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Identification of lead molecules with anti-hepatitis B activity in *Bacopa monnieri* (L.) Wettst. and *Cassia fistula* L. through *in silico* method

[1]Shefin B, [2]Sreekumar S, [3]Biju C.K
[123]*Biotechnology and Bioinformatics Division, Saraswathy Thangavelu Centre, Jawaharlal Nehru Tropical Botanic Garden and Research Institute Puthenthope, Thiruvananthapuram, Pin 695586*
[2]*Corresponding author:drsreekumar@rediffmail.com*

***Abstract**: Chronic hepatitis B virus infection is one of the leading causes of liver cancer. In the present investigation, the anti-hepatitis B virus activity of two plants viz. Bacopa monnieri (L.) Wettst. and Cassia fistula L. were evaluated through in silico method and identified potential lead molecules. The HBx protein was selected as the target protein and its three dimensional structure was retrieved from Protein Data Bank. A total of 154 phytochemicals were docked with the target protein. Of these, structures of 45 phytochemicals from B. monnieri and 51 phytochemicals from C. fistula were procured from the PubChem database. The 2D structures of the remaining 45 phytochemicals from B. monnieri and 13 phytochemicals from C. fistula were created using ACD ChemSketch and its 3D structures were generated using the tool CORINA. Out of 90 molecules from Bacopa monnieri, 30 of them and out of 64 molecules from Cassia fistula, 44 of them having free energy of binding <-5.0 kcal/mol were considered as hit molecules. However, the lead molecules were selected based on the free energy of binding and other molecular interaction parameters like H-bonds and drug-likeliness properties. The docking results revealed that the flavone compounds luteolin from B. monnieri and cassiaflavan(4α→6)epiafzelechin from C. fistula were the best lead compounds.*

***Keywords:** Bacopa monnieri, Cassia fistula, HBx, Tuberculosis, Protein, Docking, Phytochemicals*

I. Introduction

Hepatitis B is a life-threatening liver infection caused by the hepatitis B virus (HBV). According to World Health Organisation (WHO), globally 2000 million people have been infected with HBV and 350 million of them are chronically infected [1]. HBV infection is one of the major causes of hepatocellular carcinoma (HCC). It is believed that Hepatitis B virus X protein has a pivotal role in hepatocarcinogenesis because HCC incidence has been reported in animals infected with mammalian hepadnaviruses [2]. Hepatitis B virus belongs to the family Hepadnaviridae. The natural host for HBV is human, however similar viruses have been isolated from apes, woodchucks, squirrels, herons, geese and cranes [3]. In Indian traditional systems of medicine, several plant species have been used to treat liver infection and it is well acknowledged that herbal medicines induce lesser side effects when compared to modern medicine. But its efficacy and molecular mode of drug action are seldom demonstrated scientifically. Herbal medicine contains a plethora of chemical molecules evolved through a long-term evolutionary process for safeguarding the source plant from various environmental stresses such as attack of pathogens, physio-chemical and climatic changes etc. The drug activity of herbal medicine may be due to the synergistic and individual action of phytomolecules. The molecular level mechanism of such action and identification of the best lead molecules against a particular disease can be easily demonstrated through *in silico* methods. In the light of these, the present investigation was aimed to demonstrate the inhibitory activity of phytomolecules derived from two plants *viz. Bacopa monnieri* [4] and *Cassia fistula* [5] against HBx protein, which has a key role in viral multiplication, through *in silico* method.

II. Materials and Methods

2.1 Preparation of the receptor protein

The X-ray crystallographic structure of HBx (PDB ID: 3I7H) protein of Hepatitis B virus with a resolution of 2.9Å was downloaded from Protein Data Bank (PDB) [6] and its physical and chemical parameters were analysed using the tool ProtParam [7]. The structural features were also analysed to find out the presence of natural ligand molecules if any, attached to the protein. The active site of the receptor protein was resolved using CASTp server [8]. The server provides the identification and measurements of surface accessible pockets for proteins and other molecules. It also analytically measures the area and volume of each pocket and cavity, both in solvent accessible surface and molecular surface.

