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Review Paper

Pharmacognostic, Phytochemical and Pharmacological Review of *Mitragyna parvifolia* Roxb.

Abhash Singh*, Raj K. Prasad, Poonam Maurya, Shivangi Upadhyay

Shambhunath Institute of Pharmacy, Jhalwa, Prayagraj, Uttar Pradesh, 211012

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ABSTRACT

Mitragyna parvifolia (Roxb.) Korth., often called Kaim or Kadamb, is a significant medicinal tree that is a member of the Rubiaceae family. On the Indian subcontinent, it is extensively found in tropical and subtropical areas. In indigenous medical systems, different plant parts, such as bark, leaves, and roots, have long been utilized to treat metabolic problems, fever, diarrhea, inflammation, and pain. Its pharmacological qualities are influenced by bioactive components such as indole alkaloids, flavonoids, glycosides, tannins, and saponins, which have been identified by phytochemical studies. The plant has antibacterial, anti-inflammatory, analgesic, antipyretic, hepatoprotective, antioxidant, and antidiabetic properties, according to experimental research. Scientists are becoming more interested in *Mitragyna parvifolia* because of its many medicinal uses. In order to emphasize *Mitragyna parvifolia*'s importance as a potential source of natural medicinal compounds and the need for more clinical research, this study attempts to provide an overview of the plant's botanical traits, traditional applications, phytochemistry, and pharmacological activity.

INTRODUCTION

For the prevention and treatment of a wide range of illnesses, medicinal plants remain an essential source of therapeutic chemicals. Plant-derived chemicals continue to be relevant despite major advancements in synthetic medicine synthesis because of their biological activity, structural diversity, and very low incidence of side effects. The growing interest in herbal therapy throughout

the world has prompted pharmacological and phytochemical studies to validate traditionally utilized botanicals. The family Rubiaceae includes the genus *Mitragyna*, which includes a number of species of ethnobotanical and medicinal use. Among these is the deciduous tree *Mitragyna parvifolia* (Roxb.) Korth., which is found across South and Southeast Asia, including India, Nepal, and Sri Lanka. The plant, sometimes called kaim or kadamb, is found in tropical and subtropical

*Corresponding Author: Abhash Singh

Address: Shambhunath Institute of Pharmacy, Jhalwa, Prayagraj, Uttar Pradesh, 211012

Email ✉: abhashsingh177@gmail.com

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areas and has long been used in folk medicine and traditional medical systems like Ayurveda.

Fever, pain, inflammation, diarrhea, wounds, and metabolic diseases have all been treated using various parts of *Mitragyna parvifolia*, including the bark, leaves, roots, and fruits. These conventional assertions have led scientists to investigate its biological characteristics and chemical makeup. Numerous secondary metabolites, including indole alkaloids, as well as flavonoids, tannins, glycosides, and other bioactive substances that can support its medicinal potential have been identified by phytochemical investigations. A wide range of pharmacological actions, including antibacterial, anti-inflammatory, analgesic, antioxidant, hepatoprotective, and antidiabetic effects, have been linked to *Mitragyna parvifolia* in recent years, according to experimental research. Nevertheless, despite encouraging first results, there is still a lack of thorough mechanistic research and comprehensive clinical evaluation. Thus, the goal of this review is to provide a thorough overview of the literature that is currently available on *Mitragyna parvifolia*'s taxonomy, botanical description, traditional uses, phytochemical constituents, and pharmacological activities. It also seeks to identify research gaps and future directions for the plant's therapeutic development.

Geographical Distribution:

In addition to its native India, the plant may be found in tropical and subtropical regions of Asia and Africa. More well-known in India's west,

Kokan, Karnataka, Assam, Himalaya, etc. Nepal, Sri Lanka, Pakistan, Indonesia, Myanmar, and other places are also home to it. *Mitragyna parvifolia* is a tall, attractive tree with a spreading crown that has a variety of pharmacological properties. [5-7]

Religious Tree:

Rather than the famous *Neolamarkia cadamba* tree, this "true Kadamb" is associated with Lord Krishna at Vrindavan, according to ancient legend. This is unquestionably an example of mistaken identification. While *Neolamarkia cadamba* is not a native of the hot, dry Vrindavana region, *Mitragyna parvifolia* is not just native to the forest but also the dominant tree there. *Mitragyna parvifolia* is still present almost everywhere in Vrindavan. As the same seems to apply to mother goddess Durga, who resides in Kadam Forest, the tree should be called Haripriya, which means "God's favorite." It is known as the tree that Lord Krishna loves the most. [8]

