition - think about downloading, installing, running software. It has integrated scPDB, which allows selecting a target from 10,000 target structures. No need to download, upload, select binding site. With 1-ClickDocking select a target and click on Dock, then start browsing the results, Ideal for a first insight about ligand-target interactions and affinity.

Web based *in silico* pharmacokinetic tools: The chemical structure of compound 1-39 and control, unless otherwise stated, was submitted in the form of canonical simplified molecular input line entry system (SMILE), to estimate several *in silico* pharmacokinetic parameters. By applying computational methods, there are various physicochemical features and pharmacokinetic descriptors were calculated for some selected compounds 1-39 and control through the online tool Molinspiration Cheminformatics server (http://www.molinspiration.com). Drug-likeness evaluated by the Lipinski rule of five that deals four simple physicochemical parameter ranges (MWT ≤ 500, log P ≤ 5, H-bond donors ≤ 5, H-bond acceptors ≤ 10) associated with 90% of orally active drugs that have passed phase II clinical status. Other calculation methods such as ligand efficiency and lipophilic efficiency can also be used to express drug-likeness as parameters of potency. These physicochemical parameters having acceptable range associated with aqueous solubility and intestinal permeability. Physicochemical parameters take small part of the whole chemical information about the real molecule and became popular as variables in molecular modelling studies. The bioactivity score of selected compounds 1-39 and control were also evaluated using the tool Molinspiration Cheminformatics server (http://www.molinspiration.com). In this computational chemistry technique large chemical databases are analyzed in order to identify possible new drug candidates. PASS (http://www.pharmaexpert.ru/PASSonline/predict.php) was used for computational screening of possible biological effects of all the compounds of *C. guianensis*. This tool provides quantitative structure activity relationships based on decomposition of chemical structures in 2D and/or 3D descriptors, followed by generation of models obtained from bioactive ligands [9]. Prediction results were expressed in percentage of probable activity (Pa) and probable inactivity (Pi). Pa and Pi values vary from 0.000 to 1.000, thus, in this evaluation, we considered only four best activities with Pa > Pi and Pa > 0.700.

Results and Discussion

The field of molecular docking has emerged during the last few decades and now is becoming an integral aspect in drug discovery and development area. Molecular docking is utilized for the prediction of protein–ligand complexes which is composed of two components: a search algorithm, an algorithm that creates possible protein–ligand complex geometries, and thus performs the process of "pose generation" and a scoring function that predicts the binding affinity of the ligand to the protein based on the complex geometry. Binding energies are most widely used mode of measuring binding affinity of a ligand. Comparative docking results of 39 compounds of *C. guianensis* by Argus lab and 1-Click docking are listed in Table 1. With Argus lab we found compounds number 22 (trans-3,4-Dihydro-3,4-dihydroxy-7,12-dimethylbenz[a]anthracene) against target protein 3NLE and 18GS, compounds number 25 (Ipriflavone) against target protein 18GS with e-values -8.91, -8.73, -8.76 Kcal/mol respectively. Wherever the chemical structures not properly fitted in target protein software shows message, "No acceptable ligand poses were found".1-click docking gave results in terms of full fitness and ΔG Kcal/mol. From 1-click docking study best full fitness was found for compounds number 22 against target protein 3nle, compounds number 22 against target protein 18GS, compounds number 25 against target protein 18GS with e-values -10.4, -9.3, -7.9 Kcal/mol respectively (Table 1). The observed result shows that compounds of *C. guianensis* have lowest docking energy. Fig. 1 are showed diagrammatical representation of molecular docking analysis of selected ligand (compounds No. 22) with protein 3NLE by Argus lab and 1-Click docking online web server, visualization of docked protein by Discovery Studio and PyMOL. Molecular docking analysis of Ligand (compound No. 22) with protein 3NLE by ArgusLab showed interaction with amino acids TRP180, ALA183, CYS186, VAL187, GLY188, LEU195, MET341, PHE355, TRP358, MET360, GLU363, VAL420 & PHE475 by forming different types of bonds with various bond length represented using Argus Lab (Fig. 1A) and Discovery Studio software in 3D (Fig. 1B) and in 2D (Fig. 1C). Fig. 1D represents the position of ligand 22 in protein 3NLE binding site and molecular docking model presented by PyMOL visualization software showed the probable binding site of ligand 22 with protein 3NLE (Fig. 1E & F).

