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**Phytochemical and Medical Properties of *Ficus religiosa*
Specific Parts Extracts: A Review**

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Abstract

Presently there is an increasing interest worldwide in herbal plants pharmacological properties primarily due to advancement in scientific methods. The bioactive ingredients and their potential to treat various diseases of many Indian medical plants are now well established. *Ficus religiosa* is one of religious and medical plant of India, various parts of which like stem, fruit, leaves and roots are widely used in indigenous system of medicine. In recent studies *F. religiosa* has been investigated for presence of a wide range of phytoconstituents which impart a wide spectrum of pharmacological activities. The present review is an attempt to provide a detailed survey of the literature on medical properties of the plants based on scientific experimentation.

Key-Words: *F. religiosa*, Medical Properties, Phytochemistry, Pharmacology

Introduction

Numerous drugs had developed through exploration of ethnopharmacology and traditional medicine. Although scientific studies have been carried out on a large number of Indian botanicals, a considerably smaller number of effective drugs or phytochemical entities have entered the evidence-based therapeutics. *F. religiosa* is the one of Indian religious plant whose medical value was revealed by both *in vitro* and *in vivo* experiment methods. The present review describes the phytochemical and pharmacology aspects of different parts of *F. religiosa* based on scientific experimentation:

Phytochemical and Medical Properties of the Stem

Phytochemistry:

Preliminary phytochemical screening of *F. religiosa* barks, showed the presence tannins, saponins, flavonoids, steroids, terpenoids and cardiac glycosides [1-2]. Phytosterols like bergapten, bergaptol, lanosterol, β -sitosterol, stigmasterol, lupen-3-one, β -sitosterol-d-glucoside (phytosterolin), vitamin k1 have been isolated from the petroleum ether and alcoholic extracts of the stem bark of *F. religiosa*[3-6, 7-8].

Pharmacology:

Analgesic: Methanolic extract of stem bark of *F. religiosa* were administrated orally to rats at a dose level of 250mg/kg body weight was shown strong analgesic activity against acetic acid induced analgesic response [9]. *F. religiosa* need to be analyzed for specific phytochemical agent and for specific effect on the target tissue so as to develop a foolproof analgesic drug from this important plant.

Neuroprotective: Methanolic extract of stem bark of *F. religiosa* inhibited the acetylcholinesterase activity and results in increase generation of acetylcholine (Ach), as decreased level of Ach are marker of various neurodegenerative disorders (ND) thus provides the evidence of Neuroprotective drug [10]. Specific experiments are required to be conducted on *F. religiosa* to determine exact mechanism of action.

Antiulcer: Ethanolic extract of stem bark of *F. religiosa* was given to rats at dose level 100, 200 and 400 mg/kg, significantly increased the pH of gastric acid while at the same time reduced the volume of gastric juice. It also works against gastric ulcer and pylorus ligation [11]. *F. religiosa* is suggested to be analyzed for specific phytochemicals which cure the gastric ulcers.

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Hepatoprotective: *F. religiosa* stem bark powder was given to rats at a dose level of 200 mg/kg orally induce significant hepatoprotective activity against Paracetamol (2g/kg) induced hepatotoxicity [12]. Paracetamol intoxication in normal rats elevated the levels of SGPT, SGOT, ALP, total bilirubin significantly and histologically showed the disarrangement and degeneration of normal hepatic cells indicating acute centrilobular necrosis. The rat treated with alcoholic extract and aqueous extract showed a significant reduction in all the biochemical parameter elevated by paracetamol. Ethyl acetate and pet ether extract showed moderate reduction in biochemical parameters [12]. Most of the hepatotoxic chemicals damage liver cells either by lipid peroxidation or by other oxidative stress mechanisms induced cellular damage. Further work is suggested to carry out to know the specific phytochemical ingredient causing hepatoprotective activity.

Nephroprotective: Alcohol extract of *F. religiosa* stem bark reduced the blood urea nitrogen level close to normal value against the toxic effects induced by anti-Tuberculosis drugs rifampicin and isoniazid in rabbits [13]. The histopathological studies of kidney of normal rabbit indicated that in the proximal convoluted tubules nuclei were normal in appearance, renal parenchyma was also normal in structure. Kidney of treated rabbits showed severe degree of infiltration in the glomerulus with-out renal tubular space between the glomerulus, congestion in the renal parenchyma, necrosis and condensed nucleus. The rabbits treated with extract show normal appearance of the nuclei with no condensed nucleus without any necrosis but at some places there was mild congestion. Kidney tubular cells structure was normal in appearance [13]. *F. religiosa* is a potential herbal plant to work on for further details on its nephroprotective mechanism.

Anti-Diarrhoeal: Acetone extract of stem bark of *F. religiosa* was administrated to castor-oil-induced rats at a dose level of 200 mg/kg showed marked reduction in the number of diarrhoea stools and total weight of diarrhoeal faeces and, frequency and consistency of diarrhoea [14]. Further studies are needed to understand the mechanism of anti-diarrhoeal action of *F. religiosa* stem bark.

