Mediterranean Journal of Basic and Applied Sciences (MJBAS)
Volume 9, Issue 1, Pages 100-108, January-March 2025

# *Mitragyna parvifolia*: An Endangered tree

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*DOI: https://doi.org/10.46382/MJBAS.2025.9107*



*Article Received: 07 January 2025* *Article Accepted: 12 March 2025* *Article Published: 21 March 2025*

**ABSTRACT**

*Mitragyna parvifolia* (roxbi) korth commonly known as kadam is an endangered and pharmaceutically valued religious tree of the family Rubiaceae. Plant contains several alkaloids and chemical which attribute to its medicinal properties. Due to its poor seedling survival and over exploitation of its natural habitats plants reached to endangered category. Plant needs conservation of existing tree and propagation with sustainable harvesting.

**Keywords:** *Mitragyna parvifolia*; Endangered tree; Pharmacological activity; Traditional medicinal uses; Ex-situ conservation; Phytochemical; Antimicrobial activity; Anticancer.

## 1. Introduction

*Mitragyna parvifolia* is commonly known as kadamba or kaim belongs to family Rubiaceae. The majority of genus *Mitragyna* members are tree, shrubs or under shrubs and dispersed throughout the temperate part of the world. Out of total 11 species of Mitragyna only 7 species are inhabitant in India. The species are mainly distributed in tropical and arid/semiarid parts of Africa, India, China, Bangladesh, Myanmar, Srilanka and South East Asia (Govaerts et al., 2015). The part is native to Indian origin and also found in tropical and subtropical region of Africa and Asia. In India more popular in West Konkan, Karnataka, Assam, Himalayas, etc. *Mitragyna parvifolia* (Roxbi) korth is an economically useful and highly endangered deciduous tree found in well drained deep soil of Indian Thar Desert (Choudhary & Jain, 2016).

It is known by different vernacular names viz. in scientific languages Neolamarkia Cadambao in English as Burflowe tree, kalam, laran and Leichhardt Pine, In Hindi as kadam or kalam, in Marathi as kalam, in Bengali as Dharakadam and Gulikadam, in kannad as kadaari , kongre, Karaganda, kadavala, Nayekadambe, Neerkadamba and Sannakadamba, in malayalam as kadamba, rose-kadambu, kathamamaram, Neerkadamba, rooskatamp, poochakadamba, ucckkatamp, sirakadabu, sirikadamba, veembu, vimba, and vimpu, in Tamil as katampai, niculam and nirkatampu, in Telgu as Ajaghnamu, ambusaramu, jalatumburu, nirkadamba, rays and tadhidruma in nepali as kaimphaldu saano haledo and tikul, in sanskrit as Irula-kadamba-maram and vitanah etc. In some other part it is also known by vernacular names such as Boodha, China, Kaim, Kadam, Kadamba, Kadambu, Ichulam, Patta and water (Dwivedi et al., 2015; Kumar, et al., 2015, Choudhary & Jain., 2016; Phalak et al., 2020, Wikipedia etc.).

### 1.1. Religious tree

As per ancient literature this is a "true kadamb" which is associated with Lord Krishna in vrindavana rather than well-known tree Neolamarkia Cadamba. This is definitely a case of mistaken identity Neolamarkia cadamba is not found naturally in the hot, dry vrindavana region where as Mitragyna parvifolia is not only native to vrindavana

forest but is dominant tree there. Mitragyna parvifolia are still found almost everywhere in vrindavana. The same appears true for mother goddess Durga who resides in kadam forest so the tree should truly be called as Haripriya (God´s favorite). It is given name as favorite tree of Lord Krishna (Phalak et al., 2020).

### 1.2. Botany

*Mitragyna parvifolia* (Roxb) korth is a medium to large deciduous tree with rounded crown mainly arboreal in nature upto 25-27 meter tall. It is found throughout the greater parts of India upto an altitude of 1200 meters. Tree is found scattered in deciduous forests and develop best in well drained deep soil. It is found growing gregariously in low-lying areas close to the river (Bhandari et al., 1990).