Drug likeness determines if a particular molecule is similar to the known drug or not. It is a complex balance of different properties and structural features of a compound [10]. Lipinski's rule is mostly used to determine molecular properties that are vital for drug's pharmacokinetic behavior. According to Lipinski's rule of five, a compound is likely to be orally active if, i. partition coefficient (log P) is less than 5; ii. Hydrogen bond donor (OH and NH groups) is less than 5; iii. Hydrogen bond acceptor (N and O) is less than 10; iv. Molecular weight is less 500 [11] to Lipinski's rule of five. In the preset investigation, total 39 compounds of *C. guianensis* were studied and drug likeness (Lipinski's rule of five) results were shown in Table 1. In the present study, out of total 39 compounds, three compounds namely, compound number 13 (PI(P-20:0/17:2(9Z,12Z))), 16 (Gossypol) and 35 (PI(21:0/20:0)) has Physicochemical properties MLogP, natoms, MW, nON, nOHNH, nrotb, nviolations found to be

within higher acceptable range according to Lipinski's rule (Table 1). The bioactivity score profile of the all 39 compounds and 3 standards was given in Table 1.In the present study, out of total 39 compounds, compound number 7 (20-oxo-heneicosanoic acid), 18 (Sparteine), 21 (6beta, 17beta Dihydroxyandrost-4-en-3-one diacetate), 26 (5-Hydroxy-10-prenyl-7,8-dihydro-7,8-trans-dimethyl-4-phenyl-2H,6H-benzo[1,2-b:5,4-b']dipyran-2,6-dione), 27 (Ophirasterol), 29 ((22S)-1Î±,22,25-trihydroxy-26,27-dimethyl-23,23,24,24-tetradehydro-24a, 24b,24c-trihomovitamin D3), 30 (Plakortic acid), 36 (Carpaine) and 38 (Lonchocarpin) having bioactivity score, indicates they could bind more effectively. The result of the present study was found that compounds and standards are biologically active; in addition, bioactivity score provide the information about the binding cascade of the drugs that is used for the development of a new functional drug with increased binding selectivity profile and less undesirable effects.

As shown in Table 2, biological activity predicted using PASS computer program. In order to identify potential targets and pharmacological effects related to the compounds, the online platform PASS was used. The number of effects displayed by the PASS, for each compound, is provided in Table 2. PASS is based on a robust analysis of structure-activity relationships in a heterogeneous training set currently including about sixty thousand of biologically active compounds from different chemical series with about four thousand five hundred types of biological activity. The biological activity spectrum for a substance is a list of biological activity types for which the probability to be revealed (Pa) and the probability not to be revealed (Pi) are calculated. Pa and Pi values are independent and their values vary from 0.000-1.000. There are number pharmacologically important possible biological effect show for compounds of *C. guianensis* and some of these possible activities are like Growth hormone agonist, Anti-ischemic, cerebral, Pro-opiomelanocortin converting enzyme inhibitor, Mitochondrial intermediate peptidase inhibitor, Membrane integrity agonist, G-protein-coupled receptor, kinase inhibitor, Antifungal, Testosterone 17beta-dehydrogenase ($NADP^+$) inhibitor, Peptidyl-dipeptidaseDcp inhibitor, Gluconate 2-dehydrogenase (acceptor) inhibitor, etc (Table 2). The PASS predicted activities provide the basis for evaluation medicinal potential of *C. guianensis* components.

