PRELIMINARY AND PHARMACOLOGICAL PROFILE OF *FICUS RELIGIOSA L.*: AN OVERVIEW

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Summary

The present review describes the morphological, phytochemical and pharmacology aspects of *Ficus Religiosa* (*Moraceae*). The whole plant or its specific parts (leaves, stem, and roots) are known to have medicinal properties and have a long history of use by indigenous and tribal people in India. *Ficus Religiosa* is used as an Ayurvedic medicine in India and Unani medicine in Arab countries for the treatment of diabetes, stress, dyspepsia, abdominal pain, inflammation, jaundice, enlargement of spleen and congestive heart failure. The medicinal value of this plant in the treatment of a large number of human ailments is mentioned in Ayurveda, Charaka Samhita, and Sushrita Samhita. The medicinal value of this plant in the treatment of a large number of human ailments is mentioned in Ayurveda, Charaka Samhita, and Sushrita Samhita. So, an overview of phytochemical and pharmacological properties is given in the present paper.

Keywords: *Ficus Religiosa*; Pharmacognosy; Phytochemistry; Pharmacological profile.

Introduction

Medicinal plants have served through the ages, as a constant source of medicaments for the exposure of variety of diseases. The history of herbal medicine is as old as human civilization. The plants are known to provide a rich source of botanical anthelmintics, antibacterials and insecticides[1-2]. There are more than 800 species and 2000 varieties of *Ficus* genus, most of which are native to old world tropics. *Ficus benghalensis* (Banyan tree), *FicusReligiosa* (Pipal tree) and *Ficus carica* (Anjir tree) are some of the commonly occurring trees of this genus belonging to family *Moraceae*[3-5] It is a sacred tree native to India where it grows up to elevations of 5,000 ft(1,524 m). It is said to be the tree that Buddha was born under and also where he sat for six years of meditation and enlightenment[6]. *Ficus religiosa* Linn (Moraceae) commonly known as 'Peepal tree' is a large widely branched tree with leathery, heart shaped long tipped leaves on long slender petioles and purple fruits growing in pairs. The tree is regarded as a sacred tree to both Hindus as well as Buddhists. It has got mythological, religious and medicinal importance in Indian culture since ancient times[7-8]. The tree grows throughout India and widely cultivated in south-east Asia especially in vicinity of temples. In Ayurveda, *F. religiosa* belongs to a class of drugs called rasayana. Rasayana are rejuvenators, antioxidants and relieve stress in the body[9-10].

In India it is known by several vernacular names, the most commonly used ones being Asvatthah (Sanskrit), Sacred fig (Bengali), Peepal (Hindi), Arayal (Malayalam), Ravi (Telgu) and Arasu (Tamil) [11-12].

TAXONOMY
Family: Moraceae (mulberry family)
Latin name: *Ficus religiosa* L.
Synonyms: None known.
Common names: Bo tree, beepul tree, sacred tree
Taxonomic notes: Neal et al. reports that one tree was brought from India in 288 B.C. to Ceylon, is the oldest tree known historical tree, and is said to be the parent of all beepul trees there.
Nomenclature: This sacred tree is associated with Buddha and is planted beside temples, hence the species name, *religiosa*.

Ethnopharmacology

Traditional Uses
F. religiosa is a well known ethnomedicinal tree used in Ayurveda. Its use in the Indian traditional folk medicine also well documented. The use of different parts of *F. religiosa* in traditional system of medicine (Table 1)**.**

Table 1. Ethnomedicinal uses of different parts of *F. religiosa*

Plant Parts	Traditional Uses (as/in)
Bark	Astringent, cooling, aphrodisiac, antibacterial against *Staphylococcus aureus* and *Escherichia coli*, gonorrhoea, diarrhoea, dysentery, haemorrhoids and gastrohelcosis, anti-inflammatory, burns[12].
Bark Decoction	Cooling, gonorrhea, skin diseases, scabies, hiccup, vomiting[13].
Leaves and tender shoots	Purgative, wounds, skin diseases[12].
Leaf juice	Asthma, cough, sexual disorders, diarrhea, haematuria, toothache, migraine, eye troubles, gastric problems, scabies[12-13].
Fruit	Asthma, laxative, digestive[12].
Dried fruit	Tuberculosis, fever, paralysis, hemorrhoids[14].
Seeds	Refrigerant, laxative[12].
Latex	Neuralgia, inflammations, haemorrhages[12].

