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THERAPEUTIC POTENTIAL OF *FICUS RELIGIOSA* L. IN PREVENTION / TREATMENT OF CHRONIC DISEASES AND OTHER DISEASE CONDITIONS : AN OVERVIEW

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ABSTRACT

Medicinal plants have been used in healthcare since ancient time. Medicinal plants with rich source of phytochemical constituents have been found to play vital role in prevention and treatment of serious diseases like diabetes mellitus , cancer, infections, inflammation, cardiovascular diseases and gastrointestinal disorders having a major global impact on mortality and morbidity. *Ficus religiosa* (L.) is a popular bodhi tree and has got mythological, religious and medicinal importance in Indian culture since times immemorial . This plant has been used in traditional Indian medicine for a wide range of ailments such as antibacterial, antiprotozoal, antiviral, astringent, anti-diarrhoeal, in the treatment of gonorrhea, ulcers, skin diseases, cancer, asthma. The leaves of the plant has been reported to possess anti-venom activity and to regulate the menstrual cycle . Studies have demonstrated that various parts of *Ficus religiosa* (L.) possesses pharmacological properties including anti-inflammatory , anticonvulsant , anticancer, antioxidant, antidiabetic, antimicrobial, anticonvulsant, anthelmintic , antiulcer, antiasthmatic, anti-amnesic and many more due to its rich content of phytoconstituents / biomolecules like phenols, tannins, steroids, alkaloids and flavonoids, β-sitosteryl-D-glucoside, vitamin K, n-octacosanol, methyl oleanolate, lanosterol, stigmasterol, lupen-3- one etc. The present study is an attempt to present the therapeutic properties of this important medicinal plant in prevention and treatment of a wide range of conditions ranging from common ailments to chronic diseases with a view to develop plant based medicines for treatment of diseases especially chronic ailments for which our modern system of medicine has no permanent cure. Although various parts of *F. religiosa* have been found to exhibit therapeutic potential in treatment of varieties of diseases , extensive clinical studies on human subjects are needed to authenticate its therapeutic properties and to understand its mechanism of action.

***Keywords*:** *Ficus religiosa* ; Botanical classification ; Phytoconstituents; Traditional uses; Alternative and complementary medicinal uses ; Pharmacological activities; Mechanism of action

INTRODUCTION

Medicinal plants have been found to play a vital role in healthcare by serving as a primary source of therapeutic compounds, forming the basis of traditional healing systems, and contributing to modern medicine. They are used to treat a wide range of conditions, from common ailments to chronic diseases, and offer affordable, accessible treatments, especially in developing regions. Their integration into the healthcare delivery system can enhance disease prevention, promote health, and reduce reliance on synthetic drugs with potential side effects. *Ficus religiosa* (L.) is a large perennial tree, glabrous when young, found throughout the plains of India up to 170m altitude in the Himalayas, largely planted as an avenue and road side tree especially near temples . [1] It is a popular bodhi tree and has got mythological, religious and medicinal importance in Indian culture since times immemorial . [2] The plant has been used in traditional Indian medicine for various range of ailments. Traditionally the bark is used as an antibacterial, antiprotozoal, antiviral, astringent, anti-diarrhoeal, in the treatment of gonorrhea, ulcers, and the leaves are used for skin diseases. The leaves of the plant has been reported to possess anti-venom activity and to regulate the menstrual cycle
. [3,4] In Bangladesh, it has been used in the treatment of various diseases such as cancer, inflammation, or infectious diseases. [5] In case of high fever, its tender branches are used as a tooth brush. Fruits are used as laxatives , [6] latex is used as a tonic, and fruit powder is used to treat asthma [7,8]. *Ficus religiosa* (L.) has been found to possess therapeutic properties including antioxidant , anti-inflammatory, antimicrobial , antidiabetic and many more due to its rich content of compounds like flavonoids and tannins. The present study is an attempt to present the therapeutic properties of this important medicinal plant in prevention and treatment of a wide range of conditions, from common ailments to chronic diseases with a view to develop plant based medicines for treatment of diseases especially chronic ailments for which our modern system of medicine has no permanent cure.