The stem is erect and branching. Leaves are dark green in colour, smooth pattern. The tree has spreading crown. Its flowers are yellow and grow in ball shaped cluster flowers are flagrant. It has bisexual creamy white 10-12mm long in terminal heads peduncle supported by a pair of bracts like oblong leaves. It calyx tube short truncate rim and corolla tube funnel shaped 8 mm long. Stamen 5 attached towards apex of corolla tube, style fill form and stigma mitriform hollow at base. Its fruit are capsule in globose heads, 2-3 mm long wavy. Separating into two cocci, brown seeds many, small transverse by whitish ray fruits of kadamba looks like corona virus.

### 1.3. Propagation

Natural reproduction takes place by the scattering of seeds in hot season. Germination takes place in the rainy season plants grow exclusively in humid conditions and observation that geographical location and environmental conditions have a crucial role in modifying the alkaloid and the structure. (Chatterjee et al., 1982) conventionally it is grown by stem cuttings, grafting and layering but they are not much successful and there is need to multiply plant by alternative methods such as micro propagation. Micro propagation as an integrated plant conservation strategy can combine in situ as well as ex situ approaches to ensure conservation of threatened plant tax (Werden et al., 2020).

Several work for its micro propagation was carried out. Through tissue culture attempt was made but more refined work is needed (Roy et al., 1988). Poor seedling survival (due to very small size of seeds, approx 10,000 per gram) over exploitation and habitat destruction needs to conserve this species through significant, improved and repeatable microprpagation by using nodal explants of a mature tree. In an experiment nodal explants harvested during spring season from the lopped tree differentiated the maximum number of axillary shoots (5.3±0.82 per node) on full strength Murashige and Skoog (MS) medium containing 3 mg/litre, 6-benzyl amino purine (BAP) and additives (25 mg per liter each of adenine sulphate, L-arginine and Citric acid and 50mg/liter ascorbic acid). Shoots were amplified in-vitro through recurrent transfer of mother explants and sub culturing on fresh nutrient medium. Result shows greatest number of shoots (13.4±1.26) with an average length of (6.2±1.03cm) produced after 4 week on MS medium containing 0.5 mg/liter, BAP 0.25 mg/liter, Kinetin 0.1 mg/liter activated charcoal and 0.8 w/v agar. About 90 percent micro propagated shoots rooted ex vitro on pulse treatment of 500 mg/liter.Indole-3 butyric acid (IBA for 5 min) and produce 8.5±0.97 roots per shoot with an average length of 9.40±1.06 cm after 5week. Among all concurrent ex vitro rooting and acclimatization (CEVRA) plantlets over 80

percent were successfully transplanted to the soil in field. This protocol can be employed for conservation ex situ and restoration or rehabilitation in situ of *Mitragyna parvifolia* (Patel et al., 2020).

In nature plant propagated seedlings are delicate and often wash away with heavy rain or excess water (Roy et al., 1988). In one report downfall in the population of *Mitragyna parvifolia* at Keoladeo national park (KNP), Bharatpur, India, which is UNSECO world heritage site and also Ramsar site. It may be possible only natural wetland site in the Yamuna River where naturally growing *Mitragyna parvifolia* trees flourished. Moreover other constraints such as frequent droughts, herbivory and inter and intraspecific competition between species are cause of dwindling population of *M. parvifolia* (Bidalia et al., 2017).

## 2. Traditional uses

Traditionally *Mitragyna* have been used to treat fever, malaria, diarrhea, muscle pain, inflammation and hypertension. *Mitragyna* posse's wide pharmacological effects in antitumor, cardiovascular diseases and antibacterial activity (Patel et al., 2020). Its bark and roots are used to treat, fever, colic, muscular pain, burning sensation, poisoning, gynecological disorder, cough and edema as an aphrodisiac. The fruit juice augments the quantities of breast milk in lactating mothers and also work as lectodepurant (Choudhary & Jain, 2016; Jhadhav et al., 2022).

