

Phytopharmacology and Phytochemistry of Ficus Religiosa: It's Significance as Drug Carrier

Subhanshu¹, Navneet Mehan^{1,2}, Ankush¹, Sahil Dhiman¹, Ankur¹, Renu Saharan², Neeraj Kumar¹, Ritika Chouhan¹, Abhishek Kumar and Suresh Kumar Beniwal^{1*}

¹Ganpati Institute of Pharmacy, Bilaspur, Yamuna Nagar, 135102, India.

²Maharishi Markandeshwar Deemed to be University, Mullana, Ambala, Haryana, 133207, India.

Corresponding Author: Suresh Kumar*, Ganpati Institute of Pharmacy, Bilaspur, Yamuna Nagar (Haryana), India-135102; Contact No. +91-9416839762,

ABSTRACT

Ayurveda, Unani, Siddha, and Homoeopathy have all been used to build health sciences in India. The most widely used species in these traditional systems of healing is *Ficus religiosa* L. Whole plant parts including as flowers, leaves, fruit, roots, bark, inner stem sections, and seeds are used as bioactive substances in *F. religiosa*. Recently, it was revealed in several pharmacological investigations that trees are the primary source of many medicinally significant compounds that would be used in future medications. The anti-diabetic, anti-cancer, anti-ulcer, anticonvulsant, cell-reinforcing, and wound-healing capabilities of various components of *F. religiosa* were also explained by these reports. *F. religiosa* includes a variety of active ingredients in its roots, leaves, bark, fruit, and seeds that may be used to cure a variety of illnesses. Depending on the ailment, *F. religiosa* is extracted using various solvents (such as ethanol, water, methanol, etc.). As a physical method to deal with modify and enhance the pharmacokinetic and pharmacodynamic aspects of various medicinal compounds, particulate frameworks like nanoparticles have been used. The size range of nanoparticles, which span from 1 to 100 nm, is very small materials. By combining elements like copper, zinc, titanium, magnesium, gold, alginate, and silver, unique kinds of nanomaterials are being produced. *F. religiosa* nanoparticles enhance the therapeutic property against various diseases like malignant development, arthritis, and so forth. To present an advanced study on the Phytochemistry, pharmacological characteristics, and nanotechnology of *F. religiosa* is how this paper came to be written.

Keywords: Ayurveda, *Ficus religiosa*, Phyto-chemistry, Anti-cancer, Homoeopathy.

INTRODUCTION

From past thousand years different herbal plants are used for the treatment of different diseases. Since prehistoric times, men and women have had considerable knowledge of medicinal herbs in Eurasia and the Americas. Native Americans use the native plant species covered in this work in traditional medicine. The presence of different chemical compounds with complex chemical composition is the reason for therapeutic capabilities of medicinal plants. These chemical compounds are found in different potions of the plant. Due to this concept that many plants might show therapeutic responses due to its natural compounds, herbal medicine was developed. The world has recently placed a bigger focus on the study of plants, and a large amount of information has gathered to demonstrate the huge potential of the therapeutic plants which are employed in various traditional systems. The usage of herbal treatments is attracting a lot of public interest right now.

A member of the family Moraceae, ***Ficus religiosa* Linn** is also known as the peepal. It has had a significant mythological, religious, and medical significance in India since ancient times. This tree is thought to be the oldest tree in Indian art literature, Ancient sacred scriptures like the Buddhist literature, Bhagavad-Gita, Arthasastra, Ramayana, Puranas, Upanishads and Mahabharata all make reference to the *Ficus religiosa*. Many chemical compounds have been extracted from various plants because they have significant medicinal applications. These substances serve a crucial role in

medicine, whose use is expanding quickly across the globe. It is important to find alternative sources for medicines that work well and have no negative side effects. The genus *Ficus* contains approximately 800 species and 2000 varieties that are dispersed in India and all over the world, particularly within tropical as well as in subtropical regions. There are approximately 500 different species of *Ficus* in the Asian-Australasian region. Africa is home to between 110 and 130 different species of *Ficus*. The *Ficus religiosa* tree can be found in all of Asia, including India, Bangladesh, Pakistan, Nepal, Assam region, the Nicobar Islands, the Eastern Himalaya and parts of Indochina, covering Peninsular Malaysia, Thailand, the Andaman Islands, and Myanmar. It is found also in the Nicobar Islands and the Eastern Himalaya. In addition to tropical Asia, it can also be found in Florida, Venezuela, Iran, and other places. There are some more typical trees of this species, which belongs to the “family Moraceae”, include *Ficus carica* (Anjir tree), *Ficus Religiosa* (Pipal tree), and *Ficus benghalensis* (Banyan tree). There are many local names for it in India, but the ones that are most frequently used are Asvatthah (Sanskrit), Arasu (Tamil), Arayal (Malayalam), Peepal (Hindi), Holy fig (Bengali) and Ravi (Telgu). The tree has wide-spreading branches, a very massive stem, and bark that is a dark brown colour. According to numerous research, *Ficus* species are frequently employed in the treatment of number of infections, including those that affect “the respiratory tract, genital system, the CNS, the CVS, stomach, skin, diabetes”.

MECHANISM OF FICUS RELIGIOSA ON RHEUMATIC PAIN

F. religiosa have potential anti-inflammatory and analgesic action. The inhibition of PG's synthesis is the mechanism for the effect. There is an anti-inflammatory action of leaf extract of *Ficus religiosa* in contradiction of paw oedema persuaded by carrageenan.

Table 1: Different names of *Ficus religiosa* in different countries.

Sr.no	Country	Country Popular Name
1.	India	Ashathwa, Jari, Arachu, Peepal, Arasu, Pipul, Ashvallia Pipla
2.	Myanmar	Bawdi nyaung, Puerto Rico, Botree, Lagat, Mai nyawng
3.	Sweden	Tempelfikus
4.	Chinese	Puti Shu, Putishu
5.	Brazil	Figueira religiosa, Figueira-dos-Pagodes,
6.	Germany	Heiligerfeigenbaum, Indischer Pepulbaum, Bobaum
7.	Dominican Republic	Higuillo
8.	Cuba	Alamo
9.	Italy	Fico del Diavolo
10.	Israel	Ficus kadosh
11.	Spanish	Higuera de Agua
12.	French	Arbrebo, Figuier des Pagodes, Arbre de Dieu

Table 2: Taxonomical Classification of *Ficus Religiosa*.

Domain	Eukaryota
Kingdom	Plantae
Subkingdom	Viridiaeplantae
Phylum	Tracheophyta
Subphylum	Euphyllophytina
Infraphylum	Radiatopses
Class	Magnoliopsida
Subclass	Dilleniidae
Superorder	Urticanae
Order	Urticales
Family	Moraceae
Tribe	Ficeae
Genus	Ficus
Specific epithet	<i>Religiosa Linnaeus</i>
Botanical name	<i>Ficus religiosa</i>

TRADITIONAL USES

Ficus religiosa is a recognized Ayurvedic ethno-medicinal tree. Its usage in traditional Indian folk medicine is also very well known. The uses of several Ficus religiosa portions in old-style medical practises. According to numerous research, Ficus species are frequently employed in the treatment of a variety of illnesses. The present review includes a detailed description of its traditional therapeutic benefits, which are the subject of ongoing research. Traditional medicine has made considerable use of Ficus religiosa to treat a number of diseases. Its fruits, bark, leaves, latex, roots, seeds, and bark are used medicinally in many ways, usually in conjunction with other herbs.

