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Identification of Effective Phytocompounds from the Indian Medicinal Plants for the Treatment of Jaundice using *In silico* Studies

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ABSTRACT

The presence of higher levels of bilirubin in the blood is indicative of Jaundice. Unconjugated bilirubin is delivered to the liver via binding to albumin. This research aimed to find effective phytocompounds from Indian medicinal plants that could help in mitigating Jaundice. IMPPAT and PubChem databases were used to determine the 3D structure of phytocompounds. SwissADME was used to test the Lipinski rule of five for all phytocompounds. The PDB database was used to retrieve the target protein's 3D structure. PyRx was used to conduct the docking experiments, and Discovery Studio 2021 was used to evaluate the results. According to the findings, the binding affinity of Cadabicine, Voruscharin, Triptotritepenic acid A, Stigmasta-5,22-dien-3-ol and Sitogluside was -9.2, -8.9, -8.7, -8.4 and -8.1 Kcal/mol, respectively. Toxicity tests were performed on the best-interacted phytocompounds, and the results revealed that the compounds were extremely safe. Hence, the present study concludes that Cadabicine from *Crataeva nurvala*, Voruscharin from *Calotropis procera* and Triptotriterpenic acid A from *Abrus precatotius* may have a potential effect in the treatment of Jaundice.

Keywords: Jaundice, Phytocompounds, Medicinal plants, Molecular docking, Virtual screening.

INTRODUCTION

Jaundice is one of the most clinical affection indicatives of liver abnormalities that affect people all over the world. It is also a life-threatening illness, especially in developing nations. Jaundice is a condition brought on by elevated serum bilirubin levels in the body [1]. Red blood cells (RBCs) undergo hemolysis during the breakdown of bilirubin, which releases hemoglobin. Heme is broken down by the heme oxygenase within the reticuloendothelial system into biliverdin and carbon monoxide. The enzyme biliverdin reductase then transforms biliverdin into unconjugated bilirubin. Unconjugated bilirubin binds to albumin and travels to the liver in this way. Because it may pass the blood-brain barrier, unbound unconjugated bilirubin is harmful to the central nervous system (BBB) [2, 3, 4].

Hepatitis viruses A, B, C, and E cause viral hepatitis or jaundice epidemics. When at least one case is laboratory-confirmed and the others are epidemiologically connected, hepatitis outbreaks are categorised based on the causal agent. If the causal agent cannot be determined, cases are classified as hepatitis A, B, C, E, or undefined [5]. Hepatitis A is an acute, self-limiting liver illness caused by a picornavirus, the hepatitis A virus (HAV), which belongs to the genus Hepatovirus and is spread by the faecal-oral route. It infects 10 million people worldwide every year [6, 7]. In 2015, it is estimated that it caused roughly 11,000 fatalities [8]. Most children get an asymptomatic illness as a youngster and build immunity spontaneously as a result. Adult infection is usually severe, especially in naive people from infancy [9]. The Indian government's Comprehensive Disease Surveillance Program (IDSP) has released viral hepatitis surveillance data from 2011 to 2013. Hepatitis E was responsible for 78 (48 per cent) of the 163 outbreaks with known aetiology, hepatitis A for 54 (33 per cent), both hepatitis A and E for 19 (12 per cent), and hepatitis B or C for 12 (7 per cent). Most outbreaks were caused by contaminated drinking water.

During 2018, widespread hepatitis/jaundice was observed in Villupuram District, Tamil Nadu. Jaundice was a common symptom that all youngsters had, and it was present in all the clinical cases [10]. Also, Kerala has recently had multiple outbreaks of hepatitis A among the younger generation. The most recent hepatitis spread in December 2016 in Nellikuzhi, Kerala, India [11].

Viral hepatitis is a serious public health issue in India, accounting for 2.85% of all fatalities [12]. The Hepatitis B virus (HBV) is the most common kind of hepatitis virus in India, impacting almost 50 million individuals with an average prevalence of 4% [13]. In India, chronic HBV infection causes liver disease accounting for 10-20% of cirrhosis and 40-50% of hepatocellular carcinoma (HCC) [14].

The Global Health Sector Strategy (GHSS) on viral hepatitis for 2016–2021, which seeks to abolish viral hepatitis as a public health hazard by 2030, received endorsement from the World Health Assembly.

Drugs which include Levovir (Cledvudine), and Viread (Tenofovir) inhibit viral DNA polymerase and it was approved in 2006 & 2008, respectively [15]. A study reported that traditional medicinal plants such as *Acacia nicotica, Achras sapota, Baliospermum montanum* and *Bryophyllum pinnatum* had *a* potential effect against jaundice [16]. The rural inhabitants of Tamil Nadu used the medicinal plants *Azadirachta indica, Carum nothum, Cynodon dactylon, Lablab purpureus, Momordica charantia,* and *Phyllanthus amarus* to treat diabetes and jaundice [17].

Various Indian medicinal plants which include *Glycyrrhiza glabra, Abrus precatorius, Aegle marmelos, Andrographis paniculata, Boerhavia diffusa, Calotropis procera, Carica papaya* [16], *Crataeva nurvala, Cuscuta reflexa, Phyllanthus amarus, and Tephrosia purpurea* [18] were taken in this study to find the potential phytocompounds for treating Jaundice using *in silico* studies.

MATERIALS AND METHODS

Ligand selection

Around 380 phytochemical compounds were selected from various Indian medicinal plants such as *Glycyrrhiza glabra, Abrus precatorius, Aegle marmelos, Andrographis Paniculata, Boerhavia diffusa, Calotropis procera, Carica Papaya* [16], *Crataeva nurvala, Cuscuta reflexa, Phyllanthus amarus, and Tephrosia purpurea* [18] were taken using literature and the IMPPAT database [19]. These chemicals' 3D structures were obtained from the PubChem database [20], and the Lipinski Rule of Five was tested using SwissADME [21]. The Lipinski Rule of Five was observed in 236 compounds, and these compounds were chosen for the study.

