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A Review on *Mitragyna parvifolia* (Roxb.) Korth. - An Indian Medicinal Plant

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ABSTRACT

Environment has been an advanced supply of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources, many based on their use in traditional medicine. The use of herbal drugs for the prevention and treatment of different health ailments has been in practice from time immemorial. *Mitragyna parvifolia* (Roxb.) Korth. is recommended in Ayurvedic texts for prevention and treatment of Anti-arthritic, Antipyretic, Anticonvulsant, Anthelmintic, Anti-microbial, Anti-inflammatory, Anti-nociceptive, Antiproliferative and Antioxidant activity. A collection of Mitraphylline, Isomitraphylline, Pteropodine, Isopteropodine, Speciophylline, Uncarine F are the major oxindolic alkaloids isolated from *Mitragyna parvifolia* leaves. This article briefly reviews the ethnobotanical as well as medicinal uses of *Mitragyna parvifolia* with plant description. This is an attempt to compile and document information on different aspect of plant and its potential use.

INTRODUCTION

The majority of the genus Mitragyna members are trees, shrubs or undershrubs and dispersed throughout the temperate part of the world. Out of total 11 species of *Mitragyna,* only 7 species are inhabitant in India. *Mitragyna parvifolia* (Roxb.) Korth. is an economically useful and highly endangered deciduous tree found in well drained deep soil of Indian Thar Desert belonging to the family *Rubiaceae*. The Indian Thar Desert comprises about 70% part of the Western Rajasthan, incorporating 12 districts. It would become well prove crucial for any attempts of re-establishment and conservation of *Mitragyna parvifolia* (Roxb.) Korth [1].

Taxonomical Classification

Kingdom: Plantae
Phylum: Magnoliophyta
Class: Magnoliatae
Order: Rubiales
Family: Rubiaceae
Genus: Mitragyna
Species: *Mitragyna parvifolia (Roxb.) Korth.*

Mitragyna parvifolia is commonly known as Kaim (Eng) Vimpu (Malay), Kayim, Kaddam (Hindi), Vitanah (Sanskrit),Kongu(Kan),Katampai (Tam), and Nerkadamba (Tel).

PHARMACOGNOSTIC PROFILE

Mitragyna parvifolia (Roxb.) Korth is a medium to large deciduous tree (Fig. 1) with rounded crown mainly arboreal in nature up to 25 m tall. It is found throughout the greater parts of India up to an altitude of 1200 meter. Tree is found scattered in deciduous forests and develops best in well drained deep soil. It is found growing gregariously in low-lying areas close to the river [2]. Leaves simple, opposite, decussate; stipules 1 cm long, interpetiolar, ovate-oblong or obovate, foliaceous, membranous, caducous; petiole 10-40 mm long, stout, grooved above, glabrous; lamina 5-16 cm x 2.5-10 cm (Fig. 2), variable, ovate, orbicular, elliptic or ovate-oblong, base obtuse, attenuate, acute or subcordate, apex obtuse or round; margin entire, glabrous, coriaceous; lateral nerves 6-10 pairs, pinnate, prominent beneath; intercostal scalariform, slender; domatia

present. Flowers bisexual, creamy white, 10-12 mm long, in terminal heads; peduncle supported by a pair of bract like oblong leaves; bracteoles small, subulate; calyx tube short, truncate, rim even; corolla tube funnel shaped, 8 mm long, villous inside, lobes 4-5 oblong, reflexed; stamens 5, attached towards the apex of corolla tube; anthers apiculate; ovary 2-celled, inferior, ovules many; style filiform; stigma mitriform, hollow at base (Fig. 3). Fruit capsules in globose heads, 2-3 mm long, wavy, separating into two cocci, brown; seeds many, small and 10-ribbed. Bark 20-25 mm thick, grey-black, smooth exfoliations thin, unequal and fibrous (Fig. 4); blaze pink, traversed by whitish rays; Branchlets young branchlets angular to subterete, glabrous.

Natural reproduction takes place by the scattering of seeds in hot season. Germination takes place in the rainy season. *Mitragyna parvifolia* (Roxb.) Korth grows exclusively in humid conditions and observation that geographical location and environmental conditions have a crucial role in modifying the alkaloid content and the structure [3].

Fig. 1: Whole Plant

Fig. 2: Leaves

Fig. 3: Flowers

Fig. 4: Bark

Microscopy

Mitragyna parvifolia (Roxb.) Korth stem bark thickness is about 2 mm. The bark can be differentiated into an outer bark (periderm) and an inner bark (secondary phloem). The inner bark distinguished into Collapsed (outer) phloem on - collapsed (inner) phloem.

