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Research Article

COMPUTATIONAL SCREENING AND EVALUATION OF BIOACTIVE COMPOUNDS AGAINST NS3 HELICASE OF HCV

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ABSTRACT

Objective: Hepatitis C virus (HCV) infection is a major health problem worldwide causing both acute and chronic hepatitis, cirrhosis and end-stage liver diseases. Non structural protein (NS), NS3 helicase which is necessary for HCV replication is used as the potential target for the inhibition of the HCV. The present study aims to investigate the inhibitory activities of the 24 different compounds from 11 plants against the NS3 helicase protein of HCV using computational techniques.

Methods: Docking, simulation and bioactivity based screening has been applied to identify the better phytochemical(s) that can act against hepatitis. The NS3 (PDB: 1HEI) protein is docked with 24 phytochemicals of 11 various medicinal plants and subjected to the drug-likeliness and bioactivity estimation.

Results: The results reveal that tinospride from, *Tinospora cordifolia* has shown better drug-likeliness, activity and stability.

Conclusion: A number of natural antiviral compounds have been reported in the medicinal plants and tested for their efficacy in treating hepatitis. Thus by inhibiting NS3 protein one can not only prevent replication but also circumvent the problem of viral resistance.

Keywords: Hepatitis C virus, Non structural proteins, NS3, Tinosporide;

INTRODUCTION

Hepatitis C virus (HCV) is a potential cause of liver disease worldwide. Liver is the metabolic engine-room of the body [1]. Modern allopathic drugs exhibit severe toxicity, thus there is definite need to search alternate drugs having maximum therapeutic value with no or least toxicity [2]. It has been estimated that 90% of the acute hepatitis is due to the viruses. The major viral agents involved are the Hepatitis A, B, C, D (delta agents), E and G. Hepatitis C is caused by positive sense single-stranded RNA Hepatitis C virus (HCV), a member of the Flaviviridae family [3]. So far there is no universally effective therapy for all HCV genotypes. Among the protein products of HCV, the NS (non- structural) protein: NS3 and NS5B are essential for the synthesis and replication of viral RNA. [4]. Here we present our study conducted on NS3 protein of HCV.

NS3 is a 70 kDa protein and contains two functional modules, both of which are essential in the life cycle of HCV: a serine protease domain at the N terminus and an ATPase/helicase domain (NS3hel) at the C terminus [5]. NS3 RNA helicase affects two steps in the HCV replication cycle. During RNA-dependent RNA replication, NS3 is required to unwind the double-stranded RNA intermediate, which may enable movement of HCV NS5b polymerase. Second, NS3 assists in virus assembly and is likely attributable to ability to act as a scaffold for interaction with viral or cellular cofactors. In summary, NS3 helicase activity is essential for Flavivirus replication and is a potential therapeutic target against the significant human pathogen, HCV [6]. HCV NS3 is a target for therapeutic intervention of acute and chronic HCV that NS3 mediated processing of the polyprotein is essential for HCV RNA replication and maturation [7, 8]. Comparative study of phytochemicals keenly represents one of the best avenues in searching new economic plants for medicine [9]. Hence our research focuses on the replicative enzyme i.e NS3 helicase of HCV as possible target for more effective therapeutic agents through a comparative study.

MATERIALS AND METHODS

Dataset Collection

Extraction of PDB structure of NS3

The Protein Data Bank (PDB) is a repository for the 3-D structural data of large biological molecules, such as proteins and nucleic acids. PDB ID of NS3 helicase is 1HEI which is considered as the target for the phytochemicals under study.

Creation of ligand dataset

The phytochemicals that can act against the viral protein NS3 were collected from various sources like literature, text books etc (Table1). The 2D structures and the SMILES (Simplified Molecular-Input Line-Entry System) notation of twenty four bioactive compounds (ligands) are extracted from ChemSpider [10] (Table 2). The structures of bioactive compounds are converted from their SMILES format to *pdb* format using CORINA server [11].

Molecular docking

Molecular Docking is the prediction of the best ways of interaction of two molecules. For this we require rank solutions and a scoring functions or force field. AutoDock is an automated procedure for predicting the interaction of ligands with bio-macromolecular targets. Both pre-dynamics and post – dynamics docking were done. This involves docking of the NS3 protein of HCV with the 24 bioactive compounds using autodock.4 [12], followed by molecular dynamic simulation of the protein that causes energy minimization of the structure and post-dynamics docking of the minimized structure with the bioactive compounds.