Target protein selection

In the literature for jaundice, the target capsid protein for the hepatitis B virus was discovered. This target protein's 3D structure was located in the PDB database [22]. This target protein's UniProt ID was obtained from the UniProt database [23].

Docking studies

Docking experiments for the target protein capsid protein and the phytocompounds (ligands) were performed using PyRx 0.8 software. Using this program, the target protein was further prepared for docking research. All of the ligands were uploaded using PyRx 0.8's Open Babel option. The grid was created, and docking tests were carried out, using PyRx 0.8's Vina wizard tool [24]. The binding affinity values were kept in an XL file. Utilizing Discovery Studio 2021, the data were assessed, and docked 2D and 3D images were taken. The best outcomes are indicated by the lowest binding affinity.

ADMET and CYP properties

SwissADME was used to examine the ADMET and CYP characteristics of all the phytocompounds that interacted the best [21]. All the compounds with the best interactions were assessed for Lipinski, BBB (Blood-Brain Barrier), HIA (Human Intestinal Absorption), PGP (P-glycoprotein), XLogP3, TPSA (Topological Polar Surface Area), LogS, Fraction Csp3, Rotatable bonds, CYP enzyme inhibitor properties, Skin permeation, and Bioavailability score.

RESULTS

Ligand and Target protein selection

From the PubChem database, the 3D structure of ligands (phytocompounds) was obtained. The target capsid protein's 3D structure was retrieved from the PDB library; its PDB ID is 2G33. Figure 1 depicts the target protein's 3D structure.

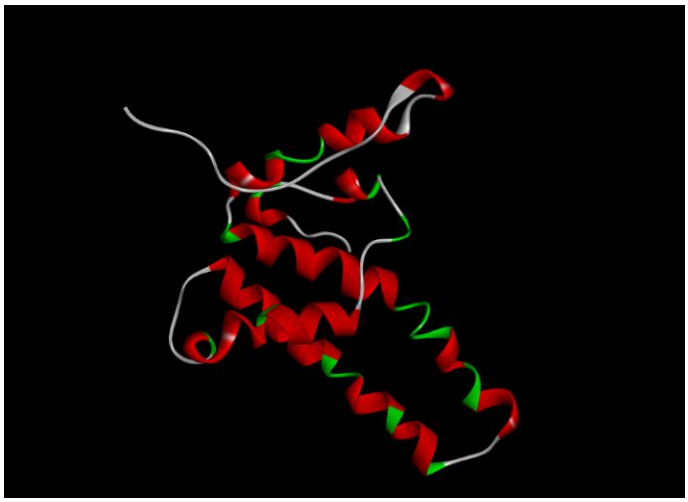

Figure 1: The 3D structure of Target Capsid Protein

Docking studies

PyRx 0.8 software was used to conduct docking studies for the phytocompounds (ligands) and the target capsid protein for the hepatitis B virus. According to the findings, the majority of the compounds interacted with the target protein, and the next 10 compounds shown excellent binding affinities with the protein. Table 1 displays all the findings, and Figures 2 to 9 display the 2D and 3D interactions of phytocompounds with the target protein.

Table 1: Interaction of Phytocompounds with the target protein

S. No.	PubChem (CID)	Compound Name	Plant Name	Binding Affinity (Kcal/mol)	No. of Bonds	Interacting Residues	Bond Length (Å)
1)	100921101	Cadabicine	*Crataeva nurvala*	-9.2	6	THR33 ASP32 ILE105 SER106 LEU30 PRO25	1.62 3.77 3.92 1.66 5.36 4.26
2)	44387915	Voruscharin	*Calotropis procera*	-8.9	5	ARG56 ILE59 ILE31 TRP62 ARG28	3.07 5.45 4.51 4.46 1.76
3)	21594203	Triptotriterpenic acid A	*Abrus precatorius*	-8.7	9	SER106 PRO25 ALA137 ILE139 LEU140 TRP102 PHE23 PHE23 PHE23	1.90 5.02 4.37 4.70 4.98 5.08 4.09 4.52 4.79
4)	53870683	Stigmasta-5,22-dien-3-ol	*Andrographis paniculata*	-8.4	9	SER106 TRP102 PRO25 PHE23 PHE23 PHE23 ALA137 PHE122 PRO25	1.97 5.44 5.19 4.88 4.07 5.06 4.85 5.44 5.19
5)	5742590	Sitogluside	*Carica papaya*	-8.1	5	TRP125 TRP125 ALA137 PRO25 THR109	5.48 4.89 4.50 5.13 2.79
6)	6427357	Epilupeol (20[29]-lupen-3A-ol) acetate	*Crataeva nurvala*	-8.1	1	LEU37	5.15
7)	156338	Apollinin	*Tephrosia purpurea*	-8	8	ILE139 SER106 TRP102 ILE105 PHE110 LEU37 LEU140 LEU140	3.1 1.81 3.30 5.32 5.41 4.98 5.11 5.37
8)	92803	5-beta-Cholanic acid	*Abrus precatorius*	-7.9	5	ILE139 ALA137 PHE23 PHE23 TRP102	4.60 5.22 4.25 4.51 2.37
9)	10569999	(+)-Tephrosone	*Tephrosia purpurea*	-7.9	5	ILE139 PRO25 ALA137 TRP102 TRP102	3.77 4.72 4.77 2.74 2.17
10)	101321335	[(4'R,5'S,23'R,25'S,26'R)-3,6a,10',11',12',15',16',17',31',32',36',37'-dodecahydroxy-2',5,7',20',28',40'-hexaoxospiro[3,3a-dihydro-2H-furo[3,2-b]furan-6,39'-	*Phyllanthus amarus*	-7.9	6	THR114 THR114 ILE139 ILE139 TYR118 ASN136	 2.23 2.33 5.49 1.78 3.39