2.2 Preparation of the ligand molecules

The detailed information on 90 phytochemicals from *Bacopa monnieri* and 64 phytochemicals from *Cassia fistula* were collected from literature and other web resources. Of the total 154 phytomolecules, structures of 45 phytomolecules from *B. monnieri* and 41 phytomolecules from *C. fistula* were procured from the PubChem database [9]. The 2D structures and SMILES format of the remaining 45 phytomolecules from *B. monnieri* and 13 phytochemicals from *C. fistula* were created using ACD ChemSketch [10]. The 2D SMILES were converted into 3D structures by using the tool CORINA [11]. A list of phytochemicals derived from the two plants used for docking was depicted in TABLE 1.

2.3 AutoDock simulations

All the selected phytochemicals were docked into the binding site of the HBx protein using AutoDock software [12], an automated molecular docking software package currently maintained by 'The Scripps Research Institute and Olson Laboratory. AutoDock uses Monte Carlo Simulated Annealing, a local hybrid search GA, also known as Lamarckian Genetic Algorithm (LGA) for docking. It mainly involves 3 steps. They are preparation of receptor and ligand files, calculation of affinity maps by using a 3D grid followed by defining the docking parameters and finally running the docking simulation. All the water molecules in the HBx protein were removed and added polar hydrogen atoms during the initial stages of docking process. All docking parameters were set as default value before run the docking process. Once the docking simulation was over, the stability of the docked poses was evaluated by determining the hydrogen bond interaction between the receptor and ligand. Molecular descriptors [13] and drug-likeliness [14,15] properties of the compounds were analyzed using the tool Molinspiration. It provides significant calculation on molecular properties as well as prediction of bioactivity score for the most important targets like GPCR ligands, kinase inhibitors, ion channel modulators, enzymes and nuclear receptors.

III. Results and Discussion

3.1 Role of HBx target protein

The HBx protein is a 17 kDa small regulatory protein conserved among mammalian hepadnaviruses [6]. The structure contains cullin 4-DNA damage-binding protein1 (CIL4-DDB1) in complex with a central fragment of hepatitis B virus X protein (HBx), its DDB1 binding activity is important for viral infection. HBx protein contains two main domains namely N-terminal negative regulatory domain and a C-terminal trans-activation domain. It is a multifunctional protein that exhibits effects on gene transcription, signalling pathways, genotoxic responses, protein degradation, cell-cycle control, cell proliferation and apoptosis which all are related to HBV associated pathogenesis, especially hepato-carcinogenesis [16].

The key role of HBx protein is to promote the transcription of the viral genome which remains as an extrachromosomal circular DNA in the infected cells. During infection, a specialized host protein complex present in human host known as Structural Maintenance of Chromosomes (Smc) complex, Smc 5/6 recognizes the HBV genome and it acts as a restriction factor to prevent virus replication. The most remarkable feature is that the virus counter attack by producing the small X protein, which can destroy Smc 5/6 complex [17]. Henceforth, inhibiting the expression of the HBx protein, we can inhibit the expression of the viral genome and also protect the Smc 5/6 complex that recognizes new HBV infection.

The crystal structure of HBx protein consists of 1139 amino acids, 9 helices and 100 beta sheets. It has a molecular weight of 126.8367 kDa and a theoretical pI value of 5.14. The target protein is predicted as a stable protein with an instability index of 38.10 and aliphatic index of 95.80 using ProtParam. The active site of the protein consists of 18 amino acid residues. Docking between phytochemicals and HBx protein using the tool AutoDock revealed the best compounds that can inhibit the activity of HBx protein.

3.2 Docking of HBx protein with phytochemicals from *Bacopa monneiri*

Docking between the HBx target protein and phytomolecules (ligand) from *B. monnieri* revealed that out of 90 phytomolecules, 30 of them showed free energy of binding $\leq$-5 kcal/mol and hence considered as hit molecules. In this circumstances, molecule having free energy of binding $\leq$-6.90 kcal/mol was chosen as the criteria for lead selection and five molecules such as bacogenin A1 (-7.79 kcal/mol), luteolin (-7.24 kcal/mol), stigmastanol (-7.12 kcal/mol), curcurbitacin D (-7.01 kcal/mol) and quecertin (-6.93 kcal/mol) were selected as the lead molecules (TABLE 2). Analysis of hydrogen bond interaction between HBx protein and the selected lead molecules revealed that both apigenin and luteolin form five hydrogen bonds whereas, cucurbitacin D and quercetin form four hydrogen bonds with the HBx receptor molecule. In fact, bacogenin A1 has the least free energy of binding and it forms only two hydrogen bonds with the receptor molecule. From the Molinspiration calculation, luteolin (Fig.1) a flavonoid compound was identified as the best lead compound from *B. monnieri* as

it assures all the essential molecular and drug-likeliness properties. Also, lutoelin possess only one rotatable bond when compared to other hit molecules (TABLE 4). Hydrogen bond interactions were shown in TABLE 3.

