Journal of Scientific and Innovative Research 2017; 6(4): 151-163
Available online at: www.jsirjournal.com

Review Article

ISSN 2320-4818
JSIR 2017; 6(4): 151-163

Received: 17-07-2017
Accepted: 21-12-2017

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A review of pharmacognostic, physicochemical, phytochemical and pharmacological studies on *Ficus bengalensis* L.

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Abstract

Since the birth of humans on this planet, plants have been utilized for diagnosis, treatment and prevention of various ailments. *Ficus bengalensis* L., belonging to family Moraceae, commonly known as Banyan tree, is one the most utilized plants. It is a very large tree with spreading branches bearing multiple aerial roots hanging downward. In traditional systems of medicines, various plant parts such as stem bark, aerial roots, vegetative buds, leaves, fruits and latex are used in diabetes, dysentery, seminal weakness, menorrhagia, leucorrhoea, erysipelas, nervous disorders, burning sensation, hemorrhages and applied topically on pimples, abscesses, wounds, ulcers, sores, cracked soles of the feet and rheumatic inflammations. Pharmacognostic studies have been done to set its quality control parameters and various phytochemicals *viz.* phytosterols, anthocyanidin derivatives, fatty acids, amino acids, polysaccharides, flavonoids, flavonols, leucoanthocyanidins and triterpenoids have been identified and isolated. This plant is reported to possess many useful pharmacological activities also *viz.* antihyperglycemic, antidiabetic, Antihyperlipidemic, hypocholesterolemic, anti-inflammatory, analgesic, antibacterial, antifungal, larvicidal, anti-diarrhoeal, antimutagenic, antioxidant, cytotoxic, hepatoprotective, anti-arthritic, antiallergic and immunostimulatory. The present review is an effort to give a detailed survey of the literature on its ethnomedical uses, pharmacognosy, physicochemical parameters, phytochemistry, pharmacological studies and other commercial uses.

Keywords: *Ficus bengalensis*, Banyan tree, Bargad, Bohar.

INTRODUCTION

Plants are the oldest and the most importantsource of medicines [1]. At the end of nineteenth century, after synthesis of aspirin, research on herbal products was halted and researchers started focusing on synthetic and semi-synthetic drugs. But from last few decades, there is an upsurge in the use and research ofnatural origin,especially botanical drugs. About 25% of the prescribed drugs are derived from higher plants and this value is increased to 50%, if animal and microbial products are also included [2].

Ficus bengalensis L., belonging to family Moraceae, is commonly known as Banyan tree (English), Darakht-e-Reesh and Bargad (Unani medicines) and Bohar (Urdu) [3, 4]. It is native to a wide area of Asia i.e. India, Burma, Southeast Asia, Southern China, Thailand, and Malaysia. The tree is cultivated in botanical gardens and parks throughout the tropical regions of the world [5].Many pharmacological activities and useful phytoconstituents of this plant have been reported. Besides other useful chemical constituents, the tree also contains a high amount of good quality natural rubber [6]. Brief taxonomic information about *F. bengalensis* is;

Kingdom: Plantae; Phylum: Tracheophyta; Class: Magnoliopsida; Order: Rosales; Family: Moraceae; Genus: *Ficus*; Species: *bengalensis* [7]. Various stages of the plant are shown in figure 1.

a **b** **c** **d**

Figure 1: *Ficus bengalensis*: **a)** mature tree; **b)** leaf and leaf primordium; **c)** aerial roots; **d)** fruits

Uses in traditional medicine systems

The plant has been extensively used in Ayurvedic and Unani medicines to treat various health problems. Infusion of the bark is used in dysentery, diabetes, seminal weakness, menorrhagia, leucorrhoea, erysipelas, nervous disorders and burning sensation. Decoction of the buds in milk is given in hemorrhages. Aerial roots are antiemetic and also applied topically to pimples. A paste of the leaves or milky juice is applied topically to abscesses and wounds for promoting suppuration. Milky juice and seeds are applied topically to ulcers, sores and rheumatic inflammations [3]. Young stem is used as tooth brush (miswak) and stem latex is applied topically to cracked soles of the feet [8]. Latex from aerial parts of plant mixed with honey is used orally to control hyperglycemia in Pakistan [9].

Morphology of the plant

F. bengalensis is a latici ferous tree, up to 30 m in height with widely spreading branches bearing many aerial prop roots. Bark is greenish white. Leaves are simple, alternate and arranged often in clusters at the ends of branches. They are stipulate, 5-12 cm broad and 10-18 cm long, entire, broadly elliptic to ovate. Fruits are achenes, which are small, crustaceous and enclosed in the common fleshy receptacles, having red outside color. The young bark is somewhat smooth having transverse and longitudinal row of lenticels, while in the older bark, the lenticels are numerous and closely spaced. Outer bark flakes off easily. The fresh cut surface of the bark is pink to flesh colored and exudes plenty of latex. The inner most part of the bark adjoining the wood is nearly white and fibrous [10].

Pharmacognostic characters

Stem bark

Shade dried stem bark is of brownish grey color with dark patches from outer surface and reddish brown to yellowish brown on inner surface possessing stimulant odor, astringent taste and rough texture due to the presence of lenticels. Thickness of bark varies with the age of the tree; normally 0.8 to 2.5 cm. Fracture is brittle in outer bark and fibrous in inner portion [11, 12].

Microscopically, stem bark is differentiated into outer and inner bark having width of 288–576 and 2.9–3.5 mm respectively. Periderm consisting of phellem and phelloderm originates from the deeper portion of the secondary phloem. Phellem cells are thin walled, homogeneous, rectangular and suberized. Phelloderm is distinct and wide, its cells are turned into radially arranged cubical sclereids. Next to the vascular cambium, secondary phloem forms a distinct zone consisting of companion cells, sieve tube members and axial parenchyma. Most of these parenchyma cells have abundance of tannin. Outside of this zone phloem appears collapsed, consisting of collapsed and destroyed sieve elements and wide dilated rays. In the peripheral part of the bark, cells of these rays are turned into thick walled lignified sclerenchyma cells. The phloem rays may beuniseriate, multiseriate, homocellular or heterocellular. Breadth and height of multiseriate rays is up to 72 mm and 900 mm respectively and height of sieve tube members is about 288–360 mm. Large and vertically oblong p-proteins can be found consistently, adjacent to sieve plates. Laticifers are abundant in the inner bark and each laticiferous canal is surrounded by distinct epithelial cells [12].

Leaf

Leaves are coraceous having slight bitter taste, green in color, opposite in arrangement, ovate to elliptic in shape (lanceolate shape) with obtuse apex and reticulately pinnate venation. Length and width are 10-30 cm and 7-20 cm respectively with2.5-5 cm long petiole. Powder of leaf is pale green colored and odorless possessing a slightly bitter taste. Trichomes, fibers, calcium oxalate crystals, spiral thickenings and epidermal cells with anticlinal walls are visible under microscope [13].