Leaves

Constipation is treated exclusively with the leaves. The leaves, when combined with young shoots, have a good laxative effect. In Nepal, a mixture of leaf juice and honey is used for a variety of ailments, including diarrhoea, gonorrhoea, hiccups, vomiting, asthma, and cough. The leaves also have anti-venomous activity, memory enhancing activity and help to regulate the menstrual cycle.

Leaf decoction

Toothaches can be relieved by leaf decoction.

Bark

Inflammation and glandular swellings of the neck can be treated using the bark's cooling and astringent properties. The powdered bark paste is applied to burns as well as anal fistulas to act as an absorbent for inflammatory swellings. There are claims that the Ficus religiosa bark has antiulcer and wound-healing properties. Ficus religiosa bark is useful in treatment of “diarrhoea, diabetes, anxiety, leucorrhoea, vaginal and other urinary and genital diseases”.

Bark Decoction

Bark decoction is used in Cooling, gonorrhoea, skin diseases, scabies, hiccup, vomiting.

Fruit

The fruits and seeds are laxative, and digestive, refrigerant. Asthma is cured by taking the dried fruit in water for a fortnight after it has been crushed. It works as a cardiac tonic and can be used to treat vaginal diseases.

Seeds

Seeds are used as Refrigerant, laxative.

MORPHOLOGY

One of the longest living trees, *Ficus religiosa* (L) is a tree that can have aerial roots or not and is typically found up to 170 metres above sea level in the Himalayas of India. It is native to India and South-east Asia, growing up to 5000 feet tall with a trunk that can reach 1 metre in length. Seeds, cottages, and stacking are all methods of reproduction. The stem, which connects the several roots, is a pale golden colour. The 5-7 alternating, long, petiolate, alternately serrate, heart-shaped, or occasionally rounded veins on the leaves' surface are exceedingly glossy, thin, and bear. The colour of the immature leaves changes from pink to copper to green as they mature. Between the months of March and April, it sheds its leaves. The bark's exterior is grey with membranous flaking and frequently coated in crustose lichen that is ash or brown in colour. Due to the exfoliation of cork, the surface is uneven and features shallow vertical cracks. Smooth, fibrous, and yellowish to orange-brown on the inner surface. The *Ficus religiosa* bark is flat or otherwise slightly curled. Its depth ranges from 05-08 mm. The purple Peepal fruits are hidden among the figs. Fruits are green when raw during the summer, but turn black after ripening during rainy seasons.

MICROSCOPY

The external characteristics of the bark of *Ficus religiosa* revealed that the bark is distinguished into inner secondary phloem and outer thick periderm. The periderm is further subdivided into phelloderm and phellem. In transection, the phellem zone is wavy, having thickness of 360 mm and irregular. Cells of phellem are stacked in tangential thin layers of membranes, and the grown-up layers shed as thin membranes. Phelloderm region is distinct as well as wide. Sclereids that have undergone lignification from phelloderm cells. Exterior wide collapsed region and inner narrow non-collapsed region are the two distinct types of secondary phloem. Axial parenchyma, radial files of sieve tube members and gelatinous fibres make up the non-collapsed zone. Dilated rays, thick walled and lignified fibres, crushed obliterated sieve tube members, and rich tannin-filled parenchyma cells characterise the outer collapsed phloem. Laticifers are common in external inferior zone of phloem. Uniseriate as well as multiseriate phloem rays exist. Uniseriate rays can be heterocellular or homocellular while multiseriate rays are homocellular.

PHYTOCHEMISTRY

By phytochemical analysis of *F. religiosa*, amino acids, phytosterols, furanocoumarins, hydrocarbons, phenolic components, volatile components, aliphatic alcohols and a few more kinds of secondary metabolites have been isolated from the plant's various parts. About all of the sections of *F. religiosa* include phenolic elements, such as tannins and flavonoids, as well as amino acids. It has been noted that only polyphenolic compounds are present in roots.

Constituents of the bark

Alcohol and petroleum ether are employed to extract the phytosterols from the *Ficus religiosa* bark. Two substituted furanocoumarins, "4-methoxy-7H-furo [3,2-g] chromen-7-one (Bergapten) (4) and 4-hydroxy-7H-furo [3,2-g] chromen-7-one (Bergaptol)", were discovered in benzene extract of the bark of *F. religiosa*. The total tannin content contained by the bark of *F. religiosa* is 8.7%. From the petroleum ether extract of bark, lupen-3-one(9), n-octacosanol(7) vitamin K1(6) and methyl oleonate(8), have been isolated.

Constituents of the fruits

In the pulp of fruit the most prevalent amino acids are asparagine and tyrosine. Moreover, the fruit pulp includes the free forms of the amino acids alanine, glycine, aspartic acid, norleucine, threonine and

norvaline. In the fruit's protein hydrolysate, serine, cysteine, phenylalanine, and isoleucine are common.

An important class of metabolites that are found in the *Ficus* genus includes phenolic elements such as flavonoids. Flavonoids and other phenolic components can be found in significant amounts in the fruits of *F. religiosa*. Flavonols such as myricetin (10), quercetin (11), and kaempferol (12) are contained in the fruit powder in amounts of up to 694, 256.3, and 160.8 mg/kg, respectively. The immature fruits have also been observed to contain condensed tannins. It has been discovered that the extraction method and solvent have an impact on the amount of flavonoids as well as phenolic components that can be extracted from *F. religiosa* fruits. The maximum yield is obtained from extraction using hydro-methanol (80%) when compared to other solvents like hydro-ethanol (80%), ethanol, and methanol. Some volatile substances are present in fruits including "simple aliphatics undecane (13), (Z)-3-hexenol (16), tetradecane (15), tridecane (14) and 1-hexanol (17), β -bourbonene (20), aromadendrene (23), β -caryophyllene (21), α -bergamotene (22), α -copaene (19), α -ylangene (18), α -humulene (24)".