3.3 Docking of HBx with phytochemicals from *Cassia fistula*

Of the 64 phytomolecules from *C. fistula*, 44 of them having a free energy of binding ≤-5 kcal/mol and these molecules were considered as hit molecules. Over 68% of the phytomolecules from *C. fistula* were qualified as the hit molecules and therefore the molecules having free energy of binding ≤-7.0 kcal/mol such as isofucosterol (-8.50kcal/mol), cassiaflavan(4α→6)epiafzelechin (-8.06kcal/mol), oxyanthraquinone (-7.67 kcal/mol), betulinic acid (-7.35 kcal/mol) and emodin (-7.12 kcal/mol) were selected as lead molecules (TABLE 2). The details of hydrogen bond interactions of the foregoing lead molecules were depicted in TABLE 3. The hydrogen bond interactions showed that both cassiaflavan(4α→6)epiafzelechin and citreorosein form seven hydrogen bonds whereas fistucacidin forms six hydrogen bonds. Also, emodin showed three hydrogen bonds. However, isofucosterol has the highest AutoDock score, but it forms only one hydrogen bond with the receptor. Hence, a flavonoid, cassiaflavan-(4 α →6)-epiafzelechin (Fig.2), which has all the required molecular properties (TABLE 4) together with drug likeliness properties and therefore, it was chosen as the best lead molecule from *C. fistula*.

IV. Conclusion

The overall results revealed that out of 90 molecules screened from *B. monnieri*, 30 of them and from *C. fistula* out of 64 molecules, 44 of them showed the free energy of binding ≤-5 kcal/mol and were qualified as hit molecules. From both the plants, five molecules having the least free energy of binding <-6.9 kcal/mol with HBx protein were selected as the lead molecules and through the analysis of molecular interaction of the docked structures as well as drug likeliness properties, the molecule luteolin from *B. monnieri* and cassiaflavan-(4 α →6)-epiafzelechin from *C. fistula* were suggested as the best lead molecules. The results also indicated that both plants contain several phytochemicals with inhibitory activity on HBx protein and its synergistic activity may significantly retard viral replication. The results support the traditional knowledge and further investigation based on the foregoing results may lead to the discovery of novel safe drugs against Hepatitis B virus from these plants.

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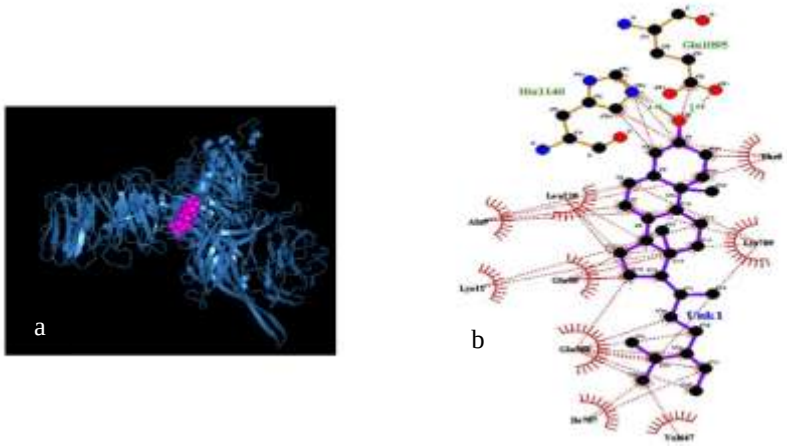

Figure 1: (a) Interaction of HBx with luteolin (b) Hydrogen bond interaction of luteolin with target residues.

