Section : Research Paper
ISSN 2063-5346

EVALUATION OF PHYTOCHEMICALS CONSTITUENTS OF *GYROCARPUS ASIATICUS* WILLD AND *LACTUCA RUNCINATA* DC FOR HEPATOPROTECTIVE ACTIVITY BY MOLECULAR DOCKING STUDY

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Source of support: Nil.

Conflict of interest: None.

ABSTRACT

Hepatitis, Cirrhosis of liver, fatty liver, liver disease, liver diseases caused by various drugs are now globally problem. Tumor necrosis factor (TNF-Alpha), Cyclooxygenase –II, Heme oxygenase –I play a vital role in various liver diseases. From ancient time various medicinal plants are used in various hepatic disorders. The plants of *Gyrocarpus asiaticus* Willd and *Lactuca runcinata* DC are collected and hydroalcoholic extract were prepared. Phytochemicals analysis was done by GC-MS (SHIMAZDU QP 2010 ULTRA). By Molecular docking interaction between drugs molecule and target proteins was done by various software ligand preparation by Chemdraw professional 16.0 and target protein 3D structure downloaded from PDB data bank and prepared by Autodock tools. Molecular docking and docking score was generated by Autodock vina software. From all docking score three best compounds Stigmasta-3,5-diene, Stigmasta-5,22-dien-3-ol, Tris (2,4-di-tert-butylphenyl) phosphate of *Gyrocarpus asiaticus* Willd and Stigmasterol, Olean-12-en-11ne,3 beta -hydroxy acetate, Germanicol of *Lactuca runcinata* DC were selected . By visualizing software Biovia discovery studio 2D diagram of all compounds interaction were generated. Affinity between various amino acids like Tyrosine, Glysine, Arginine , Histidine , Alanine etc interact with these phytoconstituents with conventional hydrogen bonding, Pi bonding , Alkyl bonding. Three molecules from each plant show good interaction with all target proteins. All three compounds from each plant show drug likeness properties follow Lipinskies rule of five with one violation predicted by Swiss ADME. All these compounds can show good result in In vivo hepatoprotective study. By further research process these three molecules can be used as hepatoprotective agents.

Keywords- Molecular Docking, GC-MS, Autodock vina, Biovia discovery studio, Swiss ADME.

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INTRODUCTION

In our body liver plays a vital role, liver can have detoxified toxic materials from blood circulating system. Hepatitis, Cirrhosis of liver, fatty liver, liver disease, liver diseases caused by various drugs are now globally problem. Tumor necrosis factor (TNF-Alpha) is a cytokine responsible for the inflammation and this cytokine mainly responsible for the liver inflammation and this liver inflammation causes liver fibrosis Cyclooxygenase –II plays a vital role in hepatic fibrosis formation. By the hepatic stellate cell activation it can causes development of liver fibrosis. Inhibition of these two protein can prevent the liver fibrosis[(1)]. In mammalian cell Heme oxygenase –I acts as a protective molecules, it breaks haemoglobin into bilirubin and carbon monoxide and these heme oxygenase –I degrades products acts as a protective agents against liver IR injury [(2)].Molecular docking is a computational drug discovery technique, by molecular docking technique can predict the interaction between drugs molecule and target proteins[(3)]. In the molecular docking study various type software can be used like Auto dock tools, Autodock vina , visualizing software like Biovia discovery studio , these can give a very clear idea about interaction between drug molecules and amino acids of target proteins[(4)]. The plants of *Gyrocarpus asiaticus* Willd and *Lactuca runcinata* DC are collected and extract prepared, various phytochemicals constituents present in *Gyrocarpus asiaticus* Willd[(5)] and lactuca runcinata DC[(6)]. Physicochemical properties lipophilicity, molecular weight, hydrogen bond donor and acceptor capacity of a drug molecules is a very important factor for biological activity [(7)]. Nowadays toxicity prediction of a drug molecules can be done by Orisis properties explorer, which can be used as a very important tools in drug discovery process.

MATERIALS METHODS

Collection of Plant materials

The plants of *Gyrocarpus asiaticus* Willd and *Lactuca runcinata* DC are collected on dated 11/03/2021 from Palayamkottai, Tamilnadu and these plants was identified and authenticated by Dr. S. Mutheeswaran , Scientist, Xavier research foundation, Xavier college, Palayamkottai, Tamilnadu ,

Phytochemicals constituents

Phytochemical analysis was done by GC-MS (SHIMAZDU QP 2010 ULTRA). For GC-MS analysis Helium and Nitrogen gas used as carrier gas and 5.00 min to 63.00 min runtime was used, and normal injection mode and 5% phenyl polysilphenylene-siloxane used as non-polar stationary phase. Some other important parameters like 70^{o}C Column oven temperature, flow rate 14.00ml/min, 61.3 kPa pressure, 1ml/min column flow rate are maintaining throughout the analysis process. From phytochemical analysis of *Gyrocarpus asiaticus* Willd (Table No-1) and *Lactuca runcinata* DC (Table No-2) extract 10 compounds are selected on the basis of highest % area and % Height from the 30 compounds reported.

