

A Review of *MitragynaParvifolia* (Roxb) Korth – An Important Medicinal Plant

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Abstract: Herbal plants are potent in curing various diseases from common cold to dreaded diseases like variety of cancers as they have comparatively lesser side effects than synthetic drugs. Corona-virus 2019 (COVID-19) pandemic has identified and experimented many drugs in its management and these agents included both new and old drugs. *MitragynaParvifolia* (Roxb.) korth popularly known as kaim, is a deciduous traditional medicinal plant belongs to genus Rubiaceae. It is a true kadamba. *MitragynaParvifolia* is one of the medicinal plants considered for repurposing in the management of covid-19 because it is crucially significant as it contains rich fraction of alkaloids. *MitragynaParvifolia* is crucially significant as it has largest number of phytochemicals (such as alkaloids, flavanoids, tannins, glycosides, carbohydrates, phenols, aldehydes, ketones, phytosterols, triterpenes, triterpenoids, saponins, indole alkaloids etc.) and Secondary metabolites (viz. quinolic acid, quinovic acid, β -sitosterol, methyl acetate, pyroligenous acid, scopoletine, therophylline, daucosterol, cadambagenic acid, cadamine, cadambine, isocadambine, isodihydrocadambine etc.) In Ayurveda medicinal effect of kadamba is described in different sunhitas like Charak Samhita, Sushrutasamhita, Ashtanga hridaya, Haritsamhita, Chakardatta etc. Kadamba is used as antihepatotoxic, antibacterial, antimalarial, antimicrobial, analgesic, anti-inflammatory, antipyretic, anti-oxidant wound healing activities, diuretic and laxative. Antiarthritic, Anticonvulsant, Anthelmintic, antinociceptive, Antiproliferative activity. *MitragynaParvifolia* plant extract also possess Antifungal, Antidiarrheal, Antiviral activity leads to the development of potent antiviral drug, which can be safer, cost effective and can be used in the Medical field in promoting rural development and prosperity.

Key Word: *MitragynaParvifolia*, Traditional medicinal plant, Phytochemical constituent, Pharmacological Activity.

I. Introduction

MitragynaParvifolia is commonly known as kadamba or kaim belongs to family Rubiaceae [1] It is an ornamental tree use for their fine timber throughout the area where they grow. It has potential role of traditional medicinal plants for the treatment of various ailments of ancient times and several viral infections focusing on Covid -19. *MitragynaParvifolia* have largely contributed to the treatment of several human diseases and different phytoconstituents have been previously described to impede the replication of numerous viruses. Plant crude contains several metabolites and it is extremely crucial to identify which component make it potential candidate for an effective antiviral drug. Different antiviral compounds of plants including alkaloids, flavonoids, terpenoids, peptides, Lignans, polysaccharides, polyacetylenes effective against different targets of viruses such as DNA, RNA, genomes, membranes, the replication process and ribosomal activity. [2,3,4] Kadamba is a miraculous tree having enormous Pharmacological implication. [5] India is largest Producer of Ayurvedic medicinal herbs in the World due to which it is often called as botanical paradise. The genus *mitragyna* is a short genus comprising of 10 species.

Geographical Distribution:

The plant is native to Indian origin and also found in tropical and subtropical region of Africa and Asia. In India more popular in west, Kokan, Karnataka, Assam, Himalaya etc. It is also found in Nepal, Sri Lanka, Pakistan, Indonesia, Myanmar etc. *Mitragynaparvifolia* is a tall and handsome tree with spreading crown with different Pharmacological activities. [6], [7], [8].

In Religion:

According to Ancient literature, this is a 'true Kadamb' which is associated with Lords Krishna in Vridavana rather than well-known tree *Neolamarkia Cadamba*, but this is definitely a case of mistaken Identity. *Neolamarkia Cadamba* is not found naturally in the hot, dry Vridavana region. *Mitragynaparvifolia* is not only native to the Vridavana forest but is their dominant tree. Interestingly, *Mitragynaparvifolia* are still found almost everywhere in Vridavana. The same appears true for mother goddess Durga, who resides in Kadamb forest (Kadamb V Van Vasini) So, the tree should truly be called as HariPriya, God's favourite ! It is favourite tree of Lord Krishna. [8].

Plant Profile:

Binomial Name : *MitragynaParvifolia* (Roxb.) Korth
ScientificName : *MitragynaParvifolia* (Roxb.) Korth
MitragynaParvifolia Var. *Parvifolia*
*NucleaParvifolia*Roxb.
*NucleaParvifolia*willd [Illegitimate]
StephegyleParvifolia (Roxb.) Korth

MitragynaParvifolia (Roxb.) Korth is an accepted name: The Plant list retrieved 17th July, 2013.