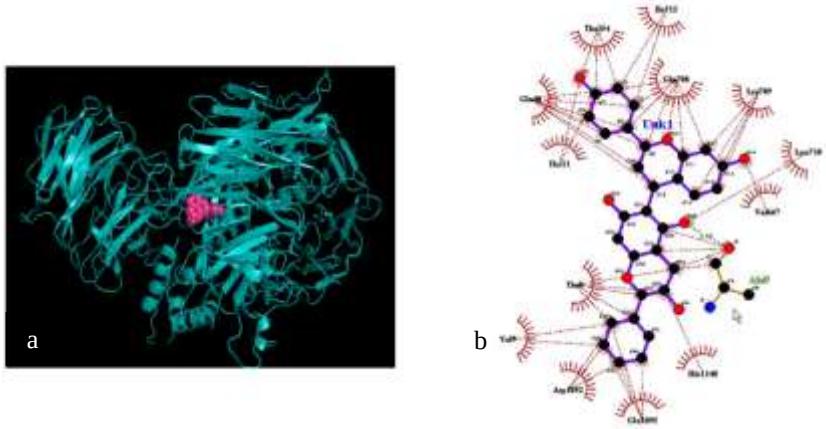

Figure 2: (a) Interaction of HBx with cassiaflavan-(4 α →6)-epiafzelechin (b) Hydrogen bond interaction of cassiaflavan-(4 α→6)-epiafzelechin with target residues

TABLE 1 : List of compounds from *Bacopa monnieri* and *Cassia fistula* selected for docking

Sl No.	Molecule Name	Molecular Formula	Sl No.	Molecule Name	Molecular Formula
Bacopa monnieri					
1	Nicotine	$C_{10}H_{14}N_2$	46	BacopasideVI	$C_{40}H_{62}O_{15}S$
2	D-mannitol	$C_6H_{14}O_6$	47	BacopasideVII	$C_{44}H_{70}O_{17}$
3	Saponin (Hersaponin)	$C_{58}H_{94}O_{27}$	48	BacopasideVIII	$C_{50}H_{80}O_{23}$
4	Bacoside A	$C_{41}H_{68}O_{13}$	49	BacopasideIX	$C_{52}H_{84}O_{22}$
5	Bacoside A1	$C_{40}H_{64}O_{12}$	50	BacopasideX	$C_{52}H_{84}O_{22}$
6	Bacoside A2	$C_{46}H_{74}O_{17}$	51	BacopasideXI	$C_{42}H_{68}O_{15}$
7	Bacoside A3	$C_{46}H_{74}O_{18}$	52	BacopasideXII	$C_{36}H_{58}O_6$
8	Bacoside A4	$C_{35}H_{56}O_8$	53	BacopasideA	$C_{14}H_{26}O_8S$
9	Bacoside A5	$C_{35}H_{56}O_8$	54	BacopasideB	$C_{23}H_{26}O_{12}$
10	Bacoside A6	$C_{40}H_{64}O_{11}$	55	BacopasideC	$C_{26}H_{32}O_{12}$
11	Bacoside B	$C_{41}H_{68}O_{13}$	56	BacopasideN1	$C_{42}H_{68}O_{14}$
12	Bacoside C	$C_{44}H_{70}O_{18}$	57	BacopasideN2	$C_{42}H_{68}O_{14}$
13	Bacopasaponin A	$C_{40}H_{64}O_{12}$	58	Monnierasides 1	$C_{21}H_{24}O_9$
14	Bacopasaponin B	$C_{39}H_{62}O_{12}$	59	Monnierasides 2	$C_{24}H_{28}O_{11}$
15	Bacopasaponin C	$C_{46}H_{74}O_{17}$	60	Monnierasides 3	$C_{21}H_{24}O_{10}$
16	Bacopasaponin D	$C_{41}H_{66}O_{13}$	61	Bacobitacin A	$C_{31}H_{42}O_9$
17	Bacopasaponin E	$C_{51}H_{82}O_{21}$	62	Bacobitacin B	$C_{31}H_{42}O_9$
18	Bacopasaponin F	$C_{52}H_{86}O_{21}$	63	Bacobitacin C	$C_{53}H_{78}O_{23}$
19	Bacopasaponin G	$C_{40}H_{64}O_{12}$	64	Bacobitacin D	$C_{53}H_{78}O_{24}$
20	Bacopasaponin H	$C_{42}H_{66}O_{13}$	65	Plantainoside B	$C_{23}H_{26}O_{11}$
21	BacopasideI	$C_{46}H_{74}O_{20}S$	66	BacosaponinA	$C_{43}H_{71}O_{10}$