Receptors and binding sites

For hepatoprotective activity study Potential receptors drug targets like Heme Oxygenase –I (PDB id - 1N3U), Cyclooxygenase -2 (COX-2) (PDB id- 4PH9), and Tumor necrosis factor (TNF-Alpha) (PDB id -2AZ5). 3D structure of these proteins was retrieved from RCSB protein data bank. With every protein one ligand is attached. The affinity and binding site of these receptors with identified compound by GC-MS analysis were determined by flexible molecular docking study by Auto dock Vina Software. Docking Score and affinity with the receptor of GC-MS identified compounds compared with the docking score and affinity of ligand previously attached with the receptor. 3D images of receptor and GC-MS identified compounds interaction were visualized and generated by visualizing software Biovia Discovery Studio.

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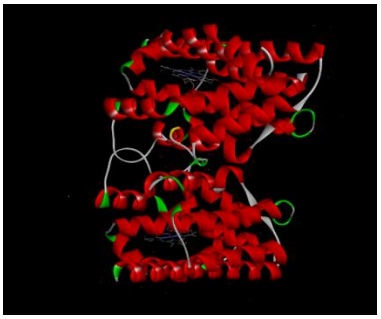


Figure 1: (1N3U) Heme Oxygenenase-I,

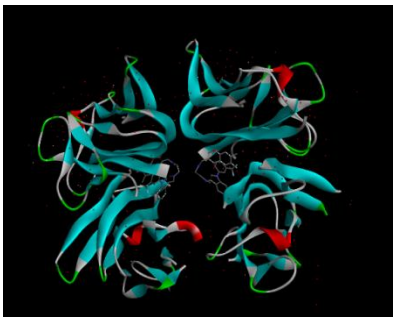


Figure 2: (2AZ5) TNF Alpha

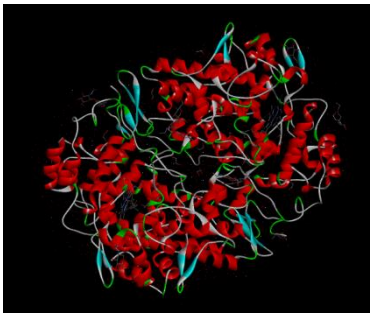
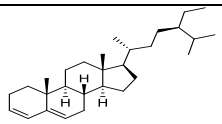
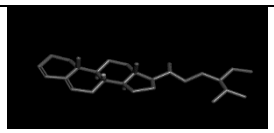
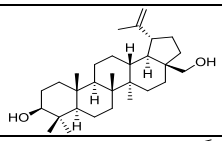
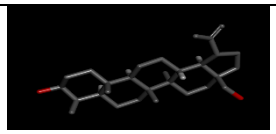
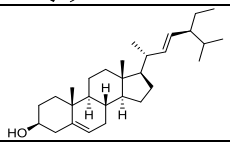
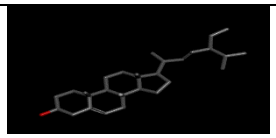
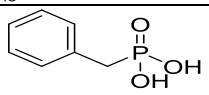
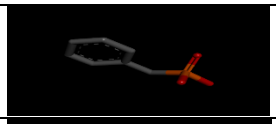
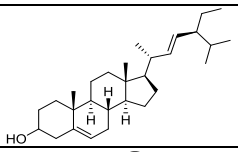
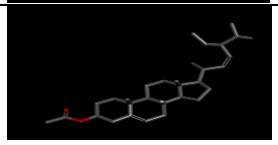
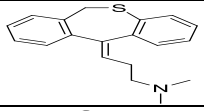
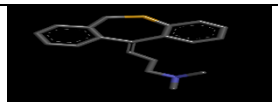
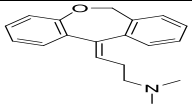
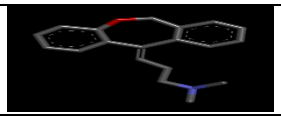


Figure 3: (4PH9), Cyclooxygenase-2

Ligand generation

2D structures of identified phytochemicals constituents of *Lactuca runcinata* DC and *Gyrocarpus asiaticus* Willd by GC-MS were drawn by Chem draw professional 16.0 version software, these identified compounds 2D structure further converted to SDF format by Chemdraw professional 16.0. Then with the help of Biovia discovery studio visualizing software and Autodock tools software SDF format converted to PDB format and then PDB to PDBQT format for molecular docking.