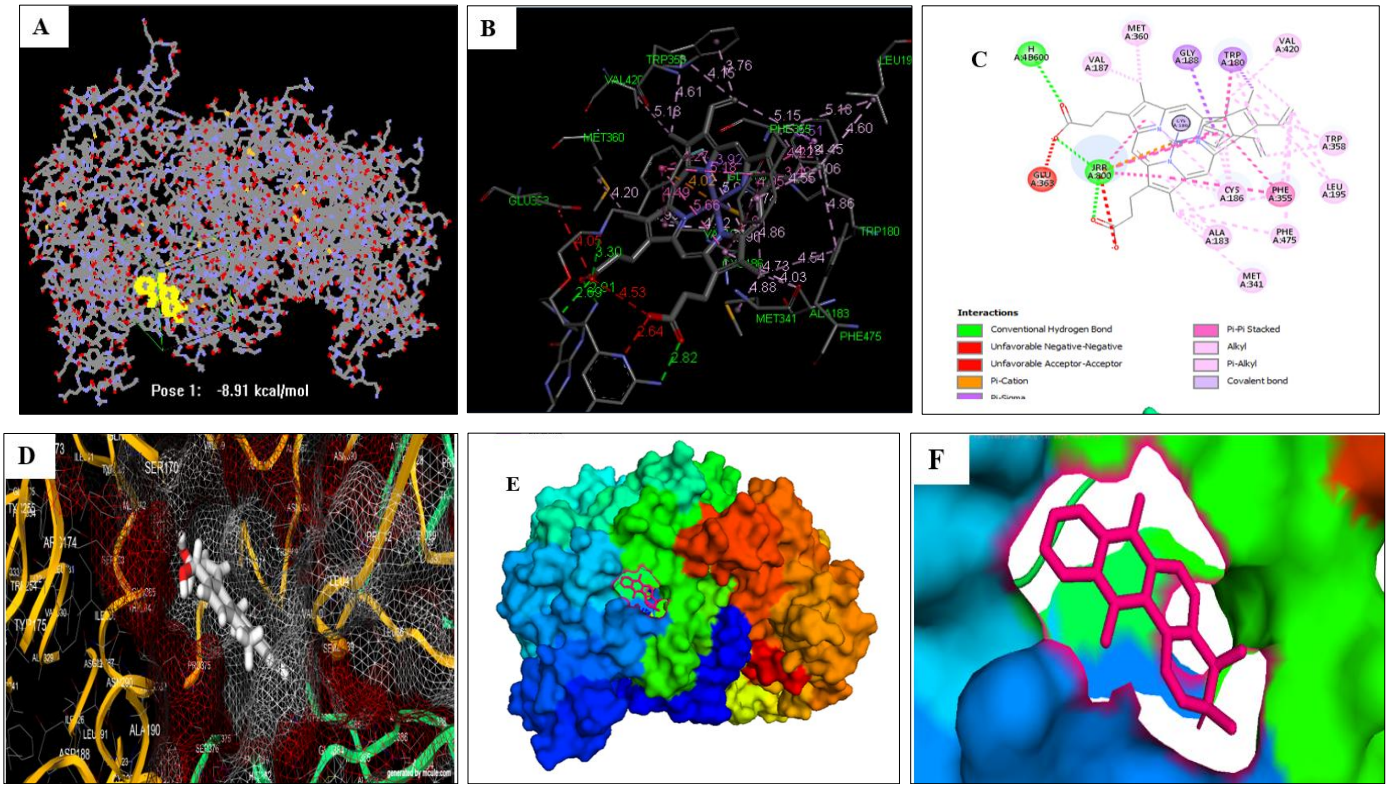

Fig 1: Molecular docking analysis of ligand 22 with protein 3NLE **(A)** Binding position of ligand by using ArgusLab, **(B)** 3D visualization of ligand and amino acid residues of protein by using Discovery studio, **(C)** 2D representation of ligand and protein interaction visualized by Discovery studio, **(D)** Position of ligand inside protein from 1-click dock, **(E)** Binding site of ligand with protein presented by PyMOL visualization software, **(F)** Binding pose in magnified view using PyMOL.

Table 1: Docking Score against receptor 1JNK, 3NLE & 18GS using Argus Lab and 1-Click Docking, physicochemical parameters and bioactivity predicted by Molinspiration of compounds.

