

Phytochemistry, pharmacology, toxicology, and clinical trial of *Ficus racemosa*

Rajnish Kumar Yadav, Bankim Chandra Nandy¹, Siddhartha Maity², Srimanta Sarkar³, Sudipta Saha

Department of Pharmaceutical Sciences, Babasaheb Bhimrao Ambedkar University, Lucknow, Uttar Pradesh, ¹Department of Pharmaceutical Sciences, Jyoti Vidyapeeth Women's University, Jaipur, Rajasthan, ²Department of Pharmaceutical Technology, Jadavpur University, Kolkata, West Bengal, India, ³Department of Pharmacy, National University of Singapore, Singapore

Submitted: 26-02-2014

Revised: 27-03-2014

Published: 05-05-2015

ABSTRACT

Ficus racemosa is an important medicinal plant, found in India, Australia, and Southeast Asia. It is popularly known as 'gular.' It reduces blood glucose concentration due to the presence of β -sitosterol. Many active constituents that have been isolated from various parts of this plant possess useful pharmacological activities. The literature survey proposed that it has multiple pharmacological actions that include antidiabetic, antioxidant, antidiarrhoeal, anti-inflammatory, antipyretic, antifungal, antibacterial, hypolipidemic, antifilarial, and hepatoprotection. This review article elaborately describes the traditional uses, phytochemistry, pharmacology, and toxicology of this plant. We also provide useful structures of the secondary metabolites along with their nuclear magnetic resonance (NMR) data. Some clinical trial data have also been provided in this review. This review would assist researchers to gather scientific information in future.

Key words: Clinical trial, *Ficus racemosa*, pharmacology, phytochemistry, toxicology, traditional uses

INTRODUCTION

The demands of herbal medicines are increasing because their potent pharmacological activity and economical values have been proving to be beneficial for the people. However, a lot of research is necessary to standardize and validate Ayurveda medicines for their potency, safety, and efficacy.^[1] *Ficus racemosa* (*F. racemosa*) is native to India, Australia, and Southeast Asia. It is distributed widely from the outer Himalayan ranges, Punjab, Khasia Mountain, Chota Nagpur, Bihar, Orissa, West Bengal, Rajasthan, Deccan, and is common in South India.^[2,3] The active constituent, β -sitosterol, isolated from the leaves and stem bark, has a good antidiabetic potential. This plant has multiple pharmacological activities that include antidiabetic, antioxidant, antidiarrheal, anti-inflammatory, antipyretic,

antifungal, antibacterial, hypolipidemic, and antifilarial, and hepatoprotective actions.^[4-6] We describe the pharmacology, toxicology, phytochemistry, and clinical trials of this plant elaborately in this review article. We also provide structures and nuclear magnetic resonance (NMR) data of active constituents and their pharmacological actions, in a tabular format, in this review.

Phytochemistry

The following active chemical constituents have been reported in *F. racemosa* and their structures are shown in Figure 1. Few spectral data of active constituents are summarized in Table 1.

Leaf

The leaves of this plant are rich in flavonoids, triterpenoids (basically lanosterol), alkaloids, and tannins. A new triterpene namely gluanol acetate and racemosic acid were isolated from the same part.^[14]

Stem bark

Bergenin (flavonoid) was the major component of the stem bark, which was isolated using both the hot and cold water extraction methods. In addition, kaempferol and coumarin were also extracted in a purified form by using the hot water extraction method. The other major components obtained from the stem bark were glycosides (leucocyanidin-3-O- β -D-glucopyranoside, leucopelargonidin-3-O- β -D-glucopyranoside, leucopelargonidin-3-O- β -D-glucopyranoside, and leucopelargonidin-3-O- α -L-rhamnopyranoside); sterols (β -sitosterol, stigmasterol, α -amyrin acetate, lupeol, and lupeol acetate); and tannins (ellagic acid).^[15]

Address for correspondence:

Dr. Sudipta Saha, Department of Pharmaceutical Sciences, Babasaheb Bhimrao Ambedkar University, Vidya Vihar, Rai Bareilly Road, Lucknow - 226 025, Uttar Pradesh, India.
E-mail: sudiptapharm@gmail.com

Access this article online

Quick Response Code:



Website:

www.phcogrev.com

DOI:

10.4103/0973-7847.156356

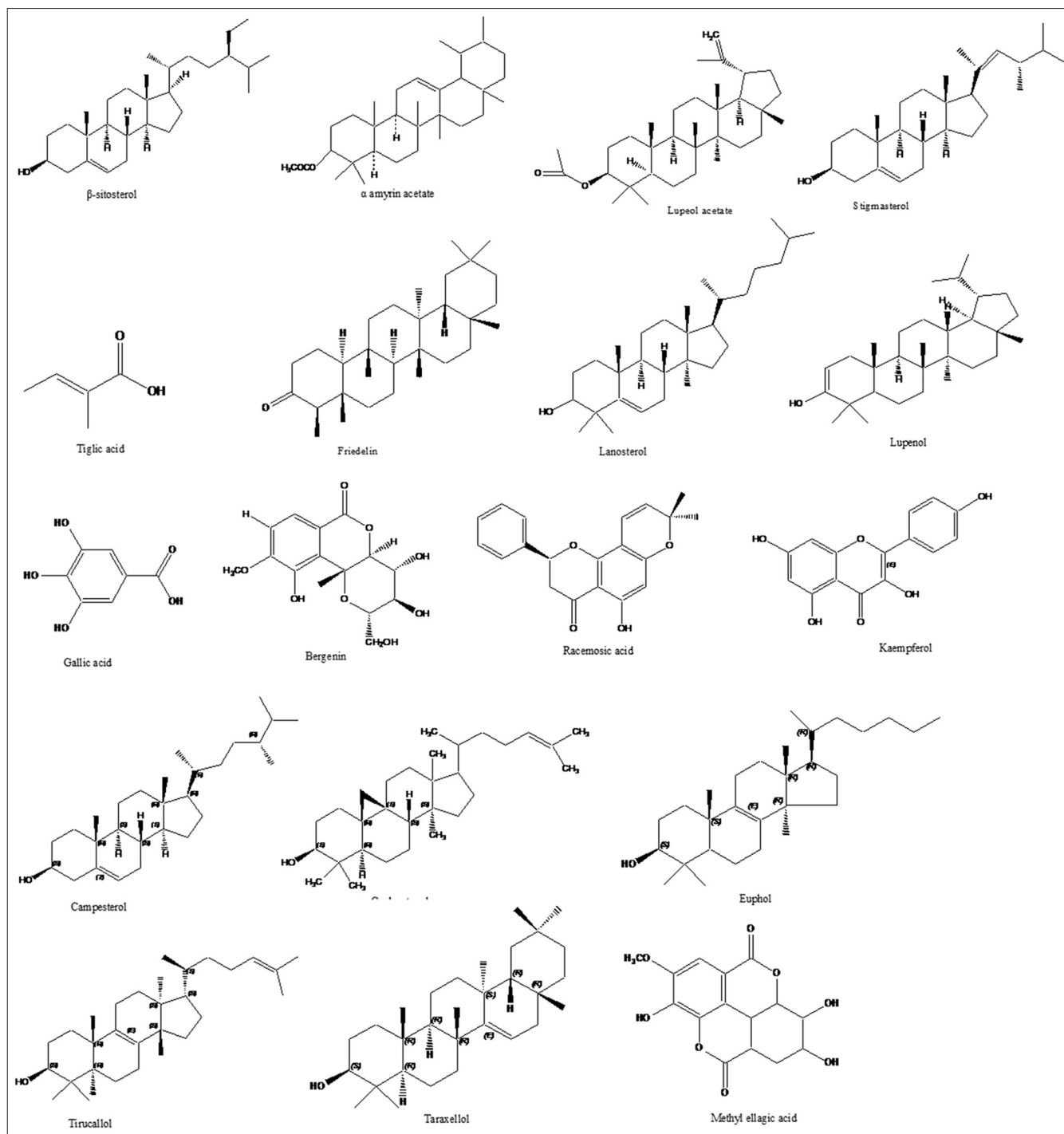


Figure 1: Chemical structure of the active constituents of *F. racemosa*

Trunk bark

The trunk bark is rich in various types of sterols like β -sitosterol, lupenol, and stigmasterol.^[14]

Fruits

Glucanol acetate is the major component of fruits. The other components are glucanol, tiglic acid, taraxasterol, lupeol acetate, friedelin, and hydrocarbons.^[16]

Latex

The latex contains various types of steroids such as euphol, isoeuphorbol, β -sitosterol, 4-deoxyphorbol, cycloartenol, and cycloeuphordenol.^[16]

Traditional uses

From ancient times all the parts of this plant have been used for their medicinal value. It is basically used for its antidiuretic effect. In the Ayurvedic System of Medicine, the roots are popularly used