Sl. No.	Compound Name	2D Structure	3D Structure
1.	Stigmasta-3,5-diene		
2.	Betulin		
3.	Stigmasterol		
4.	Alpha -toluenephosphoric acid		
5.	Stigmasta-5,22-dien-3-ol		
6.	Dothiepin		
7.	Doxepin		

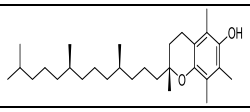
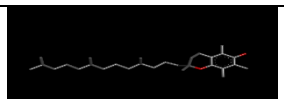
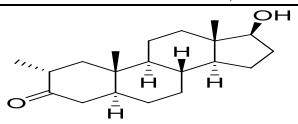
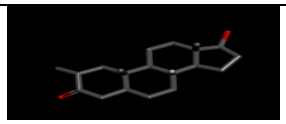
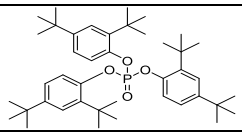
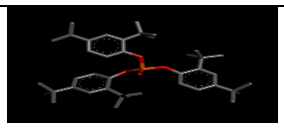
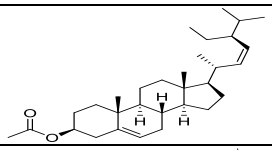
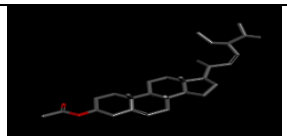
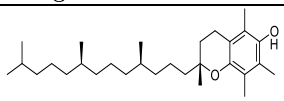
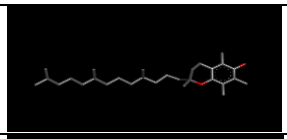
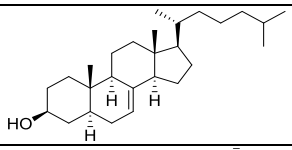
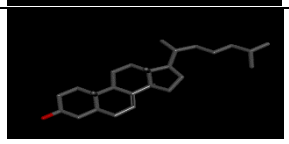
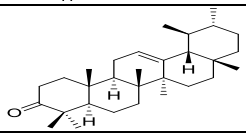
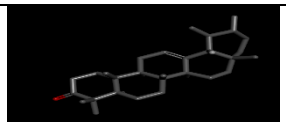
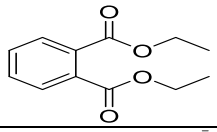
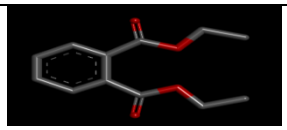
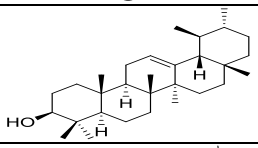
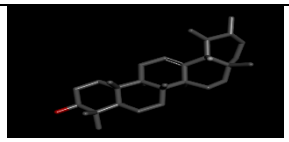
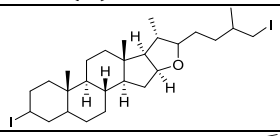
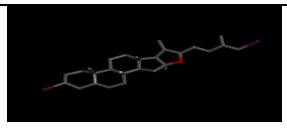
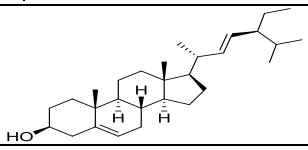
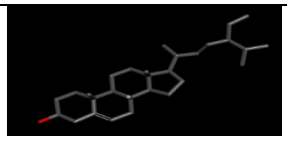
8.	Vitamin E		
9.	Drostanolone		
10.	Tris(2,4-di-tert-butylphenyl) phosphate		

Table 1. 2D & 3D structure of identified compounds of *Gyrocarpus asiaticus* Willd by GC-MS

Sl. No.	Compound Name	2D Structure	3D Structure
1	Stigmasta -5,22 -diene-3-ol, acetate (3, beta 22Z)		
2	Vitamin E		
3	Lathosterol		
4	Urs-12-en-one		
5	1,2 –Benzenedicarboxylic acid,diethyl ester		
6	Urs-12-en-3-ol, (3. beta)		
7	3,26-Diiodofurostan		
8	Stigmasterol		

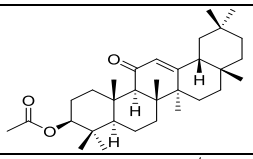
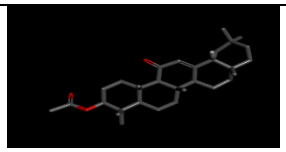
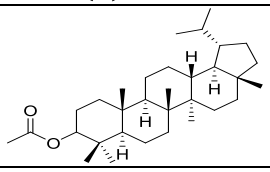
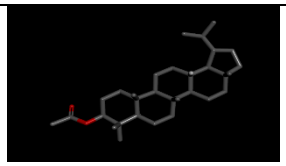
9	3 beta -hydroxy acetate		
10	Lupan -3-ol, acetate		

Table 2. 2D & 3D structure of identified compounds of *Lactuca runcinata* DC by GC-MS.

Flexible docking and Ligand –Receptor interaction

The binding affinity of all 10 selected phytochemicals constituents of these two plants with the 3 receptors by Autodock vina software by using command promt, the affinity and docking score were generated and compared with docking score and affinity with the ligand previously attached with the receptor. With the reference's compounds docking score and binding affinity three phytochemicals constituents were selected for its physicochemical and toxicity properties prediction by Swiss ADME and Orisis properties explorer.

