



REVIEW ARTICLE

Pharmacological Studies in *Ficus religiosa*

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ABSTRACT

In traditional medicine, medicinal plants have been used for the treatment of various diseases. *Ficus religiosa* is known to be a sacred plant in India. Since very ancient time, it has great medicinal and religious significance. In Ayurveda, Unani and Homeopathy, this plant serves as important source of medicine. The various parts of the plants like stem bark, fruits, buds, latex are used in treatment of different diseases like dysentery, mumps, jaundice, heart diseases, constipation, skin diseases, etc. According to Ayurvedic system of medicine, F. Religiosa (Peepal tree) is well known to be useful in diabetes. Since last couple of years it has also been investigated for the presence of various phytoconstituents (phenolics, sterols, flavonoids etc). *F. religiosa* showed diverse range of pharmacological activities like, anticonvulsant, antidiabetic, anti-inflammatory, antimicrobial, analgesic, wound-healing, antioxidant, acetylcholinesterase, proteolytic, and anti-amnesic. The present review is to compile up-to-date information of this plant that covers its natural phytochemical, biochemical, ethnobotanical and pharmacological significance.

KEYWORDS

Ficus Religiosa, Phytochemical, Pharmacological Significance

INTRODUCTION

Ficus religiosa Linn is commonly known as Peepal belongs to family Moraceae. In India, since ancient times it has got great mythological, religious and medical importance. This is considered as the oldest tree in Indian art literature. There are many chemical compounds which have been extracted out from different plants as they as they have very important use in medicinal field. These compounds play a very important role in as medicinal usages is increasing worldwide very rapidly, it is very important to get alternate sources of drugs with effective results and with no side-effects.

Since ancient times, plants have been an exemplary source of medicine. Ayurveda and other Indian literature mention the use of plants in treatment of various human ailments. Plants have been the major source of drugs in Indian system of medicine and other ancient systems in the world. Medicinal plants are found in Rig-veda. Charaka Samhita and Sushrasha Samhita give extensive description on various medicinal herbs¹. Information on medicinal plants in India has been systematically organized¹⁻⁴. India has an ancient heritage of traditional medicine. The Materia Medica of India provides a great deal of information on the folklore practices and traditional aspects of therapeutically important natural products. Indian traditional medicines based on various systems including Ayurveda, Siddha, Unani and Homeopathy².

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The genus *Ficus* consists of about 800 species and 2000 varieties which are widely distributed in India and throughout the world especially in tropical and sub-tropical regions³⁻⁴. *F. religiosa* has got mythological, medical and religious importance since ancient times. According to religious point of view, *F. religiosa* is very important as it is believed that Gautam Buddha achieved enlightenment under this tree. Because of this, it is also named as “Bodhi tree or Bo tree”. In medicinal field, *F. religiosa* is gaining great attention because it has many compounds which are beneficial in treatment of many diseases like diabetes, skin diseases, respiratory disorders, central nervous system disorder, gastric problems etc⁵⁻⁶.

Plants have played a significant role in maintaining human health and improving the quality of human life for thousands of years and have served humans well as valuable components of medicines, seasonings, beverages, cosmetics and dyes. Herbal medicine is based on the premise that plants contain natural substances that can promote health and alleviate illness. In recent times, focus on plant research has increased all over the world and a large body of evidence has collected to show immense potential of medicinal plants used in various traditional systems. Today, we are witnessing a great deal of public interest in the use of herbal remedies⁷⁻¹⁰. This review emphasizes the traditional use and clinical potentials of *Ficus religiosa*. Through which the authors hope to attract the attention of natural product researchers throughout world on the explored potential of *F. religiosa*. This review has been compiled using references from major database such as Chemical Abstracts, Medicinal and Aromatic Plants Abstracts, Pubmed, Duke’s Phytochemical and Ethnobotany database, and Image database. The available information on *F. religiosa* has been divided into four sections, which are ethnopharmacology, morphology, phytochemistry and pharmacological studies.