22	BacopasideII	$C_{30}H_{48}O_4$	67	BacosaponinB	$C_{40}H_{66}O_{14}$
23	BacopasideIII	$C_{41}H_{65}O_{16}S$	68	BacosaponinC	$C_{48}H_{78}O_{16}$
24	BacopasideIV	$C_{39}H_{62}O_{14}$	69	BacosaponinD	$C_{42}H_{68}O_{12}$
25	BacopasideV	$C_{39}H_{62}O_{14}$	70	Betulinic Acid	$C_{30}H_{48}O_3$
26	Stigmastanol	$C_{29}H_{52}O$	71	CucurbitacinA	$C_{32}H_{46}O_9$
27	Stigmasterol	$C_{29}H_{48}O$	72	CucurbitacinB	$C_{32}H_{46}O_8$
28	Bacogenin A1	$C_{30}H_{48}O_4$	73	CucurbitacinC	$C_{32}H_{48}O_8$
29	Bacogenin A2	$C_{27}H_{41}O_4$	74	CucurbitacinD	$C_{30}H_{44}O_7$
30	Bacogenin A4	$C_{30}H_{50}O_3$	75	CucurbitacinE	$C_{32}H_{44}O_8$
31	Bacosterol	$C_{34}H_{58}O_6$	76	Luteolin 7 O glycoside	$C_{21}H_{20}O_{11}$
32	Bacosine	$C_{30}H_{48}O_3$	77	Stearic acid	$C_{18}H_{36}O_2$
33	Beta sitosterol	$C_{29}H_{50}O$	78	Hydroxyl benzoic acid	$C_7H_6O_3$
34	Heptacosane	$C_{27}H_{56}$	79	B daucosterin	$C_{35}H_{60}O_6$
35	Octacosane	$C_{28}H_{58}$	80	Rosavin	$C_{20}H_{28}O_{10}$
36	Nonacosane	$C_{29}H_{60}$	81	28 hydroxy lupeol	$C_{29}H_{48}O_2$
37	Triacontane	$C_{30}H_{62}$	82	3,4-dimethoxycinnamic acid	$C_{11}H_{12}O_4$
38	Hentriacontane	$C_{31}H_{64}$	83	20 hydroxy lupeol	$C_{29}H_{48}O_2$
39	Dotriacontane	$C_{32}H_{66}$	84	Pectic acid	$C_6H_{10}O_7$
40	Apigenin	$C_{15}H_{10}O_5$	85	Ascorbic acid	$C_6H_8O_6$
41	Quercetin	$C_{15}H_{10}O_7$	86	Asiatic acid	$C_{30}H_{48}O_5$
42	Ursolic acid	$C_{30}H_{48}O_3$	87	Brahmic acid	$C_{30}H_{48}O_6$
43	Lupeol	$C_{30}H_{50}O$	88	Wogonin	$C_{16}H_{12}O_{11}$
44	Luteolin	$C_{15}H_{10}O_6$	89	Oroxindin	$C_{22}H_{19}O_{11}$
45	Asiaticoside	$C_{48}H_{78}O_{19}$	90	Loliolide	$C_{11}H_{16}O_3$
Cassia fistula					
1	Octacosan-5,8-diol	$C_{28}H_{58}O_2$	33	Benzyl 2-hydroxy-3,6-dimethoxybenzoate	$C_{16}H_{16}O_5$
2	5-(2-hydroxy phenomethyl) furfural	$C_{12}H_{10}O_4$	34	Benzyl 2β-O-D-glucopyranosyl-3,4-dimethoxy benzoate	$C_{22}H_{26}O_{11}$
3	(2'S)-7-hydroxy-5-hydroxymethyl-2-(2'-hydroxypropyl) chromone	$C_{13}H_{14}O_5$	35	5-hydroxymethylfurfural	$C_6H_6O_3$