RESULT AND DISCUSSION

Molecular docking study of all ten compounds from Gyrocarpus *asiaticus* Willd and *Lactuca runcinata* DC was performed against Heme Oxygenenase-I (1N3U), Tumor Necrosis Factor alpha (2AZ5), Cyclooxygenase-2 (4PH9) receptor using Autodock Vina. In the docking study these three receptors show interaction with different amino acids of the receptors with these 10 identified compounds. Binding energy or Docking score for *Gyrocarpus asiaticus* Willd are shown (Table No-3). From the table no -3, according to lowest binding energy required to interact with these thee receptors, three identified molecules Stigmasta-3,5-diene, Stigmasta-5,22-dien-3-ol, Tris (2,4-di-tert-butylphenyl) phosphate of *Gyrocarpus asiaticus* Willd are selected. These three molecules interaction with amino acids of each receptor are shown, for Heme Oxygenenase-I (Figure No-4), Human TNF Alpha (Figure No-5), Cyclooxygenase-2 (Figure No-6). Stigmasta-3,5-diene, Stigmasta-5,22-dien-3-ol, Tris(2,4-di-tert-butylphenyl) phosphate of *Gyrocarpus asiaticus* Willd shows different types of bonding like Pi bonding, Sigma bonding, Conventional hydrogen bonding, Alkyl bonding with Different amino acids like Alanine, Glycine, Lucien etc shown in (Table No-4).

Sl No	**Ligand**	**Binding Affinity with Receptor**		
		Heme oxygenenase-I (KJ/mol)	TNF Alpha (KJ/mol)	Cyclooxygenase-2 (KJ/mol)
1	Stigmasta-3,5-diene	-9.7	-9.2	-8.9
2	Betulin	-8.4	-7.6	-7.6
3	Stigmasterol	-7.8	-8.1	-8.0
4	Alpha -toluenephosphoric acid	-7.8	-8.1	-9.6
5	Stigmasta-5,22-dien-3-ol	-9.4	-7.9	-8.7
6	Dothiepin	-8.5	-7.6	-8.1
7	Doxepin	-8.1	-7.0	-7.4
8	Vitamin E	-8.2	-6.6	-6.5
9	Drostanolone	-7.8	-6.2	-8.7
10	Tris(2,4-di-tert-butylphenyl) phosphate	-9.8	-8.8	-9.5

Table 3. Binding affinity of identified compounds of *Gyrocarpus asiaticus* Willd with receptors.

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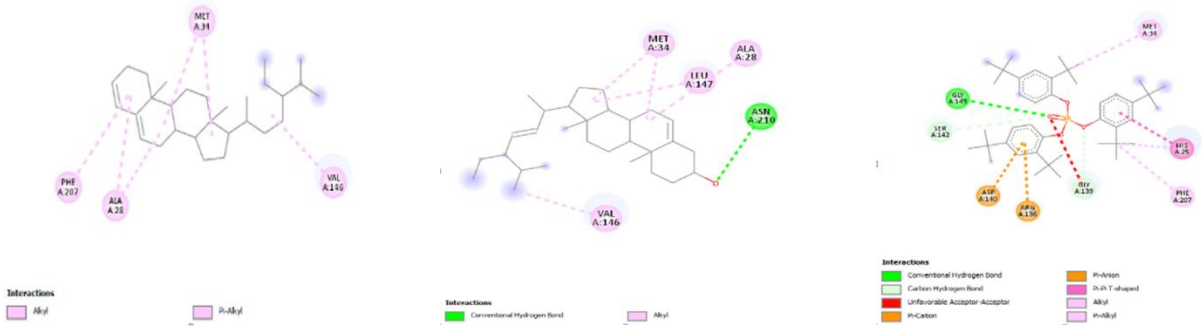
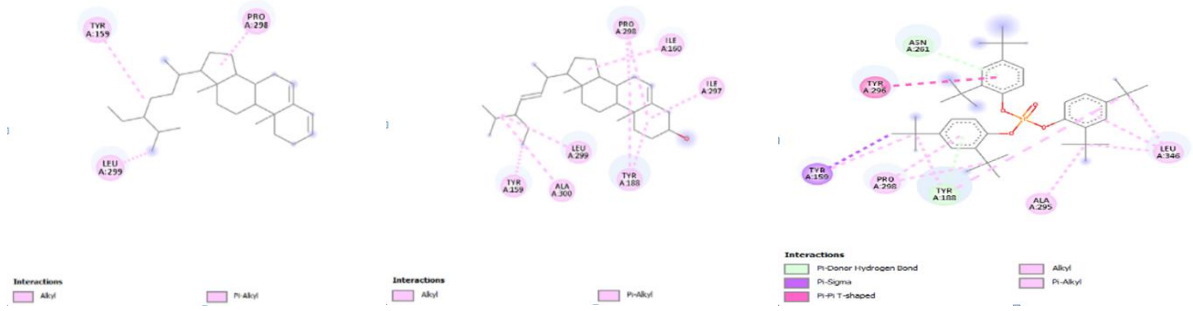