		3,6,21,24,27,38,42-heptaoxanonacyclo[35.2.2.133,36.01,35.04,23.05,26.08,13.014,19.029,34]dotetraconta-8,10,12,14,16,18,29,31,33-nonaene]-25'-yl] 3,4,5-trihydroxybenzoate					3.65
Synthetic drug							
11)	73115	Levovir	Synthetic Drug	-5.5	2	SER106 TRP102	2.05 4.91

From the results (Table 1), among other compounds, 10 compounds showed very good results with the target protein. Of which, the phytocompound Cadabicine showed excellent binding affinity (-9.2 Kcal/mol) with the amino acid residues THR33, ASP32, ILE105, SER106, LEU30, and PRO25 of the target protein. The phytocompound Voruscharin also gave excellent binding affinity of -8.9 Kcal/mol with the amino acid residues ARG56, ILE59, ILE31, TRP62, and ARG28. The binding affinity -8.7 Kcal/mol was observed between the phytocompound Triptotriterpenic acid A and the amino acid residues SER106, PRO25, ALA137, ILE139, LEU140, TRP102, and PHE23 of the target protein. Among the other compounds, the lowest binding affinity (-7.9 Kcal/mol) was observed between the phytocompound [(4'R,5'S,23'R,25'S,26'R)-3,6a,10',11',12',15',16',17',31',32',36',37'-dodecahydroxy-2',5,7',20',28',40'-hexaoxospiro[3,3a-dihydro-2H-furo[3,2-b]furan-6,39'-3,6,21,24,27,38,42-heptaoxanonacyclo[35.2.2.133,36.01,35.04,23.05,26.08,13.014,19.029,34]dotetraconta-8,10,12,14,16,18,29,31,33-nonaene]-25'-yl]3,4,5- trihydroxybenzoate and the amino acid residues THR114, ILE139, TYR118 and ASN136 of the target protein. Besides, the binding affinity of the Synthetic drug Levovir with the target protein was -5.5 Kcal/mol and the interacted amino acid residues were SER106 and TRP102. Thus, in the results of the present study, all the phytocompounds showed very good binding affinity when compared to the Synthetic drug Levovir, of which, the phytocompounds Cadabicine, Voruscharin, Triptotriterpenic acid A showed highest binding affinity among the other phytocompounds.

In the same way, the present *in silico* docking studies identified that the phytocompound Cadabicine from *Crataeva nurvala*, Voruscharin from *Calotropis procera*, and Triptotriterpenic acid A from *Abrus precatorius* had the potential ability to act as a drug for treating Jaundice.