4	Chrysophanol/Chrysophanein	$C_{15}H_{10}O_4$	36	2,5- dimethyl-7-Hydroxychromone	$C_{11}H_{10}O_3$
5	Betulinic acid	$C_{30}H_{48}O_3$	37	2,5-dimethyl-7-Methoxychromone	$C_{11}H_{10}O_3$
6	Sitosterol	$C_{29}H_{50}O$	38	Vanillic acid	$C_8H_8O_4$
7	Sennosides A/B	$C_{42}H_{38}O_{20}$	39	Isovanillic acid	$C_8H_8O_4$
8	Isofucosterol	$C_{29}H_{48}O$	40	Cephalin	$C_9H_{18}NO_8$
9	Fistucacidin	$C_{15}H_{14}O_6$	41	Anthraquinone	$C_{14}H_8O_2$
10	Oxyanthraquinone	$C_{14}H_8O_3$	42	Isoflavone	$C_{15}H_{10}O_2$
11	Dihydroxyanthraquinone	$C_{22}H_{28}N_4O_6$	43	biochanin A	$C_{16}H_{12}O_5$
12	Epiafzelechin	$C_{15}H_{14}O_5$	44	1,8-dihydroxy-3-methylanthraquinone	$C_{15}H_{10}O4$
13	Epicatechin	$C_{15}H_{14}O_6$	45	Barbaloin / Aloin	$C_{21}H_{22}O_9$
14	Procyanidin B2	$C_{30}H_{26}O_{12}$	46	Pectin	$C_6H_{10}O_7$
15	Rhein	$C_{15}H_8O_6$	47	Phytol	$C_{20}H_{40}O$
16	Rhein glucoside	$C_{21}H_{16}O_{11}$	48	2-hentriacontanone	$C_{31}H_{62}O$
17	Physcion	$C_{16}H_{12}O_5$	49	(E)-nerolidol	$C_{17}H_{28}O_2$
18	Kaempferol	$C_{15}H_{10}O_6$	50	Sterculic acid	$C_{19}H_{34}O_2$
19	Leucopelargonidin	$C_{15}H_{14}O_6$	51	Triacontane	$C_{30}H_{62}$
20	Emodin	$C_{15}H_{10}O_5$	52	4-Isopropyl benzaldehyde	$C_{10}H_{12}O$
21	Indoleacetic acid	$C_{10}H_9NO_2$	53	Limocitrol	$C_{18}H_{16}O_9$
22	Catechin	$C_{15}H_{14}O_6$	54	3,5,7,3',4'-Pentahydroxy-6,8-dimethoxyflavone 3- α -L-arabinopyranoside	$C_{22}H_{22}O_{13}$
23	Beta sitosterol	$C_{29}H_{50}O$	55	Scopoletin	$C_{10}H_8O_4$
24	Stigmasterol	$C_{28}H_{48}O$	56	Dihydrokaempferol	$C_{15}H_{12}O_6$
25	Lupeol	$C_{30}H_{50}O$	57	Epiafzelechin 3-O- β -D-glucopyranoside	$C_{21}H_{24}O_{10}$
26	Citreorosein	$C_{15}H_{410}O_6$	58	Cassiaflavan-(4 α →6)-epiafzelechin	$C_{30}H_{26}O_7$
27	Ziganein	$C_{15}H_{12}O_3$	59	Guibourtinidol	$C_{15}H_{14}O_4$
28	1,4,5-Trihydroxyanthraquinone	$C_{16}H_{14}O_3$	60	Quercetin 7-methyl ether 3-gentiobioside	$C_{28}H_{32}O_{17}$
29	Isoscopoletin	$C_{10}H_8O_4$	61	dimethyl-7-	$C_{11}H_{10}O_3$

