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Pharmacognostical, phytochemical evaluation and *insilico* lead finding of *Callicarpa macrophylla with* hepatoprotective potentials

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ABSTRACT

Present communication deals with the study of Pharmacognostical, phytochemical screening and antihepatotoxic activity prediction of compounds isolated from Callicarpa macrophylla Linn in order to search lead compound. Dried leaves and bark powder material was used for determination of ash value, extractive value, and phytochemical constituents. fifteen compounds from the whole plant of Callicarpa macrophylla were subjected to molecular properties prediction and drug-likeness by Lipinski rule of five & Molinspiration software. Phytochemical screening proved the presence of chemical constituent like tannins, alkaloids, proteins, starch, flavanoids, and glycoside. 12 compounds of the plant fulfill the requirements of Drug likeness were taken for biological activity calculation with the help of Molinspiration software and compared with standard drug Silibinin. On comparison of compounds with silibinin, Calliterpenone, Luteolin, Apigenin, Ursolic acid, Crategolic acid, β-Sitosterol, Betulinic acid, α-Amyrenol, Daucosterol, Luteolin-7-O-glucuronide, Apigenin-7-O-glucuronide and Calliterpenone monoacetate almost fulfills the Lipinski rule of five and showed good bioactivity score than Silibinin. Out of 15 compounds Calliterpenone, Ursolic acid, Crategolic acid, β-Sitosterol, Betulinic acid, Luteolin-7-O-glucuronide, Apigenin-7-O-glucuronide and Calliterpenone monoacetate has good bioactivity score as compared to Silibinin which is potent hepatoprotective drug. So these compounds can be considered as lead compounds with hepatoprotective activity from Callicarpa macrophylla.

Key words: *Callicarpa macrophylla*, Hepatoprotective, *Insilico* lead finding, Molinspiration, Lipinski's rule, Phytochemical screening

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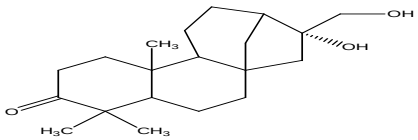
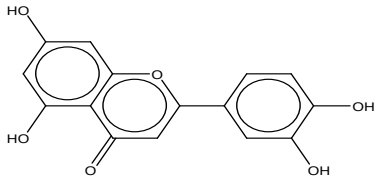
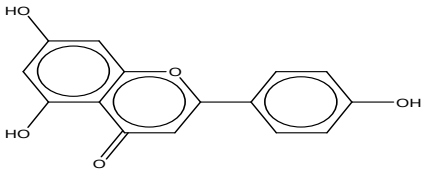
INRODUCTION