Botanical classification

Kingdom: Plantae

Phylum: Tracheophyta

Class: Magnoliopsida

Order: Urticales

Family: Moraceae

Tribe: Ficeae

Genus: Ficus

Botanical name: *Ficus religiosa*

Phytoconstituents

F. religiosa has been found to possess a large number of bioactive molecules with diverse varieties of pharmacological properties .[8a] Research studies have shown that the stem bark of *F. religiosa* possesses phytoconstituents of phenols, tannins, steroids, alkaloids and flavonoids, β-sitosteryl-D-glucoside, vitamin K, n-octacosanol, methyl oleanolate, lanosterol, stigmasterol, lupen-3- one. [9] The active constituent from the root bark *F. religiosa* was found to be β-sitosteryl-D-glucoside, which showed a per oral hypoglycemic effect in fasting and alloxan-diabetic rabbits and in pituitary-diabetic rats. The fruits contain 4.9% protein having the essential amino acids, isoleucine, and phenylalanine . [10] The seeds of the plant have been found to contain phytosterolin, β-sitosterol, and its glycoside, albuminoids, carbohydrate, fatty matter, coloring matter, caoutchoue 0.7–5.1% . [11] *F. religiosa* fruits contain flavonols namely kaempeferol, quercetin, and myricetin. [12] Leaves and fruits contain carbohydrate, protein, lipid, calcium, sodium, potassium, and phosphorus. [13] The aqueous extract of dried bark of *F. religiosa* has been reported to contain phytosterols, flavonoids, tannins, furanocoumarin derivatives namely bergapten and begaptol. The fruit of *F. religiosa* contained appreciable amounts of total phenolic contents, total flavonoid, and percent inhibition of linoleic acid. Generally higher extract yields, phenolic contents, and plant material antioxidant activity were obtained using aqueous organic solvents, as compared to the respective absolute organic solvents. Although higher extract yields were obtained by the refluxing extraction technique, in general higher amounts of total phenolic contents and better antioxidant activity were found in the extracts prepared using a shaker. [14, 15] In another study , an comprehensive review of *F. religiosa* covering its ethnobotanical, natural product chemistry, pharmacological data has been presented . [14,15] Preliminary phytochemical screening of *F. religiosa* barks showed the presence tannins, saponins, flavonoids, steroids, terpenoids and cardiac glycosides. [16,17] 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. [14,18,19,20] 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. [21] Leaves yield campestrol, stigmasterol, isofucosterol, α-amyrin, lupeol, tannic acid, arginine, serine, asparticacid, glycine, threonine, alanine, proline, tryptophan, tryosine, methionine, valine, isoleucine, leucine, n-nonacosane, n-hentricontanen, hexa-cosanol and n-octacosan . [22,23,24] 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. [25] Alanine, threonine, tyrosine have been reported in seeds of *F. religiosa* . [26] The crude latex of *F. religiosa* shows

the presence of a serine protease, named religiosin. Religiosin is an acidic protein acts optimally at 8.0-8.5 and temperature 50°C. The enzyme exhibits milk clotting as well as detergent activity .[27] Reverse Phase High Performance Liquid Chromatographic analysis of flavonoids in *F. religiosa* using kaempferol, rhamnetin, myricetin isorhamnetin and quercetin as a standard. The findings showed that quercetin was most abundant flavonol present in *F. religiosa* . [28]

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. [29]

(1] Leaves

The leaves alone are used to treat constipation. The leaves used together with young shoots acts 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. [30a]. In addition, the leaves of Ficus religiosa have also been shown to possess significant memory enhancing activity. [30]

(2) 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. [31,32] The bark of Ficus religiosa is reported to possess antiulcer and wound healing It is used in diabetes, diarrhoea, leucorrhoea, anxiety, for vaginal and other urinogenital disorders and to improve the complexion . [35,36]

(3) 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 acts as cardiac tonic and is useful to cure the diseases of vagina. It also cures vomiting, anorexia and edema. [37a] The fruit extract of plant has anti- tumor and antibacterial activity. [37]

Alternative and complementary medicinal uses

The bark of *F. religiosa* is an important ingredient in many Ayurvedic formulations, such as *Nalpamaradi tailam, Chandanasavam, Nyagrodhadi churna* and *Saribadyasavam*. [38,39] **PHARMACOLOGICAL**

ACTIVITIES

Various parts including leaves , bark, fruits of *Ficus religiosa* have been found to exhibit wide range of pharmacological activities such as anticancer, antioxidant, antidiabetic, antimicrobial, anticonvulsant, anthelmintic, antiulcer, antiasthmatic, anti-amnesic etc. as given below.

