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Pharmacognostical, Phytochemical Evaluation and *in silico* lead finding of *Ficus bengalensis* Linn 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 *Ficus bengalensis* 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. Twelve compounds from the whole plant of *Ficus bengalensis* 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. 9 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, Friedelin, β - sitosterol, 3,5,7-trimethyl ether of delphinidin-3-O-α-L rhamnoside, 3,5 dimethyl ether of leucocynaidin-3-O-β-D-glactosylcellobioside and 20-tetratriacontene-2-one fullfill Lipinski rule of five & showed good bioactivity score than Silibinin.

Out of 12 compounds Friedelin, β-sitosterol and 5 dimethyl ether of leucocynaidin-3-O-β-D-glactosylcellobioside showed good bioactivity score as compared to Silibinin. So these compounds can be considered as lead compounds with hepatoprotective activity from *Ficus bengalensis.*

Keywords: *Ficus bengalensis*, Hepatoprotective, Insilico lead finding, Molinspiration, Lipinski's rule.

1. Introduction

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. It exhibits a wide range in topography and climate, which has a bearing on its vegetation and floristic composition. Moreover, the agro-climatic conditions are conducive for introducing and domesticating new exotic plant varieties.[1] In recent years, secondary plant metabolites (phytochemicals), previously with unknown pharmacological activities, have been extensively investigated as a source of medicinal agents.[2]

Ficus bengalensis Linn. (Syn: *Ficus indica*: Family: *Moraceae*), commonly known as Bargad grows in tropical and subtropical region of India. *Ficus bengalensis* has been reported different bioactive compound such as Bengalenosides, Flavanoids and Leucocyanidin, Taraxasterol tiglate from heart wood; qucertin -3-galatosideand rutin isolated from leaves.[3] Various scientific studies have been carried out on *F. benghalensis* and various pharmacological activities have been reported. It has been reported to possess immunomodulatory [4], hypoglycemic [5], antioxidant [6], antistress and antiallergic[7] and anthelmintic[8] activities. A glucoside, bengalenoside was isolated from *F. benghalensis* and evaluated for hypoglycemic activity.[9] 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 aerial root is styptic, aphrodisiac, and useful in gonorrhea, syphilis, dysentery. In addition several therapeutic effects have been shown for different parts of *Ficus bengalensis* such as Anti-tumor activity.[10]

On the basis of literature survey we find may compound isolated from plant *Ficus bengalensis* Linn some of them are Friedelin, β – sitosterol, Quercetin-3-galactoside, 3,5,7- trimethyl ether of leucocyanidine, 3,5,7-trimethyl ether of delphinidin-3-O-α-L rhamnoside, 3,5 dimethyl ether of leucocynaidin-3-O-β-D-glactosylcellobioside, 5,7 dimethyl ether of leucopelargonidin-3-O-α-L-rhamnoside, β sitosterol-α-Dglucose, 20-tetratriacontene-2-one, 6-heptatriacontene-10-one, Pentatriacontene-5-one, Mesoinositol.[11-15]

In this paper we describes the morphological and phytochemical aspects of *Ficus bengalensis* and compare different compounds isolated from plant *Ficus bengalensis* Linn 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.