The NS3 protein (receptor) structure is prepared for docking by removing water molecules, adding hydrogen molecules and saving it in .pdbqt format. All the 24 molecules under study are docked to the NS3 protein. All the ligand structures are prepared in a required way and saved in .pdbqt format. The dimension of the grid box is set to 126 points which can completely cover the active site of the receptor protein. The docking parameters are set as follows: translation: 0.2, Quaternion: 5.0, Torsion: 5.0, RMS cluster Tolerance 1.5.

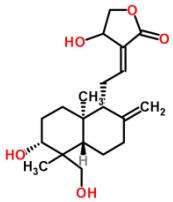
Molecular dynamic simulation

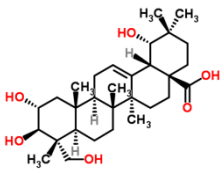
We carry out molecular dynamic simulations in the hope of understanding the properties of assemblies of molecules in terms of their structure and the microscopic interactions between them using GROMACS (GROningen MAchine for Chemical Simulations) [13, 14, 15 and 16]. The PDB structure 1HEI is processed for position-restrained molecular dynamics. However, the docking energy and scoring function came out well for energy minimized protein (post dynamics docking). Therefore we continued our further analysis with post-dynamics docking data shown in Table 3.

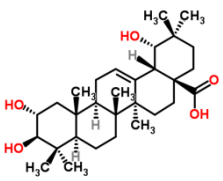
Table 1: Dataset table - 24 phytochemicals from 11 different plants used for the study

S. No.	Phytochemical	Plant name	Common name	Family	Part used
1	Andrographolide	Andrographuis paniculata	Kalmagh, maha-tita	Acanthaceae	Leaves and roots
2	Arjungenin	Terminalia arjuna	Kumbuk,arjuna	Combretaceae	Leaves and bark
3	Arjunic Acid	Terminalia arjuna	Kumbuk,arjuna	Combretaceae	Leaves and bark
4	Berberine	Mahonia leschenaultia	Mullukadambu,mullmanjanathi,thovari	Berberidaceae	Roots
5	Chasmanthin	Tinospora cordifolia	Guduchi	Menispermaceae	Roots and stem
6	Columbin	Tinospora cordifolia	Guduchi	Menispermaceae	Roots and stem
7	Desmethylwedelolactone	Eclipta alba	Bhringraj	Asteraceae	Leaves
8	Esculetin	Cichorium intybus	Chicory	Asteraceae	Roots
9	Friedelin	Swertia chirata	Kiratatikta	Gentianaceae	Roots
10	Gossypin	Hibiscus vitifolius	Bhasadwaji	Malvaceae	Roots
11	Hyperforin	Hypericum perforatum	Tipton's weed, chase devil	Hypericaceae	Flower
12	Hypericin	Hypericum perforatum	Tipton's weed, chase devil	Hypericaceae	Flower
13	Hypophyllanthin	Phyllanthus amarus	Keezhanelli, stonebreaker	Phyllantheae	Leaves and aerial part
14	Jatrorrhizine	Mahonia leschenaultia	Mullukadambu, mullmanjanathi,thovari	Berberidaceae	Roots
15	Kutkoside	Picrorhiza kurroa	Kutka	Scrophulariaceae	Roots
16	Phyllanthin	Phyllanthus amarus	Keezhanelli,stonebreaker	Phyllantheae	Leaves and aerial part
17	Picroside	Picrorhiza kurroa	Kutka	Scrophulariaceae	Roots
18	Pseudohypericin	Hypericum erforatum	Tipton's weed, chase devil	Hypericaceae	Flower
19	Silymarin	Andrographuis paniculata	Kalmagh, maha-tita	Acanthaceae	Leaves and roots
20	Sitosterol	Swertia chirata	Kiratatikta	Gentianaceae	Roots
21	Swertinin	Swertia chirata	Kiratatikta	Gentianaceae	Roots
22	Thaliporphyine	Mahonia leschenaultia	Mullukadambu, mullmanjanathi,thovari	Berberidaceae	Roots
23	Tinosporide	Tinospora cordifolia	Guduchi	Menispermaceae	Roots and stem
24	Wedelolactone	Eclipta alba	Bhringraj	Asteraceae	Leaves

Table 2: The 2D structures of the phytochemicals used for the study, obtained from ChemSpider database.