Morphology: *F. religiosa* is a large, deciduous tree. It has a heart shaped leaves. It shed its leaves in the month of March and April. The purple fruits of the Peepal are hidden with the figs. It is one of the longest living trees. It is often epiphytic with the drooping branches bearing long petioled, ovate, cordate shiny leaves. Leaves are bright green, the apex produced into a linear-lanceolate tail about half as long as the main portion of the blade. The receptacles occurring in pairs and are axillary, depressed globose, smooth and purplish when ripe. The bark is flat or slightly curved, varying from 5 to 8 mm in thickness, outer surface is grey or ash with thin or membranous flakes and is often covered with crustose lichen brown or ash coloured, surface has shallow irregular vertical fissures and uneven due to exfoliation of cork, inner surface smooth, yellowish to orange brown and fibrous[12-17]. (Figure 1)

Microscopy: An external features of bark of *F. religiosa* showed that bark differentiated into outer thick periderm and inner secondary phloem. Periderm is differentiated into phellem and phelloderm. Phellem zone is 360 mm thick and it is wavy and uneven in transection. Phellem cells are organized into thin tangential membranous layers and the older layers exfoliate in the form of thin membranes. The phelloderm zone is broad and distinct. Phelloderm cells are turned into lignified sclereids. Secondary phloem differentiated into inner narrow non-collapsed zone and outer broad collapsed zone. Non-collapsed zone consists of radial files of sieve tube members, axial parenchyma, and gelatinous fibres. Outer collapsed phloem has dilated rays, crushed obliterated sieve tube members, thick walled and lignified fibres, and abundant tannin filled parenchyma cells. Laticifers are fairly abundant in the outer secondary phloem zone. Phloem rays are both uniseriate and multiseriate. Multiseriate rays are homocellular and uniseriate rays are either homocellular or heterocellular[17].

Physical constants: Total ash 7.86 % w/w, acid insoluble ash 0.41 % w/w, alcohol soluble extract 7.21 % w/w and water soluble extractive 15.76 % w/w[17].

Phytochemistry

Preliminary phytochemical screening of *F. religiosa* barks, showed the presence tannins, saponins, flavonoids, steroids, terpenoids and cardiac glycosides[17-18]. The barks of *F.religiosa* showed the presence of bergapten, bergaptol, lanosterol, β-sitosterol, stigmasterol, lupen-3-one, β-sitosterol-d-glucoside (phytosterolin), vitamin k1[19-22]. The bark also contains tannin, wax, saponin, β-sitosterol, leucocyanidin-3-0-β-D-glucopyrancoside, leucopelargonidin- 3-0-β-D-glucopyranoside, leucopelargonidin-3-0-α-L- rhamnopyranoside, lupeol, ceryl behenate, lupeol acetate, α-amyrin acetate, leucoanthocyanidin and leucoanthocyanin[23]. Leaves yield campestrol, stigmasterol, isofucosterol, α-amyrin, lupeol, tannic acid, arginine, serine, aspartic acid, glycine, threonine, alanine, proline, tryptophan, tryosine, methionine, valine, isoleucine, leucine, n-nonacosane, n-hentricontanen, hexa-cosanol and n-octacosan[24-26]. The fruit of *F. religiosa* contains asgaragine, tyrosine, undecane, tridecane, tetradecane, (e)-β-ocimene, α-thujene, α-pinene, β-pinene, α-terpinene, limonene, dendrolasine, dendrolasine α-ylangene, α-copaene, β-bourbonene, β-caryophyllene, α-trans bergamotene, aromadendrene, α-humulene, alloaromadendrene, germacrene, bicyclogermacrene, γ-cadinene and δ-cadinene[27]. Alanine, threonine, tyrosine have been reported in seeds of *F. religiosa*[28]. The crude latex of *F. religiosa* shows the presence of a serine protease, named religiosin. Religiosin is an acidic protein acts optimally at pH 8.0 5 and temperature 50°C. The extinction coefficient (°ε1%280) of religiosin is 29.47 m−1 cm−1 with 16 tryptophan, 26 tyrosine, and 11 cysteine residues per molecule. The enzyme exhibits milk-clotting as well as detergent activity[29]. Reverse Phase High Performance Liquid Chromatographic analysis of flavonoids in *F. religiosa* using kaempferol, rhamnetin, myricetin, isorhamnetin and quercetin as a standards. The findings showed that quercetin was most abundant flavonol present in *F. religiosa*[30]. The structures of active constituents reported in *F. religiosa* are given in (Figure 2).