*Mitragyna parvifolia* fresh leaf sap is used by tribals in treatment of jaundice in the chenchus, yerukalas yanadis and sugalis of gundur district, Andhra Pradesh. Its leaves alleviate pain and swelling and are used for better healing from wounds and ulcer (Phalak et al., 2020). Its stem bark is used in the treatment of biliousness and muscular pains by the local inhabitant of Tumkur district, Karnataka, India. The tribals of sonaghati of sonbhadra district, Uttar Pradesh heal fever by a decoction of the *Mitragyna parvifolia* bark. Valaiyans tribe, population of sirumalai hills, Madhurai district, Western Ghats. Tamil nadu use barks of stem for rheumatic pain (Alka et al., 2015). The caterpillars of the commander (*Limentitis procis*) a brush footed butterfly uses this species as a food plant (Gong et al., 2012). Beside these if is used for making furniture, agricultural implements, cooperages paper industry etc. (Kunte, 2000).

## 3. Phytochemical constituents and activities

Stem and bark of *Mitragyna parvifolia* yield alkaloids, flovonoids, tennis and glycosides. An alcoholic extract of bark yield carbohydrate, phenols and sterols. Leaves yield six major oxindolic alkaloids viz mitraphylline, isomitraphylline, pteropodine, isopterepodine, speciophylline and uncarine, other plant alkaloids are rotundifoline, rhynocophylline, isoroutundifoline, rhychociline, scopolectin, thermophulline daucosterol, quinonic acid, beta-sitosterol and methyl acetate (Phalak et al., 2020).

Leaves of plant have two alkaloids 16, 17-dihydro-17 beta hydroxyl mitraphylline together. Mitraphylline was main alkaloid constituents (Panday & Gupta et al., 2006).

The aerial parts stem, bark and roots of tree contain indolic (tetrahydro alstonine, alkyamigine, hirsuteine etc) and exiidollic alkaloids (Roy et al., 2013).

It has been tested on various clinic trials on animals for its pharmacological activities. They are-

### 3.1. Antibacterial and Antifungal activity

Its extract in different concentration was tested for antibacterial activity using agar well diffusion method. It shows some degree inhibition against *pacruginosa and E. coli*. However plant extract did not show antibacterial potential against *staphylococcus aureus, Bacillus subtitis, Escherichia coli and Pseudomonas acruginosa* (Ankit et al., 2009; Padamavati, 2021).

### 3.2. Antiproliferative and Antioxidant activity

*Mitragyna parvifolia* bark and leaves were evaluated for total phenolic content, total flovonoids content, antioxidant potential, lipid per oxidation and Antiproliferative effect on Hella cell lines. Antioxidant potential and flovonoids estimation were investigated using DPHH radical scavenging activity and aluminum chloride methods respectively. Further lipid per oxidation and Antiproliferative effect were observed using TBARS and MTT assay followed by cell morphology using Giemsa and Acridine orange staining (Jain et al., 2009). In another experiment 5 different extract of its dried bark and leaves in distill water, methanol, acetone, ethyl acetate and hexane were evaluated for its antioxidant potential, lipid peroxidation and antiproliferative effect on Hella cell lines. Results show distilled water extract of bark (94%) and leaf (95.6%) antioxidant potential.

### 3.3. Anticancer activity

Dichloromethane extract of *Mitragyna parvifolia* stem bark was tested for anticancer potential using MTTT assay and molecular docking studies. IC50 values were found as 402 gm/ml and 207.4 Hg/ml and 104.4 Hg/ml on MCFT, A549 and Hep G2 cell lines respectively. Phytoconstituents of extract were determined by GC-MS analysis. Molecular docking study conducted on selected compound by choosing respective anticancer drug target proteins,VEGFR2, kinase (Lung cancer, breast cancer)and EGFR kinase (Liver cancer) using auto dockivine. During study the binding energy and interaction of steroidal derivatives were comparable to those of standards (Sorafenib, SYR and Erlotinib) indicating anticancer activity of extract.