No.	Docking Score (ΔG kcal/mol)						Molinspiration prediction													
	ArgusLab			1-Click Docking			Physicochemical parameters									Bioactivity				
	1JNK	3NLE	18GS	1JNK	3NLE	18GS	miLogP	TPSA	natoms	MW	nON	nOHNH	nviolations	nrotb	volume	Gpcr	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1	-4.607	-6.032	-8.267	-6.2	-6.0	-6.1	0.76	78.42	16	244.32	5	3	0	5	214.36	-0.10	-0.57	-0.62	-0.63	0.27	0.25
2	-	-5.844	-7.146	-6.7	-6.8	-5.7	-3.56	184.84	27	388.46	10	8	1	14	370.03	0.59	0.40	0.05	0.22	0.95	0.50
3	-	-5.161	-5.266	-7.1	-7.1	-7.4	-1.00	145.91	24	344.32	9	5	0	5	293.29	0.06	0.05	-0.14	0.11	0.01	0.33
4	-	-3.677	-4.160	-7.4	-8.8	-7.9	-1.95	177.89	34	482.40	13	4	1	8	383.26	0.24	0.06	-0.13	-0.06	0.12	0.26
5	-	-7.136	-9.627	-	-	-	4.54	20.23	21	294.45	1	1	0	0	300.53	0.46	0.48	-0.04	1.11	0.42	0.84
6	-	-5.737	-6.788	-6.7	-7.0	-6.7	0.88	108.02	22	314.38	7	3	0	9	301.34	0.37	0.19	0.08	0.29	1.07	0.30
7	-	-	-	-5.3	-5.8	-4.7	8.04	43.38	25	354.57	3	0	1	20	395.14	-0.09	-0.09	-0.41	0.06	0.01	0.07
8	-	-	-	-9.6	-10.2	-8.9	5.55	89.14	31	418.44	6	2	1	1	366.73	0.10	-0.26	0.01	0.68	-0.12	0.42
9	-	-	-	-6.5	-6.2	-5.7	5.56	66.40	25	353.55	4	2	1	17	383.61	0.20	0.01	-0.24	0.01	0.34	0.17
10	-	-	-	-8.6	-9.5	-7.8	3.92	159.05	37	514.53	10	5	1	6	450.80	-0.00	-0.24	-0.03	-0.27	-0.13	0.40
11	-	-4.444	-5.856	-6.4	-5.6	-5.4	-5.17	224.03	21	350.16	13	9	2	10	263.83	0.99	0.73	0.28	-0.01	1.16	1.44
12	-	-6.407	-	-8.5	-9.2	-7.7	1.70	201.27	40	552.53	11	8	3	5	468.02	0.18	-0.29	0.05	0.16	-0.02	0.33
13	-	-	-	-	-	-	9.75	192.45	59	861.15	12	6	4	40	870.39	-1.73	-2.77	-2.62	-2.78	-1.26	-2.11
14	-	-	-	-10.7	-9.5	-9.4	0.28	225.06	46	642.61	14	8	3	8	540.83	-0.25	-0.91	-0.37	-0.54	-0.17	-0.20
15	-	-	-	-8.3	-8.8	-7.9	1.13	209	42	590.58	13	6	3	10	509.12	0.12	-0.44	-0.40	0.10	0.14	0.24
16	-	-	-	-7.7	-10.1	-8.1	6.57	155.51	38	518.56	8	6	3	5	462.53	-0.02	-0.13	-0.07	0.08	-0.17	-0.11
17	-	-	-	-7.2	-7.5	-5.6	8.10	113.29	44	624.94	7	3	2	28	658.70	-0.01	-0.71	-0.49	-0.22	0.17	0.08
18	-4.882	-6.337	-7.006	-5.6	-7.1	-6.0	2.90	6.48	17	234.39	2	0	0	0	246.97	0.06	0.10	-0.46	-0.65	-0.08	-0.05
19	-	-	-	-	-	-	9.51	131.76	46	680.95	9	3	2	38	707.59	0.19	-0.51	-0.16	-0.32	0.22	0.09