Leaf primordium

Fresh leaf primordium has light green thick outer covering. Leaf primordia are arranged alternatively and occur in predictable positions. Length and width of primordium are 2-4 cm and 0.4-0.6 mm respectively. In dry form, these possess abundant trichomes on outer surface. Primordia have agreeable odor and slight bitter taste. In transverse section, different sequence of arrangements in concentric rings is visible. Abundant uniseriate trichomes are present on epidermis. Thin walled, elongated and compactly arranged parenchymatous cells with chloroplast form the ground tissue and later on develop into spongy and palisade parenchymatous cells. These parenchymatous cells have clustered crystals of calcium oxalate. Small rounded vascular bundles with poorly developed phloem and xylem are present in between these parenchymatous cells. Lignified, thick walled, rectangular and elongated stone cells with narrow and broad lumen are also present [14].

Physicochemical parameters

Stem bark

Physicochemical parameters of *F. bengalensis* stem bark are as follows;

Foreign matter (1.53% w/w); Total ash (11% w/w); Acid insoluble ash (2.46% w/w); Water soluble ash (5.13% w/w); Loss on drying (10% w/w); Water soluble extractive (13% w/w); Alcohol soluble extractive (8.2% w/w) [11, 15].

Leaf

Physicochemical parameters of *F. bengalensis* leaf are as follows;

Vein termination number (12.6/mm^2); Vein islet number (10.7/mm^2); Stomatal index (lower epidermis) (16/mm^2); Stomatal index (upper epidermis) (7.5/mm^2); Total ash (11.63% w/w); Acid insoluble ash (4.5% w/w); Water soluble ash (7.56% w/w); Water soluble extractive (6.4% w/w); Ethanol soluble extractive (4.8% w/w); Chloroform soluble extractive (1.2% w/w); Petroleum ether soluble extractive (1.8% w/w) [13].

Leaf primordium

Physicochemical parameters of *F. bengalensis* leaf primordium are as follows;

Foreign matter (0.65%); Moisture (10.75%); Total ash (10.95% w/w); Acid insoluble ash (0.75% w/w); Water in soluble ash (1% w/w); Water soluble extractive (0.63% w/w); Benzene soluble extractive (0.54% w/w); Chloroform soluble extractive (0.23% w/w); Petroleum ether soluble extractive (2.19% w/w) [14].

Phytochemistry of *F. bengalensis*

General phytochemical screening of *F. bengalensis* is enlisted in table 1 [16]. Detail of various phytoconstituents in different parts of the plant is described below and summarized in table 2.

Table 1: Phytochemical analysis of *F. bengalensis*

Phytoconstituents	Leaves	Stem bark	Root
Alkaloids	+	−	+
Carbohydrates	+	+	−
Glycoside	+	+	+
Terpenoids	+	+	+
Saponins	+	+	+
Phenols	+	+	+
Xanthoproteic	+	+	−
Flavonoids	+	+	+
Tannins	+	+	+

Stem bark

Phytosterols

From methanolic extract of stem bark, lanostadienylglucosyl cetoleate (01), bengalensisteroic acid acetate(02), α-amyrin acetate (03) and lupeol (04) were isolated by elution of the silica gel packed column with chloroform, chloroform:methanol (97:3), petroleum ether:chloroform (1:1) and petroleum ether:chloroform (1:1) respectively [17].

Anthocyanidin derivatives

From the water soluble fraction of the ethanolic extract of the defatted stem bark, 5,7-dimethylether of leucopelargonidin-3-*O*-α-L-rhamnoside (05) and from water insoluble fraction, 3',5,7-trimethyl ether of delphinidin-3-*O*-α-L-rhamnoside(06), 3',5,7-trimethylether of leucocyanidin (07) and 3',5-dimethyl ether of leucocyanidin-3-*O*-β-D-galactosylcellobioside (08) have been isolated by silica gel column. No NMR data was reported and these compounds were characterized by methylation, demethylation, acetylation, use of color reagents, degradation methods and elemental analysis by UV spectroscopy.

From hot ethanol extract of the defatted stem bark, meso inositol (09) and from hot petroleum ether extract, β-sitosterol-α-D-glucose (10), 6-heptatriacontene-10-one (11), 20-tetratriacontene-2-one (12) and pentatriacontan-5-one (13) have been isolated by column chromatography on silica gel [18].

Fruit and seed

Fatty acids

Seed oil is found to contain many unusual fatty acids *viz.* palmitic acid (35.2%) (14), oleic acid (20.3%) (15), linoleic acid (15.4%) (16), linolenic acid (8.7%) (17), vernolic acid (8.2%) (18), stearic acid (4.2%) (19), malvalic acid (3.7%) (20), sterculic acid (1.6%) (21), lauric acid (1.5%) (22) and myristic acid (1.3%) (23) [19].

Amino acids

Analysis of the concentrated aqueous extract of the fresh fruits revealed the presence of many amino acids in fruit proteins i.e. cysteine(24), glutamine(25), methionine(26), tryptophan(27), arginine(28), methionine(29), citrulline (30)and hydroxyproline(31). Isolation of glutathione (32) from fruits is also reported in earlier works [18].

Polysaccharide

The hot ethanolic extract, after dissolving in water, revealed the presence of D-glucose(33), D-fructose (34)and D-galactose (35)by paper chromatography.From water insoluble residue, xylan was precipitated after extraction with chloroform. Hydrolysis of the xylan with acid and analysis by paper chromatography showed the presence of mainly D-arabinose (36) and D-xylose (37)together with traces of galactose and glucose [18].

Heart wood

From benzene extract of the heartwood, tiglic acid ester of taraxasterol **(38)** has been isolated; characterized by mixed melting point, IR spectra and co-spot TLC of alkaline hydrolysis products with authentic tiglic acid and taraxasterol [18].

Leaf

Flavonoids

Two flavonoids catechin (39) and genistein (40) were isolated from methanol extracts of the leaves of Sudanese varieties of *F. bengalensis* by using column chromatography and their structures were identified by IR, ^{1}H-NMR, ^{13}C-NMR, MS spectral data, UV and comparison with published data [20].

Flavonols

Flavonols quercetin-3-galactoside (41) and rutin (42) have been isolated from ethyl acetate extract of the leaves [18].

Leucoanthocyanidins

A leucoanthocyanidin leucocyanidin (43) was isolated from the leaf and its hypoglycemic effect was testified [21, 22].

Triterpenoids and sterols

A triterpene friedelin (44) and a sterol β-sitosterol (45) have been isolated from the leaves by column chromatography using petroleum ether and benzene respectively, as eluants. Their structures were determined by mass spectral data, elemental analysis, mixed melting point and co-spot TLC with that of an authentic sample [18].