Antimicrobial: Aqueous extract of the *F. religiosa* stem bark show antimicrobial activity at 100 mg/ml concentration against the *Escherichia coli*, *Enterobacter aerogenes*, *Pseudomonas aeruginosa*,

Aeromonas hydrophila, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Aspergillus niger* and *Candida albicans* [15]. Comparatively acetone extract inhibit growth of *Bacillus subtilis* at lower concentration whereas *E. coli* show sensitivity at higher concentrations of the same extract [38]. Methanol extract was very active against *Escherichia coli*, *Proteus vulgaris*, *Bacillus subtilis* and *Staphylococcus aureus* but showed no activity against *P. aeruginosa* [38]. The various extracts have antimicrobial activity against selected microorganisms and after further scientific evaluation of bioactive compound from the plant can be used for production of new antibiotics.

Anti-diabetic: Methanolic extract of *F. religiosa* bark administered orally at a dose of 100 mg/kg to streptozotocin induced diabetic rats showed significant anti-hyperglycemic activities. The extract showed asignificant reduction in blood glucose level and showed improved in body weight [44]. Further phytochemical and pharmacological investigations are needed to identify the active molecule and to elucidate its exact mechanism anti-diabetic effect.

Anti-inflammatory: Aqueous extract of *F. religiosa* bark administrated to Carrageenan induced albino rats at a dose level 25, 50 and 100 mg/kg; s.c. significantly reduced the volume of paw edema in a dose dependent manner [45]. Further detailed phytochemical analysis of *F. religiosa* and more research work will possibly make this a prospective anti-inflammatory agent for clinical trial.

Phytochemical and Medical Properties of the Leaves

Phytochemistry:

Leaves of *F. religiosa* composed of campesterol, 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 [16-18]. Leaves and fruits contain carbohydrate, protein, lipid, calcium, sodium, potassium, and phosphorus [19].

Pharmacology:

Anti-inflammatory: The extract of *F. religiosa* was showed the anti-inflammatory activity in albino rats against carrageenan induced pedal oedema [39]. Methanolic extract inhibited the production of nitric

oxide (NO), pro-inflammatory cytokines (tumor necrosis factor-alpha (TNF-alpha), interleukin beta (IL-1beta) and IL-6) and inflammatory mediators through the down regulation of extracellular signal-regulated kinase (ERK), c- Jun N-terminal kinase (JNK) & p38 mitogen-activated protein kinase (MAPK) signaling pathway [20]. It is suggested to find out the dominant phytochemicals which particularly affects the inflammatory mediators.

Antibacterial: The antibacterial activity of *F. religiosa* leaves had tested against various bacteria like *P. vulgaris*, *E. coli*, *B. Subtilis*, *S.aureus*, *Pseudomonas aeruginosa* and *K. Pneumonia*. Chloroform extract inhibited the growth of various Salmonella species, *P. vulgaris*, *E. coli*, *B. Subtilis* and *K. Pneumonia* [21, 41]. Diethyl ether and methanol extracts were showed maximum inhibition on *S.aureus* followed by *E.coli* and *Pseudomonas aeruginosa* [37]. Hence the proper development procedures and formulations are needed to be investigated whether single phytochemical or combination of two or more phytochemical cause the antibacterial activity.

Antioxidant: Ethanolic extract of leaves of *F. religiosa* was tested at different dilutions from 200µg/ml to 1000µg/ml shows antioxidant activity [22]. The molecular mechanism of the antioxidation process need to be investigated.

Anti-diabetic: Ethanolic extracts of *F. religiosa* leaves were administrated orally to alloxan induced diabetic albino rats at a dose level of 250 mg/kg and 100mg/kg body weight. The extract was found effective to lower the blood glucose level significantly in diabetic rats [23]. The *F. religiosa* leaves can be used as an adjuvant in the diabetic therapy and can be further more screened for the chemical entity responsible for the activity.

Wound-Healing: Hydroalcoholic extract of *F. religiosa* leaves applied on wounded Wistar albino rats result in high rate of wound contraction, decrease in the period for epithelia lisation, high skin breaking strength leading to wound healing [24]. Further phytochemical studies are needed where the extract will be subjected to further fractionation and purification to identify and to isolate the active compounds responsible for wound healing activity.

Anti-ulcer: Ethanolic extract of leaves of *F. religiosa* given to rats at a dose level 250 mg/kg and 500 mg/kg

significantly decreased the volume of gastric acid secretions, free acidity and total acidity and ulcer index in aspirin induced ulcer and pylorus ligation in dose dependent manner [25]. But the exact mechanism of this observed anti-ulcer activity of the plant extract is still required to be investigated.

Memory Enhancing: Ethanolic extract of *F. religiosa* leaves was studied for memory enhancing activities in Wistar albino rats and Swiss albino mice by five models: Elevated-Plus Maze, Step through passive avoidance test, Sodium nitrite intoxication, Hebb-Williams Maze and Radial Arm Maze [40]. Scopolamine (1mg/kg, i.p) and sodium nitrite (95mg/kg, s.c) was used as inducing agent and Piracetam (200mg/kg, i.p) was used as standard nootropic agent. The extract significantly improved memory and reversed the amnesia induced by scopolamine and hypoxia induced by sodium nitrite [40]. However further isolation and identification of the active constituents present in the leaves of *F. religiosa* are required to postulate the precise underlying mechanisms.