Table 1: Spectrometry data of few active constituents of *F. racemosa*

Name	¹ H NMR	¹³ C NMR	Others (IR, Mass spectra)	References
β-Sitosterol	δ- 3.2 (1H, m, H-3), δ- 5.6 (1H, m, H-6), δ-5.19 (1H, m, H-23), δ-4.68 (1H, m, H-22) δ- 4.68 (1H, m, H-3), δ-2.38 (1H, m, H-20), δ- 0.76-0.89 (M, 9H), δ-0.91-1.05 (m, 5H), δ- 1.35-1.42 (m, 4H), δ- 0.69-0.73 (m, 3H), δ- 1.8-2.00 (m, 5H), δ- 1.07-1.13 (m, 3H), δ- 1.35-1.6 (m, 9H)	150.98, 145.2 (C-5), 139.8 (C-22), 121.7, 118.89 (C-6), 79.03 (C-3), 55.3 (C-14), 55.18 (C-17), 50.45 (C-9), 48.3 (C-9), 40.8 (C-20), 40.1 (C-12), 39.2 (C-13), 38.9(C-4), 38.6 (C-12), 37.18 (C-1), 37.12 (C-10), 36.3 (C-8), 35.59 (C-20), 34.29 (C-22), 34.24 (C-7), 32.66 (C-8), 26.1 (C-11, 26), 21.6 (C-27), 19.32 (C-19), 17.71 (C-21), 15.6 (C-18,29)	IR spectra: O-H stretching - 3373.6 cm ⁻¹ Aliphatic C-H stretching - 940.7, 2867.9 cm ⁻¹ C=C - 1641.6 cm ⁻¹ CH ₂ -1457.3 cm ⁻¹ OH- def - 1381.6 cm ⁻¹ Cycloalkane - 1038.7 cm ⁻¹ Mass spectra: Molecular formula- C ₂₈ H ₅₀ O m/z=367, 271, 255, 229, 189, 175, 161, 133, 121, 105, 107, 95, 81, 69, 55, 41	[7]
Stigmasterol	δ- 7.30 (s, OH-3) δ-5.14 (m, 1H, H-6) δ-4.60 (s, 1H, H-23) δ-4.23 (s, 1H, H-23) δ-3.51 (tdd, H-3, H-3) δ-1.21 (s, 3H, H-19) δ-1.17 (s, 3H, H-28) δ-1.03 (s, 3H, H-27) δ-0.99 (s, 3H, H-26) δ-0.97 (s, 3H, H-24) δ-0.90 (s, 3H, H-29)	140.9 (C-22), 158.53 (C-5), 129.50 (C-23),121.89 (C-6), 71.9 (C-3), 57.1 (C-4), 56.2 (C-5), 51.4 (C-24), 50.40 (C-17), 42.5 (C-9), 42.4 (C-13), 40.7 (C-10), 39.9 (C-10), 37.5 (C-20), 32.9 (C-25), 31.9 (C-21), 29.1 (C-23), 25.6 (C-12), 24.6 (C-11), 21.5 (C-25), 21.3 (C-26), 19.2 (C-29), 12.3 (C-27)	IR spectra: O-H broad band - 3335, 3431 cm ⁻¹ , intense- 1193, 667 cm ⁻¹ , C-H out of plane - 879 cm ⁻¹ , C=C - 1667 cm ⁻¹ , CH ₃ -2934 cm ⁻¹ , CH ₂ -2866 cm ⁻¹ , medium - 1459 cm ⁻¹ C-C - 1036 cm ⁻¹ Mass spectra: m/z=412, 144, 198, 229, 243, 264, 265, 289, 346, 382, 391, 396	[8]
Lipeol acetate	δ-4.69 (1H, s, H-29b) δ-4.57 (1H, s, H-29a) δ-4.47 (1H, dd, H-3) δ-2.05 (3H, s, H-2) δ-1.69 (3H, s, H-30) δ-1.03 (3H, s, H-25) δ-0.94 (3H, s, H-27)	171.3 (C-1), 151.2 (C-2), 109.6 (C-29), 81.2 (C-3), 55.6 (C-5), 50.5 (C-9), 48.5 (C-18), 48.2 (C-19), 43.2 (C-17), 43 (C-14), 41 (C-8), 40.2 (C-22),38.6 (C-1), 38 (C-4), 37.3 (C-10), 36.2 (C-13), 35.8 (C-16), 34.4 (C-7), 30.0 (C-21), 28.2 (C-2), 27.6 (C-23), 25.3 (C-15), 24.0 (C-12), 21.7 (C-2), 21.1 (C-11), 18.2 (C-28), 16.7 (C-24), 16.4 (C-25), 16.2 (C-25), 14.7 (C-27)	Mass spectra: m/z=468,453, 408, 357,218, 189,109	[9]
Lupeol	δ- 4.70, 4.55 (2H, s, H-29a, 29b), δ- 3.2 (1H, m, H-3) Seven singlet δ= 0.77, 0.79,0.85, 0.94, 0.97, 1.05, 1.65 (each 3H, s)	151.0 (C-20), 109 (C-29), 70.0 (C-3), 55.5 (C-9), 48.3 (C-18), 48.0 (C-19), 43 (C-17), 42.9 (C-14), 40.9 (C-8), 40.0 (C-22), 38.9 (C-4), 38.7 (C-1), 38.1 (C-13), 37.2 (C-10),35.5 (C-16), 34.2 (C-7), 29.9 (C-21), 28.0 (C-23), 27.4 (C-2),27.1 (C-15), 25.2 (C-12), 21.0 (C-11), 19.5 (C-30), 18.5 (C-6), 18.0 (C-28), 16.1 (C-25), 16.0 (C-26), 15.5 (C-24), 14.8 (C-27)	IR spectra: OH - 3056 cm ⁻¹ C-O - 1265 cm ⁻¹ C-H unsaturated - 893 cm ⁻¹ C=C - 1593 cm ⁻¹ CH ₃ Stretching - 2929 cm ⁻¹ Bending - 1593 cm ⁻¹ CH - 1435 cm ⁻¹ Mass spectra : Molecular formula C ₃₀ H ₅₀ O m/z=426, 365, 207, 189, 161, 135, 107	[9,10]
α-Amyrin	δ- 0.79 (3H, s, H-28) δ-0.88 (12H, s, H-23, 24, 29, 30) δ-0.98 (3H, s, H-26) δ-1.01 (3H, s, H-25) δ- 1.07 (3H, s, H-27) δ-2.05 (3H, s, OAc) δ-4.50 (1H, dd, H-3α) δ-5-12 (1H, t, H-12)	38.5 (C-1), 23.4 (C-2), 80.9 (C-3), 37.7 (C-4), 55.3 (C-5), 18.3 (C-6), 32.9 (C-7), 39.7 (C-8), 47.7 (C-9), 36.8 (C-10),22.8 (C-11), 124.2(C-12), 139.5 (C-13), 42.1 (C-14), 28.2 (C-15), 26.7 (C-16), 33.8 (C-17), 59 (C-18), 39.7 (C-19), 39.7 (C-20),31.3 (C-21), 41.6(C-22), 28.1 (C-23), 15.8 (C-24), 14.2 (C-25), 16.8 (C-26), 17.6 (C-27), 28.8 (C-28), 23.3(C-29), 21.4 (C-30)	IR spectra: C=O - 1730 cm ⁻¹ C=C - 1640 cm ⁻¹ CH ₃ -1380 cm ⁻¹ CH ₂ -1250 cm ⁻¹ CH - 1030, 1000, 985, 960 cm ⁻¹ Mass spectra: m/z=468, 453, 408, 218, 203	[11,12]
Kaempferol	δ- 6.12 (1H, d, H-6), δ-6.32 (1H, d, H-8), δ-6.86 (2H, d, H-3' and H-5'), δ-7.97 (2H, d, H-2' and H-6')	93.20 (C-8), 98.07 (C-6), 102.95(C-10), 115.11(C-3'and C-5'), 121.67(C-1'), 129.13 C-6'), 135.49 (C-3), 146.27 (C-2), 156.12 (C-9), 158.89 (C-4'), 160.65 (C-5), 163.67 (C-7), 175.54 (C-4)	Mass spectra: m/z: 287, 288, 319,	[13]

