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Review on Ethanomedicinal and Pharmacological Properties of *Ficus religiosa*

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ABSTRACT

Ficus religiosa (Bo tree) is the most popular member of the genus *Ficus*, commonly named as Peepal. Various parts of the plant, like bark, fruit, leaves and seeds are widely used in indigenous system of medicine. *F. religiosa* showed a wide spectrum of pharmacological activities like, anticonvulsant, anthelmintic, anti-amnesic, anti-anxiety, anti-asthmatic, antibacterial, antioxidant, anti-inflammatory and antiulcer. The present review is an attempt to provide a detailed survey of the literature on traditional uses and pharmacological properties of the plant.

Key words: *Ficus religiosa*, anticonvulsant, anthelmintic, anti-amnesic, anti-inflammatory, antiulcer.

INTRODUCTION

Numerous plants synthesize substances that are useful in the maintenance of health in humans and animals (Sawarkar et al., 2011). With a view to increasing the wide range of medicinal usages, the present day entails new drugs with more potent and desired activity with less or no side effects against particular disease (Roy et al., 2009). The genus Ficus (Moraceae) constitutes one of the largest genera of angiosperms includes with more than 800 species and 2000 varieties of *Ficus* genus, occurring in most tropical and subtropical forests worldwide (Hamed, 2011). Ficus religiosa, commonly known as Peepal, is the most popular member of the genus Ficus and it is known by more than 150 names. Ficus religiosa has got mythological, religious and medicinal importance in Indian culture. References to Ficus religiosa are found in several ancient holy texts like Arthasastra, Puranas, Upanisads, Ramayana, Mahabharta, Bhagavadgita and Buddhistic literature etc (Prasad et al., 2006). Ficus religiosa (Bo-Tree) is well-known symbol for happiness, prosperity, longevity and good luck. The name 'Sacred Fig' was given to it because it is considered sacred by the followers of Hinduism, Jainism and Buddhism (Yadav et al., 2011). F. racemosa, F. bengalensis and F. deltoidea are some of the commonly occurring trees of this genus belonging to family Moraceae (Sawarkar et al., 2011). About half of the species of Ficus are monoecious and the rest are functionally dioecious (Singh et al., 2011). All Ficus species possess latex-like material within their vasculatures that provide protection and self-healing from physical assaults (Sirisha et al., 2010). Various studies indicates that Ficus species are widely used in the management of various types of diseases like Respiratory disorders, sexual disorders, central nervous system disorders (CNS), cardiovascular disorders (CVS), gastric problems, skin infections and diabetes etc (Sirisha et al., 2010, Vinutha et al., 2007).



Fig 1 Pharmacological activities of Ficus religiosa.

Ficus religiosa possess a wide range of pharmacological activities, Shown in fig 1. Among various pharmacological properties, Ficus religiosa imparts an important role in CNS. It has been shown that methanolic extract of leaves of Ficus religiosa inhibited the production of nitric oxide (NO), pro-inflammatory cytokines (tumor necrosis factor-alpha (TNF-alpha), interleukinbeta (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) signalling pathway. Further, it has found to suppresses the nuclear factor kappaB (NF-kappaB) activation which proven the protective role of F. religiosa in various neurodegenerative disorders (ND) like Alzheimer disease (AD), Parkinson's disease (PD) and Huntington disease (HD) (Jung et al., 2008). Another study which also provides the evidence of drug in neuroprotection indicates that the methanol extract of stem bark of Ficus 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) (Vinutha et al., 2007). Further, the aqueous aerial root extract of Ficus religiosa possess anticonvulsant activity through the glycenergic pathway as it increased the inhibitory effect of glycine at all glycine receptors. Anticonvulsant effect of *F. religiosa* also involve additional Gama amino butyric acid (GABA) ergic pathway (Patil et al., 2011). *Ficus religiosa* also found to exhibit anti-ulcerogenic potential by decreasing the level of malondialdehyde (MDA), superoxide dismutase (SOD). Further it has been reported to stimulate the synthesis of endogenous prostaglandin (PG's) and thus act as ulceroprotectant (Saha and Goswami, 2010, Khan et al., 2011). Morover, it has been found that *Ficus religiosa* exhibit antidiabetic activity by increasing the serum insulin level, body weight and glycogen content and also shown antilipidperoxidative effect against streptozotocin induced diabetic rats (Pandit et al., 2010). Fig 2 indicates various potential target sites of *Ficus religiosa*.