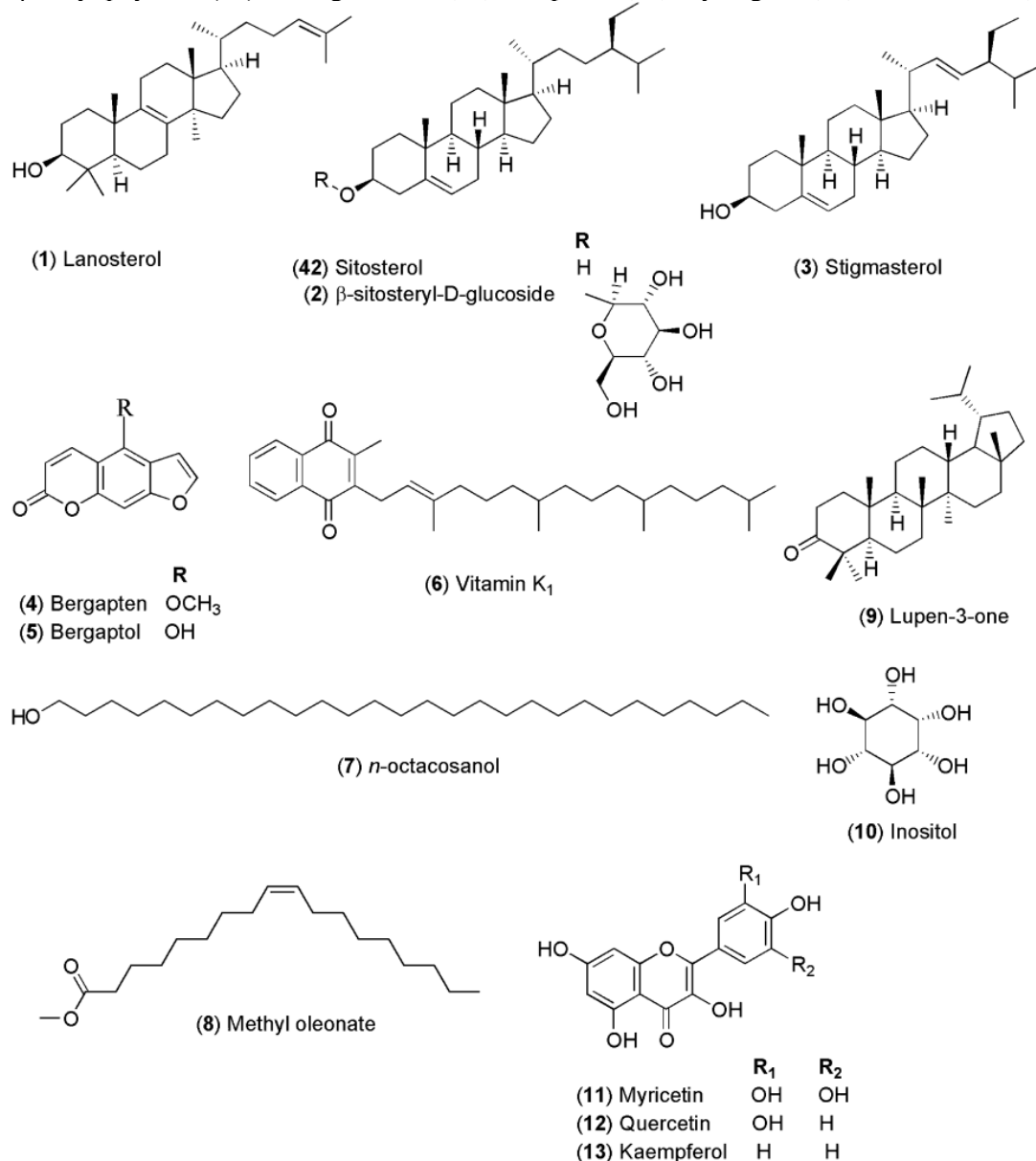
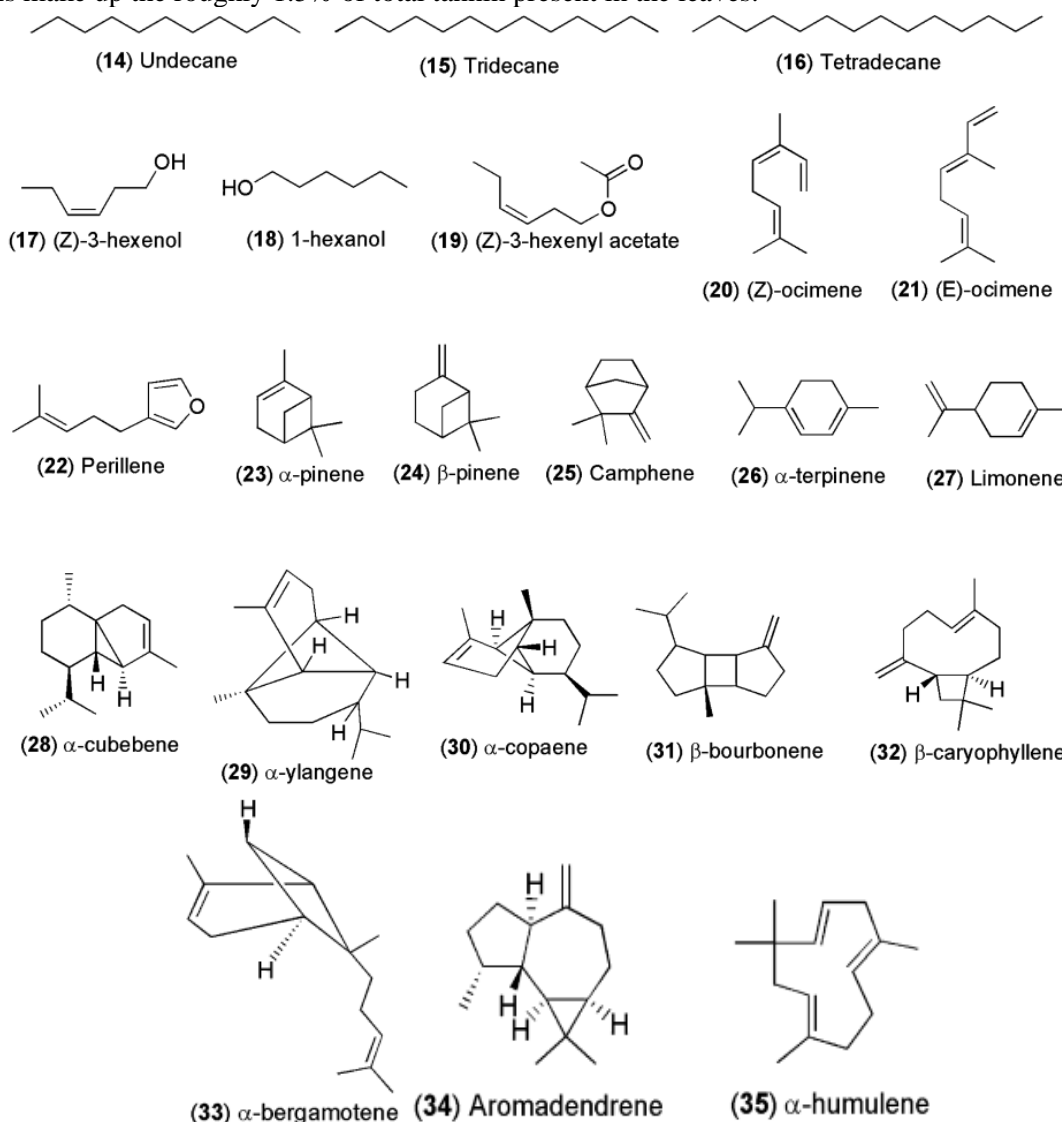


Fig. 1. Compounds with chemical structures from *F. religiosa*

Constituents of the leaves

Phytosterols (2.8%) including "stigmasterol (3), 28-isofucosterol (43), sitosterol (42), and campesterol (41), and triterpene alcohols (28.5%) including lupeol (46), -amyrin (45) and -amyrin (44)" were identified from non-saponifiable portion of the leaf extract of *F. religiosa*. The same fraction has also produced 7.9% of aliphatic alcohols, including n-octacosanol (50) and n-hexacosanol (49), 7.1% long-chain hydrocarbons, including "n-hentriacontane (48), n-nonacosane (47) in addition to phytosterols and triterpenes.