Classification

Kingdom: Plantae
Division: Magnoliophyta

Class: Magnoliopsida
Order: Rosales
Family: Moraceae
Genus: *Ficus*
Species: *F. religiosa*
Scientific Name: *Ficus religiosa*

Vernacular Names

Pippala (Sanskrit), Ahant (Assamese), Asvattha, Ashud, Ashvattha (Bengali), Pipal tree (English), Piplo, Jari, Piparo, Pipalo (Gujrati), Pipala, Pipal (Hindi), Arlo, Ranji, Basri, Ashvatthanara, Ashwatha, Aralimara, Araleghida, Ashvathamara, Basari, Ashvattha (Kannada), Bad (Kashmiri), Arayal (Malayalam), Pipal, Pimpal, Pippal (Marathi), Aswatha (Oriya), Pipal, Pippal (Punjabi), Ashwarthan, Arasamaram, Arasan, Arasu, Arara (Tamil), Ravichettu (Telugu).

Other Names

Bo tree, Bodhi tree, Sacred tree, Beepul tree, Pipers, Pimpal, Jari, Arani, Ashvattha, Ragi, Bodhidruma, Shuchidruma, Pipalla, Ashvattha and the Buddha tree are the other names used for the Banyan tree.

Botanical Description



Figure 1: *Ficus Religiosa*

Peepal is a large, fast growing deciduous tree. It has a heart shaped leaves. It is a medium size tree and has a large crown with the wonderful wide spreading branches. It shed its leaves in the

month of March and April. The fruits of the Peepal are hidden with the figs. The figs are ripen in the month of May. The figs which contain the flowers grow in pairs just below the leaves and look like the berries. Its bark is light gray and peels in patches. Its fruit is purple in colour. It is one of the longest living trees.

F. religiosa is a large deciduous tree with or no aerial roots which is commonly found in India. It is mainly grown in State of Haryana, Bihar, Kerala and Madhya Pradesh. It is also found in the Ranthambore National Park in India It is native from India to Southeast Asia which grows up to 5000ft with the trunk which reaches up to 1 meter. Reproduction is done by layering, cottage and seeds. The stem is pale yellow by which several roots are fused.

Leaves are very shiny, thin and bear 5-7 veins which are alternate, long, petiolate, and serrate or heart shaped at the base or sometimes rounded. The young leaves are pink in color, changes to copper and finally to green at maturity. The bark is of white or brown in color. Fruits are circular in shape called as Figs which is enclosed in florescences. When fruits are raw, they are green in color during summer but after ripening they turn black through rainy season.

Ethnopharmacology

Traditional Uses

F. religiosa is a well-known ethnomedicinal tree used in Ayurveda. Its use in the Indian traditional folk medicine also well documented. The use of different parts of *F. religiosa* in traditional system of medicine.

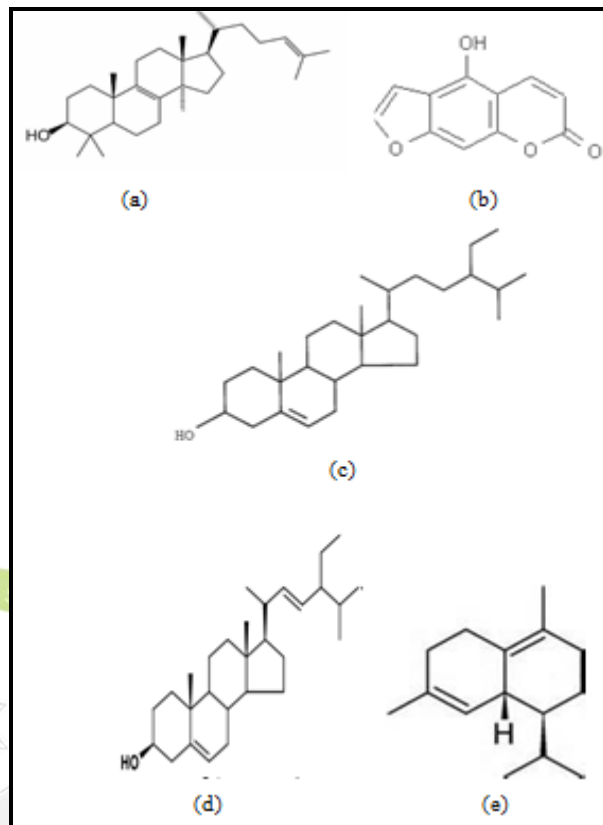
Table 1: Chemical Compounds Contained By Different Parts of *F. Religiosa*