NMR=Nuclear magnetic resonance, IR=Infrared spectroscopy

for the treatment of hydrophobia, whereas, the bark has multiple actions. It is used as a galactagogue and is helpful in gynecological disorders.^[14] The fruits are active against leprosy, menorrhagia,

leucorrhoea, and blood disorders, burns, intestinal worms, dry cough, and urinary tract infections. Bronchitis, bowel syndrome, and piles are treated with its leaves, in the Unani System of

Medicine.^[16] The leaf buds are effective against skin infection, and a decoction of the leaves is used in wound washing and healing.^[16]

A decoction of the bark is given for the treatment of piles, ulcerative colitis, diarrhea, and dysentery. It is also given in the treatment of diabetes and asthma. The latex is externally applied on wounds to decrease inflammation, pain, and edema, and promote its healing. It is also used with sugar to reduce diarrhea and dysentery, especially in children, and improves the sexual power in males.^[16]

The roots of the plant are used in dysentery, pectoral complications, and diabetes, and also applied in inflammatory glandular enlargement, mumps, and hydrophobia.^[16] The summary of traditional uses is tabulated in Table 2.

Pharmacological activity

The various parts of the plant showed good pharmacological actions and these are summarized in Table 3.

Hypoglycemia activity

β -Sitosterol isolated from stem bark is reported to have potent antidiabetic activity.^[32] Kar *et al.*, has reported that ethanol extract (250 mg/kg/day, once, twice, and thrice daily, per oral [PO]) normalized the blood glucose, lowered the

urine sugar, and helped it to reach a level of zero within two weeks, in alloxan-induced diabetic albino Wistar rats.^[33] In another experiment, a researcher has proposed that methanol extract (200 and 400 mg/kg, PO) from the stem bark exhibited a similar effect in both normal and alloxan-induced rats and the efficacy was comparable to the standard drug glibenclamide (10 mg/kg).^[34] Another experiment has also revealed that the methanol extract of fruits had good hypoglycemic activity at doses of 1, 2, 3, and 4 g/kg, p.o., both in normal and alloxan-induced diabetic rats.^[35] Another investigation by Ahmad and Urooj revealed that the stem bark aqueous extract possessed higher glucose adsorption activity and a reduced glucose retardation index, which was comparable to wheat bran and acarbose.^[36]

Antioxidant activity

Ethanol and water extract of the *F. racemosa* stem bark had potent free radical scavenging activity in both nanosecond pulse radiolysis and stopped-flow spectrophotometric analysis. The ethanol extract showed a significantly higher steady state antioxidant activity than the water extract. Veerapur *et al.*, performed an antioxidant assay through the traditionally known procedures. They also studied the radioprotective potential of the same extract using a micronucleus assay in V79 cells and observed maximum radioprotection at the 20 μ g/ml concentration. There was no blockage of the proliferative index by the cytokines in the same experiment. Based on the above observation, the *F. racemosa* ethanol extract had potent antioxidant and radioprotection activities.^[37]

Jahan *et al.*, isolated 3-O-(E)-Caffeoyl quinate, which had potent antioxidant activity via the diphenyl picryl hydrazine free radical scavenging assay.^[38]

Hepatoprotective activity

The methanol extract of the stem bark exhibited hepatoprotection action against the carbon tetrachloride (CCl₄)-induced model at 250 and 500 mg/kg doses, PO, in rats. All enzyme

Table 2: Traditional use of different parts of *F. racemosa*

Plant material	Uses in Ayurvedic medicines
Fruits	Aphthae, menorrhagia, hemoptysis
Fruits, boiled and strained	Gargle for sore throat
Ground leaves mixed with honey	Bilious affections
Latex (milky juice)	Diarrhea, hemorrhoids
Bark powder	Diabetes
Roots	Dysentery
Latex boiled with milk	Aphrodisiac
Oil infused with root bark	Eczema, leprosy, rheumatism
Fruits	Laxative, digestive