Glycine, 1-leucine, 1-alanine, tryptophan, dl-threonine, 1-proline, and 1-tyrosine are among the amino acids. The leaves comprise considerable amounts of dl-isoleucine, dl-valine and dl-methionine. The leaves have been shown to contain fibres such as ADF, NDF, and ADL. Tannic acid and condensed tannins make up the roughly 1.5% of total tannin present in the leaves.



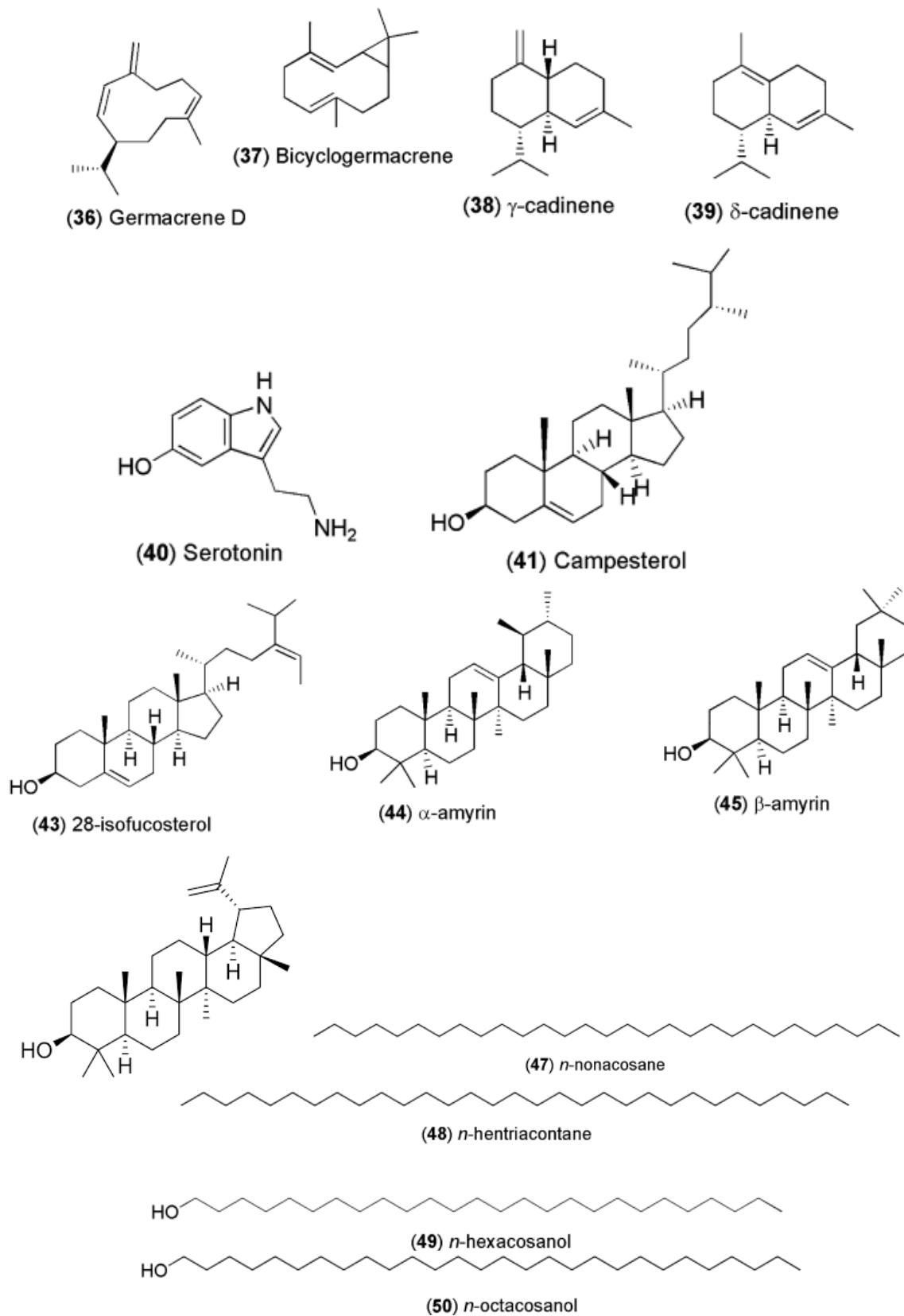


Fig. 1.Continued

PHARMACOLOGICAL ACTIVITIES PRESENT IN *F. RELIGIOSA*

A wide number of pharmacological actions are present in *F. religiosa*. The pharmacological activities of *F. religiosa* included antidiabetic, anti-inflammatory, wound healing, analgesic, anticonvulsant, antimicrobial, antitumor, antioxidant, anti-asthmatic, antiulcer, anthelmintic, antianxiety and proteolytic activity. The pharmacological effects of crude extracts, raw plant materials, and extracted components were all extremely varied.

1. Antidiabetic activity:

Many cultures have shown the efficacy of the ficus religiosa in the treatment of diabetes using a reliable experimental investigation. The hypoglycemic effect was first observed in albino rabbits when root and aqueous bark extract was used. After fasting for 18 hours, this experiment showed that normal rabbits' blood sugar levels decreased by 2.5 gm/kg. Sugar was injected into the rabbits' systems at a rate of 1 gm/kg an hour prior to the experiment. The dose of tolbutamide is typically administered at 0.5 g/kg. This study revealed that bark extract lowers blood sugar levels, however the bioactive compounds' exact mechanism is unknown. Phytosterolin beta-sitosterol-d-glucoside was extracted in 1967 from *F. religiosa* tree. The bark was extracted with 95% ethanol using the soxhlet assembly. Further it is diluted after 48 hours with water, then extraction is done with ether. After washing with water and 5% HCL, the ether extract is eliminated. Pure phytosterolin was produced after the substance was cleaned with petroleum ether and recrystallized with acetone. Fasting rabbits (weighing 2.3–3 kg) administered phytosterolin dosages of 5 mg/kg, 7.5 mg/kg intravenously, and 25 mg/kg orally. After two hours, blood sugar levels of 5 and 7.5 mg/kg significantly decreased, and after four hours, a 25 mg/kg PO drop was seen.