20	-	-	-	-	-	-	8.55	26.30	34	468.77	2	0	1	2	497.21	0.11	-0.07	-0.41	0.55	0.06	0.58
21	-	-7.974	-6.152	-6.4	-8.9	-7.7	3.74	39.68	28	388.50	5	0	0	4	372.61	0.00	-0.05	-0.64	0.79	0.00	0.65
22	-	-8.914	-8.73	-10.7	-10.4	-9.3	3.91	40.46	22	290.36	2	2	0	0	271.42	0.27	0.02	0.10	0.26	-0.05	0.46
23	-	-5.847	-5.433	-6.8	-7.0	-6.6	0.99	99.38	22	314.38	6	4	0	4	297.46	0.36	0.36	-0.11	0.49	0.16	0.76
24	-	-	-	-	-	-	10.55	48.92	75	1029.59	6	0	2	53	1111.96	-3.71	-3.81	-3.80	-3.80	-3.65	-3.74
25	-	-7.238	-9.05	-8.1	-8.5	-7.9	4.31	49.45	21	280.32	3	0	0	3	258.93	-0.28	-0.75	-0.24	0.01	-0.75	-0.09
26	-	-6.619	-	-9.4	-9.4	-8.8	5.45	109.36	33	450.49	7	3	1	4	402.12	0.04	-0.20	0.06	0.51	-0.12	0.47
27	-	-	-	-	-	-	8.37	20.23	32	438.74	1	1	1	6	478.06	0.11	0.02	-0.14	0.78	-0.10	0.55
28	-	-	-	-10.9	-11.0	-8.7	1.24	226.71	50	693.66	15	7	3	10	581.63	-0.39	-1.43	-1.05	-0.88	-0.27	-0.61
29	-	-	-	-	-	-	6.51	80.91	36	498.75	4	4	1	8	518.73	0.42	0.37	-0.06	1.33	0.17	0.87
30	-	-7.195	-5.223	-6.9	-6.6	-6.5	4.01	55.77	21	298.42	4	1	0	8	308.22	0.49	0.45	-0.13	0.48	0.38	0.68
31	-	-	-	-	-	-	9.64	131.76	56	809.12	9	3	2	42	838.49	-1.10	-2.36	-1.93	-2.08	-0.79	-1.46
32	-	-	-	-	-	-	5.83	144.29	47	648.75	10	3	2	11	586.48	-0.28	-0.12	-0.09	-0.27	0.01	-0.23
33	-	-	-	-	-	-	10.24	78.92	48	679.08	6	0	2	40	744.93	-0.37	-1.15	-0.79	-0.77	-0.18	-0.60
34	-	-	-	-	-	-	2.36	165.90	39	548.59	11	3	2	6	483.09	-0.02	-0.20	-0.40	0.63	0.15	0.45
35	-	-	-	-	-	-	10.16	209.52	64	937.29	13	6	4	47	958.34	-2.81	-3.44	-3.33	-3.51	-2.35	-2.97
36	-	-	-	-	-	-	6.40	76.66	34	478.72	6	2	1	0	497.37	0.11	-0.00	-0.12	-0.12	0.71	0.07
37	-	-	-	-9.6	-10.5	-8.6	5.95	80.35	51	696.84	10	0	2	11	646.70	-0.55	-1.50	-1.22	-1.27	-0.49	-1.02
38	-	-7.722	-7.348	-8.8	-8.7	-8.0	4.72	46.53	23	306.36	3	1	0	3	285.06	0.08	-0.12	-0.20	0.33	0.06	0.34
39	-5.856	-7.093	-7.846	-8.7	-8.8	-8.1	-2.94	200.63	30	419.44	11	9	2	10	369.85	0.58	0.17	0.14	0.17	0.76	0.41
40*	-5.980	-6.438	-6.007	-5.7	-5.6	-5.3	0.59	97.98	12	170.12	5	4	0	1	135.10	-0.77	-0.26	-0.88	-0.52	-0.94	-0.17
41*	-6.417	-6.756	-6.319	-5.1	-4.9	-5.1	-1.40	107.22	12	176.12	6	4	0	2	139.71	-0.53	-0.24	-1.09	-0.01	-0.81	0.20
42*	-4.906	-7.067	-8.200	-6.7	-7.0	-6.4	5.43	20.23	16	220.36	1	1	1	2	241.00	-0.34	0.00	-0.48	-0.08	-0.57	-0.07