Table 3: Pharmacological actions of *F. racemosa*

Pharmacological actions	Parts used	Extract	Experimental models	References
Antihyperglycemic	Stem bark	Ethanol	Alloxan-induced	[17-19]
	Stem bark	Methanol	Alloxan-induced	
	Fruits	Methanol	Alloxan-induced	
Antitussive	Stem bark	Methanol	Cough-induced model by sulfur dioxide gas	[20]
Hepatoprotective	Stem bark	Methanol	Hepatotoxicity induced by CCl ₄	[21,22]
	Leaf	Ethanol	Hepatotoxicity induced by CCl ₄	
Antioxidants	Fruits	Ethanol	DPPH free radical scavenging assay	[23]
Wound healing	Stem bark	Ethanol	Excised and incised wound model	[24]
Antidiarrheal	Stem bark	Ethanol	Castor oil-induced diarrhea PGE2-induced enter pooling	[25]
Anti-inflammatory	Leaf		Carrageenan-, serotonin-, histamine-, and dextran-induced rat paw edema	[26]
Antiulcer	Fruit	Ethanol	Pylorus ligation, ethanol induced, cold restraint stress	[27]
Antibacterial	Leaf	Petroleum ether	<i>E. coli</i> , <i>B. pumilus</i> , <i>B. subtilis</i> , <i>P. aeruginosa</i> , <i>S. aureus</i>	[28]
Hypolipidemic	Bark	Ethanol	Alloxan-induced	[29]
Renal anticarcinogenic			Potassium bromate-induced nephrotoxicity, Ferric nitrilotriacetate-induced nephrotoxicity	[30,31]

levels (aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase) were decreased in the extract-treated animals than in the controls.^[17] The researcher measured some oxidative parameters in a similar experiment and they proposed that there was a reduction in oxidized lipid and elevation of superoxide dismutase and catalase enzyme levels in the serum, kidney, and liver.^[17] In another experiment, the ethanol extract of the leaves expressed a similar trend in an *in vivo* rat model.^[18]

Antitussive activity

The stem bark methanol extract expressed good antitussive action against the sulfur dioxide-induced cough model in mice. There was 56.9% inhibition of cough at 200 mg/kg PO in mice.^[19]

Antiulcer activity

The fruit extract (50% ethanol) exhibited antiulcer activity in different well-known animal models of rats with three doses (50, 100, and 200 mg/kg, twice daily, PO) for five days. The researchers used various animal models like ethanol, pylorus ligation, and cold strain-induced ulcer to perform the antiulcer effect. The extract inhibited an ulcer in all the above-mentioned models in a dose-dependent manner. A similar extract reduced oxidative damage in the mucosal lining of the stomach by inhibiting the enzyme activity like that of H⁺/K⁺ ATPase and superoxide dismutase.^[20]

Wound healing

The stem bark (ethanol extract) had wound healing properties in various wound models in rats.^[21]

Anthelmintic activity

The aqueous extract from the bark exhibited an anthelmintic activity on adult earthworms (dose 50 mg/ml) in a spastic paralysis model and this action was similar to 3% piperazine citrate (standard). The aqueous extract caused 100% spastic paralysis, whereas, the worms came to a normal stage within five hours of standard treatment. This action showed the anthelmintic property of the bark.^[22]

Antidiuretic effect

The hot aqueous extract of *F. racemosa* barks (250, 500, and 1000 mg/kg) have a lowered antidiuretic effect of up to 50%, with respect to the standard antidiuretic hormone. This action might be due to the reduced levels of Na⁺ and K⁺ and increased osmotic action of the nephron.^[23]

Antidiarrhoeal effect

The stem bark extract (ethanol) had a significant antidiarrheal effect (castor oil and prostaglandin-E₂ enter pooling induced models) in rats. In another experiment, this action was more pronounced by reducing the gastrointestinal tract motility in the charcoal meal test in rats.^[24]

Chemopreventive effect on the nephron

The *F. racemosa* extract (200 and 400 mg/kg, PO) exhibited a

chemopreventive effect, where nephrotoxicity was produced by potassium bromate in rats. The results indicated that there was a significant reduction of the peroxidized lipid, hydrogen peroxide, and xanthine oxidase in rats. Serum glutathione, blood urea nitrogen, and serum creatinine levels were also decreased in that experiment.^[25] A similar result was also reported in ferric nitrilotriacetate-induced nephrotoxicity.^[26]

Anticancer effect

A researcher proposed that the methanol extract of *F. racemosa* produced a cytotoxic effect on various hepatic cancerous cell lines like HL-60, HepG2, NCI-H23, and HEK-293T. The results obtained from their investigation suggested that the methanol extract produced higher cytotoxic effects on HL-60 and HepG2 cells with respect to other used cell lines with very low (50% inhibitory concentration) IC₅₀ values.^[27]

Anti bacterial activity

The hydroalcoholic extract from the leaves showed potent antibacterial activity, with an IC₅₀ value of 0.08 mg/ml against *Actinomyces viscosus*. Petroleum ether extract of leaves exhibited an antibacterial potential higher than the other extracts against *Escherichia coli*, *Bacillus pumilis*, *Bacillus subtilis*, and *Pseudomonas aureus*.^[28]

Anti-inflammatory effect

The ethanol extract of leaves (400 mg/kg, orally) exhibited an anti-inflammatory activity on carrageenan-, histamine-, serotonin-, and dextran-induced paw edema models of rats. In the chronic inflammatory model of the cotton granuloma weight method, there was a reduction of 41.5% granuloma weight, which demonstrated its good anti-inflammatory activity as compared with phenylbutazone.^[29] Li *et al.*, reported that the ethanol extract inhibited both cyclooxygenase-1 and 5-lipoxygenase *in vitro* (90 and 18 μM concentration, IC₅₀ values) due to the presence of a new glycoside compound, namely, racemosic acid.^[30]