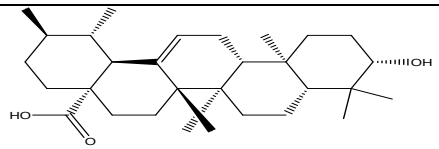
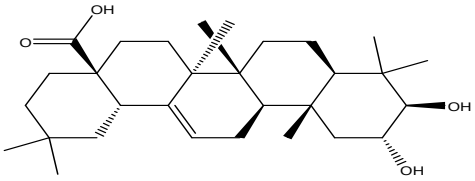
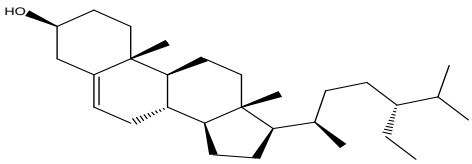
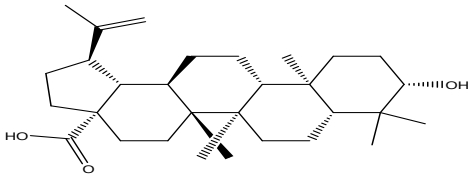
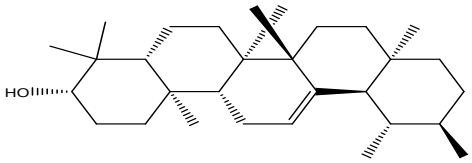
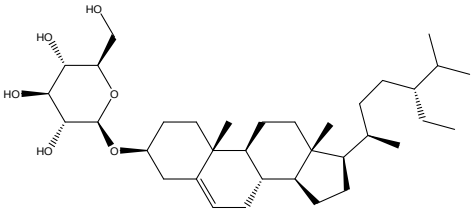
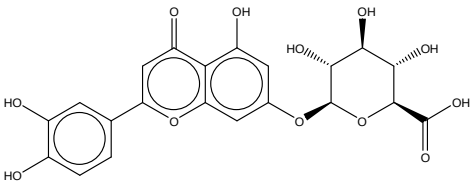
It is estimated that about 7,500 plants are used in local health traditions in, mostly, rural and tribal villages of India. Out of these, the real medicinal value of over 4,000 plants is either little known or hitherto unknown to the mainstream population. The classical systems of medicine such as Ayurveda, Siddha, Amchi, Unani and Tibetan use about 1,200 plants [1]. Due to exhibition of wide range in topography and climate, which has a bearing on vegetation and floristic composition of plants, India is a varietal emporium of medicinal plants and is one of the richest countries in the world in regard to genetic resources of medicinal plants.. Moreover, the agro-climatic conditions are conducive for introducing and domesticating new exotic plant varieties [2]. In recent years, secondary plant metabolites (phytochemicals), previously with unknown pharmacological activities, have been extensively investigated as a source of medicinal agents [3].

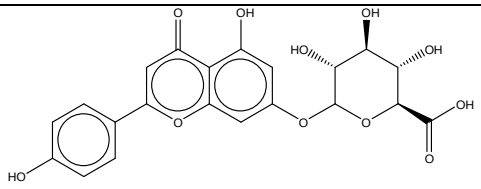
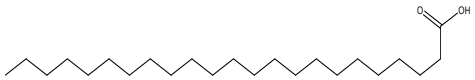
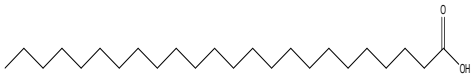
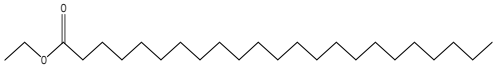
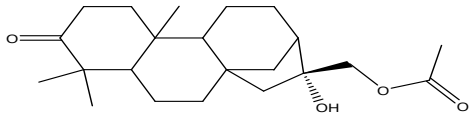
Herbal drugs play major role in the treatment of hepatic disorders. A number of medicinal plants and their formulations are widely used for the treatment of these disorders [4]. *Callicarpa macrophylla* Vahl. of family Verbenaceae, is an indigenous plant of India, have with a wide spectrum of therapeutic properties. Its leaves are reported to have anti-inflammatory, analgesic and antipyretic effects [5, 6], while roots have are anti-inflammatory and analgesic effects [7]. Its stems of *C. macrophylla* has been evaluated for its anti-fungal activity and results are very significant [8]. *Callicarpa macrophylla* Vahl. (fam-Verbenaceae) is an erect shrub which is globally distributed across India, Nepal, Bhutan, Myanmar, South East Asia, and China. In India it is distributed in Jammu & Kashmir, Himachal Pradesh, Uttar Pradesh, Bihar, Sikkim, West Bengal, Arunachal Pradesh, Assam, Meghalaya, Nagaland, Manipur, Mizoram, Tripura, and Andhra Pradesh, up to an altitude of 1800 meters. Leaves are 12.5-23 cm long, ovate or ovate-lanceolate, acuminate, base cuneate or rounded. Upper surface wrinkled, glabrate when mature, white-tomentose beneath with compound stellate hairs, Petiole 6-13mm long [9]. It is flowering in August-November and fruiting October-December [10]. Efforts are being made all over the world to discover agents that can promote healing and thereby reduce the cost of hospitalization and save the patient from amputation or other severe complications. The need for safer and effective wound healing agents and the lack of enough scientific data to support the claims made in ancient literature prompted the present study.