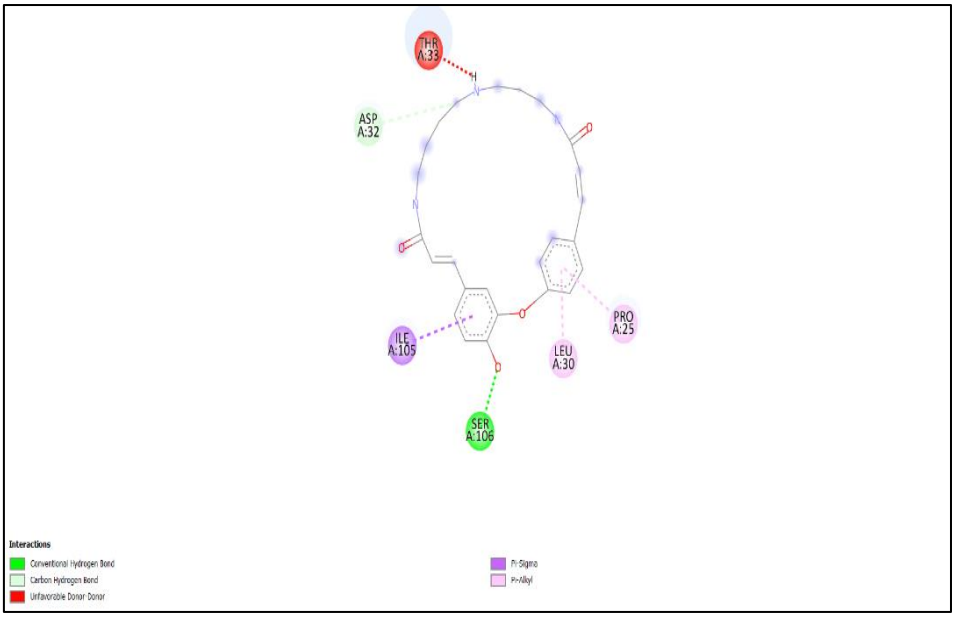

Figure 2: The 2D interaction of phytocompound Cadabicine with the target protein

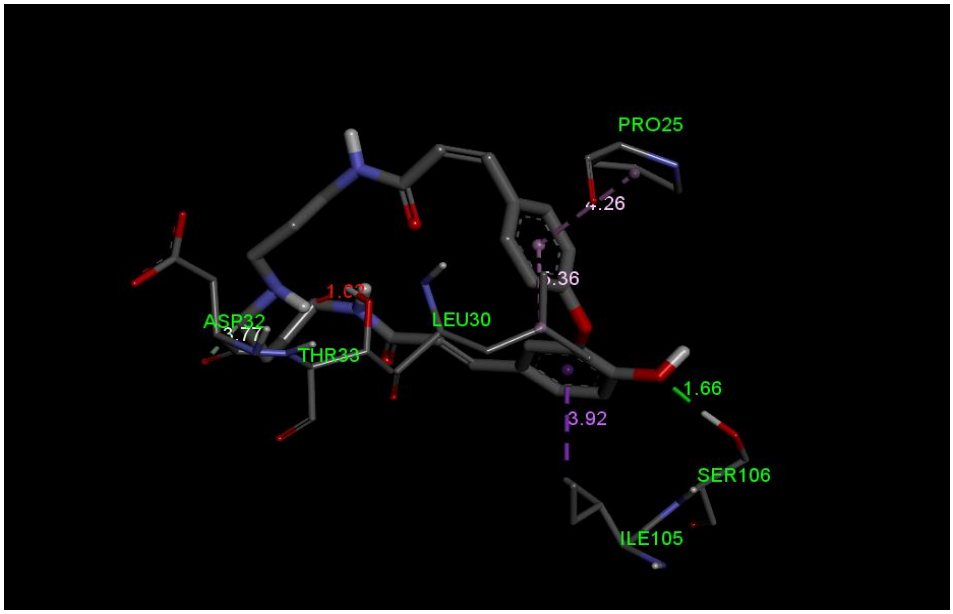

Figure 3: The 3D interaction of phytocompound Cadabicine with the target protein.

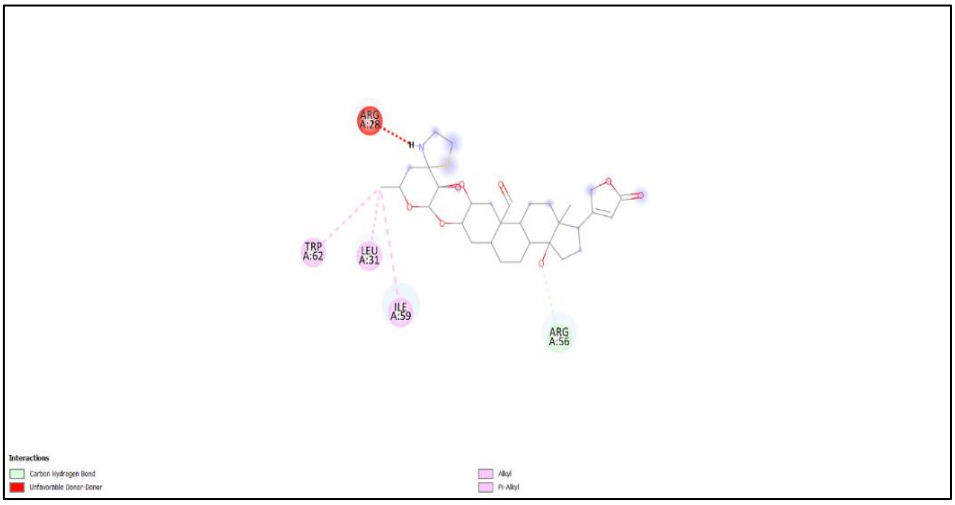

Figure 4: The 2D interaction of phytocompound Voruscharin with the target protein

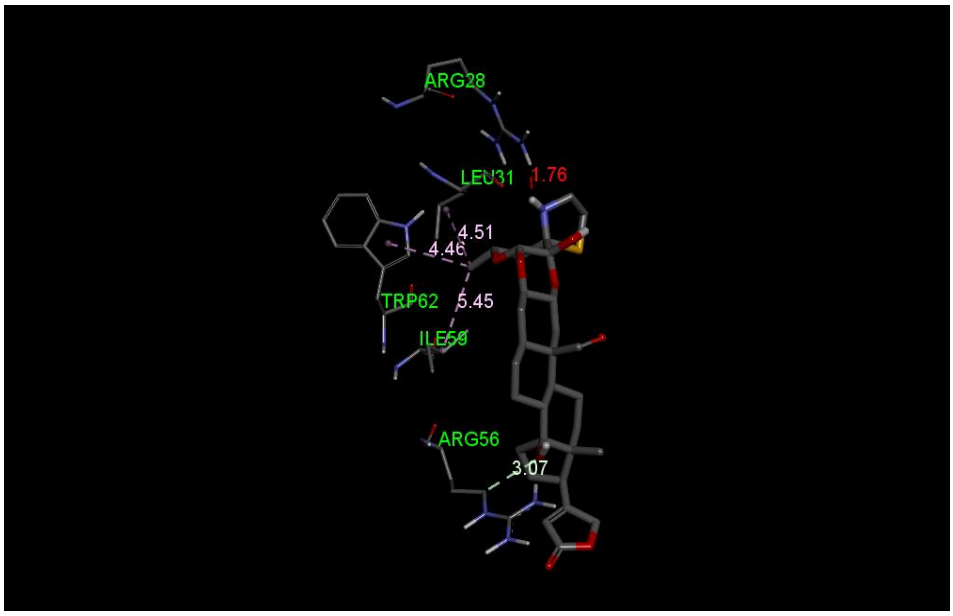

Figure 5: The 3D interaction of phytocompound Voruscharin with the target protein