Memory enhancing activity

The *F. racemosa* bark (aqueous extract) demonstrated an anticholinesterase activity, which was evaluated for its ability to enhance the acetylcholine levels. The outcome from their research revealed that it produced an antidementia activity in rats.^[31]

Hypolipidemic effect

The bark (ethanol extract) had a hypolipidemic action, as it potentiated the secretion of insulin. The study was performed using alloxan-induced diabetic rats (100 – 500 mg/kg, PO) for 45 days. The extract showed similar results like glibenclamide (standard).^[31]

Renal and testicular protective action

The acetone extract of the *F. racemosa* bark (250 and 500 mg/kg, orally) showed a protective effect against doxorubicin-induced renal and testicular toxicity. At 500 mg/kg dose, the sperm count and spermatogenesis were higher than in the normal control and 250 mg/kg dose test groups. Antioxidant activity was also observed at the same dose due to the presence of

various phenolic compounds and flavonoids such as quercetin, gallic acid, ellagic acid, and terpenoids lupeol, lupeol acetate, and α -amyrin. Finally, this extract reduced the oxidative toxicity on both renal and testes.^[40]

Toxicity study

Acute toxicity studies were performed previously using the aqueous extract of *F. racemosa* bark on albino mice. The aqueous extract was given in doses of 100, 300, and 1000 mg per 100 gm body weight, once, to the mice and the animals were sacrificed after 72 hours of dosing. Blood samples were collected to determine the hemoglobin, red blood cell (RBC) count, white blood cell (WBC) count, blood urea, blood glucose, serum creatinine, serum cholesterol, and serum glutamate pyruvate transaminase (SGPT). Some physiological changes were also observed in the liver and kidney by the researcher. The extract was safe up to the highest dose, but it produced abnormality in the liver and kidney. The fasting blood sugar level pointed toward hypoglycemia. Small amounts of fatty acids were also deposited in the kidney.^[41]

The researcher also performed acute and subacute toxicity studies of the aqueous extract of *F. racemosa* bark in both albino mice and albino Wistar rats. They administered the extract in 30 mg/100 gm dose for three weeks. Liver damage was seen in the subacute toxicity study and reversible hepatotoxicity was also observed during the experiment. There were no signs of renal damage during the histopathological studies, but the creatinine and urea levels had increased dramatically.^[42]

Clinical trials

The platelet-aggregating activity of the *F. racemosa* aqueous extract was studied on healthy human volunteers recently. Both extracts exhibited a platelet-aggregating activity to an extent of 3 – 51% when compared to the controls. The platelet-aggregating activity of both extracts was dose-dependent and had no significant difference. The cold water extract of the bark was reported to have bergenin as a major chemical constituent, while the hot water extract contained ferulic acid, kaempferol, and coumarin, along with bergenin.^[43]

The clinical trials of β -sitosterol in a randomized, double-blind, and placebo-controlled multicenter study showed effectiveness of treatment against benign prostate hyperplasia. β sitosterol produced adverse effects like dizziness, decreasing blood pressure, tachycardia, and orthostatic problems during the study.^[44]

Another double-blinded, randomized, placebo-controlled design clinical trial was performed, to check the antihyperglycemic activity of the *F. racemosa* bark on human volunteers (18 men and 12 women). The researchers maintained a few inclusion criteria like volunteers' age to be between 35 and 50 years; they should be free from diabetic retinopathy, nephropathy or cardiomyopathy; should not be pregnant; should have a normal lipid profile; had to be metabolically stable; and should not have been taking insulin, lipid-lowering drugs or herbs / supplements. They established

a human equivalent dose (HED) of 1.2 g/day (400 mg, three capsules) based on *in vivo* animal studies. After one month of study, the biochemical parameters like fasting blood glucose, postprandial blood glucose, and insulin were measured, and they reported that the body mass index (BMI) of the subjects from both groups were above normal levels and no significant changes were observed during the study period. The subjects showed good tolerance to the treatment and no volunteer had withdrawn from the study. A significant reduction of blood glucose level was observed during the extract treatment without alteration of cholesterol or triglyceride levels.^[45]

Mechanism of action

After the preclinical and clinical studies, some mechanism of action had been proposed through the antihyperglycemic activity of the *F. racemosa* extract.^[46]

On postprandial hyperglycemia

The extract reduced postprandial hyperglycemia via increasing the viscosity of the intestinal contents, resulting in entrapment of the glucose molecules by the adsorption method, thereby reducing diffusion of glucose from the intestinal barrier to the blood stream.

On glucose absorption

The extract reduced glucose absorption via inhibiting carbohydrate hydrolyzing enzymes (α -amylase, α -glucosidase, β -glucosidase) and delaying the release of glucose into the blood stream.

Utilization of glucose

The *F. racemosa* extract controlled the plasma glucose level by regulating the glucose metabolizing enzymes in the glycolysis and gluconeogenesis pathways.

Peripheral utilization of glucose

This action was increased via the glucose uptake across target cells and secretion of insulin into the blood stream.

Pancreatic β -cell regeneration

It increased through synthesis and secretion of insulin in to blood stream.