Taxonomical Classification:

Kingdom	Plantae
Sub kingdom	Tracheophytes
Phylum	Magnoliophyte
Class	Magnoliatae
Order	Rubiales
Family	Rubiaceae
Genus	<i>Mitragyna</i>
Species	<i>Mitragyna Parvifolia (Roxb) korth</i>

Synonyms of *Mitragyna Parvifolia* along with their different Names:

Bionomical Name	<i>Mitragyna parvifolia (Roxb.) Korth</i>
Scientific Name	<i>Mitragyna parvifolia (Roxb.) Korth</i> <i>Mitragyna parvifolia</i> Var. <i>Parvifolia</i> <i>Nuclea parvifolia</i> Roxb. <i>Nuclea parvifolia</i> wild [Illegitimate] <i>Stephegyle Parvifolia (Roxb.) Korth</i>
English	Burflowertree, Kaim, Laran and Leichhardt pine
Hindi	Guri, kaaylum, kaddam, Kadambkaim, Kayim
Marathi	Kalam



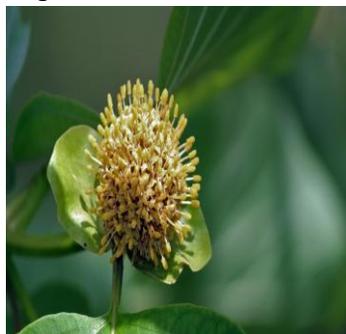
Gujrati	Kalam
Bengali	Dharakadam, Gulikadam
Kannad	Kadaani, Kadagada, Kadavala, kongu, Nayekadambe, Neerkadamba, Sannakadamba
Malayalam	Kadamba, Rooskatamp, Kathamamaram, Neerkadambu, Rosekadambu, Poochakadambu, uccakkatamp, Sirakadambu, Sirikadamba, Veembu, Vimba, Vimpu.
Nepali	KaimPhalduSaanoHaledo, Tikul
Sanskrit	Irula- kadambamaram, Vitanah
Tamil	Katampai, Niculam, Nirkatampu
Telgu	Ajaghnamu, Ambusaramu, Jalatumburu, Nirkadamba, Rsya, Tadhidruma

PHARMACOGNOSTIC PROFILE

With branches extending over 15 feet, *Mitragyna Parvifolia* can grow to a height of 50 feet (about 27 meters). It has an upright, branching stem. The leaves are spherical, smooth, dark green, and grow in the opposite direction. *Mitragyna Parvifolia* is a tall, attractive tree with a crown that spreads. Ball-shaped clusters of yellow flowers are produced.^[9] Flowers are blatant. The terminal heads have bisexual, creamy white flowers that are 10–12 mm long. The peduncle is held up by two bracts that resemble oblong leaves, and the bractioles are tiny, subulate, and the calyx tube is short with an even truncate margin. Corolla tube tunnel, 8 mm long, with 4-5 oblong reflexive lobes within that are villous. The corolla tube has five stamens linked to its apex, apiculate anthers, a two-celled ovary,

many internal ovules, a filiform style, and a mitriform, hollow stigma at its base.

Fruit capsules with globose heads that are wavy and 2-3 mm long. dividing into two cocci with many, tiny, ribbed brown seeds. Gray-black, 20–25 mm thick, with thin, smooth exfoliations that are uneven and fibrous, and flame pink with a whitish ray running through it. Young, glabrous branches.^[10,11] *Mitragynaposses* stepules have a lot of finger-shaped collectors on their diaxial bases. Collectors are of the usual form, with radially elongated epithelial cells around a core of parenchyma cells.^[12] Roxb. *Mitragyna parvifolia* Korth (Rubiaceae) is a valuable medicinal tree that is threatened. Economically speaking, *mitragynaparvifolia* micropropagation is advantageous for ex-situ discussions and for supplying raw materials for the extraction of many important alkaloids.^[13]





Different plant parts of *Mitragyna parvifolia*: (Fig.1) Leaves, (Fig. 2) Fruit, (Fig. 3) Bark, (Fig. 4)Plant.