Pharmacological activity of *F. Religiosa*

Anti-inflammatory and analgesic activity

The methanolic extract of stem bark of *Ficus religiosa* has shown significant anti-inflammatory activities orally. At a doses of 125, 125 and 500 mg/kg, 30 min prior to 0.1 ml carrageenan injection (1% in 0.9% saline) into the sub plantar region of the left hind paw. Where compared

using an aqueous solution of indomethacin as standard reference group. The paw volume was measured plethysmographically just before and 3h after carrageenan administration. The group treated with 3 doses of crude extract showed inhibition of oedema formation of 52.99, 55.41 and 56.29%, respectively by the 3rd h[31-32]. Aqueous extract of dried powdered bark of *F. religiosa* used in paw oedema, were induced by an injection of carrageenan (0.1 ml in a 1% solution) into the plantar surface of the right hind limb. Control group received phenylbutazone (100 mg/kg). For testing the effect in chronic inflammation sterile cotton pellets (10 mg) were implanted and the animals were treated with three different doses (50, 100 and 200 mg/kg) of the extract for seven days. A significant anti-inflammatory effect was observed in both acute and chronic models of inflammation; the extract also protected mast cells from degranulation induced by various degranulators[33]. A paste of the powdered bark is a good absorbent for inflammatory swellings and can be used to treat burns[34-35]. Earlier study on the same methanol extract demonstrated that the extract inhibited the production of nitric oxide and proinflammatory cytokines in LPS-stimulated microglia via the MAPK pathway[36]

Antidiabetic activity:

Aqueous extract of *F. religiosa* in a doses of 50 and 100 mg/kg show pronounced reduction in blood glucose levels in normal, glucose-loaded hyperglycemic and streptozotocin (STZ) induced diabetic rats and effect was compared with glybenclamide, a well known hypoglycemic drug. Aqueous extract of *F. religiosa* showed significant increase in serum insulin, body weight, glycogen content in liver and skeletal muscle of STZ-induced diabetic rats, also reduced the serum triglyceride and total cholesterol level. The results suggested potential traditional use of *F. religiosa*[37]. Ambike et al. investigated that a phytosterolin isolated from *F. religiosa* root bark when given at a dose of 25 mg/kg orally to fasting rabbits produced a maximum fall of the blood sugar level, equivalent to81% of the tolbutamide standard, after 4 hrs, while with *i.v.* injections of 5-7.5 mg/kg a maximum effect was achieved after 2 h[22]. Aqueous extract of *F.religiosa* at a dose of 100mg and 200mg/kg given orally decreased the fasting blood glucose, and also decreased the exaggerated activity of superoxide dismutase SOD in streptozotocin induced type II diabetic rats. *F.religiosa* modulated the enzymes of antioxidant defense system to combat oxidative stress .As a result glutathione was restored and inhibited the formation of malondialdehyde, proving its anti-diabetic activity along with antioxidant potential[38].