2. Anti-inflammatory and analgesic activity:

The body's primary response to viruses, toxic stimuli like chemicals, or physical harm that damages its tissue and cells is inflammation. It is an attempt by the organism to protect itself by removing the harmful stimuli and starting the healing process. Chemokines and cytokines, PGs, histamine and platelet activating factor (PAF), among other mediators, are some of the several factors that involved in inflammation. The common consensus is that PGs are strong pro-inflammatory mediators. Due to the release of many histamine-like mediators, which are associated with allergies and inflammation, it has been found that inflammation is also influenced by mast cell degranulation. *Ficus religiosa* have been discovered to have potential analgesic and anti-inflammatory properties. The extract of *Ficus religiosa* leaves with methanol may have anti-inflammatory action against paw oedema caused by carrageenan. The suppression, serotonin (5HT), histamine, PG and kinin release led to detection of the inhibitory activity. Moreover, numerous studies have shown that the tannin in bark has an anti-inflammatory impact.

30 minutes before injecting 0.1 ml of carrageenan (1% in 0.9% saline) into the left hind paw's sub plantar region, provide dosages of 120, 125, and 500 mg/kg. The standard reference group used for comparisons was an indomethacin aqueous solution. Plethysmographic measurements of the paw volume were taken before and three hours after carrageenan administration. At the third hour, the group that received 3 doses of the crude extract had inhibited the development of oedema by 52.99, 55.41, and 56.29%, respectively. Burns can be treated with a paste made from the powdered bark, which works well as an absorbent for inflammatory swellings. An earlier investigation on the methanol extract showed that the extract blocked LPS-stimulated microglia's ability to produce nitric oxide and proinflammatory cytokines via the MAPK pathway.

3. Antioxidant activity:

The root extract, both aqueous and alcoholic, exhibits excellent antioxidant activity, with elevated levels of "Reduced levels of lipid peroxidation (LPO) and increased levels of glutathione peroxidase, glutathione S-transferase, glutathione reductase, catalase and superoxide dismutase". Using a dosage of 500 mg/kg, the *F. religiosa* root extracts FRWE and FRAE demonstrated considerable antioxidant protection against rats' liver damage brought on by carbon tetrachloride. Its highest

reductive potential is comparable to tannic acid and gallic acid, and its potential of good superoxide scavenging is comparable to ascorbic acid. Also, a recent study found that the extract of *F. religiosa* with methanol, which contains high levels of flavonoid and phenolic components, acts as antioxidant.

It was discovered that leaves extract combined with methanol helps in the inhibition of nitric oxide production and pro-inflammatory cytokines in lipopolysaccharide stimulated microglia via the mitogen activation protein kinase pathway (ELISA) using nitric oxide assay, enzyme-linked immunosorbent assay and cell viability assay. During microglial activation, strong anti-inflammatory effects of the extract are seen. The extract protects the nervous system from inflammation caused by mediators including cytokines and nitric oxide.

Lately, acetylcholinesterase inhibitory activity and neurotrophic effects of the extract of *F. religiosa* with methanol have been found.

DPPH radical scavenging was used to test the ethanolic extract for antioxidant activity. The range of the percentage peroxide value for the 200 g/ml to 1000 g/ml strength extract of *Ficus religiosa* was found to be between 6.34% and 13.35%.

4. Antimicrobial activity:

Ficus religiosa has been found to be used as therapy for a number of diseases. *F. religiosa* aqueous extract exhibits strong antibacterial action against a number of pathogenic pathogens. *B. subtilis* exhibits high activity, with an inhibition zone of around 24mm. Moreover, *P. Aeruginosa*, a multidrug resistant bacteria, has had its development noticeably suppressed by the plant extract. Antibacterial property of *Ficus religiosa* was investigated with the help of an agar-well diffusion assay. *F. religiosa* has previously been shown to have antibacterial activity against *Bacillus cereus* and *Escherichia coli*; similarly, At MICs of 5, 39, and 20 g/ml, respectively, the extracts by chloroform shown a robust inhibitory property against the growth of *Proteus vulgaris*, *Salmonella typhimurium* and *Salmonella typhi*.

With a zone of inhibition of 10–21 mm, *F. religiosa* chloroform extract displayed strong antibacterial activity.

5. Anticonvulsant activity:

The Serotonergic neurotransmission is well recognised for controlling a number of experimentally induced seizures and implicated in prevention of seizure by modifying numerous glutamatergic and GABAergic activity. If the concentration of serotonin is reduced it increase seizure susceptibility. Pharmacological treatments facilitate the serotonergic neurotransmission and help to inhibit seizures in animal models of epilepsy. Serotonin, which causes the anticonvulsant action, has been discovered to be most abundant in *F. religiosa* figs. Singh and Goel also studied into anticonvulsant properties of a extract (by methanol) from *F. religiosa* figs on convulsions (electroshock induced and picrotoxin induced) and no neurotoxic impact. In the aforementioned mice, a nonselective serotonin antagonist (4 mg/kg, i.p.) was combined with cyproheptadine to examine whether the protective effects of the extract may be reversed. The extract was tested on animal models of strychnine-induced convulsions and pentylenetetrazole-induced convulsions.

6. Wound healing activity:

Roy et al. (2009) investigated the wound healing property of leaf extract (hydroalcoholic) of *F. religiosa* in Wistar albino rats. 70% hydro-alcoholic solvent was used to extract leaf powder and to produce the semisolid extract the leaf of *Ficus religiosa* was dried in low pressure (32.5%, w/w yield). Glycosides and tannins were detected during phytochemical screening of the extract. Using rat wound models created by excision and incision, the extract's action was identified. When it was compared with the group of controlled animals treated with the conventional medicine Povidine iodine, animals which are treated with an ointment of 10% leaf extract showed a higher rate of contraction in wound, a higher skin breaking strength and a shorter time for epithelialization. According to reports, tannins have the power to boost collagen levels, which is known as one of the broad factor that helps wounds heal faster.

7. Anti-ulcer activity:

A "peptic ulcer" is the medical name for a break in the depth of the duodenal or gastric mucosa that endures because of pepsin and acid present in gastric region. The main pathogenic conditions that can benefit from reducing acid secretion are reflux oesophagitis and duodenal and gastric peptic ulcers. The side effects of using commercially available antiulcer medications to treat peptic ulcers are typically more prominent. Thus, it is necessary to discover new antiulcerogenic compounds that may have less or no negative effects. One of the herbs traditionally used in Malay and Indian folk medicine to heal stomach ulcers is *F. religiosa*.

The *Ficus religiosa* stem bark ethanol extract (EBFR) shown potential antiulcer efficacy. In vivo testing of *Ficus religiosa*'s antiulcer properties was done using cold-restrained stress, indomethacin, and pylorus ligation assays to generate gastric ulcers. The antiulcer impact was determined using the ulcer index decrease. The ulcer index was significantly decreased by the extract (100, 200, and 400 mg/kg) in all experiments.

8. Anthelmintic activity:

F. religiosa has traditionally been used in the treatment of infections caused by parasites both humans as well as animals. Anthelmintic property of *F. religiosa* bark (extracted with methanol) was investigated by Iqbal et al. on the adult *Haemonchus contortus* Worm. From the Faisalabad slaughterhouse a slaughtered sheep was chosen to collect *H. Contortus* adult motile. It was discovered that ficin was a reason for methanolic extract of *F. religiosa*'s anthelmintic properties. Additional research demonstrates that as compared to other *Ficus* species (earthworms), the fruit of *F. religiosa* has powerful anthelmintic properties against *Pheretima posthuma*. *Ficus religiosa* has also been found to be toxic to *Ascaridia galli*.