Sr.No	Plant Part	Compounds present
1	Bark	Phenols, tannins, steroids, alkaloids and flavonoids, β -sitosteryl-d-glucoside, vitamin K, noctacosanol, methyl oleanolate, lanosterol, stigmasterol, lupen-3-one. Tannin, wax, saponin, Leucoanthocyanins. delphinindin-3-0- α -Lrhamnoside (11), Pelargonidin-3-0- α -Lrhamnoside, Leucocyanidin-3-0- β -D-galactosyl-cellobioside (111), Leucoanthocyanidin, 20- tetratriaconten-2-one , pentatriacontan- 5-one , 6 heptatria content-10-one, meso anisosital ¹¹
2	Root	β -sitosteryl-dglucoside ¹¹
3	Fruit	Protein (4.9%), Essential amino acids (isoleucine, and phenylalanine), Flavonols (kaempferol, quercetin, and myricetin), Also contains good amount of total phenolic contents, total flavonoid, and percent inhibition of linoleic acid ¹¹ , 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 ¹¹
4	Seed	Phytosterolin β -sitosterol, and its glycoside, albuminoids, carbohydrate, fatty matter, Coloring matter, Caoutchoue 0.7-5.1% ¹¹
5	Leaves	campesterol, stigmasterol, isofucosterol, α -amyrin, lupeol, tannic acid, arginine, serine, aspartic acid, glycine, threonine, alanine, proline, tryptophan, tryosine, methionine, valine, isoleucine, leucine, n-nonacosane, n-hentricontanen, hexa-cosanol and n-octacosan ¹¹
6	Latex	Neuralgia, inflammations, haemorrhages ¹¹

Phytochemistry

Phytochemistry can be defined as chemistry of plants or chemical composition of plants. In pharmacy, it is described as the chemistry of those natural products which can be used as drugs or plant parts with the emphasis on biochemistry. These compounds can be therapeutically active or inactive¹². The inactive constituents are structural constituents of the plants like starch, sugars or proteins. They have good pharmaceutical uses. Preliminary phytochemical screening of *F. religiosa* barks, showed the presence tannins, saponins, flavonoids, steroids, terpenoids and cardiac glycosides¹³. The barks of *F. religiosa* showed the presence of bergapten, bergaptol, lanosterol, β -sitosterol, stigmasterol, lupen-3-one, β -sitosterol-d-glucoside (phytosterolin), vitamin k¹⁴. The bark also contains tannin, wax, saponin, β -sitosterol, leucocyanidin-3-O- β -D-glucopyranoside, leucopelargonidin-3-O- β -D-glucopyranoside, leucopelargonidin-3-O- α -L-rhamnopyranoside, lupeol, ceryl behenate, lupeol acetate, α -amyrin acetate, leucoanthocyanidin and leucoanthocyanin¹⁵. Leaves yield campesterol, stigmasterol, isofucosterol, α -amyrin, lupeol, tannic acid, arginine, serine, aspartic acid, glycine, threonine, alanine, proline, tryptophan, tyrosine, methionine, valine, isoleucine, leucine, n-nonacosane, n-hentricontanen, hexa-cosanol and n-octacosan¹⁶. 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 -cadinene¹⁷. Alanine, threonine, tyrosine have been reported in seeds of *F. religiosa*¹⁸. The crude latex of *F. religiosa* shows the presence of a serine protease, named religiosin. Religiosin is an acidic. Reverse Phase High Performance Liquid Chromatographic analysis of flavonoids in *F. religiosa* using kaempferol, rhamnetin, myricetin, isorhamnetin and quercetin as standards. The findings showed that quercetin was most

abundant flavonol present in *F. religiosa*. the structures of active constituents reported in *F. religiosa* are given in



(a) Lanosterol (b) Bergaptol (c) B-sitosterol (d) Stigmasterol (e) δ -cadinene

Figure 2: Active Compounds Present In *F. Religiosa*

Pharmacological Activities Present in *Ficus Religiosa*

F. religiosa possess a broad range of pharmacological activities as shown in figure 4. Fresh plant materials, crude extracts and extracted components of *F. religiosa* showed a wide spectrum of *in vitro* and *in vivo* pharmacological activities like, antidiabetic, anti-inflammatory, wound healing, anticonvulsant, anti-inflammatory, analgesic, antimicrobial, antioxidant, antiasthmatic, antitumor, antiulcer, antianxiety, antihelmintic, and proteolytic activity.