*Standard

Desh (-) symbol indicates no acceptable ligand poses were found]

Table 2: Biological activity predicted by PASS for compounds.

No.	Compounds	Main predicted properties by PASS online	Pa	Pi
1	D-Biotin	Growth hormone agonist	0.977	0.000
		8-Amino-7-oxononanoate synthase inhibitor	0.972	0.000
		Antiischemic, cerebral	0.952	0.004
		Biotinidase inhibitor	0.945	0.000
2	Lys LeuGlu	Pro-opiomelanocortin converting enzyme inhibitor	0.969	0.001
		Cytosol alanylaminopeptidase inhibitor	0.964	0.001
		Protein-glutamate methylesterase inhibitor	0.961	0.002
		Mucositis treatment	0.958	0.003
3	4',6'-Dihydroxy-2'-methoxy acetophenone 6'-glucoside	Membrane integrity agonist	0.965	0.003
		3-Phytase inhibitor	0.958	0.001
		CDP-glycerol glycerophosphotransferase inhibitor	0.950	0.004
		Membrane permeability inhibitor	0.930	0.003
4	Fluconazole glucuronide	Anaphylatoxin receptor antagonist	0.921	0.003
		Benzoate-CoA ligase inhibitor	0.871	0.008
		Chitinase inhibitor	0.855	0.002
		Antifungal	0.811	0.004
5	3beta-Fluoro-5alpha-androstan-17beta-ol	Testosterone 17beta-dehydrogenase (NADP+) inhibitor	0.961	0.002
		Alkylacetylglycerophosphatase inhibitor	0.944	0.002
		Alkenylglycerophosphocholine hydrolase inhibitor	0.944	0.003
		Acylcarnitine hydrolase inhibitor	0.939	0.003
6	E-64c	Peptidyl-dipeptidaseDcp inhibitor	0.985	0.001
		Thiol protease inhibitor	0.985	0.001
		Enteropeptidase inhibitor	0.966	0.001
		Dipeptidase E inhibitor	0.960	0.000
7	20-oxo-heneicosanoic acid	Gluconate 2-dehydrogenase (acceptor) inhibitor	0.947	0.002
		Acrocylindropepsin inhibitor	0.928	0.003
		Chymosin inhibitor	0.928	0.003
		Saccharopepsin inhibitor	0.928	0.003
8	Cyclomorusin	HIF1A expression inhibitor	0.934	0.004
		Antiosteoporotic	0.928	0.004
		Bone diseases treatment	0.888	0.004
		NOS2 expression inhibitor	0.865	0.001
9	N-oleoyl alanine	Acrocylindropepsin inhibitor	0.960	0.002
		Chymosin inhibitor	0.960	0.002
		Saccharopepsin inhibitor	0.960	0.002
		Polyporopepsin inhibitor	0.951	0.003
10	Icariside II	Free radical scavenger	0.990	0.001
		Membrane integrity agonist	0.983	0.001
		Hemostatic	0.982	0.001
		Lipid peroxidase inhibitor	0.980	0.001
11	N-Phospho-D-lombricine	Glyceryl-ether monooxygenase inhibitor	0.908	0.003
		Homoserine kinase inhibitor	0.894	0.001
		Glutamate-5-semialdehyde dehydrogenase inhibitor	0.885	0.007
		Serine-sulfate ammonia-lyase inhibitor	0.865	0.001
12	Cucumerin B	Membrane integrity agonist	0.889	0.014
		Cardioprotectant	0.874	0.003
		Hepatoprotectant	0.852	0.003
		Cytostatic	0.853	0.005
13	PI(P-20:0/17:2(9Z,12Z))	Phosphatidate phosphatase inhibitor	0.952	0.002
		Beta-adrenergic receptor kinase inhibitor	0.950	0.003
		G-protein-coupled receptor kinase inhibitor	0.950	0.003
		Phosphatidylinositol diacylglycerol-lyase inhibitor	0.937	0.000
14	Haemocorin	Caspase 3 stimulant	0.937	0.003
		Anaphylatoxin receptor antagonist	0.937	0.003
		CDP-glycerol glycerophosphotransferase inhibitor	0.937	0.005
		Membrane permeability inhibitor	0.932	0.003
15	Matteuorienate B	Antihypercholesterolemic	0.969	0.002
		Membrane integrity agonist	0.924	0.006
		CDP-glycerol glycerophosphotransferase inhibitor	0.918	0.007
		Chemopreventive	0.910	0.002
16	Gossypol	Bcl2 antagonist	0.945	0.001
		Apoptosis agonist	0.930	0.004
		Ubiquinol-cytochrome-c reductase inhibitor	0.850	0.017
		L lactate dehydrogenase B inhibitor	0.829	0.000
17	Squamoxinone	Electron transport complex I inhibitor	0.834	0.000
		Lipid metabolism regulator	0.828	0.005