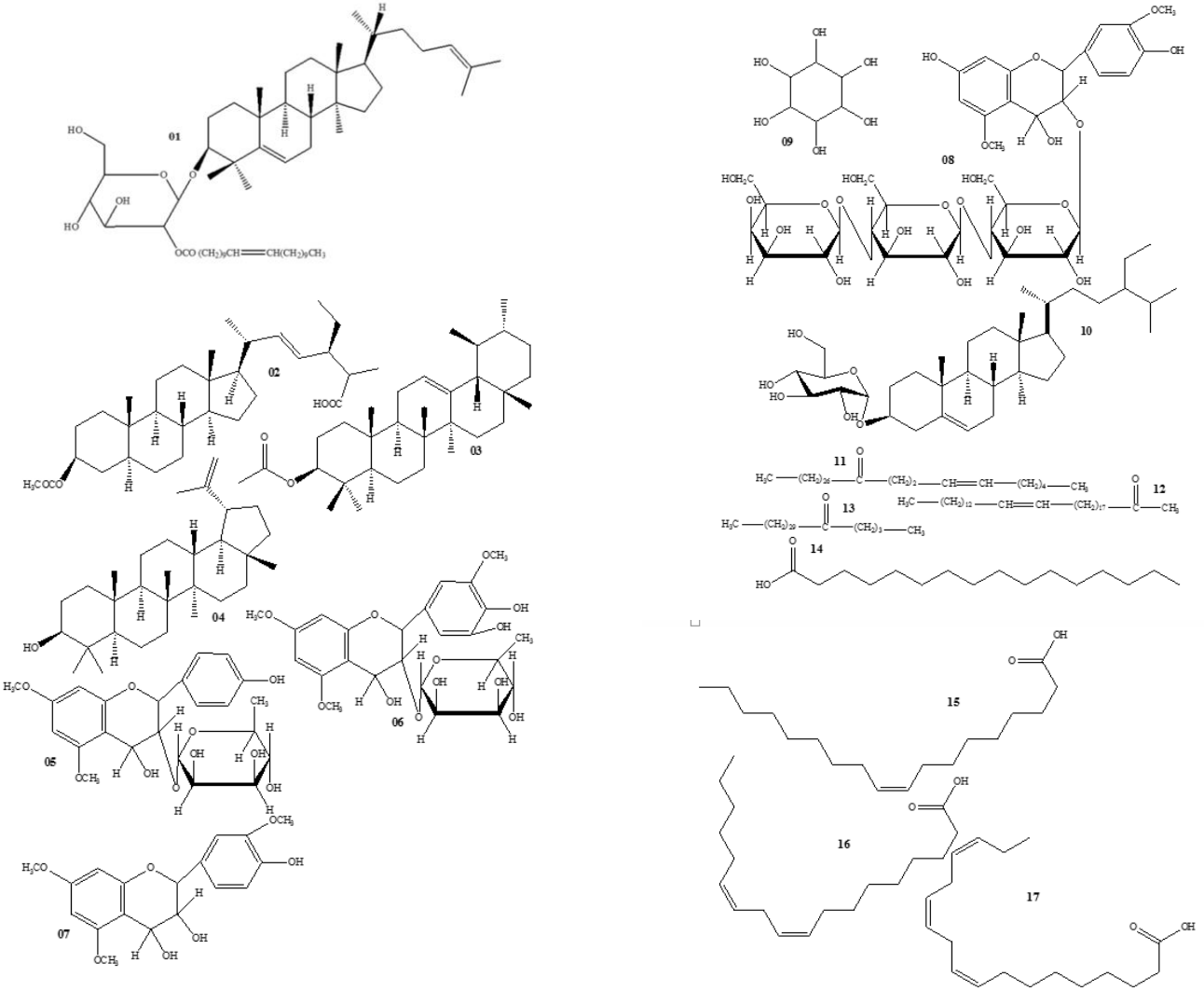
Aerial root

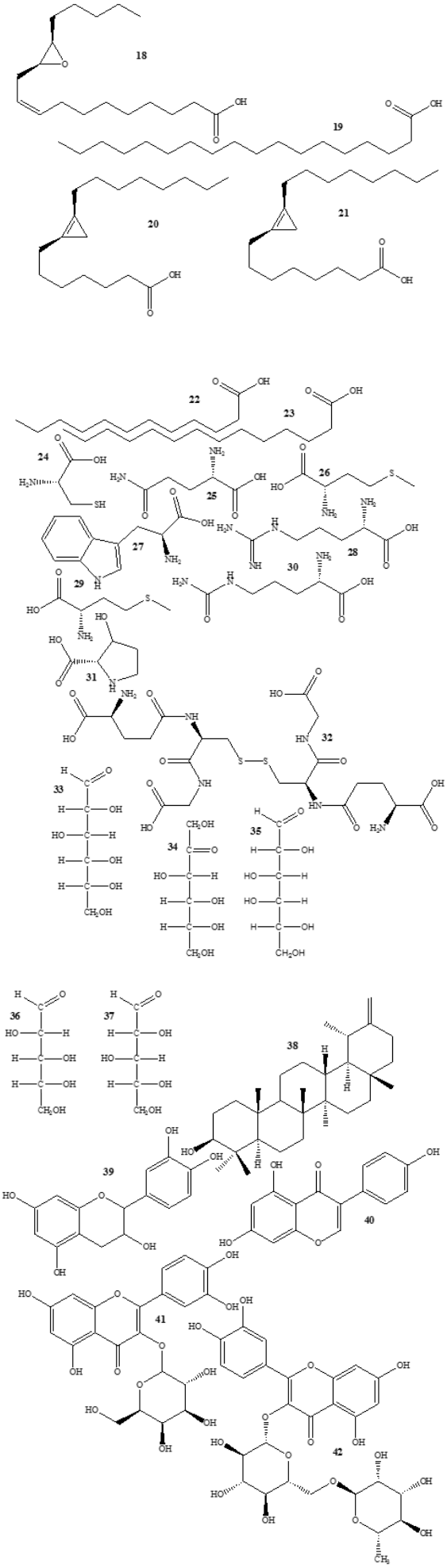
Triterpenoids

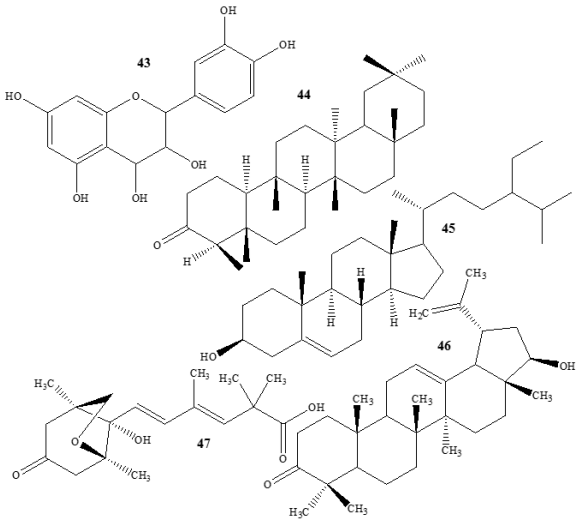
From methanolic extract of the aerial roots, Bengalensinone (46) and benganoic acid (47), possessing cholinesterase inhibitory activity, have been isolated [23].