Antioxidant activity:

Antioxidant activity of the aqueous (FRWE) and alcoholic extract (FRAE) of *Ficus religiosa* roots was evaluated in rats by inducing liver injury with carbon tetrachloride:olive oil (1:1). The extract possessed remarkable antioxidant activity showing increased levels of glutathione peroxidase (GPX), glutathione S-transferase (GST), glutathione reductase (GRD), superoxide dismutase (SOD) and catalase (CAT) and decreased level of lipid peroxidation (LPO). *F. religiosa* root extracts, FRWE and FRAE, at a dose level of 500 mg/kg showed significant antioxidant activity against carbon tetrachloride-induced liver injury in rats[39]. The methanolic extract of *F. religiosa* showed significant antiradical activity by bleaching 1,1- diphenyl-2picrylhydrazyl (DPPH) radical, EC_{50} from 11.75 µg was comparable to pyrogallol. It showed good superoxide scavenging potential, EC_{50} from 50.65 µg comparable to that of ascorbic acid and maximum reductive potential at a concentration of 400 µg, which was comparable to that of gallic acid and tannic acid. These finding suggest the rich phytochemical content of *F. religiosa* have good antioxidant activity[18]. Recent study has also revealed that the methanol leaf extract of *F. religiosa*, which contained high total phenolic and total flavonoids contents, exhibited high

antioxidant activity[40]. The ethanolic extract was subjected to screen for antioxidant activity using DPPH radical scavenging method. The percentage peroxide value for *F. religiosa* extract was found in the range of 6.34% to 13.35% for the extract with 200 µg/ml to 1000 µg/ml strength extract[41]. A study was carried to localize the oxidative stress enzymes, peroxidase and catalase; and to quantify the main reactive oxygen species, hydrogen peroxide in *F. religiosa*. The results explained that plants grown in adverse habitat showed 55% higher H_2O_2 production with about 30% increase in peroxidase activity. The three substrates tested for peroxidase activity (guaiacol, ascorbate and *o*-dianisidine), *o*-dianisidine was most preferred substrate of *F. religiosa*. Cytosolic peroxidase activity showed eleven fold increase over cell wall bound peroxidase. Similarly, catalase activity in specimens from adverse habitat showed about two fold increase during day time [42].

Anticonvulsant activity:

The methanol extract of figs of *F. religiosa* was also reported to exhibit a dose-dependent anticonvulsant activity against maximum electroshock- and picrotoxin-induced convulsions through serotonergic pathways modulation[43]. The anticonvulsant activity of the extract (25, 50 and 100 mg/kg, p.o.) was investigated in strychnine-, pentylenetetrazole-, picrotoxin- and isoniazid-induced seizures in mice. Rat ileum and fundus strip preparations were used to study the effect of the extract on acetylcholine (Ach)- and serotonin (5-HT)-induced contractions, respectively. The extract also exhibited dose-dependent potentiation of Ach in rat ileum but failed to potentiate the effect of 5-HT in rat fundus strip preparation[44].

Antimicrobial activity:

Aqueous extract of *F.religiosa* showed high antimicrobial activity against selected pathogenic organisms .High activity was found on *B. subtilis* with about 24mm inhibition zone. And also the growth of *P. aeruginosa* (multi drug resistant) was remarkably inhibited by the plant extract[45].

Nair and Chanda et al. showed antibacterial of *F.religiosa* activity against *Bacillus cereus*[46] whereas the methanol-, followed by chloroform- and aqueous-, extract, at the concentration of 200 mg/ml, were effective against the enterotoxigenic *Escherichia coli*[47]. Zaidi et al. reported the potential *in vitro* anti-*Helicobacter pylori* activity of medicinal plants from Pakistan that is used to cure GI disorders. *Helicobacter pylori* was isolated from the antral biopsy specimens and confirmed through the standard microbiology procedures. The 70% aqueous-ethanol extracts of *Ficus religiosa* completely inhibited the growth of *Helicobacter pylori* at 500µg/ml in all strains and demonstrate anti-*Helicobacter pylori* activity with MBC value ranged from 125 to 250µg/ml[48].