Anticonvulsant Activity

An exhaustive study was performed on figs (fruit) of *F. religiosa* showed promising

anticonvulsant activity in experimental model were seizure induced by maximum electroshock (MES), picrotoxin and pentylenetetrazol (PTZ). Along with cyproheptadine, a nonselective serotonin antagonist (4 mg/kg, i.p.) was used to study the reversal of protective effect of extract in the above mentioned models. Acute toxicity, neurotoxicity and potentiation of phenobarbitone induced sleep by extract were also studied. The highest amount of serotonin (5-HT) in figs of this plant as compare to figs of other species reported in Ayurveda. Furthermore serotonergic neurotransmission is known to modulate a wide variety of experimentally induced seizure and is involved in seizure protection in various animal models of epilepsy by altering various GABAergic and glutamatergic functions. *F. religiosa* was measured by using high-performance liquid chromatography (HPLC). The analysis was carried out at 277 nm using 5µm particles Hypersil GOLD C-18 RP column as a stationary phase. While 25mM phosphate buffer (pH 2.5) and acetonitrile used as mobile phase at flow rate of 1ml min⁻¹. It showed an absorption peak with a retention time of 12.563 min same retention time as that of standard serotonin solution. Hence indicate the presence of serotonin in the extract. The study showed significant decrease in the duration of tonic hind limb extension in a dose dependent manner in MES model. In picrotoxin model study extract caused a delay of the latency to clonic convulsions and activity was found to be equipotent as that of diazepam treated group at a dose of 100 mg/kg. The extract showed no protection against PTZ induced convulsion at any dose. Pretreatment with cyproheptadine showed inhibition of anticonvulsant effect of the extract in both models (MES and picrotoxin). Further the extract showed no mortality and behavioural changes in acute toxicity model. This study used rotarod test to determine neurotoxic effect like ataxia, abnormal gait, reduced or inhibited righting reflexes and muscle relaxation. The extract showed no neurotoxicity and all animals able to maintain equilibrium on rotating rod for more than 3 min. The results confirm and justify the use of *F. religiosa* in ethnomedical treatment of epilepsy and presence of high serotonin

content in its figs led to hypothesize that figs of *F. religiosa* may possess anticonvulsant properties via modulating brain serotonin levels, which will be of clinical usefulness¹¹.

Antimicrobial Activity

Aqueous extract of *F. religiosa* shows high antimicrobial activity against selected pathogenic organisms. High activity has been found in *B. subtilis* with about 24mm inhibition zone. And also the growth of *P. Aeruginosa* (multi drug resistant) has been remarkably inhibited by the plant extract¹⁹. The preliminary screening of antibacterial activity of *F. religiosa* by agar-well diffusion assay was investigated. Antibacterial activity of *F. religiosa* against *Bacillus cereus*²⁰ and *Escherichia coli*²¹ has also been reported earlier; similarly the chloroform extracts of *F. Religiosa* showed a strong inhibitory activity against growth infectious *Salmonella typhi*, *Salmonella typhimurium* and *Proteus vulgaris* at a MIC of 39, 5 and 20 µg/ml respectively²².

Wound Healing Activity

The wound healing activity was investigated by excision and incision wound models using *F. religiosa* leaf extracts. 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 treated with standard drug Povidine iodine. It has been reported that tannins possess ability to increase the collagen content, which is one of the factor for promotion of wound healing^{23,24}.