Table 2: Summary of phytochemistry of *F. bengalensis*

Chemical class	Plant part	Components	References
Phytosterols	Stem bark	Lanostadienylglucosyl cetoleate (01); bengalensisteroic acid acetate (02); α-amyrin acetate (03); lupeol (04)	[17]
Anthocyanidin derivatives	Stem Bark	5,7-dimethylether of leucopelargonidin-3-*O*-α-L-rhamnoside (05); 3',5,7-trimethyl ether of delphinidin-3-*O*-α-L-rhamnoside (06); 3',5,7-trimethylether of leucocyanidin (07); 3',5-dimethyl ether of leucocyanidin-3-*O*-β-D-galactosylcellobioside (08)	[18]
Fatty acids	Seed oil	Palmitic acid (14); oleic acid (15); linoleic acid (16); linolenic acid (17); vernolic acid (18); stearic acid (19); malvalic acid (20); sterculic acid (21); lauric acid (22); myristic acid (23)	[19]
Amino acids	Fruits and Seeds	Cysteine (24); glutamine (25); methionine (26); tryptophan (27); arginine (28); methionine (29); citrulline (30); hydroxyproline (31)	[18]
Polysaccharides	Fruits and seeds	D-glucose (33); D-fructose (34); D-galactose (35); D-arabinose (36); D-xylose (37)	[18]
Sterols	Leaf	β-sitosterol (45)	[18]
Flavonoids	Leaf	Catechin (39), genistein (40)	[20]
Flavonols	Leaf	Quercetin-3-galactoside (41); rutin (42)	[18]
Leucoanthocyanidins	Leaf	Leucocyanidin (43)	[21, 22]
Triterpene	Leaf	Friedelin (44)	[18]
	Aerial root	Bengalensinone (46), benganoic acid (47)	[23]
Miscellaneous	Stem Bark	Meso inositol (09); β-sitosterol-α-D-glucose (10); 6-heptatriacontene-10-one (11); 20-tetratriacontene-2-one (12); Pentatriacontan-5-one (13)	[18]
	Fruits and seeds	Glutathione (32)	[18]
	Heart wood	Tiglic acid ester of taraxasterol (38)	[18]







Pharmacological activities

Antihyperglycemic and antidiabetic activity

Antihyperglycemic activity of α-amyrin acetate, isolated from aerial roots of *F. bengalensis* was testified in STZ-induced diabetic rats and in db/db mice at dose level of 50 mg/kg p.o. Antihyperglycemic results were compared with the same dose of metformin. α-amyrin acetate caused 22.3% improvement of glucose tolerance in normoglycemic rats and 35.6% (comparable to metformin 37.8%) fall in blood glucose of STZ-induced diabetic rats. Multiple dose oral administration in db/db mice, lowered blood glucose level on day 3, 5, 7 and 10 by 18.7%, 27.1%, 40.0% and 51.6% respectively, comparable to the effect of metformin i.e. 17.8%, 30.5%, 39.4% and 52.5% respectively. Average antihyperglycemic effect of α-amyrin acetate on glucose tolerance in db/db mice was calculated to be around 35.6%, comparable to that of metformin 43.2% [24].

In a comparative study, using glibenclamide (5 mg/kg) as reference standard, ethanolic extract of stem bark showed relatively more hypoglycemic activity in alloxan induced diabetic rats than that of aerial roots, at same dose level i.e. 100 mg/kg [25].

Inhibitory activities of the aqueous extracts of the heat treated and untreated stem bark was studied on α-amylase, α-glucosidase and sucrase. Honda and Hara method was used to evaluate inhibitory potential [26]. Both heat treated and untreated extracts showed significant inhibitory activities. Heat treated extracts showed IC_{50} values of 77 and 141 µg/ml and untreated extracts showed IC_{50} values of 158 and 193 µg/ml for α-glucosidase and sucrase respectively. This is the possible mechanism of antidiabetic effect of this plant [27].

Antidiabetic and ameliorative potential of aqueous extract of the stem bark at dose level of 500 mg/kg/day p.o. was studied in streptozotocin induced diabetic rats by using tolbutamide (100 mg/kg/day p.o.) as reference standard. Results revealed the hypoglycemic activity comparable to that of tolbutamide and restoration of hepatic cytochrome P-450 dependent enzymes (PNPH, PROD and EROD), kidney and liver lipid peroxidation (malondialdehyde and hydroperoxides) and glycolytic enzymes to near normal levels; also decrease in the levels of serum electrolytes (potassium, sodium and calcium) was observed. Histological examination revealed reduction in swelling and inflammation of pancreatic tissue [28].

In another study, using the same extract and experimental conditions, results with regard to total protein (g/dl), albumin (g/dl), urea (m mol/l), uric acid (m mol/l), creatinine (µ mol/l), Hb (g/dl), RBC, WBC and platelets were almost equivalent to that of tolbutamide [29].

Antidiabetic effect of aqueous extract of *F. bengalensis* aerial roots at dose level of 300 mg/kg p.o. was studied in streptozotocin induced diabetic rats using glipizide (2.5 mg/kg p.o.) as reference standard. Results revealed 43.8% reduction in BGL of normal rats at 6 h. 40.7%, 54.8% and 51.7% improvement in glucose tolerance of normal, sub diabetic and mild diabetic rats respectively, was observed at 3 h during GTT [30].

Aqueous extract of the stem bark at dose level of 50 mg/kg/day p.o. when tested on normal, alloxan recovered, mildly diabetic and severely diabetic rabbits caused improvement in glucose tolerance in alloxan recovered and mildly diabetic rabbits. It also caused 55.8% and 68% fall in FBG in mildly diabetic and severely diabetic rabbits respectively [31].

In a comparative study performed on alloxan induced diabetic rats, ethanolic extract of fruit, at a dose of 120 mg/kg/day p.o., showed more diabetic activity than that of aerial root and stem bark. Glibenclamide at a dosage of 0.5 mg/kg/day p.o. was used as reference standard [32].

A partially purified preparation from aqueous extract of the stem bark demonstrated significant hypoglycemic and hypocholesterolemic effect on diabetic rabbits. ED_{50} and LD_{50} were determined to be 10 mg/kg and 1000 mg/kg p.o. respectively. For chronic toxicity studies, 50 mg, 100 mg and 150 mg/kg of this preparation, about 5, 10 and 15 times of the ED_{50} value respectively, were given to diabetic rats for three months. Fall in FBG, cholesterol and triacylglycerol and improvement in GTT were similar to those of normal control group. Weight gain and values of SGOT, SGPT, S. alkaline phosphatase, serum protein, blood urea, serum cholesterol, hemoglobin, total leukocyte count, differential count were not affected. So, partially purified aqueous extract of stem bark is nontoxic and safe even in a dose of 5, 10 and 15 times of the ED_{50}, but the crude extract is hepatotoxic [33].

Antihyperlipidemic and hypocholesterolemic activity

Administration of α-amyrin acetate, isolated from aerial roots of *F. bengalensis*, to db/db mice for 10 consecutive days decreased triglycerides, cholesterol and LDL-C by 21.5%, 24.1% and 21.2%; increased HDL-C and HDL-C to TC ratio by 21.0% and 59.1% respectively. It is concluded that α-amyrin acetate improves plasma lipid profile not only by lowering total plasma cholesterol and LDL-C levels significantly but also by increasing HDL-C level and HDL-C/TC ratio [24].