The phytochemical screening of the plant revealed the presence of different type of chemical like seeds contain oleanolic acid. Besides diterpenoids, leaves contain favonoids, C22-C24 fatty acids, Calliterpenone monoacetate and Calliterpenone isopropylidene derivative. Calliphyllin, betulinic acid,5,4'-dihydroxy-3,7,3' trimethoxyflavone,5,4'-dihydroxy-3,7,-trimethoxyflavone & β-sitosterol are present in the leaves [11]. Diterpene (Calliterpenone) [12], (3β, 16α, 17-trihydroxy Phyllocladane) [13], Diterpenoids (16α,17-Isopropylideno-3-oxo-phyllocladane [14]; flavanoids (β- sitosterol, ursolic acid, luteolin and apigenin) [15], 16,17-dihydroxy-kauranoids [16], fatty acids and other constituents [17]. *C. macrophylla* leaves contains *α*-amyrenol, α-amyrin, 2*α*,3*α*,19*α*-trihydroxy -12-dien-28- ursolic acid [18]. luteolin-7-O-glucuronide, apigenin-7-O-glucuronide, *β*-sitosterol-*β*-*D*-glucoside, 2*α*-hydroxy ursolic acid, crategolic acid, docosanoic acid, tricosanoic acid, tetracosanoic acid, ethyl tricosanoate, 3,7,3′-trimethoxy-4′,5-dihydroxyflavone [19, 20]. Some of compounds isolated from *Callicarpa macrophylla* Vahl. are summarized in Table 1.

Table 1: Some of chemical constituents of *Callicarpa macrophylla*

S. N.	Compound	Structure	Reference
1	Calliterpenone		[12]
2	Luteolin		[15]
3	Apigenin		[15]
4	Ursolic acid		[11, 15]

			
5	Crategolic acid		[19]
6	B-Sitosterol		[19]
7	Betulinic acid		[19]
8	*A*-amyrenol		[18]
9	Daucosterol		[20]
10	Luteolin-7-O-glucuronide		[19]
11	Apigenin-7-O-glucuronide		[19]

			
12	Tricosanoic acid		[19, 20]
13	Tetracosanoic acid		[19, 20]
14	Ethyl tricosanoate		[19, 20]
15	Calliterpenone monoacetate		[19, 20]

In this paper we describes the morphological and phytochemical aspects of *Callicarpa macrophylla* Vahl. and compare different compounds isolated from plant *Callicarpa macrophylla* Vahl. with the standard drug Silibinin on the basis of Lipinski's rule of five and physiological interpretation by Molinspiration software to explore the hepatoprotective activity of this plant.

Brief Review of Plant

Callicarpa macrophylla (Figure 1) belong to Family Verbenaceae, a well known plant in the Indian subcontinent for its range of uses.

Plant Taxonomy:

Kingdom	-	Plantae
Order	-	Lamiales
Family	-	Verbenaceae
Genus	-	Callicarpa
Species	-	macrophylla

Common Name:

Priyangoo, Daya, Beauty Berry

Descriptions:

Habit **:** It is a perennial deciduous shrub, Height up to 1.2–2.4 m.

Branches **:** Virgate, usually shaggy as well as the tomentose tips.

Leaves **:** 12.5-23 cm. long, ovate or ovate-lanceolate, acuminate, Base cuneate or rounded; upper surface wrinkled, glabrate when mature, white-tomentose beneath with compound stellate hairs; main lateral nerves 12-16 pairs Petioles 6-13mm long.