Antiulcer Activity

It has been observed that commercially available antiulcer drugs produce side effects in treatment of conditions due to peptic ulcer [40,41] which necessitates to developing new drugs with minimal side effects to treat complex medical condition like peptic ulcer. The medicinal plant *Ficus religiosa* has been used as folklore medicine to treat gastric ulcer in India and Malays . [42,43] The ethanol extract of stem bark of *Ficus religiosa* has been found to possess potential antiulcer activity. [33] In another study the hydroalcoholic extract of leaves of *Ficus religiosa* also exhibited antiulcer activity [44] where the activity of extract was evaluated against pylorus ligation-induced ulcers, ethanol-induced ulcers and aspirin-Induced ulcers.

Anti-inflammatory Activity

The pathogenesis of inflammation and mechanism underlying the process have been studied by researchers suggesting the involvement of mediators like cytokines and chemokines, PG's, platelet activating factor (PAF), NO and histamine etc. in inflammation. [45, 46, 47] In addition to above , increased generation of ROS [47] and mast cell degranulation [48] have also been suggested during inflammation. Ficus religiosa has been found to possess potential anti-inflammatory and 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 results of the study have suggested that the inhibitory activity might be due to inhibition of release of histamine, serotonin (5-HT), kinins and PG's . [49] 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 cylooxygenase (COX) leading to inhibition of PG's synthesis. [50] Further, various studies revealed that tannin present in the bark possess anti-inflammatory effect . Moreover, it has been shown that methanolic extract of stem bark of Ficus religiosa is known to suppress inflammation by reducing both 5-HT and bradykinin (BK). Mangiferin isolated from drug has anti-inflammatory activity against carrageenan-induced paw oedema . [51] Another study has found the antiinflammatory and mast cell proliferative effect of aqueous extract of bark of *Ficus religiosa* [48] where the antiinflammatory effect was evaluated against acute (carrageenan-induced 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 [48] . The study has suggested that the resulted anti-inflammatory and mast cell protective effect may be responsible for the beneficial effect of Ficus religiosa in kumkum dermatitis and other inflammatory conditions . [48]

Anthelmintic Activity

Ficus religiosa has been used to treat the parasitic infections in man and animals. The anthelmintic effect of methanolic bark extract of F. religiosa on the adult Haemonchus contortus Worm has been found in a

study suggesting that ficin may be responsible for the anthelmintic effect in the methanolic extract of F. religiosa . [52] The aqueous extract of fruit of *F. religiosa* has been shown to possess potent anthelmintic activity as compared to other species of *Ficus* against Pheretima posthuma (earthworms). [53] Stem and bark extract of *Ficus religiosa* was also found lethal to Ascaridia galli (Parasitic worm belonging to phylum nematoda). [52] The research studies have shown that methanolic extract of F. *religiosa* bark was found to be 100% lethal for *Haemonchus contortus* worms . [54] the stem and bark extracts of *F. religiosa* proved lethal to *Ascaridia galli in vitro*. The latex of some species of *Ficus* (Moraceae), i.e., *Ficus inspida, F. carica* was also reported to have anthelmintic activity against *Syphacia obvelata, Aspiculuris tetraptera*, and *Vampirolepis nana* . [55] The pharmacological studies on *F. glabrata* latex with live *Ascaris* demonstrated a lethal effect at concentrations reduced to 0.05% latex in physiological saline solution. It can be considered that anthelmintic activity might due to a proteolytic fraction called ficin. The study suggests that methanolic extractof *F. religiosa* possibly exerted anthelmintic effect because of ficin . [56]

Anticonvulsant Activity

Various mechanisms involving serotonergic neurotransmission and alteration in GABAergic and glutamatergic functions have been suggested in epileptic seizures protection. [57,58, 59] . Figs of the plant *F. religiosa* have been shown to contain highest amount of serotonin which may be responsible for its anticonvulsant effect. [60] The anticonvulsant effect of methanolic extract of Ficus religiosa figs on deferent study models like maximal electroshock-induced convulsions (MES), picrotoxin-induced convulsions, and pentylenetetrazole-induced convulsions (PTZ) has been reported. [61] . Further , the leaves of *Ficus religiosa* also possess anticonvulsant activity as claimed in Ayurveda where 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. [62] A study has demonstrated that the anticonvulsant effect of the aqueous aerial root extract of *F. religiosa* is effective in management of chemically -induced seizures in rats. [63] The extract was evaluated against strychnine-induced convulsions and pentylenetetrazole- induced convulsions in animal models. The results of another study revealed that methanolic extract of figs of *F. religiosa* had anticonvulsant activity against maximum electroshock (MES) and picrotoxin-induced convulsions, with no neurotoxic effect, in a dose-dependent manner suggesting that the extract might be mediating its effect via modulating serotonin-dependent GABAergic and/or glutamatergic neurotransmission. [64]