Hypolipidemic and antioxidant effect of aqueous extract of the stem bark at dose level of 50 mg/kg/day p.o. was studied in hypercholesterolaemic rabbits (rabbits fed with cholesterol suspended in groundnut oil at a dose of 100 mg/kg/day, for 6 weeks). Results of this study revealed a decrease in triacylglycerol, serum cholesterol and LDL+VLDL cholesterol by 54%, 59% and 60% respectively, increase in levels of catalase, glutathione reductase, superoxide dismutase and glutathione peroxidase 30%, 22%, 36% and 90% respectively, compared to untreated animals [34]. In another study, under the same experimental conditions, HDL-C increased to 30.6 mg% and TAG decreased to 89 mg% while in untreated group these values were 25.6 mg% and 188 mg% respectively. 48% decrease in TC level after four weeks was also observed [35].

Anti-inflammatory

Anti-inflammatory activity of methanolic extract of the stem bark and the leaf in Carrageenan induced and formalin induced hind paw edema in rats, was comparable to that of potent drugs i.e. diclofenac sodium and aspirin [36-39]. Ethanolic extract of the stem bark also possesses anti-inflammatory activity [13].

Anti-inflammatory activity of bark of young plant of *F. bengalensis* was compared with that of mature plant using carrageenan induced hind paw edema for acute inflammation and cotton pellet induced granuloma for chronic inflammation, in rats. Ethanolic, chloroform and petroleum ether extracts at dose level of 300 and 600 mg/kg/day p.o. were studied using indomethacin at dose level of 10 mg/kg/day p.o. as standard drug. Ethanolic extract of younger plant at dose level of 300 and 600 mg/kg/day p.o. caused 37.64% and 69.04% reduction in paw volume after 3 h, while mature plant caused 55.03% and 65.54% reduction respectively, in carrageenan induced paw edema model. In cotton pellet granuloma model, ethanolic extract of younger plant at dose level of 300 and 600 mg/kg/day p.o. caused 19.27% and 39.03% reduction in paw volume after 3 h, while mature plant caused 14.12% and 34.25% reduction respectively. So, younger plant possesses relatively more anti-inflammatory activity than mature plant. Chloroform and petroleum ether extracts did not possess significant anti-inflammatory activity [40].

Analgesic activity

Analgesic activity of methanolic extract of the leaf and the stem bark in Acetic acid induced writhing and Eddy's hot plate method in rats, was comparable to that of potent drugs i.e. diclofenac sodium and aspirin [37-39].

Antibacterial activity

Catechin and genistein, isolated from methanol extracts of the leaves of Sudanese varieties *F. bengalensis* were testified for their antimicrobial activity by using disc diffusion method at dose level of 100 µg/ml. Streptomycin sulphate and nystatin at dose level of 25 µg/discs and 50µg/discs respectively, were used as reference standard. Both compounds showed antibacterial activity, comparable to that of streptomycin and nystatin, against *Bacillus cereus* and *Pseudomonas aeruginosa*. No antifungal activity was found against *Aspergillus ochraceus*, *Sacchromyces cereviseae*, *Candida lipolytica* and *Sacchromyces lipolytica* [20].

Antibacterial activity of aqueous extracts of the stem bark, leaf and root was evaluated by agar diffusion technique. Among the three extracts, stem bark extract showed maximum antibacterial activity against *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Staphylococcus aureus* and *Escherichia coli* [16].

Antibacterial activity of hydroalcoholic (70% methanol) extract of the stem bark at concentration of 0.01-0.10 mg/ml was testified against *Actinomyces viscosus* using cup plate diffusion method and broth dilution technique. MIC was found to be 0.08 mg/ml and zone of inhibition at this concentration was 9.4 mm. No zone of inhibition was found at concentration of 0.01-0.07 mg/ml [41].

Antibacterial activity of methanolic extract of the stem bark determined by disc diffusion method at the dose of 200 mg/ml against Enterotoxigenic *E. coli* was comparable to that of standard drug amikacin at the dose of 10µg/disc [42].

Antibacterial activity varies with a change in environmental conditions and geography [43].

Antifungal activity

Antifungal activity of aqueous extracts of the stem bark, leaf and root was evaluated by agar diffusion technique at dose level of 30 mg/ml using nystatin (30 µg/ml) as reference standard. Among the three extracts, stem bark extract showed antifungal activity against *Trichophyton rubrum* and *Candida albicans* comparable to that of nystatin. *T. rubrum* was resistant to the leaf extract and *K. pneumonia* was resistant to both leaf and root extracts [16].

In another study, water and ethanolic extracts of the stem bark increased breaking strength and decreased period of epithelialization and percentage wound contraction in incision and excision model respectively [44].

Larvicidal activity

Larvicidal activity of methanolic extract of the leaf was studied against early 2nd, 3rd and 4th instar larvae incorporated in different concentrations in glass beakers. Results revealed LC_{50} values against early 2nd, 3rd and 4th instar larvae of *Culex quinquefasciatus*, *Anopheles stephensi* and *Aedes aegypti* as 41.43, 58.21 and 74.32 ppm, 60.44, 76.41 and 89.55 ppm and 56.54, 70.29 and 80.85 ppm respectively. LC_{50} values against early 3rd instar larvae of *Culex tritaeniorhynchus* and *Anopheles subpictus* were 100.88 and 159.76 ppm respectively [45, 46].

Anti-diarrhoeal activity

Anti-diarrhoeal effect of ethanolic extract of *F. bengalensis* hanging roots (EEFB) was evaluated at dose level of 400 mg/kg p.o. against castor oil induced diarrhea, PGE_2 induced enter pooling and GI motility in charcoal meal test in rats using diphenoxylate (5 mg/kg p.o) and atropine (0.1 mg/kg i.p) as reference standards. In castor oil induced diarrhea, mean defecations per animal in 4 hours, treated with diphenoxylate and EEFB were1.37 and 2.21 respectively and mean number of wet faeces per animal were 0.0 and 1.96 respectively. In PGE_2 induced enteropooling, volume of intestinal fluid in PGE_2 and PGE_2+EEFB was 2.97 and 1.25 ml respectively. Movement of charcoal meal with atropine and EEFB was 34.2 and 50.2 respectively [47].

Antimutagenic and antioxidant activity

Aqueous extract of heat treated stem bark was used to determine antimutagenic and antioxidant activity by using Ames test (standard plate incorporation assay) and ex-vivo inhibition of lipid peroxidation in liver microsomes of rats respectively. Extract concentration of 500 µg inhibited mutagenic activity of sodium azide (NaN_3) in *Salmonella typhimurium* with IC_{50} value of 70.24 µg/ml and inhibited microsomal lipid peroxidation with IC_{50} value of 80.24 µg/ml [48].