Iqbal et al. investigated that *F. religiosa* bark methanolic extract was 100% lethal for *Haemonchus. contortus* worms during *in vitro* testing[49]. The acetone extracts of seven plant species *Tamarindus indica, F. indica, F. religiosa, Tabernaemontana livaricate, Murraya koenigii, Chenopodium album* and *Syzygium cuminii* were evaluated for their ovicidal activity. *Murraya, Tabernaemontana* and *Chenopodium* showed 70%, 75% and 66.6% ovicidal action at 100% dose level whereas at the same dose level *T. Indica, F. indica, F. religiosa and S. cuminii* showed 48.3%, 41.6%, 13.3%, 53.3% ovicidal action respectively[50]. The preliminary screening of antibacterial activity of *F. religiosa* by agar-well diffusion assay was investigated. The chloroform extracts of *F. religiosa* showed a strong inhibitory activity against growth infectious *Salmonella typhi, Salmonella typhimurium* and *Proteus vulgaris* at a MIC of 39, 5 and 20 µg/ml respectively[51].

Wound healing activity:
The wound healing activity was investigate by excision and incision wound models using *F. religiosa* leaf extracts, prepared as ointment (5 and 10%) were applied on Wistar albino strain rats. Povidine iodine 5% was used as Standard drug. High rate of wound contraction, decrease in the period for epithelialisation, high skin breaking strength were observed in animals treated with 10% leaf extract ointment when compared to the control group of animals. It has been reported that tannins possess ability to increase the collagen content, which is one of the factor for promotion of wound healing[52-54]. Moreover, the ethanol bark extract of *F. religiosa* was reported to possess wound healing[55]

Anti-amnesic activity:
The anti-amnesic activity was investigated using *F. religiosa* methanol extract of figs of *F. religiosa* on scopolamine-induced anterograde and retrograde amnesia in mice. Figs were known to contain a high serotonergic content, and modulation of serotonergic neurotransmission plays a crucial role in the pathogenesis of amnesia[56].

Anti-ulcer activity
The anti-ulcer activity was investigated using ethanol extract of stem bark of *F. religiosa* against *in vivo* indomethacin- and cold restrained stress-induced gastric ulcer, and pylorus ligation assays[57]**.**

Proteolytic Activity:
A comparison of the proteolytic activity of the latex of 46 species of *Ficus* was done by electrophoretic and chromatographic properties of the protein components. *F. religiosa* showed significant proteolytic activity[58].

Anticancer activity:
Fruit extracts of *F. religiosa* exhibited antitumor activity in the potato disc bioassay. None of the tested extracts showed any marked inhibition on the uptake ofcalcium into rat pituitary cells GH4C1[59]

Anti-acetylcholinestrase activity: Methanolic extract of the stem bark of *F. religiosa* found to inhibit the acetylcholinestrase enzyme, thereby prolonging the half-life of acetylcholine. It was reported that most accepted strategies in alzheimer's diseases treatment is the use of cholinesterase inhibitors. The calculated 50% inhibitory dose (ID50) value was 73.69 µg/ml respectively. The results confirm and justify the popular traditional use of this plant for the treatment of alzheimer's diseases[60].

Conclusion

The multiple benefits of *F.religiosa* made it a true miracle of nature. Numerous studies have been conducted on different parts of *F.religiosa*, but this plant has not yet developed as a drug by pharmaceutical industries. A detailed and systematic study is required for identification, cataloguing and documentation of plants, which may provide a meaningful way for the promotion of the traditional knowledge of the herbal medicinal plants. In view of the nature of the plant, more research work can be done on humans so that a drug with multifarious effects will be available in the future market.

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