Inflorescences/ **:** 5mm long, crowed in axillary peduncles globose cymes 2.5-

Flower **:** 7.5 cm. across; peduncles shorter than the petioles. Calyx less than 1.2 mm long, sellate-hairy; lobes minute, triangular. Corolla rose-coloured; lobes sub-equal spreading.

Fruit **:** Drupes white.
Geographical Distribution: Western-Himalaya from Kashmir to Assam and Arunachal Pradesh, Uttar Pradesh and in the Andhra Pradesh, Maharashtra, Uttaranchal, Pantnagar (India).
Ecology **:** Usually in open evergreen to semi-evergreen forest up to 1,800 m. (altitude).
Propagation **:** By seeds
Part used **:** Leaves, Flower and Fruits**.**

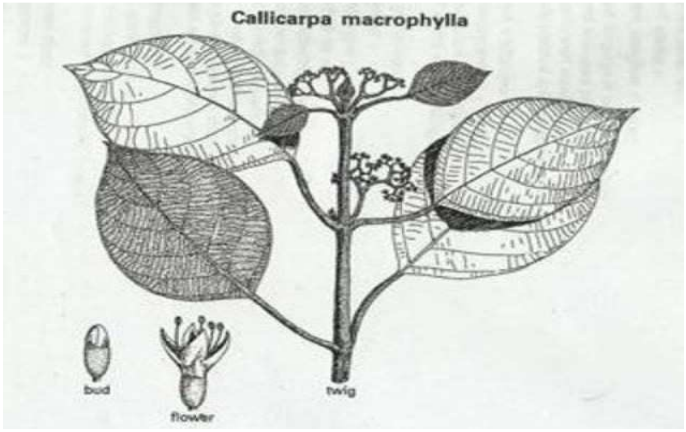


Figure 1: ***Callicarpa macrophylla***

EXPERIMENTAL SECTION

Collection of plant material

The Aerial parts of *Callicarpa macrophylla* used for the present studies were collected from Central Medicinal and Aromatic Plant (Lucknow), India. The plant was identified, confirmed and authenticated by National Botanical Research Institute (Council of Scientific and Industrial Research) Lucknow-226001, India. (Ref.No: NBRI/CIF/262/2011). The aerial parts were cut into small pieces and shade dried. The dried material was then pulverized separately into coarse powder by a mechanical grinder. The resulting powder was then used for extraction. T. S. of leaf of *Callicarpa macrophylla* is shown in Figure 2.

Figure 2: T. S. of leaf of *Callicarpa macrophylla*

Quality control parameters

Coarse powder of the Aerial parts of *Callicarpa macrophylla* has been used to perform quality control test which include determination of ash, extractable matter, moisture content.

Determination of ash
The total ash, acid insoluble ash and water-soluble ash value were determined for air dried samples using the procedure described in WHO guidelines.

Total ash value
About 2gm of powdered drug was weighed accurately into a tared silica crucible and incinerated at 450^0C in muffle furnace until free from carbon. The crucible was cooled and weighed. Percentage of total ash was calculated as following with reference to air-dried substance.

Weight of preheated crucible= g (x)
Weight of powder = g (y)
Weight of crucible with powder = g
Weight of dish+ ash (after complete incineration) = (z)
Weight of the ash = (z – x) g
Total ash value of the sample = (z-x) / y × 100

Acid in-soluble ash value
Ash obtained from total ash was boiled with 25 ml of 2N HCl for few minutes and filtered through an ash less filter paper. The filter paper was transferred into a tared silica crucible and incinerated at 450^0C in muffle furnace until free from carbon. The crucible was cooled and weighed. Percentage of acid insoluble ash was calculated as following with reference to air-dried substance.

Weight of the residue (acid insoluble ash) = 'a' g
'Y' g of the air dried drug gives - 'a' g acid insoluble ash

Therefore, 100 g of the air dried drug gives = 100 – a / y g of acid insoluble ash.