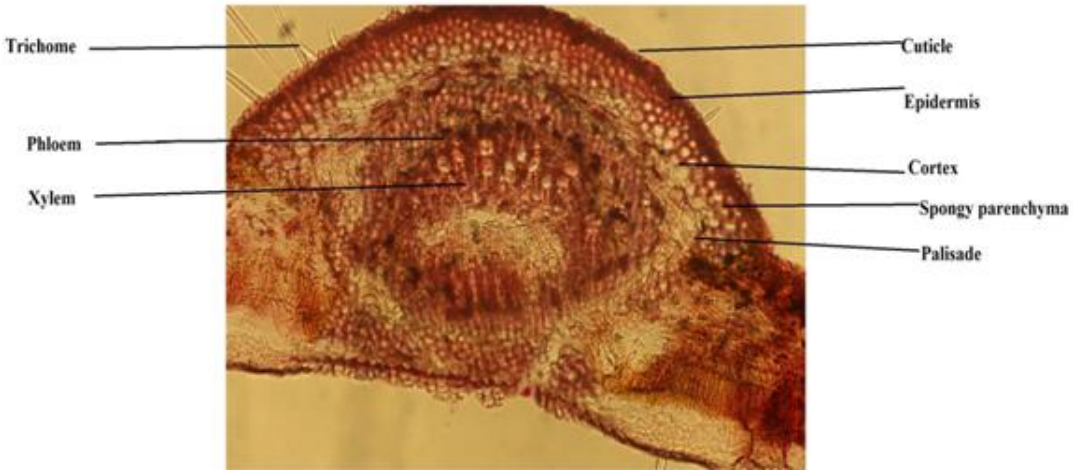
2. Material and methods

2.1 Plant material collection

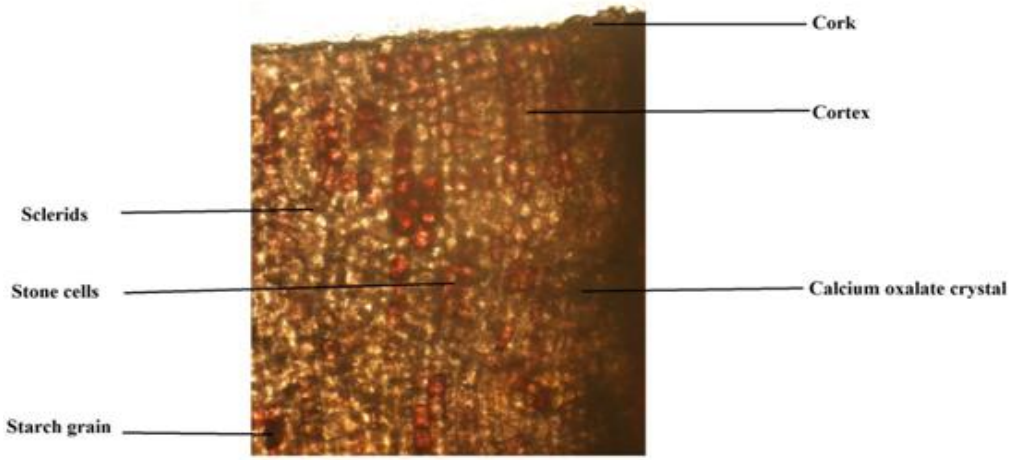
Plant sample was collected from local market of the Lucknow. Plant was authenticated (National Botanical Research Institute, Lucknow Ref. NO: NBRI/CIF/260/2011) and specimen herbarium were preserved at institute library. The leaves and bark were separated from other parts, washed, cleaned and dried for further study.

2.2 Leaf & Bark Morphology

The external leaf and bark morphology was observed and studied. Fresh mature leaf transverse section was taken. Whereas dried leaves and bark powder material was used for determination of ash value, extractive value, and phytochemical constituents. All the reagents used were of analytical grade obtained from Loba Chemical Pri Ltd, Mumbai, India, Jiangsu Huaxi International Trade Co. Ltd China, Merck specialties Pri.Ltd, Mumbai, Sigma chemical Ltd.



A. transverse section of leaf of *Ficus bengalensis*



B. transverse section of bark of *Ficus bengalensis*

Figure 1: Transverse section of leaf & bark of *Ficus bengalensis*

The leaves are green spirally arranged on branch, up to 10-30 cm long and 8-20 cm wide, coriaceous, ovate, base rounded. The microscopic character of leaf and bark shows in transverse section. (Figure 1)

2.3 Physical parameters

2.3.1 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. 5 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.

2.3.2 Ash Values

Total ash value and acid-insoluble ash value was calculated with reference to air dried drug. 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 with reference to air-dried substance.

2.3.3 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 with reference to air-dried substance.

2.3.4 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 with reference to air-dried substance.

2.3.5 Extractive Values

Extractive values in different solvent like alcohol (95%), water and chloroform was determined. 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.

2.3.6 Lipinski's rule & Druglikeness

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.[16,17]

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.[18] 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/)

2.4 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 druglikeness score of each compounds and compared with the specific activity of each compound.

3. Result and discussion

3.1 Pharmacognostical & Phytochemical Evaluation

Moisture content, ash value and extractive value of leaves and bark powder given in Table 1 and Table 2 respectively. Different phytochemical screening of crude powdered leaves and bark showed presence of tannins, starch, flavanoids, glycosides, steroids and protein, given in Table 3, Phytochemical screening of three different extract

was also done in water, alcohol and chloroform for both leaves (Table 4) and bark (Table 5). This phytochemical screening proved the presence of chemical constituent like tannins, alkaloids, proteins, starch, flavanoids, and glycoside. R_f value for Ethanolic and water extract of leaf and bark is given in table 6 and TLC plates confirms the R_f value are shown in figure 2.