		Gluconate 2-dehydrogenase (acceptor) inhibitor	0.811	0.014
		Ubiquinol-cytochrome-c reductase inhibitor	0.794	0.035
18	Sparteine	Nicotinic alpha2beta2 receptor antagonist	0.929	0.002
		Antipsychotic	0.904	0.004
		CYP2D2 inhibitor	0.890	0.001
		Nicotinic alpha6beta3beta4alpha5 receptor antagonist	0.886	0.004
19	PG(O-18:0/12:0)	Phospholipase inhibitor	0.989	0.001
		Eye irritation, inactive	0.988	0.001
		Phosphatidate phosphatase inhibitor	0.984	0.001
		Phospholipase A2 inhibitor	0.983	0.001
20	Î²-Amyrin Acetate	Lipid metabolism regulator	0.964	0.002
		Mucomembranous protector	0.960	0.003
		Caspase 3 stimulant	0.946	0.003
		Insulin promoter	0.941	0.002
21	6beta,17beta-Dihydroxyandrost-4-en-3-one diacetate	Testosterone 17beta-dehydrogenase (NADP+) inhibitor	0.971	0.002
		CYP2J substrate	0.958	0.002
		CYP2J2 substrate	0.955	0.002
		CYP2C12 substrate	0.952	0.004
22	trans-3,4-Dihydro-3,4-dihydroxy-7,12-dimethylbenz[a]anthracene	CYP2C12 substrate	0.964	0.003
		CYP1B1 substrate	0.956	0.001
		CYP1A substrate	0.953	0.003
		CYP1A1 substrate	0.952	0.003
23	(+)-trans-Carveolglucoside	Respiratory analeptic	0.943	0.004
		CDP-glycerol glycerophosphotransferase inhibitor	0.930	0.005
		Expectorant	0.918	0.001
		Caspase 3 stimulant	0.919	0.003
24	TG(22:3(10Z,13Z,16Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))[iso3]	All-trans-retinyl-palmitate hydrolase inhibitor	0.981	0.000
		Lipid metabolism regulator	0.957	0.003
		Antieczematic	0.941	0.003
		Alcohol O-acetyltransferase inhibitor	0.917	0.001
25	Ipriflavone	Aldehyde oxidase inhibitor	0.954	0.003
		Histidine kinase inhibitor	0.933	0.001
		CYP1A2 substrate	0.888	0.004
		CYP1A substrate	0.866	0.005
26	5-Hydroxy-10-prenyl-7,8-dihydro-7,8-trans-dimethyl-4-phenyl-2H,6H-benzo[1,2-b:5,4-b']dipyran-2,6-dione	Membrane integrity agonist	0.951	0.003
		NOS2 expression inhibitor	0.948	0.001
		Chemopreventive	0.934	0.002
		Free radical scavenger	0.918	0.002
27	Ophirasterol	Antihypercholesterolemic	0.963	0.002
		Cholesterol antagonist	0.959	0.001
		Hypolipemic	0.959	0.003
		Oxidoreductase inhibitor	0.918	0.002
28	Licorice glycoside E	Monophenolmonooxygenase inhibitor	0.893	0.002
		CDP-glycerol glycerophosphotransferase inhibitor	0.888	0.012
		Anticarcinogenic	0.874	0.003
		Transcription factor NF kappa B stimulant	0.843	0.002
29	(22S)-1Î±,22,25-trihydroxy-26,27-dimethyl-23,23,24,24-tetradehydro-24a,24b,24c-trihomovitamin D3	Dermatologic	0.954	0.003
		Antipsoriatic	0.950	0.002
		Antieczematic	0.943	0.003
		Antiosteoporotic	0.941	0.003
30	Plakortic acid	Antifungal	0.805	0.005
		Antineoplastic	0.785	0.014
		Antineoplastic (brain cancer)	0.751	0.003
		CYP2C9 inhibitor	0.737	0.003
31	PG(O-18:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	Phospholipase inhibitor	0.996	0.001
		Phospholipase A2 inhibitor	0.996	0.001
		Phosphatidate phosphatase inhibitor	0.984	0.001
		Eye irritation, inactive	0.983	0.002
32	Gnididin	DNA synthesis inhibitor	0.968	0.001
		Antineoplastic alkaloid	0.959	0.000
		Vanilloid 1 agonist	0.945	0.001
		Antineoplastic	0.934	0.004
33	TG(12:0/12:0/15:1(9Z))[iso3]	All-trans-retinyl-palmitate hydrolase inhibitor	0.986	0.000
		Eye irritation, inactive	0.944	0.003
		Lipid metabolism regulator	0.934	0.003
		Acylcarnitine hydrolase inhibitor	0.921	0.003
34	Bruceantin	Antiprotozoal (Amoeba)	0.993	0.001
		Myc inhibitor	0.983	0.000
		Chemopreventive	0.956	0.001