Water soluble ash
Ash obtained from total ash was boiled with 25 ml of distilled water for few minutes and filtered through an ash less filter paper. The filter paper was transferred into a tared silica crucible and incinerated at 450^0C in until free from carbon. The crucible was cooled and weighed. Percentage of water-soluble ash was calculated as following with reference to air-dried substance.

Extractive values
The parameter determines the amount of soluble matter present in the plant.

Water soluble extractive value
5g of the crude powder was taken into a conical flask and 100 ml of water was added to it. This mixture was stirred gently and warmed in a water bath for 30 minutes. The solution was shaken gently at intervals. Then the solution was taken from the water bath and cooled and filtered through a cotton plug, 25 ml of the filtrate was taken and evaporated to dryness. The residue was weighed.

Loss on drying
The percentages of active chemical constituents in crude drugs are given in terms of air-dried drugs. Hence the moisture content of drug was determined. 2 gm of powdered drug was transferred into a petridish and the contents were distributed evenly to a depth not exceeding 10 mm. The loaded petridish was heated at 105^0C in hot air oven and weighed at different time intervals until a constant weight was obtained. The difference in weight after drying and initial weight is the moisture content. Respective moisture content (%) for both the samples was calculated.

All the experiment was repeated six times for precision and results were expressed as mean ± SD.

Preparation of Hydro-alcoholic extract
The powdered drug was dried and packed well in soxhlet apparatus and extracted (48 hr) with petroleum ether (60-80^0C) for defatted and the resulting powdered dried and extracted with 60% ethanol by using soxhlet apparatus, for 24 hr. The extract was concentrated and dried using Rotary evaporator. It was stored in refrigerator and kept in desiccator few hours before use.

Preliminary Phytochemical Screening
The Aerial parts of *Callicarpa macrophylla* Hydro-alcoholic extract and its fraction were dissolved in distilled water and filtered. The filtrates were subjected to the following test.

Detection of alkaloid
Wagner's test
Test solution was treated with Wagner's reagent. No precipitate was formed indicates the absence of alkaloids.

Dragendorf's test
Test solution was treated with Dragendorf**'**s reagent. No precipitate was formed indicates the absence of alkaloids.

Hager's test
Test solution was treated with Hager's reagent. No precipitate was formed indicates the absence of alkaloids.

Detection of Flavonoids
The Aerial parts of *Callicarpa macrophylla* Hydro-alcoholic extract and its fraction were subjected to the following test to detect presence of Flavonoids.

Shinoda test
To the alcoholic solution of test sample, a few fragments of magnesium ribbon and Con. HCl was added. Appearance of magenta colour after few minutes indicates presence of alkaloids.

Ferric chloride test
Test solution was treated with few drops of 5% ferric chloride solution in water. Bluish black colour indicates the presence of flavonoids.

Sodium hydroxide test
Test solution was treated with Sodium hydroxide solution. Formation of yellow colour indicates the presence of flavonoids.

Detection of Tannins
The Aerial parts of *Callicarpa macrophylla* Hydro-alcoholic extract and its fraction were subjected to the following test to detect presence of Tannins.

Ferric chloride test
Test solution was treated with few drops of 5% ferric chloride solution in water. Bluish black colour indicates the presence of Tannins.

Lead acetate test
Test solution was treated with 10% lead acetate solution. Formation of yellow precipitate indicates the presence of Tannins.

Detection of Steroids and Triterpenes
Liberman-Burchard's test
The extract was treated with few drops of acetic anhydride, boiled and cooled. Few drops of sulphuric acid was added through sides of test tube. Formation of reddish colour ring at the interface indicates the presence of steroids and triterpenes.

Salkowski's test
Extract was treated with chloroform and filtrates were treated with few drops of Conc. Sulphuric acid, shaken and allowed to stand. Appearance of red or violet colour at the interface indicates the presence of triterpenes.

Detection of Saponins
1 ml of Hydro-alcoholic extract and its fractions were diluted with in test tubes and shaken for a few minutes. Formation of froth indicates the presence of saponins.