Anti-amnesic Activity

Research studies have found that memory being one of the complex functions of the brain involves encoding, storing, and recalling information. [65] Amnesia, a cognitive disorder is responsible for the impairment in learning and memory. [66] 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 . [67] It was reported that modulation of serotonergic neurotransmitter plays crucial role in the pathogenesis of amnesia. [68] It was found that figs of the plant contain a high serotonergic content [69] 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 and 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* has prominent antiamnesic effect as its treatment attenuated the scopolamine-induced anterograde and retrograde amnesia in a dose dependent manner. [69] 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 acts 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 results of the study concluded that amino acids present in the extract may be responsible for the anti-amnesic and memory enhancing activities of the plant. [66] **Antimicrobial Activity**

The chloroform extract of the leaves of *Ficus religiosa* has been found to inhibit the growth of various Salmonella species, P. vulgaris, E. coli, B. Subtilis and K. Pneumonia etc. which revealed the antibacterial potential of the plant. [70] According to another study, different extracts (methanol, aqueous, chloroform) of the bark of *Ficus religiosa* have been found to exhibit inhibitory effect on the growth of three enteroxigenic E. coli, isolated from the patients suffering from diarrhea. [71] Aqueous and ethanolic extracts of *F. religiosa* leaves showed antibacterial effect against *Staphylococcus aureus, Salmonella paratyphi, Shigella dysenteriae, S. typhimurium, Pseudomonas aeruginosa, Bacillus subtillis, S. aureus, Escherichia coli, S. typhi*. In another study, chloroform extract of fruits showed antimicrobial effect against *Azobacter chroococcum, Bacillus cereus, B. megaterium, Streptococcus faecalis, Streptomycin lactis, and Klebsiella pneumonia* . [72] The ethanolic extract of leaves showed antifungal effect against *Candida albicans* . [73] Aqueous, methanol, and chloroform extracts from the leaves of *F. religiosa* were completely screened for antibacterial and antifungal activities. The chloroform extract of *F. religiosa* possessed a broad spectrum of antibacterial activity with a zone of inhibition of 10–21mm. The methanolic

extracts possessed moderate antibacterial activity against a few bacterial strains. There was less antibacterial activity or none at all using aqueous extracts. The extracts of *F. religiosa* were found to be active against .*Aspergillus Niger* and *Penicillium notatum*. The extracts from the leaves exhibited considerable and variable inhibitory effects against most of the microorganisms tested. [73,70] **Anti-asthmatic 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* was studied and it has been found that the extract showed inhibitory effect on both acetylcholine-induced and histamine-induced experimental asthma. [74]

Wound Healing Activity

It has been found that *Ficus religiosa* leaf possesses wound healing , anti- inflammatory, and analgesic, anti-lipid- peroxidation activity. The bark of the plant has been found to exhibit wound healing activity, [75] anti -inflammatory, analgesic, and anti-lipid- peroxidation activity . [50] The tender shoots of this plant have been found to possess purgative properties . [76] Keeping in view of these therapeutic properties in the plant, a study has been conducted to investigate the wound healing activity by excision and incision wound models to evaluate the wound-healing activity of *Ficus religiosa* extracts, prepared as ointment form (5 and 10%) and applied on Wistar albino strain rats of either sex. In this experimental animal model study, povidine iodine (5%) was used as standard drug. The healing of the wound was assessed by the rate of wound contraction, period of epithelialization, skin breaking strength. It has been observed that both the extracts as ointments (5% and 10%) of *Ficus religiosa* leaf extract promoted the wound-healing activity significantly in all the wound models studied. 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. The results of the study indicated that leaf extracts of *Ficus religiosa* in the form of 10% ointment promote wound-healing activity better than the former concentration, 5% . [34] It has been investigated that wound healing, a complex sequence of events, is initiated by the stimulus of injury to the tissues and a positive stimulus may result from the release of some factors by wounding of tissues. Cutaneous wound repair is accompanied by an ordered and definable sequence of biological events starting with wound closure and progressing to the repair and remodeling of damaged tissue . [77] Therefore, the above study has great clinical relevance in wound healing. The effect of hydro alcoholic extract of *F. religiosa* leaves on experimentally induced wounds in rats using different wound models results in dose-dependent wound-healing activity in excision wound, incision wound, and burn wound. A formulation of leaves extract was prepared in emulsifying ointment at a concentration of 5% and 10% and applied to the