The periderm consists of a phellogen layer, a thin zone of phellem and a wide zone of phelloderm (Fig.5). Interior to the phelloderm occurs a wide zone of cortex; cortex cells have undergone widespread divisions and dilations making imaginatively oblong and radially dense cortical tissue. In cortical zone scleroids and fibres are not presence (Fig.6). *Mitragyna parvifolia* bark consists two types of calcium oxalate crystals. First type crystal fairly large druses are profuse in the cortical cells inner to the periderm and their diameter is 50-60 μm. Second type of crystal is microcrystal or sand crystal. Micro crystal are found in fewer cells and seen primarily in the phloem rays, especially in the uniseriate rays [4].

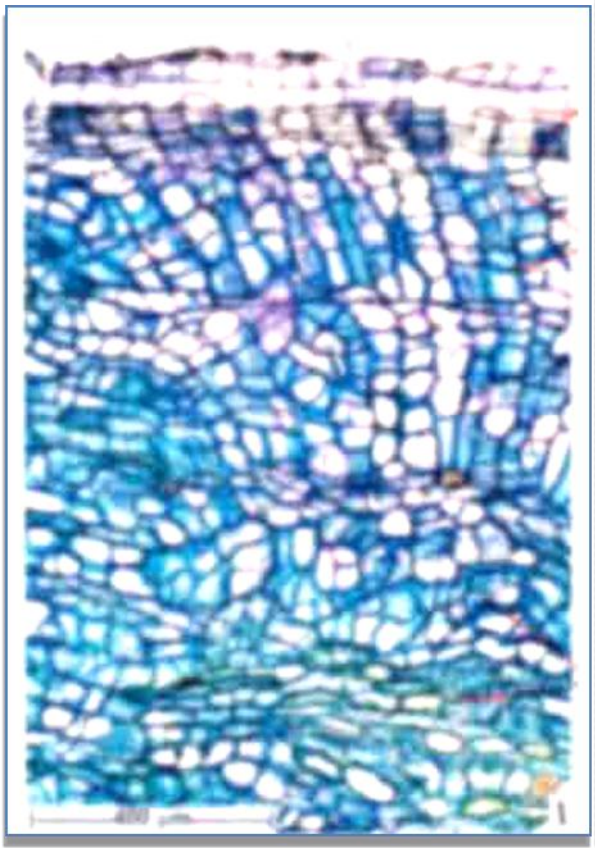

Fig. 5: Outer bark (periderm)

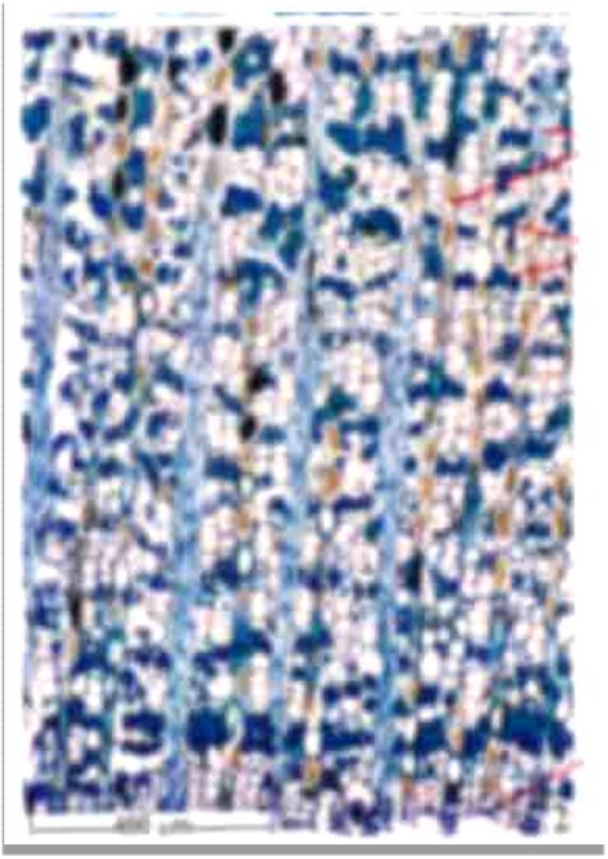

Fig. 6: Inner bark (secondary phloem)