TLC
T.L.C of the Hydro-alcoholic extract on silica gel G plate using n-Butanol: Acetic acid: Water (4:1:5) will be show under UV light (366nm) one conspicuous fluorescent spot at R_f. 0.82 (sky blue). On exposure to Iodine vapour two spots appear at R_f. 0.82 &0.92 (both yellowish).On spraying with ferric chloride (10% aqueous solution) two spots appear at R_f.0.82 & 0.92 (both grayish brown).

Lipinski's rule & Drug likeness
The rule was formulated by Christopher A Lipinski in 1997. The rule describes molecular properties important for a drug's pharmacokinetics in the human body, including their absorption, distribution, metabolism and excretion (ADME). The rule is important for drug development where a pharmacologically active lead structure is optimized stepwise for increased activity and selectivity, as well as drug like properties. The modification of the molecular structure often leads to drugs with higher molecular weight, more rings, more rotatable bond and a higher lipophilicity. The rule states that poor absorption or permeation are more likely when a ligand molecule violates Lipinski rule of 5, that is, has more than five hydrogen bond donors, the molecular weight is over 500, the log P is over 5 and the sum of N and O is over 10 [21, 22].

Druglikeness may be defined as a complex balance of various molecular properties and structure features which determine whether particular molecule is similar to the known drugs. These properties, mainly hydrophobicity, electronic distribution, hydrogen bonding characteristics, molecule size and flexibility and presence of various pharmacophoric features influence the behavior of molecule in a living organism, including bioavailability, transport properties, affinity to proteins, reactivity, toxicity, metabolic stability and many others [23]. This screening methodology was implemented to analyze the drug likeness of the proposed ligands as it influences the behavior of molecule in a living organism, including bioavailability, transport properties, affinity to proteins, reactivity, toxicity, metabolic stability, and many more. We screened the ligands against Lipinski rule of 5 using Molinspiration (http://www.molinspiration.com/)

Bioactivity Score
The drugs are also checked for the bioactivity by calculating the activity score for GPCR ligand, ion channel modulator, kinase inhibitor, nuclear receptor ligand. All the parameters were checked with the help of software Molinspiration drug-likeness score online (www. molinspiration.com). Calculated drug likeness score of each compounds and compared with the specific activity of each compound.

RESULTS AND DISCUSSION

Determination of Physiochemical parameters
Various phytochemical parameters were evaluated for aerial parts of *Callicarpa macrophylla* used as per guidelines by W.H.O. results are given in Table 2

Table 2: Physiochemical parameters of aerial parts of *Callicarpa macrophylla*

Parameter	Values % (w/w)
Total ash	5.0 %
Water soluble ash	4.8 %
Acid in-soluble ash	0.05%
Loss on drying	86.0 %

**Values are in mean, were as n=3*

Description of Hydro-alcoholic extracts of aerial parts of *Callicarpa macrophylla*
The hydro-alcoholic extracts prepared and evaluated for the different extractive values which are shown in Table 3.

Table 3: Percentage yield of the Hydro-alcoholic extract of aerial parts of *Callicarpa macrophylla*

Parameter	Values % (w/w)
Alcoholic extractive value	20.8%
Water soluble extractive value	4.80%

Preliminary Phytochemical Investigation

Phytochemical investigation of Aerial parts of *Callicarpa macrophylla* Hydro-alcoholic extracts and its fractions was done the microchemical tests and phytochemical screening results are shown in Table 4 and Table 5 respectively.