The fruit is laxative, promotes digestion, aphrodisiac and checks vomiting. Ripe fruits are alexipharmic (an antidote or defensive remedy against poison, venom or infection).The powdered fruit is taken for asthma. The fruit powder is also given to enhance fertility and used in dysentery, uterine troubles, ulcers, biliousness, bitter tonic, in blood diseases. Fresh fruit is also used to treat dehydration and prevent heart disease. Powdered dry fruit destroys sorrows of a person²⁵. The seeds are cooling and refrigerant. Seeds are useful in urinary troubles. Seeds are

laxative and if taken three days during menstruation, sterilize women for long time. The leaves are the most useful parts of *F. religiosa*. The leaves alone are used to treat constipation. The leaves and young shoots together are purgative (strong laxative). The leaves can be used to alleviate fevers, bleeding wounds, constipation, dysentery, bruises, boils and mumps. The leaves can either be consumed or poured on the wound, boil or mump. Leaf juice has been used for the treatment of asthma, cough, sexual disorders, diarrhoea, haematuria, earache and toothache, migraine, eye troubles, gastric problems and scabies. Leaf decoction has been used as an analgesic for toothache. An infusion or decoction of the bark is used with some honey for the treatment of gonorrhoea, ulcers, skin diseases and scabies. Its power bark has been used to heal the wounds for years. Charaka and Sushruta prescribed a decoction of the bark of Ashvatha in haemorrhages; leaves for covering wounds; the paste of tender roots or the bark for skin infections. Sushruta administered a decoction in urinary disorders and vaginal discharges. Milk cooked with the fruit, leaf bud, bark and the root added with sugar and honey, was prescribed as an aphrodisiac. Powder of the dried bark was dusted over burns. A paste of the bark and leaves was prescribed in stomatitis. Ash water of the dried bark was given for checking vomiting. Decoction of the root bark with salt and jaggery induce anti-diuretic property

Antioxidant Activity

The antioxidant activity of the aqueous extract of *F. religiosa* was investigated in streptozotocin-induced diabetic rats. Since the oxidative stress is the major cause and consequence of type 2 diabetes. Free radicals generated during oxidative stress damage the insulin receptors and thereby decrease the number of sites available for insulin function. The aqueous extract drug reported to contain tannins, flavonoids and polyphenols. At doses 100 and 200 mg/kg of aqueous extracts of *F. religiosa* shows significantly decrease in fasting blood glucose and increase in body weight of diabetic rats as compared to untreated rats. *F. religiosa* at 100 mg/kg dose decreased significantly ($p < 0.05$) superoxide dismutase

(SOD) and at dose of 200 mg/kg significantly enhanced catalase (CAT) ($p < 0.05$) and glutathione peroxidase (GSH-Px) ($p < 0.01$) activity in type 2 diabetic rats. It modulated the SOD activity in dose dependent manner. Decrease in CAT activity due to less availability of NADPH or gradual decrease in erythrocyte CAT concentration by excessive generation of oxygen radical that inactivates the enzyme. Aqueous extract restored the erythrocyte GSH. Decrease in MDA marker by *F. religiosa* showed the erythrocyte CAT concentration by excessive generation of oxygen radical that inactivates the enzyme. Aqueous extract restored the erythrocyte GSH. Decrease in MDA marker by *F. religiosa* showed the ability of rasayana drug (rejuvenators, antioxidant, and relieve stress). The results suggesting that the *F. religiosa*, a rasayana group of plant drug having antidiabetic along with antioxidant potential was beneficial in treatment of type 2 diabetes²⁶.

Anti-Amnesic Activity

The anti-amnesic activity was investigated using *F. religiosa* methanol extract of figs of *F. religiosa* on scopolamine-induced anterograde and retrograde amnesia in mice. Figs were known to contain a high serotonergic content, and modulation of serotonergic neurotransmission plays a crucial role in the pathogenesis of amnesia. During study, transfer latency (TL) to the preferred niche in the elevated plus-maze (EPM) and learning avoidance of passive behavior to avoid punishment in the modified passive avoidance paradigm (MPA) served as behavioral models for the assessment of memory. Scopolamine (1mg/kg, i.p.) was administered before training for induction of anterograde amnesia and before retrieval for induction of retrograde amnesia in both models. TL in the EPM, step down latency (SDL), number of trials, and number of mistakes in the MPA were determined in vehicle control, *F. religiosa* figs treated (10, 50, and 100mg/kg, i.p.), and standard groups (piracetam 200mg/kg, i.p.). Cyproheptadine, a non-selective 5-HT_{1/2} blocker (4mg/kg, i.p.), was administered along with the *F. religiosa* figs to investigate the involvement of serotonergic pathways in the

anti-amnesic effect of *F. religiosa* figs. The resulted had anti-amnesic activity against scopolamine induced amnesia, in a dose-dependent manner. Inhibition of the anti-amnesic effect of *F. religiosa* figs by cyproheptadine substantiates the involvement of serotonergic pathways for its activity²⁷.