Andrographolide


Arjungenin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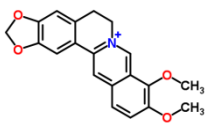
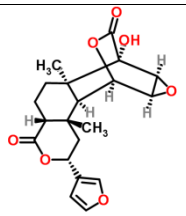

Berberine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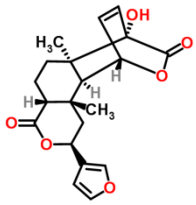
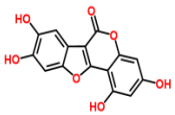

Columbin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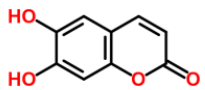
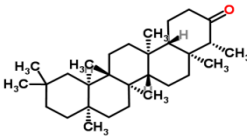

Esculetin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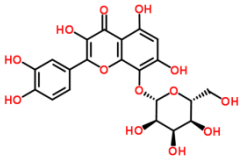
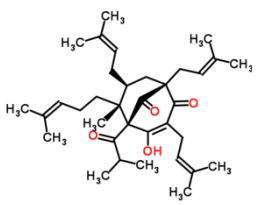
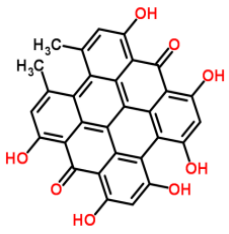
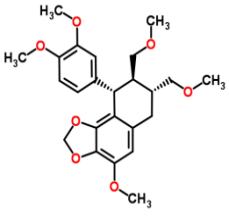

Gossypin


Hyperoforin


Hypericin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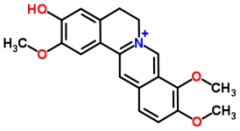
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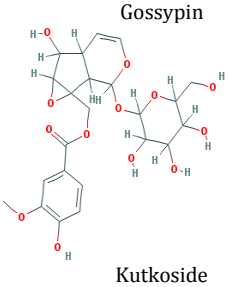
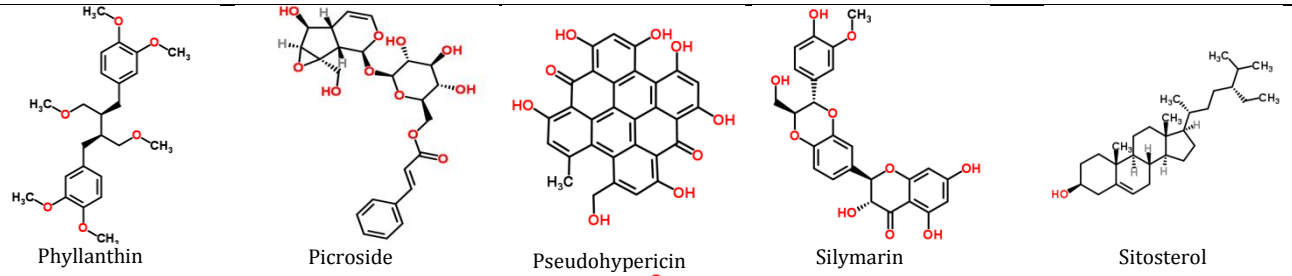

Kutkoside



Drug likeliness Prediction

In order to study the drug likeliness, we subjected the phytochemicals for its property prediction. This qualitative study is estimated from the phytochemical's 3D structure. Theoretically, a drug-like substance has a log P range of -0.4 to 5.6, molecular weight 160-480 g/mol, molar refractivity of 40-130, which is related to the volume and molecular weight of the molecule, has 20-70 atoms and follow other Lipinski's rule [17]**.** Drug likeliness can be estimated for any molecule, and does not evaluate the actual biological activity that the drug achieves. Hence the screening is extended to study the bioactivity of the drug like substance.

Biological Activity Prediction

Each biologically active compound possesses a number of biological activities. Based on the analysis of large training set consisting of tens of thousands of the known biologically active compounds, computer program PASS [18] provides the means to evaluate any new compound in huge chemical-pharmacological space. The phytochemicals which has shown the better activity is subjected to molecular dynamics simulation with the receptor for 25ns to examine its stability.

RESULTS

Biological activity is one of the important characteristics of a chemical compound reflecting its interaction with other living organisms. Twenty four compounds present in 11 major plants selected for this study have been listed in Table 1.

Molecular Docking

All molecules of plant sources (Table 1) under study were docked separately into the binding site of the receptor protein (PDB ID: 1HEI) using AutoDock 4.0 molecular docking tool. The binding energies and the interacting residues at the binding site during post-dynamics docking of the phytochemicals and the HCV NS3 helicase protein are shown in Table 3.

Molecular dynamic simulation:

To validate our docking procedure we did molecular dynamics simulation of the NS3 HCV protein. The molecular dynamics simulation results of the NS3 protein (Potential Energy plot, Total Energy plot, RMSD plot) is shown in Figure1.