Fig 2 Possible targets of *Ficus religiosa* involved in the management of various disorders.



Fig 3 Mechanism underlying anti-inflammatory activity of Ficus religiosa.

TRADITIONAL USES

Ficus religiosa has been extensively used in traditional medicine for a wide range of ailments. Its bark, fruits, leaves, roots, latex and seeds are medicinally used in different forms, sometimes in combination with other herbs (Aiyegoro and Okoh, 2009).

Leaves

The leaves alone are used to treat constipation. The leaves used together with young shoots are act as strong laxative. In Nepal leaf juice with honey is used for multipurpose such as for diarrhoea, asthma, cough, earache, toothache, and migraine, in gastric problems and in haematuria (Kunwar and Bussmann, 2006). In addition, the leaves of *Ficus religiosa* have also shown significant memory enhancing activity (Devi et al., 2011).

Bark

The Bark is cooling and astringent and is useful in inflammation and glandular swellings of neck. The paste of powdered bark is used in cases of anal fistula and as absorbent for inflammatory swellings and also used in burns (Nadkarni, 1954, Warrier et al., 1995). The bark of *Ficus religiosa* is reported to possess antiulcer and wound healing activities (Khan et al., 2011, Kalyon et al., 2009). It is used in diabetes, diarrhoea, leucorrhoea, anxiety, for vaginal and other urinogenital disorders and to improve the complexion (Pandit et al., 2010, Ratnasooriya et al., 1998).

Fruit

The seeds and fruits are digestive, laxative and refrigerant. The dried fruit, pulverized and taken in water for a fortnight removes asthma. The ripe fruit is cold in potency and good for burning sensation. It act as cardiac tonic and is useful to cure the diseases of Vagina. It also cures vomiting, anorexia and edema (Singh, 2006). The fruit extract of plant have anti tumour and antibacterial activity (Sirisha et al., 2010).

PHARMACOLOGICAL ACTIVITIES

The Whole parts of the plant exhibit wide spectrum of activities such as anticancer, antioxidant, anti diabetic, antimicrobial, anticonvulsant, anthelmintic, antiulcer, antiasthmatic, anti amnesic etc.

Antiulcer activity

The term 'peptic ulcer' describes a condition in which there is a discontinuity in the entire thickness of the gastric or duodenal mucosa that persists as a result of acid and pepsin in the gastric juice (Bansal et al., 2009). The principal pathological condition in which it is useful to reduce acid secretion is peptic ulceration (both duodenal and gastric) & reflux oesophagitis (Rang et al., 5th edition). Therapy of peptic ulcers with commercially available antiulcer drugs is usually overshadowed by various side effects. Thus there is a need to find new antiulcerogenic compound(s) with potentially less or no side effects. One of the plants that have been traditionally used in the India and Malays folklore medicine to treat gastric ulcer is *Ficus religiosa* (Ravishankar and Shukla, 2007, Kumar et al., 2011). The ethanol extract of stem bark of *Ficus religiosa* extract (EBFR) exhibited potential antiulcer activity. The antiulcer activity of *Ficus religiosa* was evaluated in vivo against indomethacin and cold restrained stress induced gastric ulcers and pylorus ligation assay. The determination of antiulcer effect was based upon the reduction of ulcer index. The extract (100, 200 & 400 mg/kg) significantly reduced the ulcer index in all assay used (Khan et al., 2011). The hydroalcoholic extract of leaves of *Ficus religiosa* also exhibited antiulcer activity (Saha and Goswami 2010). The activity of extract was evaluated against pylorus ligation-induced ulcers, ethanol-induced ulcers and aspirin-Induced ulcers. Determination of antiulcer effect was based upon ulcer index and oxidative stress. Administration of *Ficus religiosa* significantly reduced the ulcer index (Saha and Goswami, 2010).