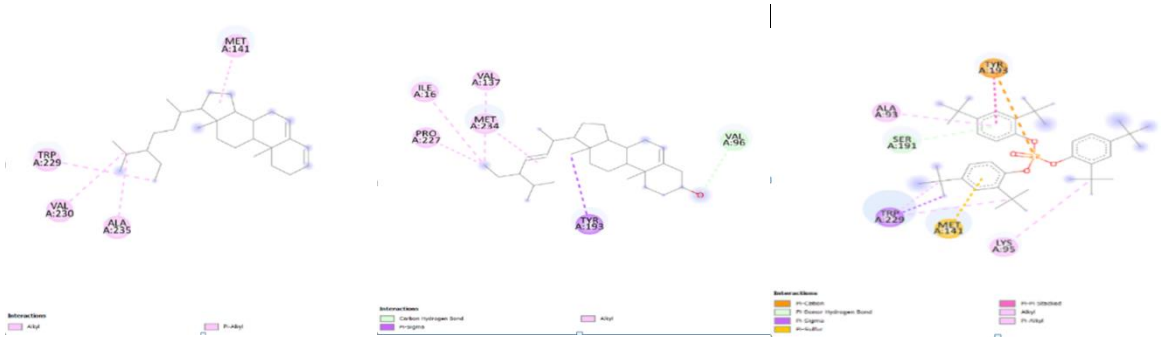
A **B** **C**

Figure 4: (A)Stigmasta-3,5-dien, (B)Stigmasta-5,22-diene-3-ol, (C) Tris (2,4-di-tert-butylphenyl) -phosphate interaction with Human Heme Oxygenase 1.



A **B** **C**

Figure 5: (A) Stigmasta-3,5-dien, (B) Stigmasta-5,22-diene-3-ol, (C) Tris (2,4-di-tert-butylphenyl) -phosphate interaction with Human TNF Alpha.



A **B** **C**

Figure 6: (A)Stigmasta-3,5-dien, (B)Stigmasta-5,22-diene-3-ol, (C)Tris (2,4-di-tert-butylphenyl) -phosphate interaction with Cyclooxygenase-2.

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Table 4. Bonding with different amino acids of receptors with identified compounds of *Gyrocarpus asiaticus* Willd.

Sl No	Ligand	Bonding with Receptor		
		Heme Oxygenenase-I	TNF Alpha	Cyclooxygenase-2
1	Stigmasta-3,5-diene	**Alkyl interaction-** PHE 207,ALA 28, MET 34, VAL 146	**Alkyl interaction-** LEU 299, TYR 159, PRO 293	**Alkyl interaction-** TRP 299, VAL 230, ALA 235
2	Stigmasta-5,22-dien-3-ol	**Conventional Hydrogen bond-** ASN 210 **Alkyl bond-** LEU 147,MET 34, ALA 28, VAL 146	**Alkyl interaction-** TYR 159,ALA 300,LEU 299,TYR 100, PRO 298, ILE 297,ILE 160.	**Conventional Hydrogen bond-** VAL 96 **Pi-Sigma Bond-** TYR 193 **Alkyl interaction-** ILE 16,PRO 227, VAL 137,MET 234
3	Tris(2,4-di-tert-butylphenyl) phosphate	**Conventional Hydrogen bond-** GLY 143, GLY 139 **Carbon Hydrogen Bond-** SER 142 **Pi cation –anion bond-** ASP 140, ARG 136 **Alkyl bond-** PHE 207, MET 34	**Pi-Donor Hydrogen bond-** TYR 108, ASN 261 **Pi-Sigma Bond-** TYR 159 **Alkyl bond-** ALA 295, LEU 346, PRO 298 **Pi-Pi T Shaped bond –** TYR 296	**Pi- Cation bond-** TYR 193 **Pi-Donor Hydrogen bond-** SER 191 **Pi- Sigma bond –** TRP 229 **Pi- Sulphur bond-** MET 141 **Alkyl bond-** ALA 93, LYS 95

The result of molecular docking of *Gyrocarpus asiaticus* Willd show that compound No 1,5,10 (Stigmasta-3,5-diene, Stigmasta-5,22-dien-3-ol, Tris (2,4-di-tert-butylphenyl) phosphate) shows highest affinity with all three receptors. These three molecules show Carbon Hydrogen Bonding, Conventional Hydrogen Bonding, Alkyl Bonding with All three receptors. These three molecules can be considering as responsible molecules for hepatoprotective activity for *Gyrocarpus asiaticus* Willd. And these three molecule obey the Lipinski rule of five with one violation when predicted by SWISS ADME software and having low absorption and limited brain permeability (Table No-5), having drug likeness properties and shows good toxicity result when prediction done by Orisis properties explorer shows (Table No-6)