SUMMARY AND CONCLUSION

F. racemosa is the well-known fig plant in the Indian Traditional System of Medicine, with multiple pharmacological actions. In this review, we have included the traditional use, phytochemistry, and pharmacology in a descriptive manner. The structures of the active constituents are shown in Figure 1 and spectrometry data are tabulated in Table 1. The traditional uses and pharmacological actions are summarized in Tables 2 and 3, respectively. The extracts and phytoconstituents isolated from this plant have been shown to produce different pharmacological responses, which include hypoglycemic, analgesic, anti-inflammatory, hypolipidemic, antidiuretic, and

renal anticarcinogenic activities. The multiple traditional uses and pharmacological responses of *F. racemosa* allowed us to write this review article. This review will provide all the scientific information in a concise manner to the scientific community.

ACKNOWLEDGEMENTS

Dr. Sudipta Saha (Corresponding Author) wishes to express his thanks to the University Grants Commission (UGC), New Delhi, India, for providing UGC-MRP Grant [Project No. 42-680/2013(SR)].

REFERENCES

- Dubey S, Maity S, Singh M, Saraf SA, Saha S. Phytochemistry, pharmacology and toxicology of *Spilanthes acmella*: A review. *Adv Pharmacol Sci* 2013;2013:423750.
- Joy PP, Thomas J, Mathew S, Skaria BP. Medicinal Plants. Tropical Horticulture. Calcutta: Naya Prakash; 2001. p. 123-5.
- Council of Scientific and Industrial Research; New Delhi, India. The wealth of India- A Dictionary of Indian Raw Material. Publications and Information Directorate, Issue 4. 1956. p. 35-6.
- Available from: http://www.herbalcureindia.com/herbs/Ficus_racemosa.html. [Last accessed on 2013 Dec 23].
- Chopra RN, Nagar SL, Chopra IC. Glossary of Indian medicinal plants, reprinted edition. New Delhi, India: Central Scientific and Industrial Research; 1986; p. 119.
- Atal CK, Kapur BM. Cultivation and Utilization of medicinal plants. Jammu-Tawi, India: Regional Research laboratory CSIR; 1982. p. 514-9.
- Kamboj A, Saluja AK. Isolation of stigmasterol and β sitosterol from petroleum ether extract of aerial parts of *Ageratum conyzoides* (asteraceae). *Int J Pharmacy Pharma Sci* 2011;3:94-6.
- Rajput AP, Rajput TA. Isolation of stigmasterol and β sitosterol from Chloroform extract of leaves of *Corchorus fasciculari*. *Int J Bio Chem* 2012;6:130-5.
- Jamal AK, Yaacob WA, Din LB. A Chemical Study on *Phyllanthus reticulatus*. *J Phys Sci* 2008;19:45-50.
- Abdullahi SM, Musa AM, Abdullahi MI, Sule MI, Sani YM. Isolation of Lupeol from the Stem-bark of *Lonchocarpus sericeus* (Papilionaceae). *Sch Acad J Biosci* 2013;1:18-9.
- Ali N. Brine shrimp cytotoxicity of crude methanol extract and antispasmodic activity of α -amyrin acetate from *Tylophora hirsute* Wall. *Comp Alter Med* 2013;13:7.
- Fingolo CE, Santos Tde S, Filho MD, Kaplan MA. Triterpene Esters: Natural Products from *Dorstenia arifolia* (Moraceae). *Molecules* 2012;18:4247-56.
- Gangwal A, Parmar SK, Sheth NR. Triterpenoid, flavonoids and sterols from *Lagenaria siceraria* fruits. *Der Pharmacia Lettre* 2010;2:307-17.
- Shikshartha AR, Mittal S. *Ficus racemosa*: Phytochemistry, traditional uses, and pharmacological properties: A review. *Int J Adv Pharm Res* 2011;4:6-15.
- Ahmed F, Chandra JN, Manjunath S. Acetylcholine and memory-enhancing activity of *Ficus racemosa* bark. *Pharmacognosy Res* 2011;3:246-9.
- Joseph B, Raj SJ. Phytopharmacological and phytochemical properties of three *Ficus* species-an overview. *Int J Pharma Bio Sci* 2010;1:246-53.
- Channabasavaraj KP, Badami S, Bhojraj S. Hepatoprotective and antioxidant activity of methanol extract of *Ficus glomerata*. *J Nat Med* 2008;62:379-83.
- Mandal SC, Maity TK, Das J, Pal M, Saha BP. Hepatoprotective activity of *Ficus racemosa* leaf extract on liver damage caused by carbon tetrachloride in rats. *Phytother Res* 1999;13:430-2.
- Bhaskara RR, Murugesan T, Pal M, Saha BP, Mandal SC. Antitussive potential of methanol extract of stem bark of *Ficus racemosa*. *Phytother Res* 2003;17:1117-8.
- Rao CHV, Verma AR, Vijay KM, Rastogi S. Gastric protective effect of standardized extract of *Ficus glomerata* fruit on experimental gastric ulcers in rats. *J Ethnopharmacol* 2008;115:323-6.
- Biswas TK, Mukherjee B. Plant medicines of Indian origin for wound healing activity: a review. *Int J Low Extreme Wounds* 2003;2:25-39.
- Chandrashekhar CH, Latha KP, Vagdevi HM, Vaidya VP. Anthelmintic activity of the crude extracts of *Ficus racemosa*. *Int J Green Pharm* 2008;2:100-3.
- Ratnasooriya WD, Jayakody JR, Nadarajah T. Antidiuretic activity of aqueous bark extract of Sri Lankan *Ficus racemosa* in rats. *Acta Biol.* 2003;54:357-63.
- Mukherjee PK, Saha K, Murugesan T, Mandal SC, Pal M, Saha BP. Screening of anti-diarrhoeal profile of some plant extracts of a specific region of West Bengal. India. *J Ethnopharmacol* 1998;60:85-9.
- Khan N, Sultana S. Modulatory effect of *Ficus racemosa*: Diminution of potassium bromate- induced renal oxidative injury and cell proliferation response. *Basic Clin Pharmacol Toxicol* 2005;97:282-8.
- Khan N, Sultana S. Chemo-Modulatory effect of *Ficus racemosa*: extract against chemically induced renal carcinogenesis and oxidative damage response in Wistar rats. *Life Sci* 2005;77:1194-210.
- Sukhramani PS, Vidyasagar G, Patel PM. In-vitro screening of *Ficus racemosa* for Anticancer activity. *Res J Pharmacog Phytochem* 2013;5:119-22.
- Mandal SC, Saha BP, Pal M. Studies on bacterial activity of *Ficus racemosa* leaf extract *Phytoether Res* 2000;14:278-80.
- Mandal SC, Maity TK, Das J, Saha BP, Pal M. Anti-inflammatory evaluation of *Ficus racemosa* Linn. leaf extract. *J Ethnopharmacol* 2000;72:87-92.
- Li RW, Leach DN, Myers SP, Lin GD, Leach GJ, Waterman PG. A new anti-inflammatory glucoside from *Ficus racemosa*. *Planta Med* 2004;70:421-6.
- Faiyaz A, Manjunath S. Acetylcholine and memory enhancing activity of *Ficus racemosa* bark. *Pharmacogn Res* 2011;3:246-9.
- Baslas RK, Agha R. Isolation of a hypoglycaemic principle from the bark of *Ficus glomerata* Roxb. *Himalayan Chem Pharm Bull* 1985;2:213-4.
- Kar A, Choudhary BK, Bandyopadhyay NG. Comparative evaluation of hypoglycemic activity of some Indian Medicinal Plants in alloxan diabetic rats. *J Ethnopharmacol* 2003;84:105-8.
- Bhaskara RR, Murugesan T, Pal M, Sinha S, Saha BP, Mandals SC. Glucose lowering efficacy of *Ficus racemosa* barks extract in normal and alloxan diabetic rats. *Phytother Res* 2002;16:590-2.
- Akhtar MS, Qureshi AQ. In vitro studies on the hypoglycemic potential of *Ficus racemosa* stem bark Pakistan. *J Pharm Sci* 1988;1:877-89.
- Ahmed F, Urooj A. In vitro studies on the hypoglycemic potential of *Ficus racemosa* Stem bark. *J Sci Food Agric* 2010;90:397-401.
- Veerapur VP, Prabhakar KR, Parihar VK, Kandadi MR, Ramakrishana S, Mishra B, et al. *Ficus racemosa* Stem