Table 1: Physical Parameters of Powdered of F. Bengalensis (Leaves)

Loss on drying	Total ash (%w/w)	Water soluble Ash (%w/w/)	Acid insoluble Ash (%w/w/)	Water soluble Extractive value (%w/w/)	Alcohol soluble Extractive value (%w/w/)	Chloroform water soluble Extractive value (%w/w/)
88.70%	8.75	3.5	0.6	15.68	16.43	3.79

Table 2: Physical Parameters of Powdered of F. Bengalensis. (Bark)

Loss on drying	Total ash (%w/w)	Water soluble Ash (%w/w/)	Acid insoluble Ash (%w/w/)	Water soluble Extractive value (%w/w/)	Alcohol soluble Extractive value (%w/w/)	Chloroform water soluble Extractive value (%w/w/)
87.6	9.5	3.6	1.2	5.056	15.16	6.32

Table 3: Phytochemical Investigation

S.N.	Chemical test for powder analysis	Powdered leaves	Powdered bark
1	Picric Acid	_ _ _ (Alkaloid)	_ _ _ (Alkaloid)
2	Con. Sulphuric acid	+++ (Steroid/Triterpenoid)	+++(Steroid/Triterpenoid)
3	Aq. Ferric chloride	+ + Tannins	+ + Tannins
4	Iodine Solution	+ + Starch	+ + Starch
5	5%PotassiumHydroxide	+ + Glycosides	+ + Glycosides
6	Mayer Reagents	_ _ _ (Alkaloid)	_ _ _ (Alkaloid)
7	Aq. NaOH	+++ Flavanoids	+++ Flavanoids
8	Aniline + Suphuric acid	_ _ _ Lignified cells	_ _ _ Lignified cells
9	Phloroglucinol+ HCl	+++Xylum,Sclerenchyma	+++Xylum,Sclerenchyma
10	Weak iodine solution	+++ Starch	+++ Starch
11	Suphuric acid	+++(Calcium oxalate, mono, di, tri radiate)	_ _ _
12	Millar reagents	+ (Protein test)	+++ (Protein test)

Table 4: Different Extract Analysis (Leaves extract)

S.N.	Name of the test	Ethanolic extract	Chloroform water extract	Aq. Extract
1	Mg-HCl	+ + + Flavanoids	_ _ _	+ + + Flavanoids
2	Benedicts test	++ Carbohydrate	_ _ _	+ + Carbohydrate
3	Mayer's test	+ + + Alkaloids	+ + + Alkaloids	+ + + Alkaloids
4	Hager's Reagent	+ + + Alkaloids	+ + + Alkaloids	+ + + Alkaloids
5	Con. Suphuric acid	+++ Steroids/Terpenoids	+++ Steroids/Terpenoids	+++ Steroids/Terpenoids

Table 5: Different Extract Analysis (Bark extract)

S.N.	Name of the test	Ethanolic extract	Ethanolic extract	Aq. Extract
1	Benedict solution	+ + Carbohydrate	_ _ _	_ _ _
2	Aq.Silver nitrate	+ + (Protein)	_ _ _	_ _ _
3	Mg-HCl	+ + + (Flavanoids)	_ _ _	+ + (Flavanoids)
4	Hager's Reagent	+ + + Alkaloids	+ + + Alkaloids	+ + + Alkaloids
5	Mayer reagent	+ + + Alkaloids	+ + + Alkaloids	+ + + Alkaloids
6	Con.Suphuric acid	+++ Steroids/Terpenoids	+++ Steroids/Terpenoids	+++ Steroids/Terpenoids

Table 6: Rf Values for different extract by TLC

S. N.	Ethanolic extract of leaves	Ethanolic extract of bark	Water extract of leaves	Water extract of bark
1	Solvent system, Ethyl acetate: Frmicacid: GAA: Water (100:11:11:26)	Solvent system Butanol: Acetic acid: Water(4:1:5)	Solvent system Ethyl acetate: Frmic acid: GAA: Water (100:11:11:26)	Solvent system Ethyl acetate: Frmic acid: GAA: Water (100:11:11:26)
2	Rf = 0.88	Rf=0.327,0.290, 0.309	Rf = 0.27, 0.70, 0.88,	Rf = 0.66, 0.68

Figure 2: showing TLC of leave and bark extract of *Ficus bengalensis* Linn

3.2 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 software 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 12 compound showed there values for different parameter and these values recorded in Table 7.