		Polarisation stimulant	0.953	0.000
35	PI(21:0/20:0)	Phosphatidylinositol diacylglycerol-lyase inhibitor	0.960	0.000
		Beta-adrenergic receptor kinase inhibitor	0.961	0.002
		G-protein-coupled receptor kinase inhibitor	0.961	0.002
		Phosphatidate phosphatase inhibitor	0.959	0.001
36	Carpaine	Nicotinic alpha6beta3beta4alpha5 receptor antagonist	0.821	0.008
		Nicotinic alpha2beta2 receptor antagonist	0.788	0.012
		Antineoplastic	0.785	0.014
		Nicotinic alpha4beta2 receptor antagonist	0.766	0.002
37	Thalicarpine	Antitussive	0.845	0.003
		Nicotinic alpha4beta4 receptor agonist	0.777	0.009
38	Lonchocarpin	HIF1A expression inhibitor	0.923	0.004
		NOS2 expression inhibitor	0.883	0.001
		Membrane integrity agonist	0.890	0.014
		Mucomembranous protector	0.880	0.005
39	TrpThrAsn	Pseudolysin inhibitor	0.908	0.002
		Mucositis treatment	0.909	0.006
		Pitrilysin inhibitor	0.863	0.004
		Biotinidase inhibitor	0.806	0.003
40*	Gallic Acid	Arylacetonitrilase inhibitor	0.955	0.002
		Chlordecone reductase inhibitor	0.954	0.002
		Dehydro-L-gulonate decarboxylase inhibitor	0.950	0.002
		Testosterone 17beta-dehydrogenase (NADP+) inhibitor	0.950	0.003
41*	Ascorbic Acid	NADPH peroxidase inhibitor	0.990	0.000
		Ubiquinol-cytochrome-c reductase inhibitor	0.988	0.001
		Dextranase inhibitor	0.984	0.001
		Arylacetonitrilase inhibitor	0.984	0.001
42*	Butylated hydroxytoluene	Mucomembranous protector	0.922	0.004
		Reductant	0.906	0.003
		Ubiquinol-cytochrome-c reductase inhibitor	0.908	0.005
		Aspulvinonedimethylallyltransferase inhibitor	0.897	0.009

*Standard

Conclusion

Molecular docking has played key role in the identification of efficient binding of receptor and ligand. Compounds with most favorable binding energy were considered as hits. Current study contributes to the identification of drug-like molecules, which can inhibit the selected target. The molecular docking was applied to explore the binding mechanism and to correlate its docking score with the activity of compounds of *Couroupita guianensis* leaf. Out of 39 reported compounds, 28 compounds showed varied level of binding score, in certain cases better than the standard as well. Compound number 22 (trans-3,4-Dihydro-3,4-dihydroxy-7,12-dimethylbenz[a]anthracene) and 25 (Ipriflavone) exhibited remarkable score against the screened receptor proteins, hence it can be recommended for the further drug discovery and development.

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