Sl. NO.	Molecule Name	Molecular Formula	Molecular Weight < 500 g/mol	Lipophilicity (logP) < 5	Hydrogen Bond Donor < 5	Hydrogen Bond Acceptor < 10
1.	Stigmasta-3,5-diene	C29H48	396.69	5.11	0	0
2.	Stigmasta-5,22-dien-3-ol	C29H480	412.69	5.01	1	1
3.	Tris (2,4-di-tert-butylphenyl) phosphate	C42H63O4P	662.92	6.93	0	4

Table 5. Physico chemical prediction of Stigmasta-3,5-diene Stigmasta-5,22-dien-3-ol, Tris (2,4-di-tert-butylphenyl) phosphate of *Gyrocarpus asiaticus* Willd by Swiss ADME.

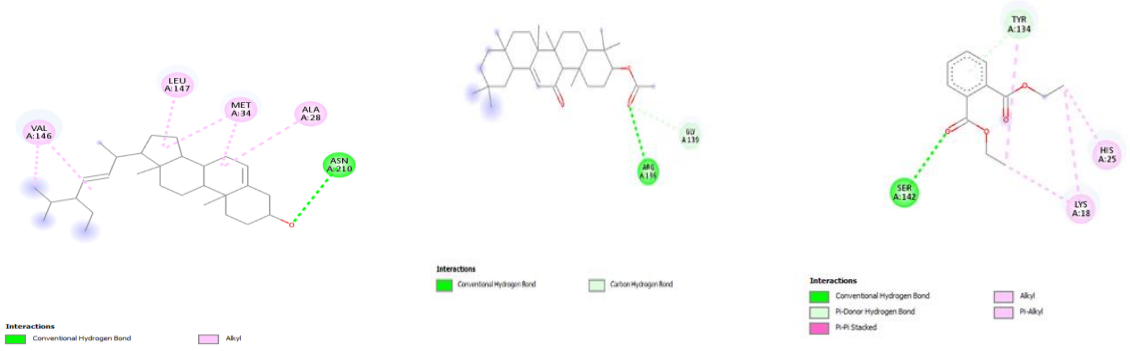
Sl. No.	Compound Name	Mutagenic	Tumorigenic	Irritant	Reproductive Effective	Permeability (Boiled Egg)
1.	Stigmasta-3,5-diene	No effect	No effect	No effect	No effect	Grey region - low absorption and limited brain permeation
2.	Stigmasta-5,22-dien-3-ol	No effect	No effect	No effect	No effect	Grey region - low absorption and limited brain permeation
3.	Tris (2,4-di-tert-butylphenyl) phosphate	No effect	Medium effect	High risk effect	Medium effect	Grey region - low absorption and limited brain permeation

Table 6. Toxicity prediction of Stigmasta-3,5-diene, Stigmasta-5,22-dien-3-ol, Tris (2,4-di-tert-butylphenyl) phosphate of *Gyrocarpus asiaticus* Willd by Orisis Properties explorer.

Binding energy or Docking score for *Lactuca runcinata* DC are shown (Table No-7). From the table no -3, according to lowest binding energy required to interact with these thee receptors three identified molecules Stigmasterol, Olean-12-en-11ne,3 beta -hydroxy acetate, Germanicol of *Lactuca runcinata* DC are selected. These three molecules interaction with amino acids of each receptor are shown, for Heme Oxygenenase-I (Figure No-7), Human TNF Alpha (Figure No-8), Cyclooxygenase-2 (Figure No-9).

Sl No	Ligand	Binding Affinity with Receptor		
		Heme oxygenenase-I (KJ/mol)	TNF Alpha (KJ/mol)	Cyclooxygenase-2 (KJ/mol)
1	Stigmasta -5,22 -diene-3-ol, acetate (3, beta 22Z)	-8.7	-5.4	-8.9
2	Vitamin E	-8.6	-6.4	-7.5
3	Lathosterol	-8.1	-7.3	-8.2
4	Urs-12-en-one	-8.0	-7.3	-9.1
5	1,2 –Benzenedicarboxylic acid,diethyl ester	-9.1	-8.4	-8.9
6	Urs-12-en-3-ol, (3. beta)	-8.2	-7.3	-7.6
7	3,26-Diiodofurostan	-8.7	-7.1	-8.6
8	Stigmasterol	-10.1	-6.9	-7.5
9	3 beta -hydroxy acetate	-9.1	-6.8	-8.2
10	Lupan -3-ol, acetate	--8.6	-6.4	-8.1

Table 7. Binding affinity of identified compounds of *Lactuca runcinata* DC with receptors.



A **B** **C**

Figure 7: (A) Stigmasterol, (B) 3 beta -hydroxy acetate (C) 1,2 –Benzenedicarboxylic acid, diethyl ester interaction with Human Heme Oxygenase 1.