Drug likeliness prediction

Estimating drug likeliness has been a major challenge in screening the phytochemicals. We have predicted the properties of the phytochemicals under study using Molinspiration property calculator [19 and 20]. The properties like MIlogP, TPSA, number of atoms, hydrogen bond donors and acceptors, molecular weight and rotational bonds were predicted (Table 4).

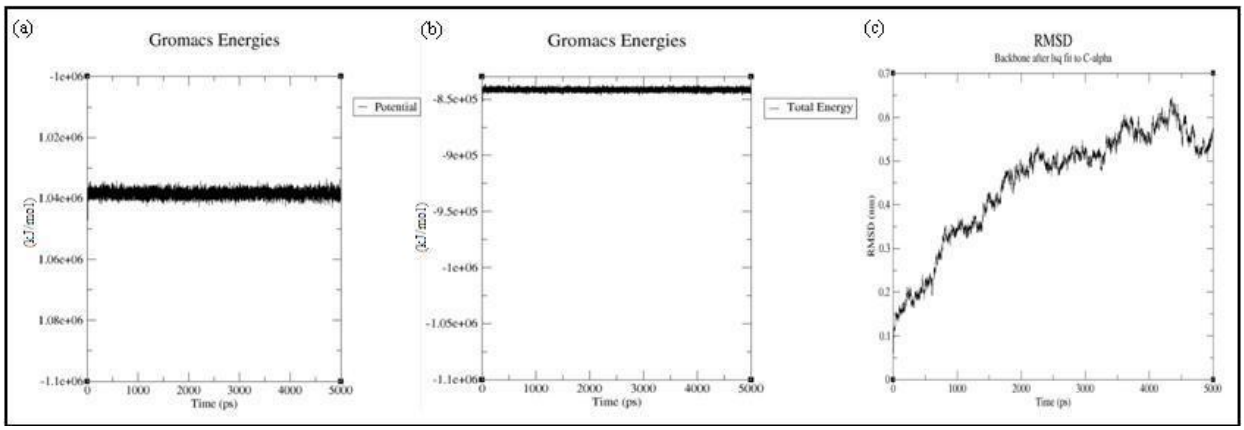


Fig. 1: Molecular dynamics simulation trajectories of NS3 protein (1HEI) that shows: (a) potential energy (b) total energy and (c) Root mean square deviation.

Table 3: Pre-Dynamics Docking and Post-Dynamics Docking results of NS3 helicase of HCV with various bioactive compounds