wounds. In excision wound and burn wound models, the extract showed significant decrease in the period of epithelization and in wound contraction (50%). A significant increase in the breaking strength was observed in an incision wound model when compared to the control. The result suggests that leaf extract of *F. religiosa* (both 5% and 10%) applied topically possess dose-dependent wound-healing activity. [78] These studies have great clinical relevance in wound healing .

Immunomodulatory Activity

The immunomodulatory effect of alcoholic extract of the bark of *F. religiosa* (moraceae) was investigated in mice as experimental animal model where various hematological and serological tests was carried out. The results of the study indicated that administration of extract remarkably ameliorated both cellular and humoral antibody response confirming that the extract possessed promising immune stimulant properties. [79]

Antioxidant Activity

The antioxidant properties of the extract of *F. religiosa* fruit and bark were investigated using different solvents on the basis of oil stability index together with their radical scavenging ability against 1, 1-diphenyl-2-picrylhydrazyl (DPPH) . [80] The research studies have indicated that the oxidative stress and oxidative damage to tissues are common end points of chronic diseases such as diabetes, atherosclerosis, and rheumatoid arthritis. Oxidative stress in diabetes coexists with a reduction in the antioxidant status, which can further increase the deleterious effects of free radicals. The aqueous extract of *F. religiosa* reduces oxidative stress in experimentally induced type 2 diabetes rats. Type 2 diabetic rats gained relatively less weight during the course of development as compared to normal rats. Decrease in uptake of glucose, free fatty acids from circulation, and accelerated β-oxidation in adipose tissue lead to weight loss in diabetes. The aqueous extract of *F. religiosa* improved the body weight of diabetic rats . [81] Aqueous extract of *F. religiosa has been found to* modulate the superoxide dismutase (SOD) activity in the diabetic rat's dose dependently and also decreased catalase (CAT) activity. It could be possible due to less availability of NADPH or gradual decrease in erythrocyte CAT concentration by excessive generation of O_2^{++} inactivates the enzyme. Since the activity of an enzyme depends upon its substrate, depletion of glutathione (GSH) may be the reason for decreased glutathione peroxidase (GSH-Px) activity. Aqueous extract of *F. religiosa* bark had upregulated the CAT and GSH-Px activities. Drug at higher dose (200 mg/kg) was better effective in modulating the enzyme. [82] In another study, it has been found that the methanolic extract of *F. religiosa* leaf inhibits the production of nitric oxide and pro- inflammatory cytokines in lipopolysaccharide (LPS) stimulated microglia via the mitogen activation protein kinase (MAPK) pathway by using cell viability assay, nitric oxide assay, and enzyme-linked immunosorbent assay (ELISA). The extract exerts strong anti-inflammatory properties in microglial activation. It is likely that extract has a neuroprotective effect against inflammation by inflammatory mediators such as nitric oxide

and cytokines . [83] Recently, the methanolic extract of *F. religiosa* has been reported to have neurotrophic effects and acetylcholinesterase inhibitory activity. [84]

Hypolipidemic Activity

It has been observed that dietary fiber content of food namely peepalbanti (*F. religiosa*), where cellulose and lignin are predominating constituents in peepalbanti, fed at 10% dietary level to rats, induced a greater resistance to hyperlipidemia than cellulose. The results of the study have shown that teent had the most pronounced hypocholesterolemic effect that appeared to operate through increased fecal excretion of cholesterol as well as bile acids. Further, dietary hemicellulose showed a significant negative correlation with serum and liver cholesterol and a significant positive correlation with fecal bile acids. The dietary fiber influenced total lipids, cholesterol, triglycerides, and phospholipids of the liver to varying extents . [85]