Table 4: Staining/Diagnosis/Microchemical tests

S.No.	Test	Observation	Characteristics
1.	Seed powder + Phloroglucinol + Conc. HCl (1:1)	Red colour	Lignified cell
2.	Dried powder +Dil. Iodine solution	Blue colour	Starch present
3.	Dried powder + Ruthenium red	Pink colour	Mucilagenous cells presents
4.	Dried powder + 1N HCl, boil, cool and filter. Residue+ Safranin	Red colour observed under microscope	Lignified tissue presents

Table 5: Phytochemical investigation of *Callicarpa macrophylla* Hydro-alcoholic extracts

S. No.	Test	Hydro-alcoholic extract of *Callicarpa macrophylla*
1.	**Test of alkaloids**	
	Wagner's test	- -
	Dragendorf's test:	- -
	Hager's test:	- -
2.	**Test of Flavonoids**	
	Shinoda test	+ +
	Ferric chloride test	+ +
	Sodium hydroxide test	+ +
3.	**Test of Tannins**	
	Ferric chloride test	+
	Lead acetate test	+
4.	**Test of Steroids and Triterpenes**	
	Liberman-Burchard's test	+
	Salkowski's test	+
5.	**Test of Saponins**	
	Foam test	+ +

(+) Indicate Presence, (-) Indicate absence

Drug likeness calculation on the basis of Lipinski rule of five

On the basis of literature survey we take 12 compounds from the plant and with the help of Molispiration softwere we calculate different properties of these compounds. These properties are calculated on the basis of Lipinski's rule of five, which states that any compound considered as drug should have partition coefficient less than 5, its polar surface area within 140 A^2, it should have H bond acceptor less than 10, it should have H bond donor less than 5 and its molecular weight within 500 doltan. The 15 compounds showed there values for different parameter and these values recorded in Table 6.

Table 6: Drug likeness score for compounds

S.N.	Compounds	milog P	TPSA	n atoms	MW	n ON	N OHNH	n violations	n rotb	volume
1.	Calliterpenone	2.84	57.53	23	320.47	3	2	0	1	321.68
2.	Luteolin	1.97	111.12	21	286.24	6	4	0	1	232.07
3.	Apigenin	2.46	90.89	20	270.24	5	3	0	1	224.05
4.	Ursolic acid	6.79	57.53	33	456.71	3	2	1	1	471.49
5.	Crategolic acid	5.81	77.75	34	472.71	4	3	1	1	479.18
6.	β-Sitosterol	8.62	20.23	30	414.72	1	1	1	6	456.52
7.	Betulinic acid	7.04	57.53	33	456.71	3	2	1	2	472.04
8.	α-Amyrenol	8.08	20.23	31	426.73	1	1	1	0	461.05
9.	Daucosterol	7.15	99.38	41	576.86	6	4	2	9	588.64
10.	Luteolin-7-O-glucuronide	0.07	207.35	33	462.36	12	7	2	4	355.37
11.	Apigenin-7-O-glucuronide	0.55	187.12	32	446.36	11	6	2	4	358.35
12.	Tricosanoic acid	9.28	37.30	25	354.62	2	1	1	21	409.04
13.	Tetracosanoic acid	9.41	37.30	26	368.65	2	1	1	22	425.84
14.	Ethyl tricosanoate	9.45	26.30	27	382.67	2	0	1	23	443.37
15	Calliterpenone monoacetate	3.54	63.60	26	362.51	4	1	0	3	358.19
13.	Silibinin	1.47	155.14	35	482.441	10	5	0	4	400.86

Biological activity of compounds

15 compounds of the plant which fulfill the requirements of Drug likeness were taken for biological activity calculation with the help of Molinspiration software and compared with standard drug Silibinin. On the basis of mechanism of action of Silibinin i.e. enzyme inhibition, we compare compound for there hipatoprotective activity. As shown in Table 7 and after comparison with Silibinin we find that 12 compounds, Calliterpenone, Luteolin, Apigenin, Ursolic acid, Crategolic acid, β-Sitosterol, Betulinic acid, α-Amyrenol, Daucosterol, Luteolin-7-O-glucuronide, Apigenin-7-O-glucuronide and Calliterpenone monoacetate showed batter enzyme inhibition than