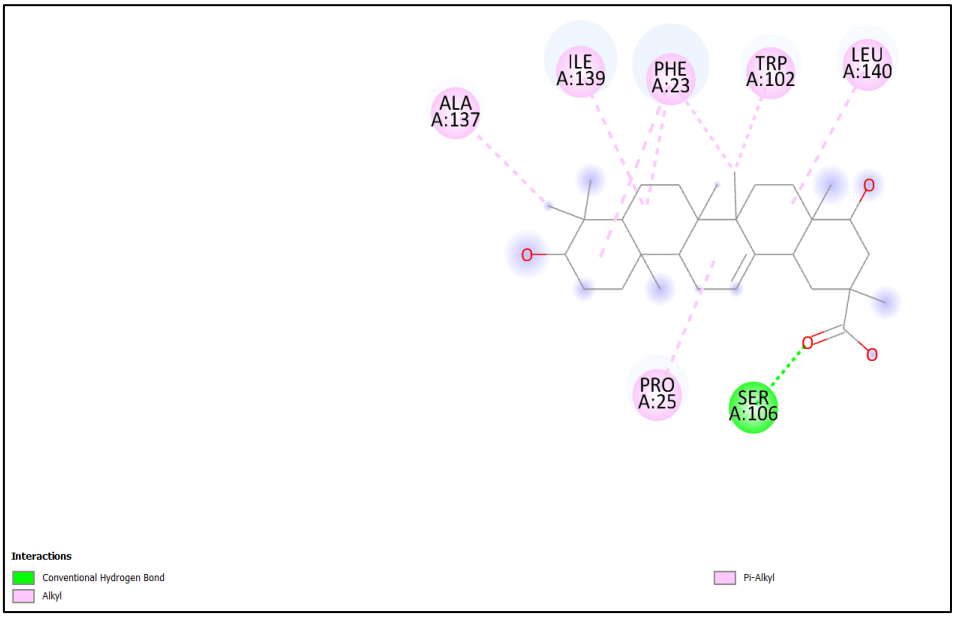

Figure 6: The 2D interaction of phytocompound Triptotriterpenic acid A with the target protein

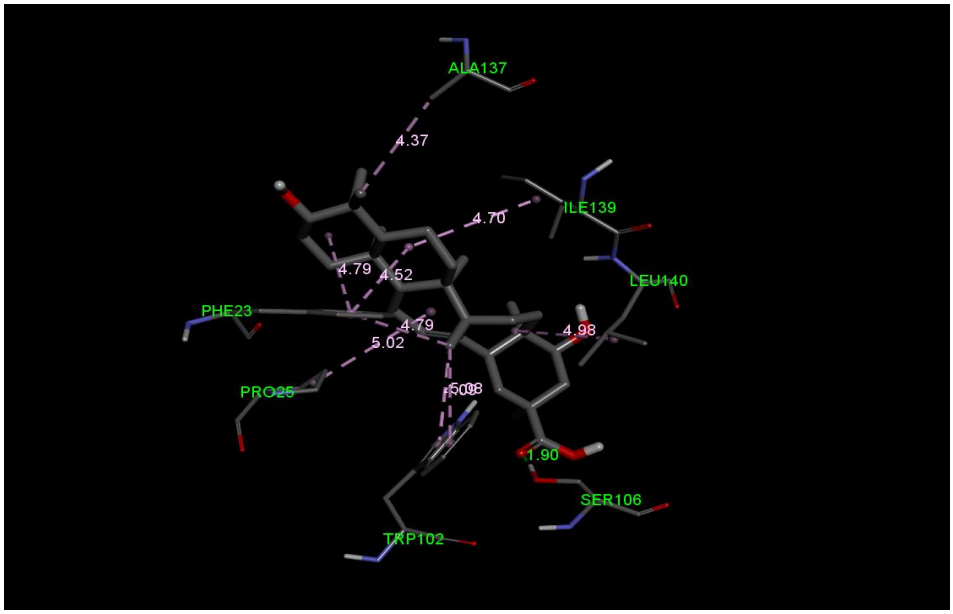

Figure 7: The 3D interaction of phytocompound Triptotriterpenic acid A with the target protein