Antioxidant (free radical scavenging) activity

F. bengalensis possesses antioxidant activity which is mostly due to phenolic compounds [49]. Anti-oxidant and free radical scavenging activity of methanolic and acetone:water (70:30) extracts of *F. bengalensis* aerial roots was studied. Antioxidant potential of the methanol extract, estimated by using potassium ferric cyanide reduction method, was comparable to that of tannic acid. DPPH free radical scavenging activity (%) of the 70% acetone and methanol extracts was about 50, nearer to each other, at concentrations of46.79 µg and 39.3 µg respectively. The values of TAA determined by $ABTS^{\cdot+}$ radical cation scavenging activity of the 70% acetone and methanol extracts were 6182.7 and 6096.1 µmol/g respectively. Hydroxyl radical scavenging activity (%) of the 70% acetone and methanol extracts at concentration of 250 µg was 24.2 and 32.4 respectively. Linoleic acid peroxidation inhibition of both extracts was comparable to that of α-tocopherol. Antihemolytic activity (%) and metal chelating activity (mg EDTA/g sample) of 70% acetone and methanol extracts was 75.0, 70.5 and 19.9, 7.4 respectively [50].

Cytotoxic activity

Fruits of *F. bengalensis* have cytotoxic activity demonstrated by brine shrimp bioassay with LC_{50} value of 900 and by potato disc bioassay with 48% tumor inhibition [51].

Hepatoprotective activity

Methanolic extract of the aerial root was tested for hepatoprotective activity against isoniazid-rifampicin induced liver injury in rats using Liv 52 at dose level of 10mg/kg p.o. as reference standard. Results of MEFB at dose level of 100, 200 and 300 mg/kg p.o. with regard to bilirubin level, total protein level, albumin level, AST and ALT were almost same as that of Liv 52. Histopathological results with regard to hepatocytic necrosis, inflammation and neutrophil infiltration were also comparable to that of Liv 52 [52].

Hepatoprotective effect of leucopelargonin derivative, isolated from the bark of *F. bengalensis*, at dose level of 100 mg/kg/day i.p. was evaluated in CCl_4 induced hepatotoxic rats, using vitamin E at dose level 50mg/kg/day i.p. as reference standard. Result with regard to decrease in biochemical parameters like total cholesterol, HDL, LDL, FFA, TAG; decrease in the activities of glucose 6- phosphate dehydrogenase, HMGCoA reductase in the liver and enzymes like ALT, ALP and AST in serum and liver; increase in the levels of antioxidant enzymes in liver; inhibition of fatty infiltration and fibrosis, was comparable to that of vitamin E [53].

Anti-arthritic activity

Anti-arthritic activity of methanolic extract of the stem bark (MESB) at dose level of 400 mg/kg/day p.o was studied in formalin and Complete Freund's adjuvant (CFA) induced arthritis in rats by using arthritis score, oxidative stress, radiographic pattern of hind legs and biomarkers *viz.* lipid peroxidation, antioxidants (non-enzymatic and enzymatic), nitricoxide, serum lysosomal enzymes (ALT, AST, and LDH), connective tissue biomarkers (sialic acid, hydroxyproline and glucosamine) and pro-inflammatory mediators (IL-6 and TNF-α). Diclofenac sodium, dexamethasone and methotrexate at dose level of 10, 0.03 and 0.007 mg/kg/day p.o. respectively were used as reference standards. Anti-arthritic activity of MESB was slightly better than that of diclofenac sodium and less effective than that of dexamethasone and methotrexate [54].

Antiallergic potential

Aqueous, ethyl acetate and ethanol extracts of the stem bark at dose level of 50 mg/kg i.p., showed antiallergic and antistress activity against milk induced asthma in male Swiss albino mice by decreasing leucocytes and eosinophils. Bhargava and Singh method was used in this study [55].

Immunostimulatory effect

Immunostimulatory effect of the aerial roots was testified by using feed containing 5% aerial root powder, in fish models (*Channa punctatus*). Levels of ALT and AST remained almost same. Serum lysozyme, SOD, phagocytotic index, %age phagocytosis, total serum protein, nitric oxide and immunoglobulin increased significantly [56].

The aqueous extract of *F. bengalensis* aerial roots was evaluated for immunostimulatory activity, using in vitro polymorphonuclear (PMN) function test and hypersensitivity and hemagglutination reactions in rats. Maximum percentage phagocytosis i.e. 64% was observed at 1.0 mg/ml, compared to 34% in the control. Maximum early and delayed hypersensitivity reactions and an increase in the antibody titer in rats were observed at a dose of 100 mg/kg p.o. for five days [57].

In another study, the hydroalcoholic extract of the leaves and its four fractions (n-hexane, chloroform, n-butanol and water) showed prominent immunostimulatory activity in phagocytosis of killed *C. albicans* and candidacidal assay [58].

Wound healing potential

Wound healing capacity of aqueous and ethanolic extract of the root was studied by incision model, excision model and dead space wound model in rats. Increased breaking strength, decreased period of epithelialization and percentage wound contraction and increased hydroxyproline content were observed in incision, excision and dead space model respectively. Results were comparable to that of standard drug povidone iodine [59].

In another study, using excision and incision wound models, wound healing ability of aqueous and ethanolic extracts of the stem bark was evaluated in excision and incision wound models. Significant wound healing activity was shown by increase in the skin breaking strength and the rate of wound contraction and a decrease in the period of epithelialization, compared with placebo [44].

Action against inflammatory bowel disease

Effect of aqueous and ethanolic extract of the stem bark at dose level of 500 mg/kg was evaluated against inflammatory bowel disease induced by 2, 4, 6-trinitrobenzenesulfonic acid in rats using prednisolone (2 mg/kg) as reference standard. Protective effect against IBD was comparable to that of prednisolone [60, 61].