### 3.4. Anthelmintic activity

The effect of ethanolic and aquous extract of leaves from *Mitragyna parvifolia* was examined for their anthelmintic activity against *Pheritima posthema* demonstrating significant paralysis of worms at higher concentration of 50 mg/ml as compared with albendazole (10mg/ml) as standard reference (Sahu et al., 2017). Methanolic extract of dried stem bark at concentration of 100 mg/ml produced significant anthelmintic activity evaluated by observing paralysis time and death time of earthworm and found dose dependent with 20mg/ml lower concentration did not produced any result. Similarly result of its fruit made anthelmintic activity with ethanolic and Methanolic extract when compared with piperazine citrate standard (with respect to earthworm paralysis and death time) were found to be dose department (Gupta et al., 2009).

Anthelmintic activity of stem barks was examined Invitro against adult earthworm using its anatomical and physiological resemblance with the intestinal. Levamisole hydrochloride (10mg/ml) was used as reference

standard and distilled water as control. The Methanolic extract of *M. parvifolia* stem bark at the concentration of 100 mg/ml produced significant anthelmintic activity. Whereas 20 mg/ml lower concentration did not produce significant result. It was found that activity is dose dependent (Badgujar et al., 2010).

### 3.5. Antimicrobial activity

Bark of *Mitragyna* and leaves of *Butea monosperma* against human pathogenic microbial strains such as two gram positive (*Staphlococcus epidermis, Bacillus substillis*), two gram negative (*E. coli, Pseudomonas aeruginosa*) and two yeast (*Saccharomyces cerviseae, Candida albicans)* assayed by using agar well diffusion assay. There different extract (ethanol, methanol and water) of *Mitragyna parvifolia* showed better activity in compare to *Butea monosperma* (Vishal et al., 2009). Similar study carried out by other researcher (Kumar and Shreya, 2011) revealed that out of three different extract of *Mitragyna parvifolia* maximum inhibition was shown by methanol extract against bacteria. Methanolic extract offered inhibition zone in the range from 14 to 25 mm. The aqueous extract did not show any inhibitory activity against any of the text bacterial strains. The MIC values of methanol extract of *Mitragyna parvifolia* for different bacterial strains ranged from 6.25mg/ml to 12.5 mg/ml. No antifungal activity was observed against the test yeast strains (Kumar & Shreya, 2011).

### 3.6. Anti convulsing activity

*M. parvifolia* leaves ethanolic extract was tested for anti convulsant activity by studying the effect of seizure`s induced by phenyl etetrazole (PTZ) and maximal electroshock convulsive method in mice. The extract was administered orally in mice at these doses (100, 250 and 500 mg/kg). Result shows protector effect only at 500 mg/kg (Vishal et al., 2009). Similar result reported by other worker (Kaushik et al., 2009).

### 3.7. Anti-inflammatory and Antinociceptive activity

Ethanolic extract of dried leaves of *M. parvifolia* was tested for anti-inflammatory effect showed in carrageen induced paw edema model was equivalent to phenyl butazone (PTZ) (80mg/kg orally). The extract also exhibited marked antinociceptive activity was comparable with standard drug ibuprofen (Pundir et al., 2011).

Ethanolic extract of dried leaves of *Mitragyna parvifolia* was investigated for anti-inflammatory and antinociceptive activity using the carrageen an-induced paw edema and tail-flick method in rodent. The maximum anti-inflammatory effect of the extract was found to be at 300 mg/kg in carrageen a test and this effect was equivalent to phenyl butazone (PBZ) with 80 mg/kg orally.

The extract also shows antinociceptic activity at a dose of 300 mg/kg and the effect was comparable to that of standard dry Ibuprofen (100 mg/kg orally) (Gupta et al., 2009).

The analgesic activity on mice by Eddy`s hot plate and acetic acid induced writhing test. The extract sows only moderate analgesic potential in acetic acid induced writhing test at all the test doses while the extract at the dose of 500 mg/kg showed strong analgesic activity comparable to standard drug diclofenac sodium(50 mg/kg) in hot plate method (Kaushik, 2009).

### 3.8. Anxiolytic activity

Various extract of stem bark of for anxiolytic activity evaluated using elevated plus maze (EPM) and marble burying test (MBT) in mice. The alkaloid rich fraction was more potent in producing anxiolytic effect. The anxiolytic activities were mediated via GAB allergic system (viii). CMC is used for treating pain, fever, skin, infection, and as a mild anxiolytic (Ghatak, 2014).