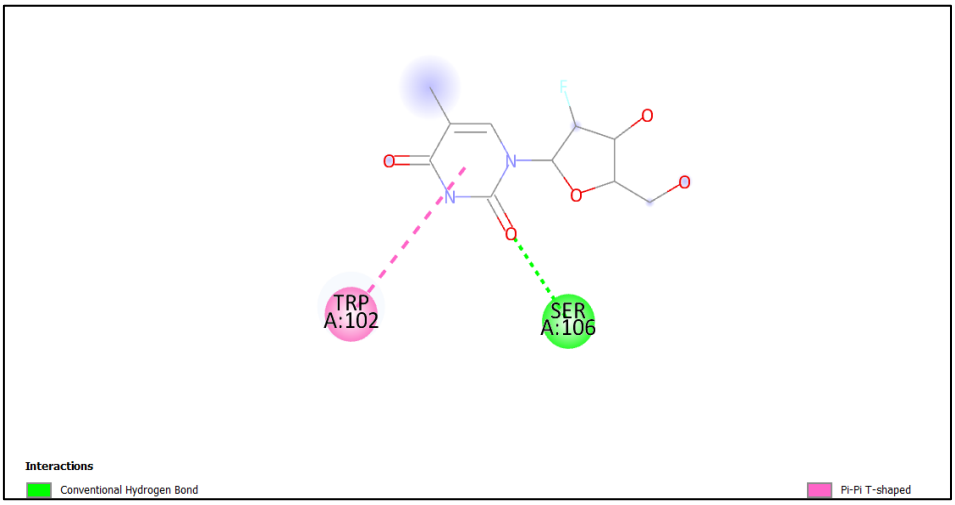

Figure 8: The 2D interaction of Synthetic Drug Levovir with the target protein

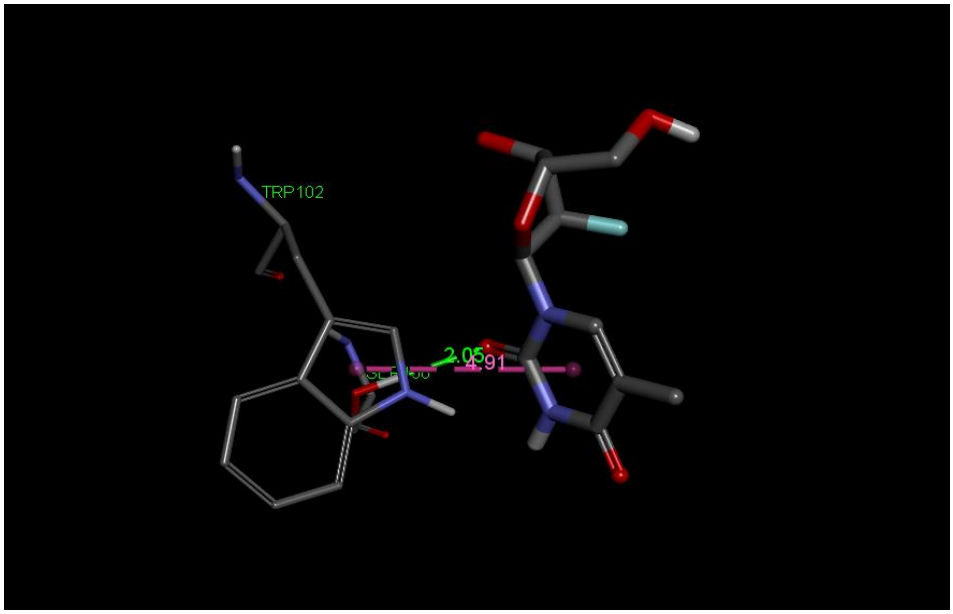

Figure 9: The 3D interaction of the Synthetic Drug Levovir with the target protein

ADMET and CYP Properties

SwissADME was used in the current investigation to examine the ADMET qualities of the best-interacting phytocompounds and the synthetic medication Levovir, and the results were tabulated (table 2). According to the findings, Levovir, a synthetic medication, and all the best-interacted phytocompounds both follow the Lipinski rule of five. The majority of the substances exhibited high intestinal absorption (HIA) and did not penetrate the blood-brain barrier (BBB). P-glycoprotein is projected to remove many phytochemicals from the CNS. Five of the ten compounds' XLogP3 values fell within the acceptable range. Most of the compounds' TPSA (Topological Polar Surface Area) and Log S values were within the permitted range. All of the compounds' rotatable bonds were inside the permitted range.

From the results of the Boiled Egg image of the phytocompounds (Figure 10), the compounds Apollinin (PubChem CID: 156338) and (+)-Tephrosone (PubChem CID: 10569999) are located in the Egg-yolk region, which means the compounds are passively absorbed by the gastrointestinal tract and can also permeate through the blood-brain barrier. And the compounds 5-beta-Cholanic acid (PubChem CID: 92803), Triptotriterpenic acid A (PubChem CID: 21594203), Cadabicine (PubChem CID: 100921101) and Levovir (PubChem CID: 73115) are located Egg-white region, which means they are passively absorbed by the gastrointestinal tract but cannot permeate through the blood-brain barrier. Additionally, it is projected that the P-glycoprotein will not remove the substances Stigmasta-5,22-dien-3-ol, 5beta-Cholanic acid, Apollinin, Sitogluside, and Levovir from the central nervous system. Additionally, it is projected that P-glycoprotein will remove substances like Triptotriterpenic acid A, (+)-Tephrosone, Cadabicine, and Voruscharin from the central nervous system.

The majority of the substances do not inhibit the CYP450 enzymes or cause any negative side effects, according to the results of CYP characteristics (Table 3). The plant chemical cadabicine blocks the CYP3A4, Stigmasta-5,22-dien-3-ol blocks CYP2C9, Apollinin blocks CYP1A2, CYP2C19, CYP2C9, CYP3A4, 5-beta-Cholanic acid blocks CYP2C9, and (+)-Tephrosone blocks CYP1A2, CYP2C9, CYP2D6 respectively. The value of log K_p (Skin Permeant) is good for all compounds and A Bioavailability Score (ABS) is good for most of the compounds.

From the results (Table 3), the Phytocompounds Voruscharin, Triptotriterpenic acid A, Sitogluside, Epilupeol (20[29]-lupen-3A-ol) acetate, [(4'R,5'S,23'R,25'S,26'R)-3,6a,10',11',12',15',16',17',31',32',36',37'-dodecahydroxy-2',5,7',20',28',40'-hexaoxospiro[3,3a-dihydro-2H-furo[3,2-b]furan-6,39'-3,6,21,24,27,38,42-heptaoxanonacyclo [35.2.2.133,36.01,35.04,23.05,26.08,13.014,19.029,34]dotetraconta-8,10,12,14,16,18,29,31,33-nonaene]-25'-yl] 3,4,5-trihydroxybenzoate did not inhibit any CYP450 enzymes.

Compounds with a high log Kp negative value have limited ability to penetrate skin. According to this statement, the Phytocompounds [(4'R,5'S,23'R,25'S,26'R)-3,6a,10',11',12',15',16',17',31',32',36',37'-dodecahydroxy-2',5,7',20',28',40'-hexaoxospiro[3,3a-dihydro-2H-furo[3,2-b]furan-6,39'-3,6,21,24,27,38,42-heptaoxanonacyclo [35.2.2.133,36.01,35.04,23.05,26.08,13.014,19.029,34]dotetraconta-8,10,12,14,16,18,29,31,33-nonaene]-25'-yl] 3,4,5-trihydroxybenzoate, Voruscharin, Cadabicine, and (+)-Tephrosone have less skin permeation ability.