Table 3: Summary of pharmacological studies on *F. bengalensis*

Activity tested	Extract	Plant part	Experimental design	Dose	Effect	References
Antihyperglycemic and antidiabetic	EtOH	Aerial roots	STZ-induced diabetic rats and db/db mice. Metformin (50 mg/kg p.o.) used as reference standard.	50 mg/kg p.o.	Antihyperglycemic effect (caused by α-amyrin acetate) was comparable to that of metformin	[24]
	Water	Stem bark	Streptozotocin induced diabetic rats. Tolbutamide (100 mg/kg/day p.o.) used as reference standard	500 mg/kg/day p.o.	Hypoglycemic activity was equivalent to that of tolbutamide. Restored glycolytic enzymes, serum electrolytes, hepatic P-450 dependent enzyme systems and formation of kidney and liver lipid peroxides to normal levels.	[28]
	Water	Aerial roots	Streptozotocin induced diabetic rats. Glipizide (2.5 mg/kg p.o.) used as reference standard.	300 mg/kg p.o.	43.8% reduction in BGL of normal rats at 6 h. 40.7%, 54.8% and 51.7% improvement in glucose tolerance of normal, sub diabetic and mild diabetic rats respectively at 3 h during GTT.	[30]
	Water	Stem bark	Normal, alloxan recovered, mildly diabetic and severely diabetic rabbits.	50 mg/kg/day p.o.	Improvement in GT in alloxan recovered and mildly diabetic rabbits. 55.8% and 68%fall in FBG in mildly diabetic and severely diabetic rabbits respectively.	[31]
Antihyperlipidemic and Hypocholesterolemic	Water	Stem bark	Hypercholesterolaemic rabbits (rabbits fed with cholesterol suspended in groundnut oil at a dose of 100 mg/kg/day, for 6 weeks).	50 mg/kg/day p.o.	Decreased triacylglycerol, serum cholesterol and LDL+VLDL cholesterol by 54%, 59% and 60% respectively, increased levels of catalase, GR, SOD and GSH.Px by 30%, 22%, 36% and 90% respectively, compared to untreated animals.	[34]
					HDL-C increased to 30.6 mg% and TAG decreased to 89 mg% (in untreated group, 25.6 mg% and 188 mg% respectively). 48% decrease in TC level.	[35]
			Alloxan induced subdiabetic and diabetic rabbits.		TC, LDL and TG decreased from 82to 42.7 mg%, 34 to 16 mg% and 121 to 45 mg% respectively in subdiabetic rabbits andfrom 118 to 51.7 mg%, 95 to 29 mg% and 416 to 81 mg% respectively in diabetic rabbits.	[62]

Anti-inflammatory	MeOH	Stem bark	Carrageenan induced hind paw edema and cotton pellet induced granuloma in rats. Diclofenac sodium (10 mg/kg/day p.o.) for 8 days used as reference standard.	400 mg/kg/day p.o.	Results were comparable to that of diclofenac sodium	[39]
	EtOH	Stem bark	Carrageenan induced hind paw edema in rats. Diclofenac sodium (5 mg/kg i.p.) used as reference standard.	200 mg/kg p.o.	Results were comparable to that of diclofenac sodium	[36]
	MeOH	Leaf	Carrageenan induced hind paw edema in rats. Aspirin (20mg/kg p.o.) used as reference standard.	100 mg/kg p.o.	Results were comparable to that of aspirin	[37]
	MeOH	Leaf	Formalin induced hind paw edema in rats. Diclofenac sodium (10 mg/kg p.o.) used as reference standard.	200 mg/kg p.o.	Results were comparable to that of diclofenac sodium	[38]
Analgesic	MeOH	Stem bark	Acetic acid induced writhing in rats. Diclofenac sodium (10 mg/kg/day) for 8 days used as reference standard.	400 mg/kg/day	Results were comparable to that of diclofenac sodium	[39]
	MeOH	Leaf	Acetic acid induced writhing and Eddy's hot plate method in albino mice. Aspirin (20mg/kg p.o.) used as reference standard.	100 mg/kg p.o.	Results were comparable to that of aspirin	[37]
	MeOH	Leaf	Eddy's hot plate method in rats. Diclofenac sodium (10 mg/kg p.o.) used as reference standard.	200 mg/kg p.o.	Results were comparable to that of diclofenac sodium	[38]
Antibacterial	MeOH	Leaf	Disc diffusion method. Streptomycin sulphate and nystatin (50 µg/discs) used as reference standard.	100 µg/ml	Antibacterial activity (caused by catechin and genistein) was comparable to that of streptomycin and nystatin, against *B. cereus* and *P. aeruginosa*	[20]
	Hyd-alc	Stem bark	Cup plate diffusion method and broth dilution technique.	0.01-0.10 mg/ml	MIC against *A. viscosus* was 0.08 mg/ml and zone of inhibition at this concentration was 9.4 mm.	[41]
	MeOH	Stem bark	Disc diffusion method. Amikacin (10µg/disc) used as reference standard.	200 mg/ml	Results against Enterotoxigenic *E. coli* were comparable to that of amikacin.	[42]
	EtOH	Stem bark	Cup and plate method. Ofloxacin (25 mg/ml) used as reference standard.	1000 µg/ml	Zone of inhibition was comparable to that of ofloxacin, against *E. coli* and *S. aureus*.	[43]
Antifungal	Water	Stem bark	Agar diffusion technique. Nystatin (30µg/ml) used as reference standard.	30mg/ml	Zone of inhibition against *T. rubrum* and *C. albicans* was comparable to that of nystatin.	[16]
Larvicidal	MeOH	Leaf	Early 2^{nd}, 3^{rd} and 4^{th} instar larvae incorporated in different concentrations in glass beakers	25 to 200 ppm concentration	LC_{50} values against early 2^{nd}, 3^{rd} and 4^{th} instar larvae of *C. quinquefasciatus*, *A. stephensi* and *A. aegypti* were 41.43, 58.21 and 74.32 ppm, 60.44, 76.41 and 89.55 ppm and 56.54, 70.29 and 80.85 ppm respectively	[45]
			Early 3^{rd} instar larvae incorporated in different concentrations in glass beakers		LC_{50} values against early 3^{rd} instar larvae of *C. tritaeniorhynchus* and *A. subpictus* were 100.88and 159.76 ppm respectively	[46]
Anti-diarrhoeal	EtOH	Aerial roots	Castor oil induced diarrhoea in rats. Diphenoxylate (5 mg/kg p.o.) used as reference standard	400 mg/kg p.o.	MDPA in 4h, treated with Diph and EEFB was 1.37 and 2.21 and MNWFPA was 0.0 and 1.96 respectively.	[47]
			PGE_2 induced enteropooling in rats		Value of VIF for PGE_2 (100 µg/kg) and PGE_2+EEFB was 2.97 ml and 1.25 ml respectively.	
			GI motility in charcoal meal test in rats. Atropine (0.1 mg/kg i.p) used as reference standard.		Value of MCM for atropine and EEFB was 34.2 and 50.2 respectively.	
Antimutagenic	Water	Stem bark (heat treated)	Ames test (standard plate incorporation assay).	500 µg (extract concentration)	Inhibited mutagenic activity of sodium azidein *S. typhimurium* with IC_{50} value of 70.24 µg/ml	[48]
Antioxidant	Water	Stem bark (heat treated)	Ex-vivo inhibition of lipid peroxidation in liver microsomes of rats.	500 µg (extract concentration)	Inhibited microsomal lipid peroxidation with IC_{50} value of 80.24 µg/ml	[48]