Hypoglycemic Activity

β-Sitosterol-D-glycoside was isolated from the root bark of *F. glomerata and F. religiosa*, which has a per oral hypoglycemic activity. [86] Oral administration of *F. religiosa* bark extract at the doses of 25, 50, and 100mg/kg was studied in normal, glucose-loaded, and STZ (streptozotocin) diabetic rats. The results of the study revealed that the three doses of bark extract produced significant reduction in blood glucose levels in all the experimental models. The effect was more pronounced in 50 and 10mg/kg than 25mg/kg. *F. religiosa* also showed significant increase in serum insulin, body weight, and glycogen content in liver and skeletal muscle of STZ-induced diabetic rats, while there was significant reduction in the levels of serum triglyceride and total cholesterol. *F. religiosa* also showed significant antilipid peroxidative effect in the pancreas of STZ-induced diabetic rats. The results indicate that aqueous extract of *F. religiosa* bark possesses significant antidiabetic activity . [35] **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. [87]

Anti- acetylcholinestrase Activity

Methanolic extract of the stem bark of *F. religiosa* has been 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 (ID_{50}) 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. [84]

Other Activities

Apart from above mentioned pharmacological activities, *Ficus religiosa* has been studied for its anxiolytic potential. It has been found that the aqueous extract of trunk bark of *Ficus Religiosa* exhibits potent

anti-anxiety activity with a rapid onset of action. [36]. The aqueous bark extract of *Ficus religiosa* has also shown antidiabetic activity against streptozotocin-induced diabetic rats .[35] The methanolic extract of *Ficus religiosa* latex at a dose level 400 mg/kg has been found to possess nephroprotective effect . [88] *Ficus religiosa* has also shown antioxidant activities. [37] Bark of the plant has also been found to exhibit aphrodisiac potential. [89]

DISCUSSION

Most modern drug discovery attempts to use one single compound to hit one target for combating the related disease. However, human body is an extremely complex network and the pathogenesis of most of diseases involves multiple factors. Thus, targeted single compound usually fails to cure multi-genic diseases adequately. A single target drug can exert unexpected side effects due to the breaking of the balance of the network. Traditional systems of medicines are still in place today because of their organizational strengths and as they focus primarily on multi-component mixtures. They contain enormous number of compounds to fight the disease at various aspects. These herbal medicinal preparations can have plus points due to (i) these may exert synergistic effects due to multi-constituents and multi-targets and these formulations can explore a wider biological space with less expense, (ii) these modulate the biological networks modestly and thus may be efficient in controlling complex disease systems, (iii) these exert effects at lower concentration of individual constituents, thus is safer than single component drugs, (iv) these can deal with drug resistance that becomes more and more severe with antibiotics, anti-malarial and anticancer drugs.

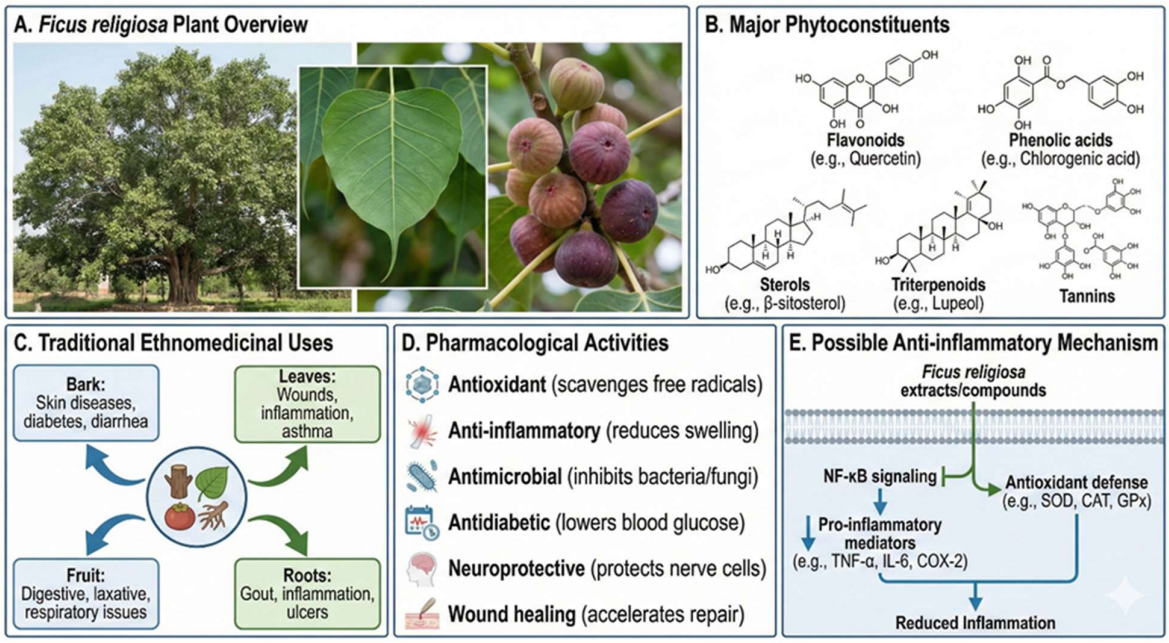
Medicinal plants, which are generally considered safer, more affordable, and more accessible than synthetic medicines, have historically served as useful therapeutic agents in ethnomedicine. According to the World Health Organization (WHO), more than 80% of the world's population still relies on traditional medicines obtained from plants to meet their basic medical needs. Over the past few decades, there has been a surge in global interest in medicinal plants as alternatives to synthetic medicines. Unlike the latter, which is based on a single chemical entity, medicines based on plant extracts contain various phytoconstituents (e.g., flavonoids, alkaloids, polyphenols, and terpenoids). Interestingly, they have been demonstrated to exert their pharmacological activities by interacting simultaneously with numerous biological targets, thereby increasing their therapeutic potential. [90, 91, 92]. Moreover, the discovery that some phytoconstituents are able to enhance the bioactivity of others within a plant extract, an effect called "synergism", is another great incentive for the use of medicinal plants . [93, 94]