PHYTOCHEMICAL CONSTITUENTS:

The stem and bark generate chemicals called alkaloids, flavonoids, tannins, and glycosides. Phenols, tannis, alkaloids, polysaccharides, and phytosterols are all present in bark alcohol extract. Benzene extracts were used to extract carbohydrates, phenols, and steroids. The six primary oxindolic alkaloids present in leaves are speciophylline, pteropodine isopteropodine, uncarine F, isothitraphylline, and mitraphylline. Other plant alkaloids include mitragynine, rotundifoline, rhynocophylline, isorotundifoline, rhynchociline, speciocilitine, and speciofoline. Methyl acetate, pyroligneous acid, aldehydes, ketones, scopoletin, thermophyllinedaucosterol, quinovic acid, and β -sitosterol are also produced by the plant.^[14] The alkaloids 16, 17-dihydro-17 β hydroxyl isomitraphylline and 16, 17, dihydro-17 β hydroxyl mitraphylline, which are both economically priced, are found in the leaves of the *Mitragyna parvifolia* plant. Mitraphylline was the main alkaloid component. The ariel sections, stem, bark, and roots of the tree contain tetrahydroalstonine, akkyamigine, hirsuteine, and other indolic and oxiindollic alkaloids.^[15] According to the preliminary distribution of the alkaloid pattern in *Mitragyna parvifolia*, the trunk bark of young plants grown from Ceylon seed contains both the closed E ring alkaloids, such as akuammigine, pteropodine, isopteropodine, speciophylline, and uncarine F, as well as the open-cell E ring alkaloids isorhynchophylline or

rhynchophylline.^[16] The root bark contained just rhynchophylline and isorhynchophylline. The root's xylem and phloem components contain corynoxine, rhynchophylline, and isorhynchophylline. Additionally, hirsutine and hirsuteine (sometimes called Als-hirsutine) are found in the root phloem. An interesting pattern of alkaloids throughout the entire plant has been revealed by a more detailed examination of the seeds or seedlings as well as every component of a young plant grown from seed.^[17] Numerous oxindolic and indolic alkaloids have been found in *Mitragyna parvifolia* leaves. There are only six major oxindolic alkaloids from *Mitragyna parvifolia* that have been documented from the Lucknow area: Pteropodine, Isopteropodine, Speciophylline, Uncarine F, Mitraphylline, and Isomitraphylline. Rotundifoline, rhynchophylline, the isorotundifoline complex, rhynchociline, speciociliatine, speciofoline, and mitragynine are among the other alkaloids found in the plant. The plant also includes aldehydes, ketones, and pyroligneous acids in addition to alkaloids. β -sitosterol, methyl acetate, quinovic acid, scopoletin, thermophyllin, and daucosterol.^[15] Four hetero yohimbine class oxindole alkaloids were obtained from an ethanolic solution of *M. parvifolia* plants treated with an acid-base chloroform fraction. They found 16, 17-dihydro-17b-hydroxy isomitraphylline, mitraphylline, and isomitraphylline, respectively, based on their spectroscopic data and a comparison with the literature. The structures of 1 and 2 were clarified

by means of heteronuclear singular quantum coherent experiment with direct coupling (HSQC), heteronuclear multiple bonds correlation spectrum (HMBC), and ¹H-¹H correlated spectroscopy (COSY). The DEPT. experiment was used to measure the number of sp, sp², sp³, and quaternary carbon atoms.^[18]

TRADITIONAL USES

In Gundur District, Andhra Pradesh, the Chenchus, Yerukalas, Yanadis, and Sugalis utilize the sap from fresh leaves of *Mitragyna parvifolia* to cure jaundice.^[19] Its leaves reduce pain and swelling and promote faster wound and ulcer healing. In Tumkur district, Karnataka, India, the native population uses the stem bark of *M. parvifolia* to alleviate muscle aches and biliousness.^[20] In the Sonbhadra district of Uttar Pradesh, the tribal people of Sonaghati use a bark decoction of *M. parvifolia* to treat fever. For rheumatic discomfort, the Valaiyans, who live in the Sirumalai Hills in the Madurai district in the Western Ghats of Tamil Nadu, use the stem bark of *M. parvifolia*. The bark and roots are used to treat gynecological diseases, fever, colic, burning sensations, muscle soreness, coughing, edema, poisoning, and as an aphrodisiac. The fruit juice acts as a lactodepurant and increases the amount of breast milk produced by nursing parents. Timber is utilized in the paper industry, furniture, and farming tools, among other things.^[21]