Antioxidant (Free radical scavenging)	MeOH Act-Wtr	Aerial root	Antioxidant potential (potassium ferric cyanide reduction method), DPPH free radical scavenging activity, $ABTS^{\cdot+}$ radical cation scavenging activity, hydroxyl radical scavenging activity, linoleic acid peroxidation inhibition, antihemolytic activity and metal chelating activity.		Showed good antioxidant, free radical scavenging, metal chelating and antihemolytic potential.	[50]
	Water	Aerial root	DPPH radical scavenging activity, hydroxyl radical scavenging activity, reducing capacity, hydrogen peroxide activity, determination of total phenolic content using Folin-Ciocalteu's phenolic reagent		Antioxidant and free radical scavenging activity was observed	[63]
Cytotoxic	CF	Fruit	Brine shrimp bioassay and potato disc bioassay		LC_{50} value of 900 and 48 % tumor inhibition respectively	[51]
Hepatoprotective	MeOH	Aerial root	Isoniazid-rifampicin induced liver injury in rats. Liv 52 (10 mg/kg p.o.) used as reference standard.	100, 200 and 300 mg/kg p.o.	Results with regard to bilirubin level, total protein level, albumin level, AST, ALT and histopathological results with regard to hepatocytic necrosis, inflammation and neutrophil infiltration were comparable to that of Liv 52.	[52]
	Leucopelargonin derivative (isolated from the bark)		CCl4 induced hepatotoxicity in rats. Vitamin E (50 mg/kg/day i.p.) used as reference standard.	100 mg/kg/day i.p.	Result with regard to decrease in biochemical parameters like total cholesterol, HDL, LDL, FFA, TAG; decrease in the activities of glucose 6-phosphate dehydrogenase, HMGCoA reductase in the liver and enzymes like ALT, ALP and AST in serum and liver; increase in the levels of antioxidant enzymes in liver; inhibition of fatty infiltration and fibrosis, was comparable to that of vitamin E.	[53]
Anti-arthritic	MeOH	Stem bark	Formalin and CFA induced arthritis in rats using paw edema volume and arthritic score. Diclofenac sodium, dexamethasone and methotrexate (10, 0.03 and 0.007 mg/kg/day p.o. respectively) used as reference standard.	400 mg/kg/day p.o.	Anti-arthritic activity was slightly better than that of diclofenac sodium and less effective than that of dexamethasone and methotrexate	[54]
Antiallergic in asthma	Water EtOH EtAc	Stem bark	Milk-induced (4 mg/kg s.c.) leucocytosis and eosinophilia in mice	50 mg/kg i.p.	Significant reduction in eosinophils and leucocytes compared to untreated group.	[55]
Immunostimulatory		Aerial root	Fish models (*Channa punctatus*)	feed containing 5% root powder	Levels of ALT and AST remained almost same. Serum lysozyme, SOD, phagocytotic index, %age phagocytosis, total serum protein, NO and immunoglobulin increased significantly.	[56]
	Water	Aerial root	In vitro PMN function test and hypersensitivity and hemagglutination reactions in rats.	1.0 mg/ml and 100 mg/kg p.o.	64% percentage phagocytosis, compared to 34% in the control. Early and delayed hypersensitivity reactions and an increase in the antibody titer was observed	[57]
Wound healing	Water EtOH	Root	Incision model, excision model and dead space wound model in rats. Povidone iodine used as reference standard.		Results were comparable to that of povidone iodine.	[59]
	Water EtOH	Stem bark	Incision model and excision model		Both the extracts increased breaking strength and decreased period of epithelialization and percentage wound contraction in incision and excision model respectively, compared with placebo	[44]
Protection against IBD	Water EtOH	Stem bark	IBD induced by 2, 4, 6-trinitrobenzenesulfonic acid in rats. Prednisolone (2 mg/kg) used as reference standard	500 mg/kg	Protective effect against IBD was comparable to that of prednisolone.	[60, 61]

A. aegypti: *Aedes aegypti*; Act-Wtr: acetone:water (70:30); AEFB: aqueous extract of *F. bengalensis*; *A. h*: *Aeromonas hydrophila*; ALT: alanine aminotransferase; *A. subpictus*: *Anopheles subpictus*; *A. stephensi*: *Anopheles stephensi*; AST: aspartate aminotransferase; *A. viscosus*: *Actinomyces viscosus*; *B. cereus*: *Bacillus cereus*; BGL: blood glucose level; *C. albicans*: *Candida albicans*; CF: Chloroform; CFA: Complete Freund's Adjuvant; CMDI: colon mucosa damage index; *C. quinquefasciatus*: *Culex quinquefasciatus*; *C. tritaeniorhynchus*: *Culex tritaeniorhynchus*; Ctrl: control; DAI: disease activity index; Diph: Diphenoxylate; *E.coli*: *Escherichia coli*; EEFB: ethanolic extract of *F. bengalensis*; EtAc: ethyl acetate; EtOH: ethanol; GR: glutathione reductase; GSH.Px: glutathione peroxidase; GT: glucose tolerance; GTT: glucose tolerance test; h: hour; Hyd-alc: hydroalcohoic (70% methanol); IBD: inflammatory bowel disease; i.p.: intraperitoneally; LC: lethal concentration; MCM: movement of charcoal meal; MDPA: mean defecations per animal; MeOH: methanol; MNWFPA: mean number of wet faeces per animal; NO: nitric oxide; Pred: prednisolone; *P. aeruginosa*: *Pseudomonas aeruginosa*; SOD: superoxide dismutase; *S. typhimurium*: *Salmonella typhimurium*; STZ: Streptozotocin; TNBS: trinitrobenzenesulfonic acid; *T. rubrum*: *Trichophyton rubrum*; VIF: volume of intestinal fluid.

Other diverse activities and uses

Silver nanoparticles synthesis

In the synthesis of silver nanoparticles, aqueous extract of the leaf reduced silver ions into silver nanoparticles with the reaction time of five minutes and without any harsh conditions. Antibacterial activity of these nanoparticles against *Escherichia coli* was verified by bacterial growth method showing MIC of 25 µg/ml [64].

Serine protease enzyme

A serine protease enzyme named benghalensin was isolated from the latex of the plant. This enzyme is very stable and retains more than 80% of its activity in the temperature (°C) and pH range of 20-80 and 5.5-10 respectively [65].

Food for animals

Leaves are food for goats [66].

As indicator of lead pollution

Lead contents of *F. bengalensis* can be measured as the sensitive indicator of lead pollution [67-69].

As source of natural rubber

F. bengalensis contains good quality natural rubber in high amounts, comparable to the commercial rubber tree *Hevea brasiliensis* [6].

As biomonitor of polycyclic aromatic hydrocarbons

F. bengalensis leaves can be used as biomonitor of polycyclic aromatic hydrocarbons in the atmosphere [70].

CONCLUSION

Plants have been serving the humanity for centuries by providing a good source of medicines. Active constituents from plants are isolated and being used for diagnosis, treatment, mitigation, and prevention of various diseases, but many crude drugs are also in use. *Ficus bengalensis* L. is one of the most important plants of traditional medicines and is still in use, to treat various diseases, particularly diabetes, reproductive system disorders, inflammatory conditions and abscesses. Because of its importance in traditional medicines, its quality control parameters are established by pharmacognostic studies and various phytochemicals have also been isolated and identified. Pharmacological studies on various parts of the plant have verified its use in traditional medicines. Many aspects of this plant are to be uncovered, for example, toxicity studies, proper dose for a particular disease when the plant is used in crude form, isolation of further phytoconstituents, synergistic studies, drug-drug interactions and drug-food interactions.

Conflict of interest

We declare that we have no conflict of interest.

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