Ligand	Energy (Pedd)	Binding Site Residues	Energy (Podd)	Binding Site Residues
Andrographolide	-5.24	HIS293 ASP487 GLY484 VAL490 VAL456 THR295 ASP454 THR433 GLN434	-5.87	ASP412 VAL432 THR433 SER489 ARG461 GLN460 SER457 ASP454 VAL456 THR295
Arjungenin	-4.68	GLY271 ALA297 THR298 GLU493 ASP296 VAL490	-6.88	TYR502 ASP396 GLY394 ARG393 GLY255 VAL399 TYR391 GLY417 THR298 ALA413 THR410 MET415
Arjunic Acid	-4.87	ALA413 ARG393 MET415 ASP412 THR433 VAL432 ASP454 SER457	-7.17	TYR502 ASP396 GLY394 ARG393 GLY255 VAL399 TYR391 GLY417 THR298 ALA413 THR410 MET415
Berberine	-5.26	ASP487 VAL490 GLU433 ARG481 PHE486 ALA297 MET485 THR295 ASP296	-6.46	ASP412 VAL432 THR433 GLN461 LEU414 GLN460 SER457 SER489
Biopegnin	-5.31	PRO230 ASP296 THR269 GLY255 GLY271 THR298 TYR502 TRP501 ALA497	-7.19	GLY271 LYE272 TYR502 TYR270 THR269 GLY394 THR416 LEU414 MET415 THR298 ALA413 VAL432
Chasmanthin	-5.81	THR295 GLY484 VAL456 GLU291 SER294 HIS293	-7.34	ASP412 ARG393 ASN556 GLU493 VAL490 VAL456 GLN460 VAL432 THR295 THR433
Columbin	-6.3	GLY271 THR297 ALA497 ALA297 TRP501 GLU493 TYR502	-7.24	LEU414 ARG393 GLN460 ARG464 ASP296 ASP412 ALA413 ARG461
Desmethyl-Wedelolactone	-5.01	MET485 GLY484 THR298 CYS431 ASP454 HIS293 ARG481 THR433	-6.07	LYS272 THR269 GLY271 TYR270 PRO230 THR298 THR416 TYR502 ASP396 GLY394
Esculetin	-4.46	ASP296 PR0230 THR269 GYL271 THR298	-5.32	GLN460 ARG464 PRO230 TYR270 SER299 THR298 SER294 THR416 ASP296
Friedelin	-8.75	THR269 GLY271 THR298 LYS272 GLY255 ALA497 TRP501 PRO558	-9.82	ALA413 TYR391 GLY394 ASP396 TYR502 THR298 THR446 GLY417 MET415 LEU414
Gossypin	-3.22	VAL456 ASP454 ARG481 MET485 GLN460 PHE486 THR295 VAL490 ASP296	-4.14	THR295 LYS272 THR269 GLY394 THR416 LEU414 TYR391 TYR502 TRP501 LY271
Hyperforin	-4.95	VAL432 THR433 GLN434 ASP487 ASP454 ARG481 THR295 VAL490 ASP296	-2.11	THR298 ASP296 LEU414 ARG461 GLN460 PHE367 THR416 GLN434 GLU493 ARG393 ASP412 GLY394
Hypericin	-6.4	VAL490 GLU493 ASP487 THR295 ASP296 GLN434 ASP454	-9.01	TYR502 GLY394 TYR391 ARG393 LYS272 GLY271 THR416 THR269 PRO230 TYR270 ASP296 THR295
Hypophyllanthin	-3.88	THR433 VAL432 SER457 MET485 ASP487 ARG481 GLU493 ASP296 ASP454 VAL490 GLN460 ALA297 CYS431 PHE486 THR298	-5.44	TYR270 GLY271 LYS272 THR298 TYR502 ASP396 TYR391 LEU395 THR416 THR269 PRO230 VAL399
Jatrorrhizine	-5.19	MET485 ASP454 THR295 GLY484 HIS293 PRO523 PRO230	-7.44	TYR502 ASP396 THR416
Kutkoside	-2.9	THR298 ALA497 TRP501 GLY271 THR269 VAL232 PRO230 ASP296 ASN556	-3.1	ALA413 MET415 TYR391 THR416 ARG393 GLU493 ALA497 GLY394 THR298 ASP396 TRP501 TYR502
Phyllanthin	-1.93	THR433 VAL432 VAL456 GLU434 ASP296 GLU493	-3.43	THR433 VAL490 GLN460 VAL432 ASP296 ALA413 LEU414 GLU394 GLU393 ALA497 ARG393 TYR502 TRP501
Picroside	-3.28	THR295 SER294 HIS293 VAL490 GLU493 GLN434 THR433	-5.57	ARG393 ASP412 GLU493 VAL432 ALA413 TYR391 CYS 431 THR416 ARG461 SER457 ASP454 VAL 456
Pseudohypericin	-6.08	TYR270 PHE273 GLY278 GLY277 LEU274 ALA275 ASP296 THR269 GLY271 THR298 LYS272 GLY255	-8.67	THR416 THR298 ASP296 PRO230 TYR270 THR269 GLY271 TYR502
Sitosterol	-6.1	ASP454 ARG481 VAL456 SER231 HIS293 PR0230 THR295 MET485	-7.52	TYR502 TRP501 THR433 GLU493 GLY394 ARG393 ALA413 LEU414 GLN460 ASP454 CYS431
Silymarin	-4.17	TRP501 TYR502 ALA275 PRO230 ALA233 VAL232 GLY255 SER231 THR269	-6.6	PRO230 SER299 THR298 TYR391 TYR270 SER294 ASP296 THR416 GLY394 TYR502 GLY271 THR269
Swertinin	-4.41	PRO230 HIS293 SER294 VAL456 SER483 ASP296 GLY484 ASP454 THR295	-4.83	ASP296 LEU414 GLN460 MET415 THR416 GLN434 TYR391 ALA413 VAL432 ARG393 GLU493
Thaliporphine	-5.37	ASP454 THR433 ASP487 GLN434 PHE486 THR295 ASP296 VAL490 SER294	-5.79	SER294 ASP296 PRO230 GLN460 THR298 TYR270 ALA413 LEU414 THR416 GLY271
Tinosporide	-6.66	THR269 ASP296 PRO230 SER231 THR254 GLY255 GLY271 THR298	-8.32	ARG253 LEU226 ASP276 GLY278 PHE273 CYS279 SER280 GLY281 ALA283 SER263
Wedelolactone	-5.43	GLU493 VAL490 ASP487 MET485 ARG481 GLN434 THR433	-6.9	SER294 ASP296 ARG464 PRO230 ARG467 THR416 SER231 ALA233

PeDD: Pre-Dynamics docking; PoDD: Post-Dynamics Docking.