9. Anti-amnesic activity:

It has been speculated that the serotonergic system, specifically by cooperating with the glutamatergic, cholinergic, dopaminergic, GABAergic systems, plays a substantial role in learning and memory. According to reports, serotonergic neurotransmitter modulation is a key factor in the aetiology of amnesia.

It was discovered that the plant's figs have a high serotonergic content. The anti-amnesic efficacy of the extract of figs with methanol from *Ficus religiosa* was examined against retrograde amnesia in mice and scopolamine-induced anterograde. The effect was studied using the experimental models modified passive avoidance paradigm and elevated plus maze. It was documented that how many times the trial is done and how many errors were there, as were parameters like the decrease in transmission potential in the EPM and step down potential. In an effort to better understand how the serotonergic system contributes to the anti-amnesic impact, *Ficus religiosa* extract was administered alongside the non-selective 5-HT blocker cyproheptadine. Considering that the scopolamine-induced anterograde and retrograde amnesia was dose-dependently lessened by the therapy, the study came to the conclusion that *F. religiosa* had a strong anti-amnesic action.

10. Hypolipidemic activity:

Peepalbanti (*F. religiosa*), cellulose, and lignin were the predominant components of peepalbanti, which was fed to rats at a 10% dietary level and resulted better than cellulose in resistance to hyperlipidaemia. Teent exhibited the strongest hypocholesterolemic impact, which appeared to be brought about by an increase in bile acid and cholesterol excretion from the faeces. Dietary hemicellulose demonstrated a statistically significant positive link with faecal bile acids and a substantial unfavourable relationship between liver and blood cholesterol. The total lipids, phospholipids, triglycerides and cholesterol in the liver were all impacted by the dietary fibre to varying degrees.

12. Immunomodulatory activity:

In mice, the alcoholic extract of *F. religiosa* (Moraceae) bark was tested for its potential to modulate the immune system. A variety of haematological and serological assays were used to conduct the investigation. The administration of extract significantly improved the immune response, both cellular and humoral. The extract was found to have potential immunostimulant effects.

14. Proteolytic activity:

F. religiosa demonstrated a large amount of proteolytic activity when the proteolytic activity of the 46 different types of *Ficus* was compared using the chromatographic and electrophoretic characteristics of the protein components.

TOXICOLOGY

Because no negative effects have been reported for *Ficus religiosa* from earliest times to the present, it is safe to use. Swiss albino mice were used in tests to determine the acute toxicity of methanolic extract, and the results showed that it was harmless. The mice showed no signs of neurotoxicity. An aqueous *Ficus religiosa* bark extract was tested using OECD (organisation for economic co-operation and development) guidelines on female Swiss albino mice, and no toxicity was reported. The alcoholic extract of leaf of the *F. religiosa* was likewise determined to be safe for oral toxicity. There aren't many studies that discuss *Ficus religiosa*'s toxicity. Allergies have been linked to large doses of bark aqueous extract. In a toxicity test on brine shrimp, a fruit extract in chloroform (CHCl₃) with a fatal Concentration 50 of 400 g/ml was harmful. Nonetheless, leaf extracts made from alcohol and water are said to be secure.

Consent for Publication

Not applicable

Availability of Data and Materials

All data available in manuscript.

Ethical Approval and Consent to Participate

None.

Supplementary Material

None.

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Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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REFERENCE

1. Sandeep, & Kumar, Ashwani & Sepla, Dimple & Tomer, Vidisha & Gat, Yogesh & Kumar, Vikas. (2018). *Ficus religiosa*: A wholesome medicinal tree. 7.
2. M.Shankar, T. Lakshmi Teja, B.Ramesh, D. Roop kumar, D.N.V. Ramanarao, M.Niranjan Babu, "Phytochemical investigation and antibacterial activity of Hydroalcoholic extract of terminalia bellirica leaf", *Asian Journal of Phytomedicine and Clinical Research*, 2(1): 33-39, 2014.
3. Singh, Shailja & Jaiswal, Shalini. (2020). Therapeutic Properties of *Ficus Religiosa*.
4. Gautam, Sanskriti & Meshram, Anju & Bhagyawant, Sameer & Srivastava, Nidhi. (2014). FICUS RELIGIOSA-POTENTIAL ROLE IN PHARMACEUTICALS. *International Journal of Pharmaceutical Sciences and Research*. 5. 1616. 10.13040/IJPSR.0975-8232.5(5).1616-23.
5. Corner E.J.H.: Check List of *Ficus* in Asia and Australasia with keys to identification. *Gard. Bull. Singapore* 1965; 21:1-186.
6. Berg CC: Classification and Distribution of *Ficus*. *Experientia* 1989; 45(7):605-611.
7. Berg CC, Corner E.J.H. *Moraceae - Ficus. Flora Malesiana Series I (Seed Plants)*, 17: 1-730.
8. Kapile, C., A. Kulkarni, P. Pardeshi, A. Sayed, and A. Nehe. "Ficus Religiosa: A Beneficial Medicinal Plant". *Journal of Drug Delivery and Therapeutics*, Vol. 12, no. 2-S, Apr. 2022, pp. 210-8, doi:10.22270/jddt.v12i2-S.5434.
9. Sawarkar, H. A., Singh, M. K., Pandey, A. K., Devendra, B., & Pranita, K. (2011). Comparative in vitro anthelmintic activity of *Ficus benghalensis*, *Ficus carica* & *Ficus religiosa*. *International Journal of PharmTech Research*, 3(1), 157-159.