				hydroxychromone	
30	2,4-dihydroxybenzaldehyde	$C_7H_6O_3$	62	Stearic acid	$C_{18}H_{36}O_2$
31	Malvalic acid	$C_{18}H_{32}O_2$	63	Oleic acid	$C_{18}H_{34}O_2$
32	Palmitic acid	$C_{16}H_{32}O_2$	64	Linoleic acid	$C_{18}H_{32}O_2$

TABLE 2: Docking results of top 10 hit compounds identified from two selected plants

Sl. No.	Plant Name	Compound Name	Estimated Free Energy of Binding Kcal/mol	Inhibition Constant Ki (uM)
1	*Bacopa monnieri*	BacogeninA1	-7.79	1.95
		Luteolin	-7.28	4.59
		Stigmastanol	-7.12	5.99
		CucurbitacinD	-7.01	7.28
		Quercetin	-6.93	8.37
2	*Cassia fistula*	Isofucosterol	-8.50	585.20
		Cassiaflavan(4α→6) epiafzelechin	-8.06	1.24
		Oxyanthraquinone	-7.67	2.40
		Betulinic acid	-7.35	4.11
		Emodin	-7.12	6.06

TABLE 3 : Hydrogen bond interaction between the target protein and the selected lead compounds from *Bacopa monnieri* and *Cassia fistula.*

Sl. No	Name of the lead molecule	No. Of H-bonds formed with the receptor	Details of H-bonds
1	BacogeninA1	2	Prtn_rig:A:LYS35:HZ2:BacogeninA1::UNK1:O1 Prtn_rig:A:LEU710:HN:BacogeninA1::UNK1:O20
2	Luteolin	5	Prtn_rig:A:LEU710:HN:Luteolin::UNK1:O19 Luteolin::UNK1:H28:prtn_rig:A:ALA9:O Luteolin::UNK1:H30:prtn_rig:A:GLU40:OE2 Luteolin::UNK1:H31:prtn_rig:A:GLU40:OE2 Prtn_rig:A:GLN708:HE21:Luteolin::UNK1:O10
3	Stigmastanol	1	Stigmastanol::UNK1:H69:prtn_rig:A:PRO12:O
4	CucurbitacinD	4	Prtn_rig:A:THR354:HG1:CucurbitacinD::UNK1:O33 Prtn_rig:A:LYS35:HZ2:CucurbitacinD::UNK1:O35 CucurbitacinD::UNK1:H55:prtn_rig:A:GLN10:OE1 Prtn_rig:A:LEU710:HN:CurcurbitacinD::UNK1:O20
5	Quecertin	4	Prtn_rig:A:LEU710:HN:Quecertin::UNK1:O19 Prtn_rig:A:GLN708:HE21:Quecertin::UNK1:O10 Quecertin::UNK1:H32:prtn_rig:A:GLU40:OE2 Quecertin:UNK1:H31:prtn:A:GLU40:OE2
6	Isofucosterol	1	Prtn_rig:A:HIS1140:HE2:Isofucosterol::UNK1:O1
7	Cassiaflavin(4 α→6) epiafzelechin	1	Cassiaflacin::UNK1:H58:prtn_rig:A:ALA9:O
8	Oxyanthraquinone	1	Prtn_rig:A:LYS11:HN:Oxyanthraquinone::UNK1:O17
9	Betulinic acid	2	Betulinic acid::UNK1:H77:prtn_rig:A:GLU1095:OE1 Prtn_rig:A:HIS1140:HE2:Betulinicacid::UNK1:O29
10	Emodin	3	Prtn_rig:A:GLN10:HE22:Emodin::UNK1:O20 Prtn_rig:A:LYS11:HN:Emodin::UNK1:O17 Prtn_rig:A:LYS709:HZ3:Emodin::UNK1:O19

TABLE 4 : Molinspiration calculation of selected lead compounds

Hit Name	miLogP	TPSA	N atoms	MW	nOH	nOHNH	Nvio	N rotb	Vol
BacogeninA1	5.64	66.76	34	472.71	4	2	1	2	479.91
Luteolin	1.97	111.12	21	286.24	6	4	0	1	232.07
Stigmastanol	8.71	20.23	30	416.73	1	1	1	6	462.73
CucurbitacinD	2.13	132.12	37	516.67	7	4	1	4	495.98
Quecertin	1.68	131.35	22	302.24	7	5	0	1	240.08
Isofucosterol	7.69	20.23	30	412.70	1	1	1	5	450.30
Cassiaflavin(4 α→6) epiafzelechin	4.83	119.61	37	498.53	7	5	0	3	435.56
Oxyanthraquinone	5.73	51.21	17	224.22	3	0	0	0	190.95
Betulinic acid	7.04	57.53	33	456.71	3	2	1	2	472.04
Emodin	3.01	94.83	20	270.24	5	3	0	1	223.19