Table 4: Molecular properties predicted using Molinspiration property calculator.

Phytochemical	miLogP	TPSA	Atoms	MW	# ON	# OHNH	#Violations	#ROTB	Volume
Arjungenin	3.72	118.21	36	504.71	6	5	1	2	495.49
Chasmanthin	2.03	98.51	27	374.39	7	1	0	1	318.35
Columbin	2.72	85.98	26	358.39	6	1	0	1	313.96
Friedelin	7.85	17.07	31	426.73	1	0	1	0	461.05
Hypericin	6.66	155.51	38	504.45	8	6	3	0	401.52
Jastrorrhizine	-0.42	51.82	25	338.38	5	1	0	3	305.94
Sitosterol	8.62	20.23	30	414.72	1	1	1	6	456.52
Tinosporide	2.03	98.51	27	374.39	7	1	0	1	318.35
Wedelolactone	2.30	113.27	23	314.25	7	3	0	1	247.74
Arjunic Acid	3.72	118.21	36	504.71	6	5	1	2	495.49

miLogP: LogP(partition co-efficient) TPSA: topological polar surface area; MW: Molecular weight; #ON: number of hydrogen bond acceptors; #OHNH: number of hydrogen bond donors; #ROTB: number of rotational bonds.

Table 5: Bio-activity prediction of the phytochemicals using the PASS server

S. No.	Phytochemical	Pa	BioAcitivity
1	Chasmanthin	0.83	AI
		0.44	HP
		0.32	HDT
2	Columbin	0.77	AI
		0.33	HP
		0.27	HDT
3	Tinosporide	0.94	HP
		0.75	AI
		0.73	HDT
4	Wedelolactone	0.62	AI
		0.54	HP
		0.52	HDT

Pa:Probability of the predicted activity, AI: Anti-Inflammatory, HP: Hepato-Protectant, HDT: Hepatic Disorder Treatment. Tinosporide is found to possess greater probability (0.94) of anti hepatic activity like AP, ADT and AI.

Bio-Activity Prediction

Bioactivity of the substance is an essential finding because non-selectiveness in the metabolism may destroy the pharmacological activity in spite of good drug likeliness. Hence, in order to improve the screening strategy, we predicted the bioactivity of the phytochemicals which showed better drug likeliness. PASS predictions have been applied to predict the biological activity of the screened phytochemicals with probability "to be active" Pa ranged from 0.5 to 0.8. Three types of bioactivity were common for all the phytochemicals under study though the probability value is varying. The observed common bioactivities are: Hepato-protectant (HP), Hepatic disorder treatment (HDT) and anti-inflammatory (AI) activities (Table 5). Jatrorrhizine cannot be subjected for bioactivity prediction in PASS server since its molecular charge is 1. The best activity against hepatitis i.e. HP, HDT and AI is predicted for tinosporide.

DISCUSSION

Modern medicines have little to offer for alleviation of hepatic diseases and it is chiefly the plant based preparations which are employed for the treatment of liver disorders [21]. Binding energies of the protein-phytochemical interaction are important to describe how well the drug binds to the target (protein) molecule. Among the ligands arjungenin, chasmanthin, columbin, friedelin, hypericin, jatrorrhizine, sitosterol, tinosporide and wedelolactone were found to best dock with NS3 protein. The docking scores were calculated based on the conformation and free energy of binding (Table 3). Thereafter Post-Dynamics docking of the minimized structures of the proteins was performed with the phytochemicals. It can be observed that the binding energy decreases after the ligand is docked with energy minimized structure of NS3 protein and the binding residues are almost same.

The phytochemicals arjungenin, hypericin, arjunic acid violated the rule of five because of its molecular weight higher than 500 D. In particular, the number of rotatable bonds (10 or fewer) and polar surface area (<=140 Å) helps to screen the drug like substance for its proven efficiency of oral activeness in rats [22]. Accordingly, hypericin which has its TPSA 155.51 Å (which is more than 140 Å) can be screened off; whereas, friedlein and sitosterol has MIlogP value 7.85 and 8.62 respectively i.e. greater than 5. Hence totally five compounds such as arjungenin, arjunolic acid, friedelin, hypericin and sitosterol can be neglected for broader analysis. Positively, other compounds like chasmanthin, columbin, jatrorrhizine, tinosporide and wedelolactone can subjected to further investigation. It should be noted that the three compounds namely chasmanthin, columbin and tinosporide are from the plant *Tinospora cordifolia*, jatrorrhizine from *Mahonia leschenaultia* and wedelolactone from *Eclita alba*.