Laxative: Aqueous extract of *F. religiosa* leaves extract was administrated to albino wistar rats at different doses (100, 200, 400mg/kg, p.o.) showed significant laxative activity and reduced loperamide induced constipation in dose dependent manner. The extract induced a significant enter pooling and excretion of Cl⁻, Na⁺, K⁺ and Ca²⁺ in the intestinal fluid [42]. Future investigation needs to be carried out to isolate the active laxative agents and elucidate the chemical structures to establish the mechanism by which the plant exerts its laxative effect.

Anticancer: Pet ether extract of *F. religiosa* leaves was tested for *in vitro* anticancer activity using human MCF 7 cell line by trypan blue exclusion method. The viable tumor cell count decreased in dose dependent manner and more predominantly beyond concentration of 200 µg/mL where the extract inhibits the entire viable tumor MCF-7 cell [43]. Further studies on mechanism of action and isolation of active components responsible for anticancer activity are required to work upon.

Phytochemical and Medical Properties of the Fruits

Phytochemistry:

The fruit of *F. religiosa* contains asparagine, 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, bicyclgermacrene, γ -cadinene and δ -cadinene [26]. The GC-MS analysis showed the presence of n-Hexadecanoic acid; 9, 12-Octadecadienoic acid; 9, 12, 15-Octadecatrienoic acid, and Butyl 9, 12, 15-octadecatrienoate [27-28]. Asparagine and tyrosine are the most abundant amino acids of the fruit pulp of *F. religiosa* [29]. *F. religiosa* fruits contain a considerable amount of flavonoids namely kaempferol, quercetin, and myricetin and other phenolic components [30]. Alanine, threonine, tyrosine have been reported in seeds of *F. religiosa* [31].

Pharmacology:

Antifertility: *F. religiosa* fruits extract was tested *in vitro* on goat uterus showed the anti-implantation activity. The fruit extract induced decrease in thickness of surface epithelium, diameter of uterine glands, diameter of gland cell and thickness of layer of myometrium according to exposure in time dependent manner [27, 32]. Further detailed study is required to establish its antifertility activity and also to understand underlying cellular and molecular mechanism of action.

Antiamnesic: Methanol extract of fruits of *F. religiosa* was tested on scopolamine-induced anterograde and retrograde amnesia in mice at a dose level 10, 50 and 100 mg/kg, *i.p.* showed a significant improvement of memory in dose dependent manner [33]. This study demonstrated anti-amnesic activity of *F. religiosa* however, further study on the phytochemicals profile, safety and active principles of the plant need to be carried out.

Phytochemical and Medical Properties of the Roots

Phytochemistry:

It contains tannin, wax, saponin, β -sitosterol, leucocyanidin-3-O- β -D-glucopyranoside, leucopelargonidin-3-O- β -D-glucopyranoside, leucopelargonidin-3-O- α -L-rhamnopyranoside, lupeol, ceryl behenate, lupeol acetate, α -amyrin acetate, leucoanthocyanidin and leucoanthocyanin [34].

Pharmacology:

Anticonvulsant: Aqueous aerial root extract of *F. religiosa* at dose level 25, 50 and 100 mg/kg was investigated in strychnine, pentylenetetrazole, picrotoxin and isoniazid induced seizures in mice. The extract showed no toxicity and protected the animals in the strychnine, pentylenetetrazole tests in a dose dependent manner [35]. The extract possesses anticonvulsant activity through the glyceric pathway as it increased the inhibitory effect of glycine at all glycine receptors. Anticonvulsant effect of *F. religiosa* also involve additional GABA amino butyric acid (GABA) ergic pathway [35]. It is suggested that further research on *F. religiosa* need to be carried out to determine how GABA pathway are modulated and what are the specific phytochemical constituents involved.

Antidiabetic: *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 to 81% 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 [36]. Further detailed phytochemical analysis of *F. religiosa* and more research work will possibly make this a prospective antidiabetic agent for clinical trial.

Conclusion

F. religiosa is widely used in the Indian system of medicine, besides which scientific experiments prove that different part of it live Stem, leaf, fruits and root have several medical properties. The stem has Analgesic, Neuroprotective, Antiulcer, Hepatoprotective, Nephroprotective, Anti-Diarrhoeal, Antimicrobial, Anti-diabetic and Anti-inflammatory properties. Beside stem the leaves exhibit the Anti-inflammatory, Antibacterial, Antioxidant, Anti-diabetic, Wound-Healing, Anti-ulcer, Memory Enhancing, Laxative and Anti-cancer activities. The fruits have also great medical value and have phytochemical which act as antifertility and Antiamnesic agents. The roots of *F. religiosa* exhibit Anticonvulsant and Antidiabetic activity.

With development of new scientific methods there is an increasing interest worldwide in search bioactive ingredients from herbal plants. Numerous drugs had discovered through exploration of ethnopharmacology and traditional medicine. More efforts are needed to find particular phytochemicals and their molecular mechanism of action to establish and validate the safety and practices of herbal medicines.

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