- Bark Extract: A Potent Antioxidant and a Probable Natural Radioprotector. *Evid Based Complement Alternat Med* 2009;6:317-24.
38. Jahan IA, Nahar N, Mosihuzzaman M. Hypoglycemic and antioxidant activity of *Ficus racemosa* Linn fruits. *Nat Prod Res* 2009;23:399-408.
 39. Sophia D, Manoharan S. Hypolipidemic activities of *Ficus racemosa* linn. Bark in alloxan induced diabetic rats. *Afr J Tradit Complement Altern Med* 2007;4:279-88.
 40. Ahmed F, Urooj A, Karim AA. Protective effect of *F. racemosa* stem bark against doxorubicin induced renal and testicular toxicity. *Pharmacogn Mag* 2013;9:130-4.
 41. Jaykaran, Bhardwaj P, Kantharia N, Yadav P, Panwar A. Acute toxicity study of an aqueous extract of *Ficus racemosa* Linn. bark in albino mice. *Int J Toxicol* 2008;6:112-9.
 42. Panwar A, Jaykaran, Chavda N, Saurabh M, Yadav P. Subacute toxicity study of an aqueous extract of *Ficus racemosa* Linn. bark in rats. *J Pharma Res* 2010;3:814-7.
 43. Ahmed F, Kumar MS, Urooj A, Kemparaju K. Platelet aggregation inducing activity of *Ficus racemosa* stem bark extracts. *J Pharmacol Pharmacother* 2012;3:329-30.
 44. Berges RR, Windeler J, Trampisch HJ, Senge T. Randomized, double blind and placebo controlled multicenter study showed effectiveness in treatment of benign prostate hyperplasia. *Lancet* 1995;345:1529-32.
 45. Ahmed F, Hudeda S, Urooj A. Antihyperglycemic activity of *Ficus racemosa* bark extract in type 2 diabetic individuals. *J Diabetes* 2011;3:318-9.
 46. Urooj A, Ahmed F. *Ficus racemosa* and *Morus indica*: Emerging alternative antihyperglycemic agents. *Open Conf Proc J* 2013;4:59-65.

How to cite this Article: Yadav RK, Nandy BC, Maity S, Sarkar S, Saha S. Phytochemistry, pharmacology, toxicology, and clinical trial of *Ficus racemosa*. *Phcog Rev* 2015;9:73-80.

Source of Support: University Grants Commission (UGC), New Delhi, India, for providing UGC-MRP Grant [Project No. 42-680/2013(SR)]. **Conflict of Interest:** No.