To gain more molecular insight, tinosporide is docked onto the active site of HCV NS3 helicase. The best predicted binding mode is illustrated in Figure 3(a). The residues interacting with tinosporide are ARG253, LEU226, ASP276, GLY278, PHE273, CYS279, SER280, GLY281, ALA283 and SER263. Tinosporide forms hydrogen bond interactions with ARG253 and GLY278; electrostatic interactions with ARG253, PHE273, GLY278, CYS279, SER280, SER263 and van der waals interactions with LEU226,ASP276,GLY281,TYR284, ALA283. The protein-ligand interaction plot (Figure 3 (b)) is obtained using Discovery Studio Visualizer 3.5 [23]. The docking energy is -8.32 when compared to the other 4 compounds chasmanthin, columbin, jatrorrhizine and wedelolactone i.e -7.34, -7.24, -7.44 and -6.9 respectively (Table 3).

Tinosporide has been subjected molecular dynamics simulation in complex with NS3 protein to examine its stability. The molecular dynamics trajectory signifies that the tinosporide - protein complex is found to be stable when simulated for 25 ns. The molecular dynamics simulation trajectories of potential energy and RMSD are shown in figure 4(a) and 4(b). The study focuses the tremendous potential of plants as prolific producers of bioactive substances against HCV and this analysis reveals that the plant *Tinospora cordifolia* provides insight to exploit the treasure for its utilization as novel drug delivery system for HCV infections.

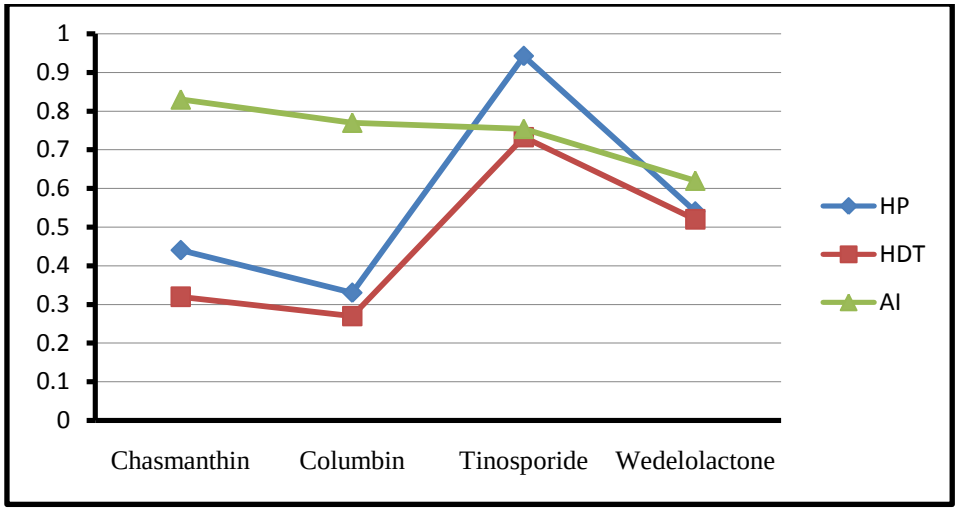


Fig. 2: The bioactivity predicted from the PASS server. It is shown that tinosporide exhibits higher probability of activity as HP, HDT and AI. HP: Hepato-Protectant, HDT: Hepatic Disorder Treatment and AI: Anti-Inflammatory.