TRADITIONAL USES

Mitragyna parvifolia fresh leaves sap is used by the tribals in treatment of jaundice in the *Chenchus*, *Yerukalas*, *Yanadis* and *Sugalis* of Gundur District, Andhra Pradesh [5]. Its leaves alleviate pain, swelling and for better healing from wounds and ulcers. *M. parvifolia* stem bark is used in treatment of biliousness and muscular pains by the local inhabitant of Tumkur district, Karnataka, India [6]. The tribals of *Sonaghati* of Sonbhadra district, Uttar Pradesh to heal fever by decoction of the *M. parvifolia* bark. *Valaiyans* tribe, population of Sirumalai hills, Madurai district, Western Ghats, Tamil Nadu utilize stem bark of *M. parvifolia* for rheumatic pain. The bark and roots used to treat fever, colic, muscular pain, burning sensation, poisoning, gynecological disorders, cough, edema and as an aphrodisiac. The fruit juice augments the quantities of breast milk in lactating mothers and also work as lactodepurant. The timber is used for furniture, agricultural implements, cooperages paper industry etc [7]

PHYTOCHEMISTRY

Preliminary distribution of alkaloid pattern in *Mitragyna parvifolia* in young plants grown from Ceylon seed showed the leaves contain the closed E ring alkaloids, tetrahydroalstonine, akuammigine, pteropodine, isopteropodine, speciophylline and uncarine F while the trunk bark contains the open E ring alkaloids isorhynchophylline and rhynchophylline in addition. The root bark contained isorhynchophylline and rhynchophylline only [8]. Xylem and phloem component of root contain isorhynchophylline, rhynchophylline and corynoxeine. Hirsutine and hirsuteine (Als-hirsutine) also occur in the root phloem. A more detailed examination of all parts of a young plant grown from seed and of the seeds and seedlings has revealed an interesting distribution of alkaloids throughout the plant.

A range of indolic and oxindolic alkaloids have been reported from *Mitragyna parvifolia* leaves. Only six alkaloids, Mitraphylline, Isomitraphylline, Pteropodine, Isopteropodine, Speciophylline, Uncarine F are the major oxindolic alkaloids isolated from *Mitragyna parvifolia* have been reported from the Lucknow region [9]. Rotundifoline, Rhynchophylline, Isorotundifoline, Rhynchociline, Speciociliatine, Speciofoline, Mitragynine are some other alkaloids found in the plant. Apart from alkaloids, other compounds like pyroligneous acids, aldehydes, ketones, scopoletin, thermophyllin, daucosterol, quinovic acid, β- sitosterol and methyl acetate are found in the plant.

A total of four hetero yohimbine type oxindole alkaloids were isolated from an acid base treated chloroform fraction of ethanolic extract of *M. parvifolia* leaves. 16, 17-dihydro-17b-hydroxy isomitraphylline (1), 16, 17- dihydro-17b-hydroxy mitraphylline (2) isomitraphylline (3) and mitraphylline (4) respectively, from their spectroscopic data and by comparison of the data with the literature [10]. The structures of 1 and 2 were elucidated using the use of ^{1}H-H correlated spectroscopy (COSY), heteronuclear single quantum coherence experiment via direct coupling (HSQC) and heteronuclear multiple bond correlation spectrum (HMBC). The DEPT experiment was used to ascertain the number of sp, sp^2, sp3, and quaternary carbon atoms [11].

PHARMACOLOGICAL REVIEW

Antiarthritic and Antipyretic activity

According to Jain et al. (2009) methanolic extract of *Mitragyna parvifolia* (MEMP) leaves were found antiarthritic and antipyretic potential in rodent. For evaluation of antiarthritic activity using Acetic acid-induced vascular permeability in mice and Freund's adjuvant induced arthritis in rats and antipyretic activity was analyzed using yeast induced pyrexia in rats; MEMP was administered orally at 125,250 and 500 mg/kg and showed significant antiarthritic, antipyretic effect ($p < 0.05$- 0.01) [12].