Table 2: ADMET Properties of Phytocompounds

S. No	PubChem (CID)	Compound Name	Lipinski	BBB	HIA	PGP-	XLOGP3	TPSA (Å)	Log S (ESOL)	Fraction Csp3	Rotatable Bonds
1)	100921101	Cadabicine	Yes	No	High	No	3.06	99.69	-4.75	0.28	0
2)	44387915	Voruscharin	Yes	No	Low	No	1.52	148.85	-4.32	0.87	2
3)	21594203	Triptotriterpenic acid A	Yes	No	High	No	6.14	77.76	-6.57	0.90	1
4)	53870683	Stigmasta-5,22-dien-3-ol	Yes	No	Low	Yes	6.36	20.23	-7.46	0.86	5
5)	5742590	Sitogluside	Yes	No	Low	No	7.74	99.38	-7.70	0.94	9
6)	6427357	Epilupeol (20[29]-lupen-3A-ol) acetate	Yes	No	Low	No	10.45	20.30	-9.13	0.91	3
7)	156338	Apollinin	Yes	Yes	High	No	5.67	65.74	-4.64	0.18	3
8)	92803	5-beta-Cholanic acid	Yes	No	High	Yes	6.14	37.30	-5.68	0.96	4
9)	10569999	(+)-Tephrosone	Yes	Yes	High	No	3.47	75.99	-4.35	0.29	3
10)	101321335	[(4'R,5'S,23'R,25'S,26'R)-3,6a,10',11',12',15',16',17',31',32',36',37'-dodecahydroxy-2',5,7',20',28',40'-hexaoxospiro[3,3a-dihydro-2H-furo[3,2-b]furan-6,39'-3,6,21,24,27,38,42-heptaoxanonacyclo[35.2.2.133,36.01,35.04,23.05,26.08,13.014,19.029,34]dotetraconta-8,10,12,14,16,18,29,31,33-nonaene]-25'-yl] 3,4,5-trihydroxybenzoate	Yes	No	Low	NA	-2.61	515.24	-5.11	0.3	3
Synthetic drug											
11)	73115	Levovir	Yes	No	High	Yes	-0.86	104.55	-1.03	0.60	2

Note: Obey Lipinski: yes, that's fantastic, no violations, Blood-Brain Barrier: Yes denotes favor, Human Intestinal Absorption (HIA): High indicates favorable PGP- (Molecules expected not to be excreted from the CNS by P-glycoprotein): XLOGP3 score between 0.7 and +5.0 indicates good lipophilicity. Polarity: Good is defined as TPSA between 20 and 130 A^2. Water Solubility (Log S scale: Insoluble = -10, Poor = -6, Moderate = -4, Soluble = -2, Very = 0, Highly): Log S value less than 6 indicates good, Saturation (Fraction Csp3): Good saturation is defined as a fraction of carbons in the sp3 hybridization that is not less than 0.25. Flexibility (Rotatable Bonds): Good if there are no more than 9 rotatable bonds.

Table 3: Cytochrome P450 properties of phytocompounds

S. No	PubChem (CID)	Compound Name	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Log K_p (Skin permeation) (cm/s)	A Bioavailability Score (ABS)
1)	100921101	Cadabicine	No	No	No	No	Yes	-6.78	0.55
2)	44387915	Voruscharin	No	No	No	No	No	-8.82	0.55
3)	21594203	Triptotriterpenic acid A	No	No	No	No	No	-4.82	0.56
4)	53870683	Stigmasta-5,22-dien-3-ol	No	No	Yes	No	No	-2.74	0.55
5)	5742590	Sitogluside	No	No	No	No	No	-4.32	0.55
6)	642735	Epilupeol (20[29]-lupen-3A-ol) acetate	No	No	No	No	No	-1.74	0.55

	7								
7)	156338	Apollinin	Yes	Yes	Yes	No	Yes	-5.90	0.55
8)	92803	5-beta-Cholanic acid	No	No	Yes	No	No	-4.14	0.85
9)	10569999	(+)-Tephrosone	Yes	No	Yes	Yes	No	-5.99	0.55
10)	101321335	[(4'R,5'S,23'R,25'S,26'R)-3,6a,10',11',12',15',16',17',31',32',36',37'-dodecahydroxy-2',5,7',20',28',40'-hexaoxospiro[3,3a-dihydro-2H-furo[3,2-b]furan-6,39'-3,6,21,24,27,38,42-heptaoxanonacyclo[35.2.2.133,36.01,35.04,23.05,26.08,13.014,19.029,34]dotetraconta-8,10,12,14,16,18,29,31,33-nonaene]-25'-yl] 3,4,5-trihydroxybenzoate	No	No	No	No	No	-14.93	0.17
Synthetic drug									
11)	73115	Levovir	No	No	No	No	No	-8.50	0.55

Note: Yes, which indicates that the substance inhibits the CYP450 enzymes and causes unexpected negative effects; No indicates that the substance has no negative effects and does not inhibit the CYP450 enzymes; The molecule is less skin permeable the more negative the log Kp is; ABS 0.55 indicates that it satisfies the rule of five, whereas 0.17 indicates that it does not.