F. religiosa has been found to possess a large number of bioactive molecules with diverse varieties of pharmacological properties. The whole parts of the plant *F. religiosa* exhibit wide spectrum of activities such as anticancer, antioxidant, antidiabetic, antimicrobial, anticonvulsant, Anthelmintic, antiulcer, antiasthmatic, anti-amnesic etc. which might be due to the presence bioactive molecules like phytoconstituents of phenols, tannins, steroids, alkaloids and flavonoids, β-sitosteryl-D-glucoside, vitamin

K, n-octacosanol, methyl oleanolate, lanosterol, stigmasterol, lupen-3- one, β-sitosteryl-D-glucoside, essential amino acids, isoleucine, phenylalanine, phytosterolin, β-sitosterol, and its glycoside, albuminoids, carbohydrate, fatty matter, coloring matter, caoutchoue. *F. religiosa* fruits contain flavonols namely kaempeferol, quercetin, and myricetin . Leaves and fruits contain carbohydrate, protein, lipid, calcium, sodium, potassium, and phosphorus..The aqueous extract of dried bark of *F. religiosa* has been reported to contain phytosterols, flavonoids, tannins, furanocoumarin derivatives namely bergapten and begaptol. All these biomolecules present in various parts of *F. religiosa* account for the effectiveness of this plant in cure of various diseases.

CONCLUSION

Medicinal plants offer therapeutic potential through their rich bioactive compounds, such as flavonoids and alkaloids, which exhibit a wide range of pharmacological activities such as antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. These compounds act on multiple biological targets, often with a synergistic effect, making them valuable for treating chronic ailments like diabetes, cancer, cardiovascular diseases, gastrointestinal disorders and many more. Modern research is exploring these ancient remedies, aiming to integrate them into healthcare for effective and cost-efficient treatments with fewer side effects. Medicinal plants have long been recognized as important components of traditional medicine and have gained popularity as alternative or adjunctive treatments for diabetes mellitus, cancer, infections , inflammation, cardiovascular diseases and gastrointestinal disorders . *F. religiosa* is an important medicinal plant commonly used in the traditional and Ayurvedic system of medicine for treatment of different ailments. *F. religiosa* , a versatile medicinal plant, is rich in phytochemicals with numerous biological activities and health benefits. Traditional medical practitioners use *F. religiosa* parts like root, fruit, leaves, stem, seeds, latex, and whole plant for treating various diseases. *F. religiosa* has been found to possess a large number of bioactive molecules with diverse varieties of pharmacological properties The plant's bioactive constituents, such as β-sitosterol and its glycoside, have shown therapeutic potential for various ailments. However, further research is needed to fully explore the clinical therapeutic benefits and elucidate the molecular mechanisms underlying the effects of the bioactive constituents present in *F. religiosa* .



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