Table 7: Drug likeness score for compounds

S.N.	Compounds	milog P	TPSA	n atoms	MW	n ON	N OHNH	n violations	n rotb	volume
1.	Friedelin	7.854	17.071	31	426.729	1	0	1	0	461.050
2.	β - sitosterol	8.051	20.228	30	414.718	1	1	1	6	456.543
3.	Quercetin-3-galactoside	1.444	210.503	39	548.541	12	8	3	5	470.192
4.	3,5,7- trimethyl ether of leucocyanidine	2.384	77.392	25	346.379	6	2	0	4	313.312
5.	3,5,7-trimethyl ether of delphinidin-3-O-α-L rhamnoside	0.299	176.772	36	510.492	12	6	3	6	436.649
6.	3,5 dimethyl ether of leucocynaidin-3-O-β-D-glactosylcellobioside	0.772	147.31	33	464.467	10	5	0	5	403.086
7.	5,7 dimethyl ether of leucopelargonidin-3-O-α-L-rhamnoside	-4.48	346.07	59	848.801	22	13	3	14	717.208
8.	β sitosterol-α-Dglucose	7.152	99.38	41	576.859	6	4	2	9	588.638
9.	20-tetratriacontene-2-one	10.135	17.071	35	490.901	1	0	1	30	579.409
10.	6-heptatriacontene-10-one	10.305	17.071	38	532.982	1	0	2	33	629.815
11.	Pentatriacontene-5-one	10.252	17.071	36	506.944	1	0	2	32	602.398
12.	Mesoinositol	-2.387	121.368	12	180.156	6	6	1	0	150.866
13.	Silibinin	1.465	155.14	35	482.441	10	5	0	4	400.862

3.3 Biological activity of compounds

9 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, protease inhibition and kinese inhibition we compare compound for there hipatoprotective activity. As shown in Table no.2 and after comparison with Silibinin we find that 5 compounds, Friedelin, β - sitosterol, Quercetin-3-galactoside, 3,5,7-trimethyl ether of delphinidin-3-O-α-L rhamnoside, 3,5 dimethyl ether of leucocynaidin-3-O-β-D-glactosylcellobioside, β sitosterol-α-Dglucose, showed batter enzyme inhibition than Silibilin, five compounds Friedelin, β - sitosterol, Quercetin-3-galactoside, 3,5,7-trimethyl ether of leucocyanidine, β sitosterol-α-Dglucose showed good Nuclear receptor ligand 2 compounds β - sitosterol, and 3,5 dimethyl ether of leucocynaidin-3-O-β-

D-glactosylcellobioside showed good protease inhibition with Silibinin and 3 compounds 3,5,7-trimethyl ether of delphinidin-3-O-α-L rhamnoside, 3,5 dimethyl ether of leucocynaidin-3-O-β-D-glactosylcellobioside, β sitosterol-α-Dglucose showed good kinese inhibition as Slilibinin. Results are given in Table 8.

Table 8: Bioactivity score of the compounds

S.N.	Compounds	GPCR ligand	Ion channel modulator	Kinese inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1.	Friedelin	0.02	-0.06	-0.39	0.39	0.02	0.21
2.	β - sitosterol	0.26	0.22	-0.42	0.68	0.18	0.51
3.	Quercetin-3-galactoside	0.03	-0.18	0.19	0.24	-0.03	0.25
4.	3,5,7- trimethyl ether of leucocyanidine	0.12	-0.04	0.00	0.25	0.04	0.18
5.	3,5,7-trimethyl ether of delphinidin-3-O-α-L rhamnoside	0.14	0.03	0.06	0.08	0.11	0.35
6.	3,5 dimethyl ether of leucocynaidin-3-O-β-D-glactosylcellobioside	0.19	0.09	0.06	0.15	0.15	0.37
7.	5,7 dimethyl ether of leucopelargonidin-3-O-α-L-rhamnoside	-2.01	-3.12	-2.81	-2.86	-1.48	-2.33
8.	β sitosterol-α-Dglucose	0.15	-0.21	-0.41	0.33	0.11	0.41
9.	20-tetratriacontene-2-one	-0.00	-0.05	-0.25	0.08	0.00	0.09
10.	6-heptatriacontene-10-one	0.03	-0.12	-0.17	0.10	0.05	0.07
11.	Pentatriacontene-5-one	0.00	-0.06	-0.17	0.08	0.05	0.05
12.	Mesoinositol	-0.67	-0.11	-0.82	-0.72	-0.67	-0.17
Std.	Silibinin	0.07	-0.05	0.01	0.16	0.02	0.23

4. Conclusion

The Phytochemical screening and Pharmacognostical evaluation parameters of *Ficus bengalensis* were performed. 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 different extract of *Ficus bengalensis* in Ethanolic and water extract useful for further studies of pharmacological parameters.