10. Warriar, P.K., Indian medicinal plants-A compendium of 500 species, Orient Longman Ltd., Chennai, Vol. III, 1996, 38-39.
11. Panchawat S. *Ficus religiosa* Linn. (Peepal): A Phyto-Pharmacological Review. *Inter J Pharm Chem Sci.* 2012; 1(1):435-446.
12. Kaur, A. & Rana, A.C. & Tiwari, V. & Sharma, Ramica & Kumar, S.. (2011). Review on ethanomedicinal and pharmacological properties of *Ficus religiosa*. *Journal of Applied Pharmaceutical Science.* 1. 6-11.
13. Singh, Shailja & Jaiswal, Shalini. (2020). Therapeutic Properties of *Ficus Religiosa*.
14. Makhija, Inder Kumar, Indra Prakash Sharma, and Devang Khamar. "Phytochemistry and Pharmacological properties of *Ficus religiosa*: an overview." *Annals of Biological Research* 1.4 (2010): 171-180.
15. Gautam, Sanskriti, et al. "*Ficus religiosa*-potential role in pharmaceuticals." *International journal of pharmaceutical sciences and research* 5.5 (2014): 1616.
16. Singh D, Singh B, Goel RK. Traditional uses, phytochemistry and pharmacology of *Ficus religiosa*: a review. *J Ethnopharmacol.* 2011 Apr 12;134(3):565-83. doi: 10.1016/j.jep.2011.01.046. Epub 2011 Feb 3. PMID: 21296646.
17. Ribeiro A, Estanqueiro M, Oliveira M, Sousa Lobo J. Main benefits and applicability of plant extracts in skin care products. *Cosmetics* 2015; 2: 48-65.
18. Aswal A, Kalra M, Rout A. Preparation and evaluation of polyherbal cosmetic cream. *Pharm Lett* 2013; 5(1): 83- 88.
19. Abdullah N, Patil AB. Designing of novel topical in situ polymeric film-forming solution spray formulation of antifungal agent: in vitro activity and in vivo characterization. *Int J App Pharm.* 2022;14(1):169-84. doi: 10.22159/ijap.2022v14i1.43581.
20. Poomkokrak J, Niamnuy C, Choicharoen K, Devahastin S. Encapsulation of soybean extract using spray drying. *J Food Sci Agric Technol.* 2015;1:105-10.
21. Manganaris GA, Goulas V, Vicente AR, Terry LA. Berry antioxidants: small fruits providing large benefits. *J Sci Food Agric.* 2014;94(5):825-33. doi: 10.1002/jsfa.6432, PMID 24122646.
22. Chaerunisaa AY, Muhaimin. Comparative study on the release of two drugs in fixed-dose combination using zero order and first derivative spectrophotometry. *Int J PharmTech Res.* 2016;9(12):581-90.
23. Deshkar S, Satpute A. Formulation and optimization of curcumin solid dispersion pellets for improved solubility. *Int J App Pharm.* 2020;12(2):36-46. doi: 10.22159/ijap.2020v12i2.34846.
24. Tolun A, Altintas Z, Artik N. Microencapsulation of grape polyphenols using malt dextrin and gum arabic as two alternative coating materials: development and characterization. *J Biotechnol.* 2016;239:23-33. doi: 10.1016/j.jbiotec.2016.10.001, PMID 27720817.
25. Shailja S and Jaiswal S: Therapeutic properties of *Ficus religiosa*. *International Journal of Engineering Research and General Science* 2014; 2(5):149-158.
26. Joseph B and Justin SR: Phytopharmacological and phytochemical properties of three *Ficus* species-an overview. *International Journal of Pharma and Bio Sciences* 2010; 1(4): 246-253.
27. Husain A, Virmani OP, Popli SP, Misra LN, Gupta MM, Srivastava GN, Abraham Z and Singh AK: *Dictionary of Indian Medicinal Plants.* CIMAP Lucknow, India, 1992: 546.
28. Makhija IK, Sharma IP and Khamar D: Phytochemistry and pharmacological properties of *Ficus religiosa*: an overview. *Annals of Biological Research* 2010; 1(4): 171-180.
29. Panda SK, Panda NC and Sahue BK: Phytochemistry and pharmacological properties of *Ficus religiosa*: an overview. *Indian Veterinary Journal* 1976; 60:660-664.
30. Verma RS and Bhatia KS: Chromatographic study of amino acids of the leaf protein concentrates of *Ficus religiosa* Linn. and *Mimusops elengi* Linn. *Indian Journal of Hospital Pharmacy* 1986; 23:231-232.
31. Behari M, Rani K, Usha MT and Shimiazu N: Isolation of active-principles from the leaves of *Ficus religiosa*. *Current Agricultural* 1984; 8:73.

32. Chao P, Deshmukh M, Kutscher HL, Gao D, Rajan SS, Hu P, et al. Pulmonary targeting microparticulate camptothecin delivery system: anticancer evaluation in a rat orthotopic lung cancer model. *Anticancer Drugs*, 21, 2010, 65-76.
33. Gupta R, Gupta MK, Bhandari A and Gupta J: Preliminary pharmacognostical and physicochemical analysis: a poly herbomineral formulation. *International Journal of Drug Development and Research* 2014; 6(3):85-92.
34. Gupta R, Gupta MK, Bhandari A, Gupta J and Pathan IK: Preparation and standardization of polyherbomineral formulation. *International Journal of Drug Development and Research* 2014; 6(2):211-219.
35. Afsar, Z. and Khanam, S. (2016). Formulation and evaluation of poly herbal soap and hand sanitizer. *IRJP*, 7(8):54-57.
36. Agarwal, V. and Chauhan, B.M. (1988). A study on composition and hypolipidemic effect of dietary fibre from some plant foods. *Plant Foods Hum. Nutr.*, 38:189-97.
37. Ahuja, D.; Bijjem, K.R.V. and Kalia, A.N. (2011). Bronchospasm potentiating the effect of methanolic extract of *F. religiosa* fruits in guinea pigs. *J. Ethnopharmacol.*, 133(2):324-328.
38. Aiyegoro, O. and Okoh, A.I. (2009). Use of bioactive plant products in combination with standard antibiotics: Implications in antimicrobial chemotherapy. *J. Med. Plants*, 3:1147-1152.
39. Akhtar, M.S.; Iqbal, Z.; Khan, M.N. and Lateef, M. (2000). Anthelmintic activity of medicinal plants with particular reference to their use in animals in the Indo-Pakistan subcontinent. *Small Ruminant Research*, 38:99-107.
40. Ambike, S. and Rao, M. (1967). Studies on a phytosterolin from the bark of *Ficus religiosa*. *Indian J. Pharm.*, 29:91-94.
41. Antony, J.J.; Sithika, M.A.; Joseph, T.A.; Suriyakalaa, U.; Sankarganesh, A.; Siva, D.; Kalaiselvi, S. and Achiraman, S. (2013). In vivo antitumor activity of biosynthesized silver nanoparticles using *Ficus religiosa* L. as a nanofactory in DAL induced mice model. *Colloids and surfaces. B. Biointerfaces*, 108:185-190.
42. Antony, J.J.; Sithika, M.A.; Joseph, T.A.; Suriyakalaa, U.; Sankarganesh, A.; Siva, D.; Kalaiselvi, S. and Achiraman, S. (2013). In vivo antitumor activity of biosynthesized silver nanoparticles using *Ficus religiosa* L. as a nanofactory in DAL induced mice model. *Colloids and surfaces. B. Biointerfaces*, 108:185-190.
43. Aqil, F. and Ahmad, I. (2007). Antibacterial properties of traditionally used Indian medicinal plants. *Methods Find Exp. Clin. Pharmacol.*, 29:79-92.
44. Asolakar, V.L.; Kakkar, K.K. and Chakre, J.O. (1992). Glossary of Indian Medical plants with active principles. Publication and Information directorate, C.S.I.R., New Delhi, pp:312-313.
45. Barnes, J. (2002). An introduction to herbal medicine products. *The Pharmaceutical Journal*, 268:304-306.
46. Behari, M.; Rani, K.; Usha, M.T. and Shimiazu, N. (1984). Phytochemistry and pharmacological properties of *ficus religiosa*: An overview. *Curr. Agri.*, 8:73.
47. Bhogaonkar, P.Y.; Chavhan, V.N. and Kanerkar, U.R. (2014). Nutritional potential of *Ficus recemosa* Linn fruits. *Biosci. Discov.*, 5(2):150-153.
48. Bushra, S. and Farooq, A. (2008). Flavonols (Kaempferol, quercetin, myricetin) contents of selected fruits, vegetables and medical plants. *Food Chemistry*, 108(3):879-884.
49. Bushra, S. and Muhraf, F.A. (2009). Effect of extraction solvent/technique on the antioxidant activity of selected medicinal plant extracts. *Molecules*, 14:2168-2180.
50. Chopra, R.N. and Chopra, S. (1958). *Indigenous Drugs of India*. 2nd ed. Calcutta, Dhur. and Sons, pp:606.
51. Damanpreet, S. and Rajesh, K.G. (2009). Anticonvulsant effect of *F. religiosa*: Role of serotonergic pathways. *J. Ethnopharmacol.*, 123:330-334.
52. DeAmorin, A.; Borba, H.R.; Caruta, J.P.; Lopes, D. and Kaplan, M.A. (1999). Anthelmintic activity of the latex of *Ficus* species. *J. Ethnopharmacol.*, 64:255-258.