PHARMACOLOGICAL ACTIVITIES

Anti-Hypertensive Activity:

Vasorelaxant and antihypertensive effects of root alcohol extract from *Mitragyna Parvifolia*. S. C. was given a deoxy corticosterone acetate injection (20 mg/kg) and an 11% w/v NaCl solution with drinking water following uninephrectomy, which resulted in hypertension. The alcohol extract from *M. P.* roots was given in doses of 200

and 400 milligrams per kilogram. We looked at heart rate, systolic blood pressure, and serum levels of TG and TC. To evaluate the extract's vasorelaxation capacity against calcium chloride-induced contractions in isolated tissue, the isolated thoracic aorta was utilized.^[22]

Anthelmintic activity:

In comparison to albendazole (10 mg/ml), a common reference, the ethanolic and aqueous extracts of *Mitragyna Parvifolia* leaves demonstrated a significant paralysis of worms at higher doses of 50 mg/ml when evaluated for anthelmintic effect against *pheritimaposthuma*. Dried stem bark methanolic extract had significant anthelmintic action at a dose of 100 mg/ml. The paralysis and death periods of the earthworms were measured to evaluate this activity, and it was shown that the impact was dose dependent; no effects were observed at a lower dosage of 20mg/ml. In contrast to the piperazine citrate standard, earthworm paralysis and death times were noted, and it was discovered that the anthelmintic activity of the methanolic or ethanolic extract from *M. Parvifolia* fruit depended on dose.^[23]

Anti – Diabetic Activity:

M. Parvifolia produced DHIM, an indole alkaloid. DHIM substantially inhibited DPP IV. Chronic DHIM therapy improved glucose tolerance in response to glucose loading and markedly reduced plasma glucose levels. GLP-1 and IL-1 levels were significantly greater in treated diabetic rats in in vivo studies on neonatal Wistar albino rats administered STZ. As per the experiment, DHIM stimulates cell division, reduces pancreatic cells, and boosts β -cell production.^[24,25]

Antimicrobial Activity:

For medicinal applications where antibacterial activity is crucial, the green produced copper nanoparticles showed promise. The aqueous extract made from the bark of the *Mitragynaparvifolia* plant offers a cost-effective, ecologically friendly, and efficient method of synthesizing copper nanoparticles in a short amount of time. Copper nanoparticle production is confirmed by the solution's color changing from pale yellow to dark brown. [26]

Antiviral Activity:

Extract from *Mitragynaparvifolia* was tested against the bovine herpes virus type-1, which causes infectious bovine rhinotracheitis, abortions in cows during months 5-7 of pregnancy, and significant financial losses. Using the MDBK cell line, the cytopathic inhibition assay was used to evaluate the plant extracts' in vitro antiviral ability against BHV-1. The MDBK cell line was identified using the MTT (microculture tetrazolium) test. [27]

Anticonvulsant Activity:

Mitragyna parvifolia leaves' ethanolic extract has an anticonvulsant effect. was examined by the use of maximum electroshock convulsive techniques and phenylenetetrazole (PTZ)-induced seizures in mice. Three dosages (100, 250, and 500 mg/kg) of the extract were given orally; only the 500 mg/kg dose showed a protective effect. As a result, both models' results indicated dosage dependence. [28]

Antiarthritic and Antipyretic activity

The methanolic extract of *Mitragyna parvifolia* (MEMP) leaves was discovered to have antipyretic and antiarthritic properties in rodents. In order to assess antiarthritic activity using acetic acid-induced vascular permeability in mice, Freund's adjuvant-induced arthritis in rats, and yeast-induced pyrexia in rats, MEMP was given orally at

125, 250, and 500 mg/kg. It demonstrated a significant antiarthritic and antipyretic effect ($p < 0.05-0.01$). [29]