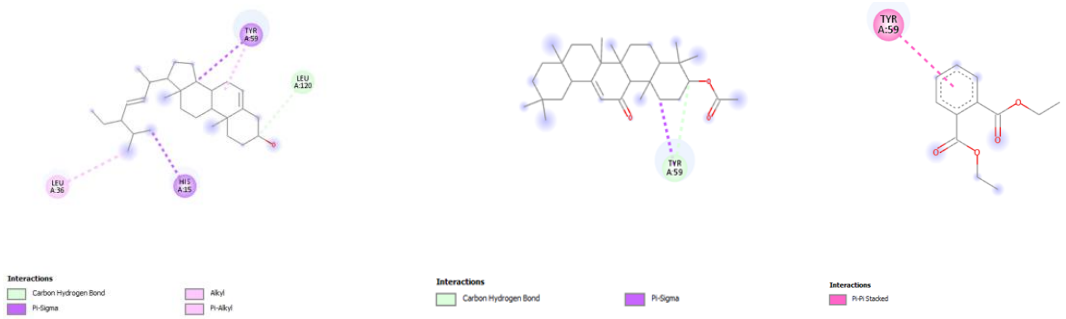
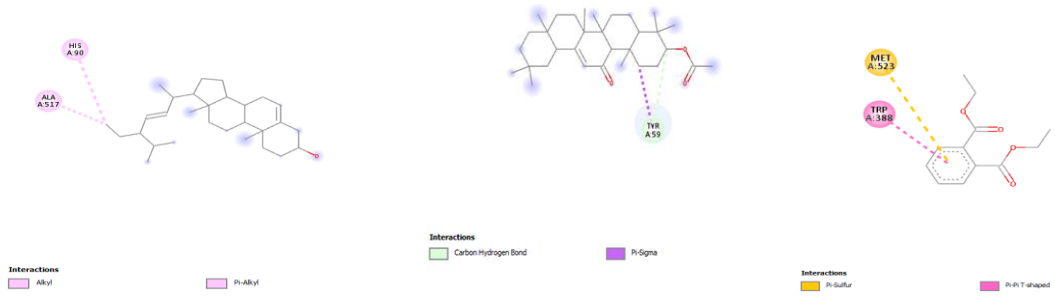


Figure 8: (A) Stigmasterol, (B) 3 beta -hydroxy acetate (C) 1,2 –Benzenedicarboxylic acid,diethyl ester interaction with TNF Alpha.



A **B** **C**

Figure 9: (A) Stigmasterol, (B) 3 beta -hydroxy acetate (C) 1,2 –Benzenedicarboxylic acid,diethyl ester interaction with Cyclooxygenase-2.

Stigmasterol, Olean-12-en-11ne,3 beta -hydroxy acetate**,** 1,2 –Benzenedicarboxylic acid,diethyl ester of *Lactuca runcinata* DC shows different types of bonding like Pi bonding, Sigma bonding, Conventional hydrogen bonding, Alkyl bonding with Different amino acids like Alanine, Glycine , Lucien etc shown in (Table No-8).

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Sl No	Ligand	Bonding with Receptor		
		Heme oxygenenase-I	TNF Alpha	Cyclooxygenase-2
1	Stigmasterol	**Conventional Hydrogen bond-** ASN 210 **Alkyl bond-** VAL 146, LEU 147, MET 34, ALA 28	**Carbon –Hydrogen bond-** LEU 120 **Pi –Sigma bond –** TYR 59, HIS 15 **Pi- Alkyl bond-** LEU 36	**Pi-Alkyl-** HIS 90, ALA 517
2	3 beta -hydroxy acetate	**Conventional Hydrogen bond-** ARG 136 **Carbon Hydrogen Bond-** GLY 139	**Conventional Hydrogen bond-** TYR 59	**Conventional Hydrogen bond-** TYR 59
3	1,2 – Benzenedicarboxylic acid,diethyl ester	**Conventional Hydrogen bond-** SER 142 **Pi Donor Hydrogen Bond-** TYR 134 **Alkyl bond-** LYS 18, HIS 25	**Pi-Pi bond –** TYR 59	**Pi-Pi bond-** MET 523 **Pi- Sulphur bond-** TRP 388

Table 8. Bonding with different amino acids of receptors with identified compounds of *Lactuca runcinata* DC.

The result of molecular docking of *Lactuca runcinata* DC. show that compound No 5,8,9 (1,2 –Benzenedicarboxylic acid, Stigmasterol , 3 beta -hydroxy acetate) shows highest affinity with all three receptors . These three molecules show Carbon Hydrogen Bonding, Conventional Hydrogen Bonding, Alkyl Bonding with All three receptors. These three molcules can be consider as responsible molecules for hepatoprotective activity for *Lactuca runcinata* DC.