53. Dubchak, S.; Ogar, A.; Mietelski, J.W.; and Turnau, K. (2010). Influence of silver and titanium nanoparticles on arbuscular mycorrhiza colonization and accumulation of radiocaesium in *Helianthus annuus*. *Span. J. Agric. Res.*, 8(1):103-108.
54. Farrukh, A. and Iqbal, A. (2003). Broad-spectrum antibacterial and antifungal properties of certain traditionally used Indian medicinal plants. *World J. Microbiol. Biotechnol.*, 19:653-657.
55. Foye, W.O.; Lemke, T.L. and Williams, D.A. (2008). *Foye's principle of Medicinal Chemistry*, Lippincott Williams and Wilkins, 44(6).
56. Gautam, S.; Meshram, A.; Bhagyawant, S.S. and Srivastava, N. (2014). *F. religiosa*: Potential role in pharmaceuticals. *Int. J. of Pharm. Sci. and Res.*, 5(5):1616-1623.
57. Gordon, M.C. and David, J.N. (2001). Natural product drug discovery in the next millennium. *Pharmaceutical Biology*, 39:8-17.
58. Hamed, M.A. (2011). Beneficial effect of *F. religiosa* on high fat-induced hypercholesterolemia in rats. *Food Chem.*, 129:162-170.
59. Hansson, A.; Veliz, G.; Naquira, C.; Amren, M.; Arroyo, M. and Arevalo, G. (1986). Preclinical and clinical studies with latex from *Ficus glabrata* HBK, a traditional intestinal anthelmintic in the Amazonian area. *J. Ethnopharmacol.*, 17:105-138.
60. Hemaiswarya, S.; Poonkothai, M.; Raja, R. and Anbazhagan, C. (2009). Comparative study on the antimicrobial activities of three Indian Medicinal Plants. *Eg. J. of Biol.*, 11:52-57.
61. Hyo, W.J.; Hye, Y.S.; Chau, V.; Young, H.K. and Young, K.P. (2008). Methanol extract of *Ficus* leaf inhibits the production of nitric oxide and proinflammatory cytokines in LPS stimulated microglia via the MAPK pathway. *Phytother. Res.*, 22:1064-1069.
62. Jannathul, F.M.; Lalitha, P. and Shubashini, K.S. (2012). Novel synthesis of silver nanoparticles using leaf ethanol extract of *Pisonia grandis* (R. Br). *Der. Pharma Chemica.*, 4(6):2320-2326.
63. Joseph, B. and Raj, S.J. (2010). Phytopharmacological and phytochemical properties of three *Ficus* species: An overview. *Int. J. of P. and BioSc.*, 1(4):246-253.
64. Joy, P.P., Thomas, J. Mathew, S. and Skaria, B.P. (1998). *Medicinal plants*. Kerala Agricultural University, Kerala, India, pp:3-8.
65. Jung, H.W.; Son, H.Y.; Min, H.C.V.; Kim, Y.H. and Park, Y.K. (2008). *Phytother Res.*, 22:1064-1068.
66. Kalpana, G. and Rishi, R.B. (2009). Ethnomedicinal knowledge and healthcare practices among the Tharus of Nawalparasi district in central Nepal. *For Ecol. Manage.*, 257:2066-2072.
67. Kaushik, R.K.; Katiyar, J.C. and Sen, A.B. (1981). A new in vitro screening technique for anthelmintic activity using *Ascaridia galli* as a test parasite. *Indian J. Anim. Sci.*, 51:869-872.
68. Kavitha, K.S.; Syed, B.; Rakshith, D.; Kavitha, H.U.; Yashwantha,; Rao, H.C.; Harini, B. and Pand, S.S. (2013). Plants as green source towards synthesis of nanoparticles. *Int. Res. J. Biol. Sci.*, 2(6):66-76.
69. Kirana, H.; Agrawal, S.S. and Srinivasan, B.P. (2009). Aqueous extract of *F. religiosa* Linn: Reduces oxidative stress in experimentally induced type 2 diabetic rats. *Indian J. Exp. Biol.*, 47:822-826.
70. Kuntal, D.; Khan, S. M.; Namratha, N.; Swetha, R. and Sevgi, G. (2019). Comparative phytochemical screening, elemental content and chromatographic evaluation for detection and quantification of polyphenolic compounds for strong antioxidant activity of various extracts of *Abutilon indicum* (Link) Sweet leaves. *Ann. Phytomed.*, 8(1):36-44.
71. Suresh Kumar, Abhishek Tiwari, Varsha Tiwari, Sukhbir Lal Khokra, Renu Saharan, Manish Kumar, Ajay Sharma, Tarun Virmani, Reshu Virmani, Girish Kumar, Abdulsalam Alhalmi, "Synthesis, Anticancer, and Antimicrobial Evaluation of Integerrimide-A", *BioMed Research International*, vol. 2023, Article ID 9289141, 11 pages, 2023. <https://doi.org/10.1155/2023/9289141>
72. Deepak Kaushik and Rajeev Kumar Sharma Abhishek Tiwari, Varsha Tiwari, Suresh Kumar, Manish Kumar, Renu Saharan, Navneet Varma, Biswa Mohan Sahoo, "Molecular Docking

- and Simulation Analysis of Cyclopeptides as Anticancer Agents”, *Current Drug Therapy* 18 (3), 247-261.
73. Renu Saharan, Sarvesh K Paliwal, Abhishek Tiwari, Varsha Tiwari, Randhir Singh, Suresh Kumar Beniwal, Preeti Dahiya, Suresh Sagadevan, “Exploring graphene and its potential in delivery of drugs and biomolecules”, *Journal of Drug Delivery Science and Technology*, 104446.
74. Randhir Singh Suresh Kumar, Renu Saharan, “ Synthesis, Characterization and Biological Evaluation of some Novel 2-Substituted Aminothiazoles,” *Research Journal of Pharmacy and Technology* 14 (6), 3104-3110.