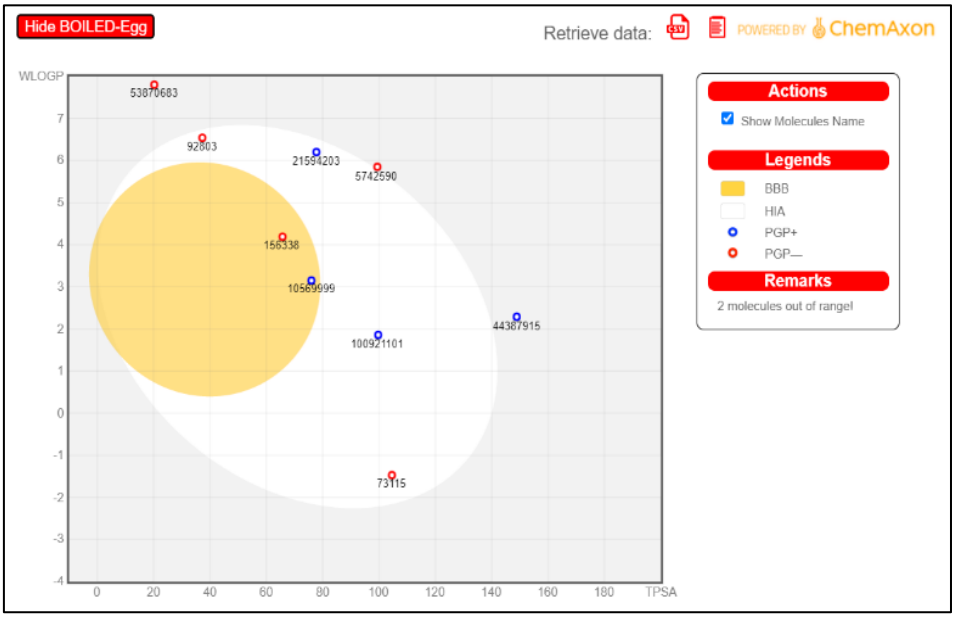

Figure 10: Boiled egg for all the compounds

Note: BBB: It is envisaged that some chemicals in the yolk of the BOILED-Egg will passively flow over the blood-brain barrier. Molecules in the white of BOILED-Eggs called HIA-Points are thought to be passively absorbed by the gastrointestinal tract. PGP+: Blue dots indicate compounds that the P glycoprotein predicts will be eliminated from the central nervous system. PGP-: Red dots indicate compounds that the P-glycoprotein predicts won't be eliminated from the central nervous system.

DISCUSSION

For the past thirty years, antioxidants derived from plants have been valued as being vital to preserving human wellbeing. A study by Jinadatta *et al.* (2019) reveals that the traditional treatment for jaundice involves using of stem part of the plant *Gnetum ula*. They examined the ethanol extract of stem of *G. ula* and its isolated compound gnetol for its *in vitro* hepatoprotective and antioxidant activity. The isolated chemical gnetol, according to the results, demonstrated strong antioxidant activity and provided protection against liver damage [25].

In another research, Ai *et al.* (2013) evaluated the total flavonoids that were isolated from the flowers of *Abelmoschus manihot* (L.) Medic for their hepatoprotective potential. They being traditionally used for the treatment of jaundice showed protection against CCI4-induced liver injury through antioxidant stress and anti-inflammatory effects. The findings suggests that this plant can be used for the treatment of liver disease [26].

A recent study by Raghuvanshi *et al.* (2022) reported that phytocompounds from *Thalictrum foliolosum* DC. and *Cordia dichotoma* G exhibited good binding affinity to the target protein which is responsible for causing jaundice. Rutin, a phytocompound which was found in those plants exhibited a binding affinity of -8.2 kcal/mol and the next best compound Ursodeoxycholic acid and Ceftriaxone exhibited a value of -7.4 kcal/mol as binding affinity. The findings of this study indicates that this may be a source for new

pharmaceuticals or medications with potent antioxidant properties by binding to the sphingomyelin phosphodiesterase *Leptospira interrogans* receptor's active site [27].

The study of Sahu *et al.* (2020) showed that Isohamnetin, a phytochemical from the *Santalum album* L. is the most active, might efficiently inactivate the sphingomyelin phosphodiesterase *Leptospira interrogans* (5EBB) enzyme, inhibiting the metabolic cycle of the *Leptospira inferrogans* spp. organism that is linked to the onset of jaundice. According to their study with total of 7 phytochemicals, 4 of them namely Isohamnetin, Isoorientin, Flavan-3-ol, and Chrysin 6-c-beta-D-glucopyranoside helps in the deactivation of the enzyme and 3 of them did not show any result [28].

A molecular docking study by Behera *et al.* (2020) suggests that caffeice acid and myricetin phytochemicals derived from *Beta vulgaris* might significantly inactivate the sphongomyelin phosphodiesterase enzyme by interrupting in the organism's life cycle [29].

Furthermore, an interesting study by Mohanty *et al.* (2020) reported that plant extract from *Eclipta alba* is being traditionally used to treat jaundice caused by *Leptospira interrogans*. The findings showed that the thioredoxin-disulfide reductase enzyme may be efficiently deactivated by pentadecane, heptadecane, and 6,10,14-trimethyl-2-pentadecanone, stopping the life cycle of Leptospira. And upon their docking studies with total of 6 phytochemicals, Pentadecane showed the maximum inhibition with the microbial enzyme [30].

In the same way, our present study shows better binding affinity. It indicates that Cadabicine from *Crataeva nurvala*, Voruscharin from *Calotropis procera* and Triptotriterpenic acid A from *Abrus precatotius* may be a source for new pharmaceuticals or medications to treat jaundice.

According to the findings, phytoconstituents derived from plants have the potential to be an alternative to the synthetic drug, particularly for infections. Cadabicine, among all the phytocompound used to treat jaundice, has demonstrated the highest protein binding ability, according to our *in-silico* research on its antioxidant properties. To fully evaluate the scientific potential of Cadabicine produced from *Crataeva nurvala*, further drug testing, including *in vitro* and *in vivo* assessment, should be done.

CONCLUSION

In the present study, the phytocompounds from the different Indian medicinal plants and the target protein capsid protein were subjected to *in silico* docking analysis to find the potential inhibitors for Jaundice. In which, 48 compounds showed better results than the Synthetic drug Levovir. Among them, 10 compounds showed very good binding affinity. Of which, the phytocompound, Cadabicine, Voruscharin, Triptotriterpenic acid A showed the highest binding affinity. Toxicity studies were also done for the 10 best-interacted phytocompounds and the results showed that the compounds had very less toxicity.

Hence, the present study concludes that the plant chemicals such as Cadabicine from *Crataeva nurvala*, Voruscharin from *Calotropis procera*, and Triptotriterpenic acid A from *Abrus precatorius* may give a potential effect in the treatment of Jaundice.

Abbreviations

BBB: Blood - Brain Barrier; HIA: Human Intestinal Absorption; PGP: P-glycoprotein; TPSA: Topological Polar Surface Area; CNS: Central Nervous System.

Conflict of Interest

The authors declare that they have no conflict of interest.

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