Anti-inflammatory and Anti-nociceptive Activity

By used the tail-flick technique and carrageenan-induced paw edema in rodents to examine the anti-inflammatory and antinociceptive properties of the ethanolic extract of dried *Mitragyna parvifolia* (MPEE) leaves. [30] In the carrageenan test, the extract's maximal anti-inflammatory activity was 300 mg/kg, which was comparable to phenylbutazone (PBZ) at 80 mg/kg, taken orally ($p < 0.05$). At a dosage of 300 mg/kg, the extract also showed notable antinociceptive action; the impact was similar to that of the common medication, Ibuprofen (100 mg/kg orally) ($p < 0.05$). [31] By used the Acetic acid-induced writhing test and Eddy's hot plate to investigate the analgesic effects on mice. In the acetic acid-induced writhing test, the extract only shown modest analgesic potential at all test dosages; however, in the hot plate technique, the extract at 500 mg/kg ($P < 0.01$) demonstrated high analgesic efficacy equivalent to the standard medication Diclofenac sodium (50 mg/Kg, i.p.). [32]

Anxiolytic Activity:

Anxiolytic effect of several extracts of *Mitragyna parvifolia* stem bark was assessed in mice using the marble burying test (MBT) and elevated plus maze (EPM). The fraction with a higher concentration of alkaloids had stronger anxiolytic effects. C.MC is used to treat pain, fever, skin, infections, and as a moderate anxiolytic. The anxiolytic properties were mediated through the GAB allergic system (VIII). [33]

Antibacterial and Antifungal Activity:



Using the agar-based well diffusion technique, the extract's antibacterial activity at different doses was assessed. *Escherichia coli*, *Pseudomonas aeruginosa*, and *Bacillus subtilis* were among the microorganisms against which the plant extract showed no antibacterial effect. Nonetheless, it showed some degree of inhibition of *E. coli* (A) and *Paeruginosa*, and it significantly inhibited five aureus.^[34]

Immunosuppressive Activity:

The in vitro effects of flavanoids derived from the leaves of the three medicinal plants on human peripheral blood mononuclear cells (PBMC) are assessed using a hepatitis B vaccine that contains surface antigens (HBs, Ag,) at concentrations of 20 µg/ml and 10 µg/ml. The growth of HBs, Ag, nitric oxide production, and the surface marker CD 14 are also measured. Higher dosages of flavanoids (25 µg/ml; 50 µg/ml) suppressed HBsAg driven human PBMC cell proliferation and nitric oxide generation. They also prevented the activation of CD-14 monocyte surface marker, which is required for T cell activation, according to the data. According to the results, it has immunosuppressive properties and also has cytotoxic effects.^[35]

Antiulcer Activity:

The research indicates that ethanolic extracts of *M. Roxb, parvifolia*. at 400 mg/kg significantly improved the cytoprotective, ulcer-healing, and anti-secretory actions. By employing the pylorus ligation technique, the antiulcer capabilities of the plant were evaluated.^[36]

Anticancer Activity:

Dichloromethane extract of *Mitragyna parvifolia* stem bark has anticancer potential according to molecular docking studies and the MTTT test. MCFT A549 and Hep G2 cell lines were subjected

to the MTT test. The results showed that the IC₅₀ values were 402.8 µg/ml, 207.4 µg/ml, and 104.4 µg/ml, in that order. By using GC-MS analysis, the phytoconstituents of the extract were identified. The NTST library was used to identify and name the most likely structures. Using autodockivina, a molecular docking research was performed on a chosen molecule by selecting the appropriate anticancer treatment target proteins, VEGFR2, Kinase (lung cancer), (breast cancer), and EGFR Kinase (liver cancer). The docking investigation revealed that the extract had significant anticancer effect since the binding energy and interactions of the steroidal derivatives were similar to those of the standards (Erlotinib, Sorafenib, and SYR).^[37]

CONCLUSION

Many studies have been conducted on the use of natural plant-based medicines. Many Indian tribal people have long used *Mitragyna parvifolia* in their traditional treatments. The parts of the plant have several therapeutic uses. Numerous pharmacological properties of the plant's various sections have been studied and scientifically confirmed. The plant's safety profile is demonstrated by the acute toxicity testing. Research on the plant's chemical profile shows that it has a high alkaloidal content that changes quantitatively as the tree's geographic position changes. These haven't, however, been examined separately for various pharmacological actions. This section requires careful research. Overall, the research demonstrates the plant's value as a secure and efficient therapy in contemporary medicine.

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