Anti-inflammatory and Anti-nociceptive Activity

Gupta et al. (2009) investigated both anti-inflammatory and antinociceptive activity of the ethanolic extract of dried leaves of *Mitragyna parvifolia* (MPEE), using the Carrageenan-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 carrageenan test and this effect was equivalent to phenylbutazone (PBZ) (80 mg/kg, orally) ($p<0.05$). The extract also demonstrated marked antinociceptive activity at a dose of 300 mg/kg and the effect was comparable to that of standard drug, Ibuprofen (100 mg/kg orally) ($p<0.05$) [13]. Kaushik D. et al. (2009) studied the analgesic activity on mice by Eddy's hot plate and Acetic acid induced writhing test. The extract showed 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 ($P<0.01$) showed strong analgesic activity comparable to standard drug Diclofenac sodium (50 mg/Kg, i.p.) in hot plate method.[14]

Anticonvulsant Activity

Kaushik et al. (2009) found that ethanolic extract of *Mitragyna parvifolia* leaves exhibits considerable Anticonvulsant Activity by pentylenetetrazole (PTZ) and maximal electroshock induce convulsion in mice. The extract was administered orally in mice at three doses (100, 250 and 500 mg/kg). The percentage inhibition of tonic hind limb extensions achieved at the doses 100, 250 and 500mg/kg were 60%, 80% and 90% respectively. Percentage of inhibition of PTZ-induced seizures for 500 mg/kg relative to controls was 60.0% ($p<0.05$) [15].

Anxiolytic activity

Badgujar Vishal B and Surana Sanjay J (2009) investigated anxiolytic activity in methanolic, ethyl acetate extract and alkaloid rich fraction of *Mitragyna parvifolia* stem bark by using elevated plus maze (EPM) and marble burying test (MBT) in mice. The extracts 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. This effect was comparable to that of negative control group treated with 0.5 % CMC (Carboxymethyl cellulose) and positive control the benzodiazepine diazepam (1.0 mg/kg p.o.) was used as a standard. When evaluated by MBT the number of marbles buried by mice was decreased significantly as compared to control group CMC 0.5 %. Fluoxetine (10 mg/kg p.o.) was used as a standard for comparison. These results indicate 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 effects by both test. Badgujar suggests that the anxiolytic-like activities of this plant are mainly mediated via the GABAergic system [16].

Anthelmintic activity

Badgujar Vishal B and Surana Sanjay J (2010) examined that anthelmintic activity of *Mitragyna parvifolia* stem bark was performed in vitro against adult earthworm (*Pheretima posthuma*) using owing to its anatomical and physiological resemblance with the intestinal. Levamisole hydrochloride (10 mg/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 results when compared with standard ($P<0.01$). The result of anthelmintic activity of methanolic extract was dose dependent paralysis time and death time of earthworms [17].

Antimicrobial activity

Kumar and Shreya (2011) revealed the possible antimicrobial efficacy of *Mitragyna parvifolia* (barks) against human pathogenic microbial strains such as two Gram positive (*Staphylococcus epidermidis, Bacillus subtilis*), two Gram negative (*Escherichia coli, Pseudomonas aeruginosa*) and two yeasts (*Saccharomyces cereviseae, Candida albicans*) assayed by using agar well diffusion assay. Out of three different extracts (ethanol, methanol and water) of *M. parvifolia*

maximum inhibition was shown by methanol extract against bacteria. Methanolic extract offered inhibition zone the range from 14 mm to 25 mm. The aqueous extracts did not show any inhibitory activity against any of the test bacterial strains. The MIC values of methanol extract of *Mitragyna parvifolia* for different bacterial strains ranged from 6.25mg/ml to 12.5mg/m.No antifungal activity was observed against the test yeast strains [18].

Antiproliferative and Antioxidant activity

Recent findings by Ghatak et al. (2014) showed that five different extract of dried bark and leaves of *Mitragyna parvifolia* in distilled water, methanol, acetone, ethyl acetate and hexane were evaluated for antioxidant potential, lipid peroxidation and antiproliferative effect on HeLa cell lines. Antioxidant potential was investigated using DPPH radical scavenging activity. Antiproliferative effect was observed using MTT (3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide) assay, followed by cell morphology using Giemsa and Acridine orange staining. Distilled water extracts of bark (94 ± 0.05%) and leaf (95.63 ± 0.34%) showed maximum antioxidant potential. Acetone extracts showed high cytotoxic effect on HeLa cells compared to other extracts with very minimal or no cytotoxicity [19]

CONCLUSIONS

Medical treatments, using plant-based natural sources have been studied extensively. A lot of plants and herbs have already been identified to have potential for therapeutic applications. Kaddam plant currently gaining popularity among researchers due to its potential health benefits. A range of indolic and oxindolic alkaloids have been reported from *Mitragyna parvifolia* leaves and stem barks and functional properties such as Antiarthritic, Antipyretic, Anti inflammatory, Antinociceptive, Anticonvulsant, Anxiolytic, Anthelmintic,Antimicrobial, Antiproliferative and Antioxidant activity. Besides, the timber is used for furniture, agricultural implements, cooperages paper industry etc.

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