Acetylcholinestrase Activity

Methanolic extract of the stem bark of *F. religiosa* is found to inhibit the acetylcholinestrase enzyme, thereby prolonging the half-life of acetylcholine. It has been reported that most accepted strategies in Alzheimer's diseases treatment is the use of cholinestrase inhibitors²⁸.

Proteolytic Activity

A comparison of the proteolytic activity of the latex of 46 species of *Ficus* has been done by electrophoretic and chromatographic properties of the protein components and *F. religiosa* has showed a significant proteolytic activity²⁹.

Anti-Acetylcholinestrase Activity

Methanolic extract of the stem bark of *F. religiosa* found to inhibit the acetylcholinestrase enzyme, thereby prolonging the half-life of acetylcholine. It was reported that most accepted strategies in alzheimer's diseases treatment is the use of cholinestrase inhibitors. The calculated 50% inhibitory dose (ID50) value was 73.69 µg/ml respectively. The results confirm and justify the popular traditional use of this plant for the treatment of alzheimer's diseases³⁰.

Anti-Inflammatory Activity

The methanolic extract of stem bark of *F. religiosa* has shown significant anti-inflammatory activities orally. A significant anti-inflammatory effect has been observed in acute and chronic models of inflammation; the extract also protected mast cells from degranulation induced by various degranulators²³. A paste of the powdered bark is a good absorbent for inflammatory swellings and can be used to treat burns 24-25. Earlier study on the same methanol extract demonstrated that the extract inhibited the production of nitric oxide and proinflammatory

cytokines in LPS-stimulated microglia via the MAPK³¹⁻³².

What Makes *F. Religiosa* Different From Other Plant?

The *F. religiosa* releases oxygen all the time which makes it different from other plant. Most plants largely uptake Carbon dioxide (CO₂) and release oxygen during the day (photosynthesis) and uptake oxygen and release CO₂ during the night (respiration). Some plants such as *F. religiosa* (Peepal) can uptake CO₂ during the night also like day because of their ability to perform a type of photosynthesis called Crassulacean Acid Metabolism (CAM). However, it is not true that they release large amounts of oxygen during the night. *F. religiosa* (Peepal) is a hemiepiphyte in its native habitat i.e. the seeds germinate and grow as an epiphyte on other trees and then when the host-tree dies, they establish on the soil. It has been suggested that when they live as epiphyte, they use CAM pathway to produce carbohydrates and when they live on soil, they switch to C3 type photosynthesis.

So, *F. religiosa* (Peepal) would either release or not release CO₂ in the night depending on if they are epiphytic or not. For other CAM plants, it would depend on if they have adequate water or not, or other environmental factors. Recently one more hypothesis has predicted that leaves of *F. religiosa* are able to charge the battery of mobile. With scientific approaches in future, this hypothesis can reduce the usage of charger and can be good source of renewable energy.

CONCLUSION

Ficus religiosa is a widely branched tree with leathery, heart shaped, long tipped leaves, used in the Indian system of medicine, besides which folklore medicine also claims its use in diarrhoea, diabetes, urinary disorder, burns, haemorrhoids, gastrohelcosis, skin diseases, convulsion, tuberculosis, fever, paralysis, oxidative stress, bacterial infection etc. Research carried out using different in-vitro and in-vivo techniques of biological evaluation support most of these claims. Presently there is an increasing interest

worldwide in herbal medicines accompanied by increased laboratory investigation into the pharmacological properties of the bioactive ingredients and their ability to treat various diseases. Numerous drugs have entered the international through exploration of ethnopharmacology and traditional medicine. Although scientific studies have been carried out on a large number of Indian botanicals, a considerably smaller number of marketable drugs or phytochemical entities have entered the evidence-based therapeutics. Efforts are therefore needed to establish and validate evidence regarding safety and practices of Ayurvedic medicines.

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