Anti-inflammatory activity

Inflammation is the body's immediate response to damage to its tissue & cells by pathogens, noxious stimuli such as chemicals or physical injury (Weiss, 2008). It is a protective attempt by the organism to remove the injurious stimuli and initiate the healing process (Singh et al., 2008). The various mediators involved in inflammation include cytokines & chemokines, PG's, platelet activating factor (PAF), NO and histamine etc. PG's are generally considered to be potent pro-inflammatory mediator (Hata and Breyer, 2004). Further, evidence suggests that during inflammation there is increased generation of ROS (Hata and Breyer, 2004). It has been found that Mast cell degranulation also imparts a role in inflammation due to release of several mediators like Histamine, which are implicated in the inflammation and allergy (Viswanathan et al., 1990). Ficus religiosa has found to be potential anti-inflammatory & analgesic property. The mechanism underlying the effect is the inhibition of PG's synthesis. It was found that the leaf extract of Ficus religiosa has potential antiinflammatory activity against carrageenan induced paw oedema. The inhibitory activity was found due to inhibition of release of histamine, serotonin (5HT), Kinins and PG's (Charde et al., 2010). The methanol extract of stem bark of *Ficus religiosa* has inhibitory effect on carrageenan-induced inflammation in rats due to the inhibition of the enzyme cycylooxygenase (COX) leading to inhibition of PG's synthesis. Further, various studies revealed that tannin present in the bark possess anti-inflammatory effect (Sreelekshmi et al., 2007). Moreover, it has been shown that methanolic extract of stem bark of Ficus religiosa is known to suppress inflammation by reducing both 5-HT & bradykinin (BK). Mangiferin isolated from drug has anti-inflammatory activity against carrageenan-induced paw oedema (Verma et al., 2010). Figure (3) indicates the activity of various extracts of Ficus religiosa on inflammation. Viswanathan et al investigated the antiinflammatory and mast cell proliferative effect of aqueous extract of bark of Ficus religiosa (Viswanathan et al., 1990). The antiinflammatory effect was evaluated against acute (carrageenaninduced hind paw oedema) and chronic (cotton pellet implantation) models of inflammation. As already discussed mast cell degranulation cause inflammation and Ficus religiosa extract significantly reduced the percentage of degranulation induced by either propranolol or carbachol (Viswanathan et al., 1990). The resulted anti-inflammatory & mast cell protective effect may be responsible for the beneficial effect of *Ficus religiosa* in kumkum dermatitis and other inflammatory conditions (Viswanathan et al., 1990).

Anthelmintic activity

Ficus religiosa have been used to treat the parasitic infections in man and animals. Iqbal el al investigated the anthelmintic effect of methanolic bark extract of F. religiosa on the adult Haemonchus contortus Worm. Adult motile H. Contortus was collected from the gastrointestinal tract of sheep slaughtered at Faisalabad slaughterhouse. It was found that ficin is responsible for the anthelmintic effect in the methanolic extract of *F. religiosa* (Akhatar et al., 2000).

Further, studies show that the aqueous extract of fruit of *F. religiosa* has shown potent Anthelmintic activity as compared to other species of Ficus against Pheretima posthuma (earthworms) (Sawarkar et al., 2011). Stem and bark extract of *Ficus religiosa* was also found lethal to Ascaridia galli (Parasitic worm belonging to phylum nematoda) (Akhatar et al., 2000).

Anticonvulsant activity

It is well recognised that serotonergic neurotransmission modulates a wide variety of experimentally induced seizures in the brain and is involved in seizure protection by altering various GABAergic and glutamatergic functions (Bagdy et al., 2007). The reductions of brain serotonin concentration leads to an increase in seizure susceptibility and the Pharmacological treatment that facilitate serotonergic neurotransmission inhibit the seizures in many animal models of epilepsy (Lazarova et al., 1983, Statnick et al., 1996). Figs of the plant F. religiosa have been reported to contain highest amount of Serotonin which is responsible for its anticonvulsant effect (Bliebtrau, 1968). Further, Singh and Goel investigated the anticonvulsant effect of methanolic extract of *Ficus religiosa* figs on Maximal electroshock-induced convulsions (MES), Picrotoxin-induced convulsions, and pentylenetetrazoleinduced convulsions (PTZ) (Singh and Goel, 2009).

In Ayurveda it is claimed that leaves of *Ficus religiosa* also possess anticonvulsant activity (Vyawahare et al., 2007). The anticonvulsant effect of the extract obtained from the leaves of *Ficus Religiosa* was evaluated against PTZ (60mg/kg, i.p) induced convulsion in albino rats. The study revealed 80 to 100 % protection against PTZ-induced convulsions when given 30-60 minutes prior to induced convulsion respectively (Vyawahare et al., 2007). Patil et al demonstrated that the anticonvulsant effect of the aqueous aerial root extract of F. religiosa is effective in management of chemically-induced seizures in rats (Patil et al., 2011). The extract was evaluated against strychnine-induced convulsions and pentylenetetrazole-induced convulsions animal models.