On comparision of compounds 1 to12 with silibinin by Molinspiration software, compounds Friedelin, β - sitosterol, 3,5,7-trimethyl ether of delphinidin-3-O-α-L rhamnoside, 3,5 dimethyl ether of leucocynaidin-3-O-β-D-glactosylcellobioside and 20-tetratriacontene-2-one fullfill Lipinski rule of five & showed good bioactivity score than Silibinin. Our study shows that compounds Friedelin, β-sitosterol and 5 dimethyl ether of leucocynaidin-3-O-β-D-glactosylcellobioside 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 *Ficus bengalensis.* These compounds may be used as lead for further synthesis of bioactive scaffolds and their SAR study.

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References

[1]. Martins AP, Saguaro L, Gonçalves MJ, da Cunha AP, Vila R, Can igueral S, Mazzoni V, Tomi F, Casanova J. Essential oil composition and antimicrobial activity of three Zingiberaceae from S. Tome e Principle. *Planta Med* 2001; 67:580-584.

[2]. Alluri VK, Tayi VNR, Dodda S, Mulabagal V, Hsin-Sheng T, and Gottumukkala V. Assessment of bioactivity of Indian medicinal plants using Brine shrimp (*Artemia salina*) lethality assay. *Int J Appl Sci Eng* 2005; 2:125-134.

[3]. Subramanian SS, Nair AGR. Sterol & Flavonols of Ficus Bengalensis. *Phytochemistry* 1970; 9:2583-2584.

[4]. Gabhe SY, Tatke PA, Khan TA. Evaluation of the Immunomodulatory activity of the methanol extracts of *Ficus benghalensis* roots in rats. *Indian J Pharmacol* 2006; 38:271-275.

[5]. Deshmukh VK, Shrotri DS, Aiman R. Isolation of a hypoglycemic principle from the bark of *Ficus bengalensis. Indian J Physiol Pharmacol* 1960; 4:182-185.

[6]. Shukla R, Gupta S, Gambhir JK, Prabhu KM, Murthy PS. Antioxidant effect of aqueous extract of the bark of *Ficus bengalensis* in hypercholesterolaemic rabbits. *J Ethnopharmacol* 2004; 92:47-51.

[7]. Taur DJ, Nirmal SA, Patil RY, Kharya MD. Antistress and antiallergic effects of *Ficus bengalensis* bark in asthma. *Nat Prod Res* 2007; 21:1266-1270.

[8]. Aswar M, Aswar U, Watkar B, Vyas M, Wagh A, Gujar KN. Anthelmintic activity of *Ficus benghalensis. Int J Green Pharma* 2008; 2:170-172.

[9]. Augusti KT. Hypoglycemic action of bengalenoside: A glucoside isolated from *Ficus benghalensis* Linn. in normal and alloxan diabetic rabbits. *Indian J Physiol Pharmacol* 1975; 19:218-20.

[10]. Mousa O, Vuorela P, Kiviranta J, Wahab SA, Hiltunen R, Vuorela H. Bioactivity of Certain Egyptian Ficus Species. *J Ethnopharmacol* 1994; 41:71-76.

[11]. Subramanian PM, Misra GS.Chemical constituents of *Ficus bengalensis. Indian J chem.* 1977; 15B:762-766.

[12]. Sheeja C, Kumar RV, Augusti KT, Kidwai JR. Antidiabetic effect of glycoside of Pelargonidin isolated from the bark of *Ficus bengalensis* linn. *Indian J Biochem biophys* 1992; 29:380-382.

[13]. Kumar RV, Augusti KT. Antidiabetic effect of a leucocynidin derivative isolated from the bark of *Ficus bengalensis* Linn. *Indian J Biochem Biophys* 1989; 26(6):400-404.

[14]. Subramanian PM, Misra GS. Chemical constituents of *Ficus bengalensis* (Part II). *Pol J Pharmacol Pharm* 1978; 30(4):559-62.

[15]. Daniel RS, Devi KS, Augusti KT. Mechanism of action of Antiatherogenic and related effects of *Ficus bengalensis* Linn. Flavonoids in experimental animals *Indian J Exp Biol* 2003; 41:296-303.

[16]. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Adv Drug Deliv Rev* 2001; 46:3-26.

[17]. Lipinski CA. Drug-like properties and the causes of poor solubility and poor permeability. *J Pharmacol Toxicol Methods* 2000; 44:235-236.

[18]. Patel R, Shukla PK, Verma A, Singh MP. Pharmacognostical, phytochemical evaluation and *insilico* lead finding of *Callicarpa macrophylla with* hepatoprotective potentials. *J. Chem. Pharm. Res* 2016; 8(3): 383-393.