Silibilin. These 12 compounds was also showed good Nuclear receptor ligand affinity and it was clearly shown that out of these 12 compounds, Calliterpenone, Luteolin, Apigenin, Ursolic acid, Crategolic acid, β-Sitosterol, Betulinic acid, α-Amyrenol, Daucosterol, Luteolin-7-O-glucuronide, Apigenin-7-O-glucuronide and Calliterpenone monoacetate showed excellent Nuclear receptor ligand affinity. 2 compounds β - sitosterol, and Crategolic acid showed good protease inhibition than Silibinin and 2 compounds Luteolin and Apigenin showed better kinese inhibition as Slilibinin.

Table 7: Bioactivity score of the compounds

S.N.	Compounds	GPCR ligand	Ion channel modulator	Kinese inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1.	Calliterpenone	0.21	0.14	-0.32	0.56	0.04	0.50
2.	Luteolin	-0.02	-0.07	0.26	0.39	-0.22	0.28
3.	Apigenin	-0.07	-0.09	0.18	0.34	-0.25	0.26
4.	Ursolic acid	0.28	-0.03	-0.50	0.89	0.23	0.69
5.	Crategolic acid	0.24	-0.16	-0.41	0.81	0.20	0.62
6.	β-Sitosterol	0.14	0.05	-0.51	0.73	0.07	0.51
7.	Betulinic acid	0.31	0.03	-0.50	0.93	0.14	0.55
8.	α-Amyrenol	0.22	-0.02	-0.41	0.29	0.19	0.60
9.	Daucosterol	0.15	-0.21	-0.47	0.33	0.11	0.41
10.	Luteolin-7-O-glucuronide	0.11	-0.03	0.01	0.40	0.01	0.42
11.	Apigenin-7-O-glucuronide	0.12	-0.03	-0.01	0.44	0.03	0.43
12.	Tricosanoic acid	0.16	0.04	-0.10	0.22	0.18	0.16
13.	Tetracosanoic acid	0.15	0.04	-0.09	0.21	0.17	0.15
14.	Ethyl tricosanoate	-0.03	-0.05	-0.18	0.03	0.03	0.01
15.	Calliterpenone monoacetate	0.20	0.16	-0.36	0.55	0.13	0.45
Std.	Silibinin	0.07	-0.05	0.01	0.16	0.02	0.23

CONCLUSION

The Phytochemical screening and Pharmacognostical evaluation parameters of *Callicarpa macrophylla* were performed and it showed the presence of many pharmacological active phyto-constituents. Effective formulations to be developed using indigenous medicinal plants, with proper pharmacological experiments and clinical trials. The manufacture of Herbal products should be governed by standards of safety and efficacy. So finally we concluded that these phytochemical screening data and phytochemical investigation of extract of *Callicarpa macrophylla* in Ethanolic and water useful for further studies of pharmacological parameters.

On comparision of compounds 1 to15 with silibinin by Molinspiration software, compounds Calliterpenone, Luteolin, Apigenin, Ursolic acid, Crategolic acid, β-Sitosterol, Betulinic acid, α-Amyrenol, Daucosterol, Luteolin-7-O-glucuronide, Apigenin-7-O-glucuronide and Calliterpenone monoacetate almost fulfills the Lipinski rule of five and showed good bioactivity score than Silibinin. Our study shows that compounds Calliterpenone, Ursolic acid, Crategolic acid, β-Sitosterol, Betulinic acid, Luteolin-7-O-glucuronide, Apigenin-7-O-glucuronide and Calliterpenone monoacetate has good bioactivity score as compared to Silibinin which is potent hepatoprotective drug. So these compounds can be considered as lead compounds with hepatoprotective activity from *Callicarpa macrophylla.* These compounds may be used as lead for further synthesis of bioactive scaffolds and their SAR study will help in the production of new drugs having hepatoprotective activity.

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