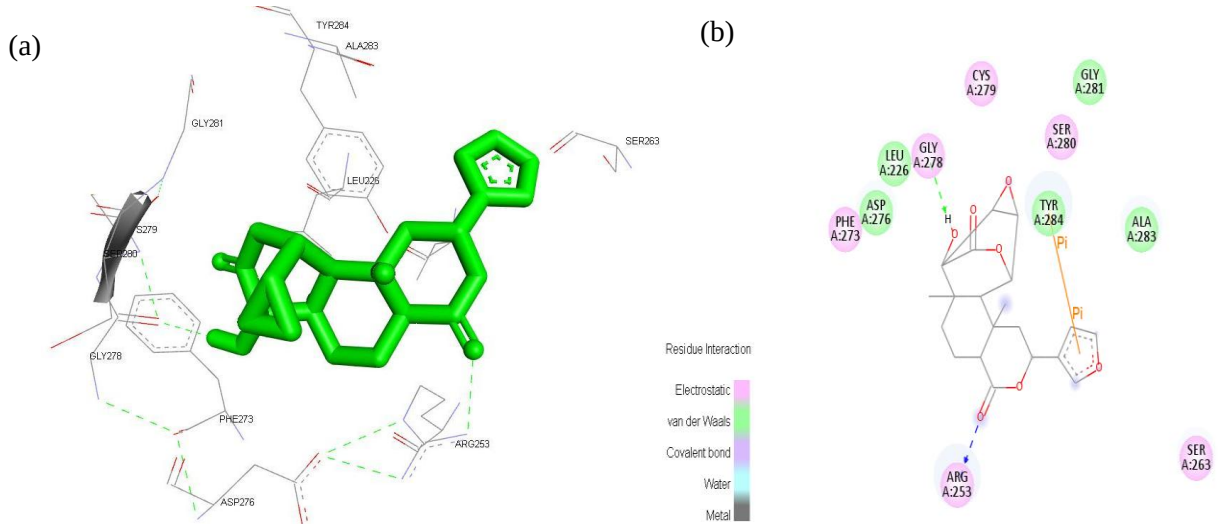


Fig. 3: Docking is done using the Autodock 4. The residues interacting with tinosporide are ARG253, LEU226, ASP276, GLY278, PHE273, CYS279, SER280, GLY281, ALA283 and SER263. Tinosporide forms hydrogen bond interaction with ARG253 and GLY278 (a) The docked image of NS3 protein (1HEI- grey wireframe) with tinosporide (green solid stick) when visualized in Pymol. (b) The interaction plot of protein ligand complex is visualized using Discovery Studio Visualizer 3.5. Tinosporide forms (i) electrostatic interactions with ARG253, PHE273, GLY278, CYS279, SER280, SER263; (ii) van der waals interaction with LEU226, ASP276, GLY281, TYR284, ALA283 (iii) hydrogen bond with ARG253 and GLY278 and (iv) Pi-Pi interaction with TYR284.

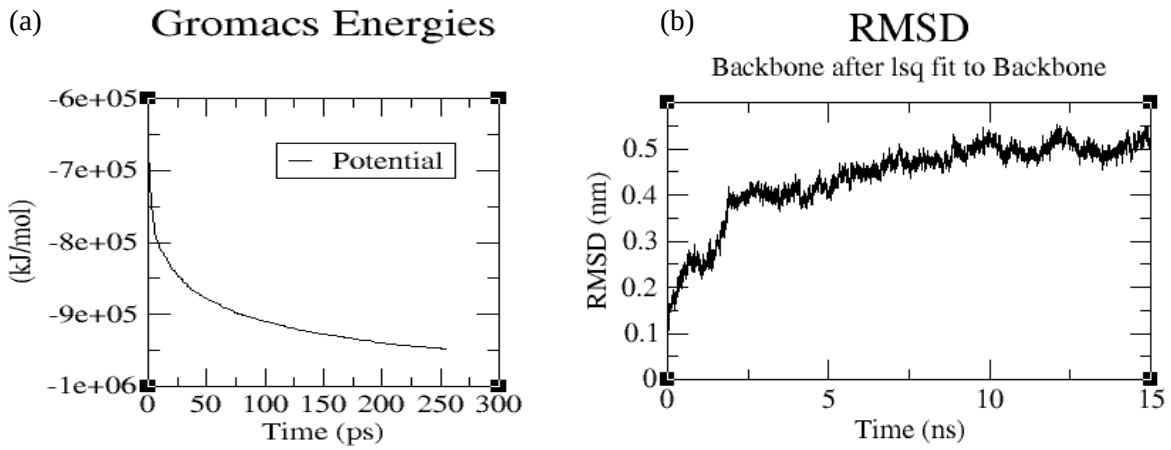


Fig. 4: Molecular dynamics simulation trajectories of 1HEI and tinosporide complex. (a) The potential energy graph of the complex that shows that the protein lignad complex attains its stability at 250ps. (b) The root mean square deviation plot of protein alone and protein ligand complex.

CONCLUSION

HCV infection is a serious global health problem necessitating effective treatment. The current interferon treatment is costly, has significant side effects and fails to cure about half of all infections. Hence, there is a need to develop anti-HCV agents from medicinal plants, which are less toxic, more efficacious and cost-effective. In the present investigation, 24 bioactive compounds from 11 medicinal plants occurring in India have been analyzed and screened for their inhibitory action against the NS3 protein of the hepatitis C virus. The majority of the reported species are wild and rare. The use of these plants to treat hepatitis is still needed by the communities, because of the poor socioeconomic conditions, the high cost, a difficult access to allopathic medicines and their low level efficacy. On the basis of results presented here the biochemical compounds represent an alternative approach for the treatment of chronic HCV infection.

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