Methanolic ethyl acetate extract and alkaloid rich fraction of *Mitragyna parvifolia* stem bark was investigated for anxiolytic activity by using elevated plus maze (EPM) and marble burying test (MBT) in mice. The extract increased the time spent on and the number of entries into the open arms of the EPM in doses of 200 and 400 mg/kg p.o. respectively. The effect as comparable to that of negative control group treated with 0.5 percent CMC (Carbomethyl cellulose) and positive control group CMC, 0.5% fluoxentine was used as a standard for comparison. The result indicates that all the extract were effective in dose dependent manner and proved statistically significant at higher doses but alkaloid rich fraction was found to be more potent in producing anxiolytic effect by both test. This activity of plant is mediated via GABAergic system (Badgujar et al., 2009).

### 3.9. Antiarthritic and antipyretic activity

Methanolic extract of leaves of *M. parviflora* was investigated for its Antiarthritic activity using acetic acid induced vascular permeability in mice. Effect was analyzed using yeast induced pyrexia in rats. MEMP was administered orally at 125, 250 and 500 mg/kg and it shows significant Antiarthritic and antipyretic effect (Gupta, et al., 2009).

### 3.10. Anti hypertension activity

Alcoholic extract of *M. parviflora* root was tested for its antihypertensive activity and vasorelaxant potential. Hypertension was induced by uninephrotectomy followed by administration of 11 percent w/v sodium chloride solution with drinking water and S.C. injection of deoxy corticosterone acetate (20 mg/kg). Alcoholic extract of plant roots was administrated at dose 200 and 400 mg/kg. Systolic blood pressure and heart rate were measured along with serum levels of TC and TG. Vasorelaxation property of the extract was evaluated an isolated thoracic aorta against calcium chloride induced contraction on isolated tissue.

### 3.11. Antidiabetic activity

From *Mitragyna parvifolia* yield DHIM an indole alkaloid which exhibited marked inhibition of DPP IV. In an in-vivo study on neonatal Wister albino rats treated with STZ. Chronic administration of DHIM marked reduced plasma glucose concentration, increased glucose tolerance in response to glucose loading GLP-1 and IL-1 were significantly increased in treated diabetic rats. Assay showed DHIM stimulates cell proliferation and formation of Beta-cell. *Mitragyna parvifolia* (Roxb) korth is an important medicinal plant belongs to family Rubiaceae. This deciduous plant has several traditional medicinal uses and it contain many alkaloids and other useful chemical constituents. The plant is widely used by tribal people and other Ayurvedic peactioners. Due to its immumerable pharmaceutical and /or commercial important, over exploitation and habitat destructions it is now categorized as an endangered tree species of Rajasthan (Panwar & Tarafdar, 2006; Rai & Lalramnghinglova, 2011). Now this

species is also facing threat of extinction in its natural habitats (Bidalia et al., 2017). It is need of the era to save and propagate this important medicinal and religious tree.

## 4. Conclusion

*Mitragyna parvifolia* is an important plant with respect to religious and medicinal value. As its seed germination are less and due to loss of its natural habitat plant is now put-up under endangered category. There is need to collect its seed from different seed source and developed its propagation technique to increase its natural habitat.

## 5. Future suggestions

Being important plant with multipurpose uses its seeds from different agro climatic zone should be collected and with pretreatment as well as putting seeds under less than 10% moisture cold storage and checking their viability is suggested.

**Declarations**

**Source of Funding**

This study was supported by MOEFCC, New Delhi on behalf of CAMPA funding under the FGR project.

**Competing Interests Statement**

The authors declare no competing financial, professional, or personal interests.

**Consent for publication**

The authors declare that they consented to the publication of this study.

**Authors' contributions**

All the authors took part in the literature review, analysis, and manuscript writing equally.

**Acknowledgment**

The authors are thankful to the CAMPA authority for providing financial support through Forest Genetic Resources project. Authors gratefully acknowledge ICFRE & MOEFCC New Delhi for CAMPA funding and other support.

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