Anti-amnesic activity

Memory is one of the complex functions of the brain involving encoding, storing, and recalling information (Pattewar et

al., 2011). Amnesia, a cognitive disorder is responsible for the impairment in learning and memory (Devi et al., 2011). It was reported that serotonergic system plays a significant role in learning and memory, in particular by interacting with the cholinergic, glutamatergic, dopaminergic or GABAergic systems (Buhot et al., 2000). It was reported that modulation of serotonergic neurotransmitter plays crucial role in the pathogenesis of amnesia (Kaur et al., 2010).

It was found that figs of the plant contain a high serotonergic content (Ahuja et al., 2011). The methanol extract of figs of *Ficus religiosa* was investigated for its anti-amnesic activity against scopolamine-induced anterograde and retrograde amnesia. Elevated plus maze (EPM) and Modified passive avoidance paradism (MPA) were used as experimental models to investigate the effect.

Parameters such as reduction in transfer latency in EPM and step down latency, no. of trials & no. Of mistakes in MPA were noted. To investigate the involvement of serotonergic pathway in antiamnesic effect of *Ficus religiosa* extract, cyproheptadine (nonselective 5-HT blocker) was administered along with the extract. Thus the study concluded that F. religiosa have prominent antiamnesic effect as its treatment attenuated the scopolamine-induced anterograde and retrograde amnesia in a dose dependent manner (Ahuja et al., 2011).

According to another study, it was investigated that ethanol extract of leaves of Ficus religiosa have memory enhancing activity. The preliminary phytochemical screening and TLC analysis of the leaf extract of F. religiosa showed the presence of sterols, glycosides, tannins and amino acids. The memory enhancing effect was evaluated against Elevated plus maze, Step through avoidance, Sodium nitrite intoxication, Hebb-William maze and Radial arm maze experimental models. Scopolamine was used as inducing agent except in sodium nitrite intoxication; in this model sodium nitrite was act as inducing agent. The extract showed improved in memory and reversed the amnesia induced by scopolamine and hypoxia induced by sodium nitrite. The effect of ethanol extract of F. religiosa (100 mg/kg) was comparable to that of piracetam and mentat (100 mg/kg). The result concluded that amino acids present in the extract may be responsible for the antiamnesic and memory enhancing activities of the plant (Devi et al., 2011).

Antimicrobial activity

It has been found that *Ficus religiosa* is used as a national therapy against various infectious disorders. The antibacterial potential of *Ficus religiosa* was investigated by Hemaiswarya et al. According to this study the chloroform extract of the leaves of *Ficus religiosa* inhibited the growth of various Salmonella species, *P. vulgaris, E. coli, B. Subtilis* and *K. Pneumonia* etc which revealed the antibacterial potential of the plant (Hemaiswarya et al., 2009).

According to another study different extracts (methanol, aqueous, chloroform) of the bark of *Ficus religiosa* has inhibitory effect on the growth of three enteroxigenic *E. coli*, isolated from the patients suffering from diarrhoea (Uma et al., 2009).

Antiasthmatic activity

Ficus religiosa is also used for the treatment of Bronchial Asthma. Malhotra et al was the first who investigated the antiasthmatic potential of the alcoholic bark extract of the *Ficus religiosa*. The exract showed inhibitory effect on both acetylcholine-induced and histamine-induced experimental asthma (Malhotra et al., 1960).

Miscellaneous activities

Apart from above mentioned activities *Ficus religiosa* has been studied for its anxiolytic potential. It has been discovered that the aqueous extract of trunk bark of *Ficus Religiosa* exhibit potent anti-anxiety activity with a rapid onset of action (Ratnasooriya et al., 1998). The aqueous bark extract of *Ficus religiosa* has also shown antidiabetic activity against streptozotocin-induced diabetic rats (Pandit et al., 2010). Yadav et al, has evaluated the nephroprotective effect of methanolic extract of *Ficus religiosa* latex at a dose level 400 mg/kg (Yadav et al., 2011). *Ficus religiosa* has also shown antioxidant activities (Sirisha et al., 2010). Bark of plant has also shown aphrodisiac potential (Singh et al., 2010)

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