These three molecule obey the Lipinski rule of five with one violation when predicted by SWISS ADME software and having low absorption and limited brain permeability (Table No-9), having drug likeness properties and shows Stigmasterol having good toxicity result and 3 beta -hydroxy acetate and 1,2 –Benzenedicarboxylic acid having mutagenic, irritant and tumergenic effects when prediction done by Orisis properties explorer shows (Table No-10)

Sl. NO.	Molecule Name	Molecular Formula	Molecular Weight < 500 g/mol	Lipophilicity (logP) < 5	Hydrogen Bond Donor < 5	Hydrogen Bond Acceptor < 10
1.	Stigmasterol	$C_{29}H4_8O$	412.69	5.01	1	1
2.	3 beta -hydroxy acetate	$C_{24}H_{29}ClO_4$	416.94	3.41	0	4
3.	1,2 – Benzenedicarboxylic acid,diethyl ester	$C_{13}H_{16}O_5$	252.26	2.39	0	5

Table 9. Physicochemical prediction of Stigmasterol, 3 beta -hydroxy acetate, 1,2 –Benzenedicarboxylic acid, diethyl ester of *Lactuca runcinata* DC by Swiss ADME.

Sl. No.	Compound Name	Mutagenic	Tumorigenic	Irritant	Reproductive Effective	Permeability (Boiled Egg)
1.	Stigmasterol	No effect	No effect	No effect	No effect	Grey region - low absorption and limited brain permeation
2.	3 beta -hydroxy acetate	No effect	No effect	No effect	High risk	The yellow region- can cross blood brain barrier and having high gastrointestinal absorption.
3.	1,2 – Benzenedicarboxylic acid,diethyl ester	High risk	Medium risk	Medium risk	High risk	The yellow region- can cross blood brain barrier and having high gastrointestinal absorption.

Table 10. Toxicity prediction of Stigmasterol, 3 beta -hydroxy acetate, 1,2 –Benzenedicarboxylic acid, diethyl ester of *Lactuca runcinata* DC by Orisis Properties explorer .

CONCLUSION-

Protein Heme Oxygenenase-I, TNF-Alpha, and Cyclooxygenase-2 having great role in hepatoprotective activity. Phytochemicals constituents identified from the hydroalcoholic extract of *Gyrocarpus asiaticus* Willd and *Lactuca runcinata* DC showing good affinity with all three receptors. Depending on the lowest binding energy and interaction three best molecules are selected. We can consider that depending on docking score with these three receptors and conventional hydrogen bonding, Pi- Sigma bonding, Alkyl bonding with receptors, due to the presence of these molecules Plant *Gyrocarpus asiaticus* Willd and *Lactuca runcinata* DC show the hepatoprotective activity.

Stigmasta-3,5-diene, Stigmasta-5,22-dien-3-ol, Tris (2,4-di-tert-butylphenyl) phosphate for *Gyrocarpus asiaticus* Willd and Stigmasterol, 3 beta -hydroxy acetate, 1,2 –Benzenedicarboxylic acid,diethyl ester for *Lactuca runcinata* DC can shows hepatoprotective activity. These compounds Stigmasta-3,5-diene, Stigmasta-5,22-dien-3-ol, Tris (2,4-di-tert-butylphenyl) phosphate for *Gyrocarpus asiaticus* Willd and Stigmasterol, 3 beta -hydroxy acetate, 1,2 –Benzenedicarboxylic acid,diethyl ester for *Lactuca runcinata* DC can be used a lead compound for hepatoprotective agents.

Physicochemical properties prediction and toxicity prediction of these six molecules also done with Swiss ADME and Orisis properties explorer and result shown three compounds of *Gyrocarpus asiaticus* Willd and *Lactuca runcinata* DC having drug likeness properties and follow the Lipinski rule of five.

Stigmasta-3,5-diene, Stigmasta-5,22-dien-3-ol having no Mutagenic, Tumorigenic, Irritant effects and no effects on reproductive system and Tris (2,4-di-tert-butylphenyl) phosphate having no mutagenic effects and having medium risk for tumorigenic, irritant effects. All three molecules having low absorption and limited brain permeation.

Stigmasterol, 3 beta -hydroxy acetate, having no Mutagenic, Tumorigenic, Irritant effects and no effects on reproductive system and 3 beta -hydroxy acetate having high risk of mutagenic and high risk on reproductive system and medium risk on tumorigenic effects. Stigmasterol having low absorption and limited brain permeation and beta -hydroxy acetate, 3 beta -hydroxy acetate can cross blood brain barrier and having gastrointestinal absorption is high.

This research can proceed further for hepatoprotective drug discovery and development considering these six molecule as a lead molecule for hepatoprotective drugs.

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ISSN 2063-5346

ACKNOWLEDGEMENT

Authors are grateful to Haldia institute of pharmacy providing me Chemdraw professional 16.0 software, Autodock Vina for molecular docking software, Biovia Discovery studio, software for molecular docking study.

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