Taxonomy:

Kingdom - Plantae
Sub Kingdom - Tracheophytes
Phylum - Magnoliophyta
Class - Magnolita
Order - Rubiales
Family - Rubiaceae
Genus - *Mitragyna*
Species - *Mitragynaparvifolia*
Common Name - True Kadamb, Kaim

Other Vernacular Name

Scientific : *NeolamarkiaCadamba*
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, Kathamamaram, Neerkadambu, Rose
kadambu, Rooskatamp, Poochakadambu, uccakkatamp, Sirakadambu,
Sirikadamba, Veembu, Vimba, Vimpu.
Tamil : Katampai, Niculam, Nirkatampu .,
Telgu : Ajaghnamu, Ambusaramu ,Jalatumburu , Nirkadamba,
Rsya, Tadhidruma .
Nepali : KaimPhalduSaanoHaledo, Tikul
Sanskrit : Irula – kadambamaram, Vitanah
Other : Boodha, China, Kaim, Kadam, Kadamba, Kadambu,ichulam, patta, Water. [5],
[6], [7], [8], [9].

Pharmacognostic Profile:

MitragynaParvifolia reaches height of 50 feet (about 27 meter) with branches spread over 15 feet. The stem is erect and branching. Leaves are dark green in colour, smooth, rounded in shape and opposite in growth pattern. MitragynaParvifolia is a tall and handsome tree with spreading crown. Flowers are yellow and grow in ball shaped cluster [10].

Flowers are fragrant. Flowers are bisexual creamy white 10-12 mm long in terminal heads, peduncle supported by a pair of bracts like oblong leaves, bractioles small, subulate, calyx tube short, truncate rim even. Corolla tube tunnel shaped, 8 mm long, villous inside lobes 4-5 oblong reflexed. Stamens 5 attached towards apex of corolla tube, anthers apiculate, ovary 2 celled, interior ovules many, style filiform, stigma mitriform hollow at base.

Fruits 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, blaze pink transversed by whitish ray. Branches young and glabrous [11], [12]. Stepules of mitragynaposseses numerous finger shaped collectors on their diaxial bases. Collectors are of standard type with central core of parenchyma cells surrounded by radially elongated epithelial cells [13]. MitragynaParvifolia (Roxb.) Korth (Rubiaceae) is an endangered tree of pharmaceutical importance. The micropropagation of mitragynaparvifolia is economically favorable for the ex-situ conversation and for providing raw material for extraction of numerous significant alkaloids [14]. Fruit of Kadamba looks like Corona Virus.

Traditional Uses:

Traditionally Mitragynagenuses has been used to treat fever malaria, diarrhea, muscle pain, inflammation and hypertension. Mitragyna possess wide pharmacological effects in antitumor, cardiovascular disease and antibacterial activity [15]. The 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 lactodepurant [7].

MitragynaParvifolia 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 ulcers [8]. Its stem bark is used in treatment of billiouness and muscular pains by the local inhabitant of Tumkur district, Karnataka India. The tribals of Sonaghati of Sonbhadra District, Uttarpradesh heal fever by a decoction of the M. Parvifolia bark. Valaiyans tribe, Population of Sirumalai hills, Madurai district, Western Ghats, Tamil Nadu use stem bark for rhematic pain [5]. The caterpillars of the commander (*Limenitis procis*) a brush footed butterfly uses this species as a food plant [16].

Other Uses:

- Timber – Used for making furniture, agricultural implements, co-operages, paper industry etc. [17].
- Kratom or yellow gold - Kratom has opiod properties and same stimulat like effect (wikipedia). Southeast Asian reports the Kratom is addictive.
- Modern Product includes formulation as a topical application of liniments, balms or tinctures may provide effective alternative for treatment of certain types of pain. [18].
- The wood - Generally used for agriculture implements, building and other domestic uses. [19].

Phytochemical Constituent:

Stem and bark yield alkaloids flavanoids, tannins and glycosides. An alcohol extract of bark yield carbohydrates, alkaloids, phenols, tannis and phytosterols. A benzene extracts yielded carbohydrates phenols and sterols. Leaves yield six major oxindolic alkaloids viz, mitraphylline, isoMitrphylline, Pteropodine isopterepodine, speciophylline and Uncarine F. Other plant alkaloids are rotundifoline, rhynocophylline, isorotundifoline, rhynchociline, speciocilitine, speciofoline, mitragynine. Plant also yields compounds like pyroligneous acid, aldehydes, ketones, scopoletin, thermophyllinedaucosterol, quinovic acid, β -sitosterol and methyl acetate. [8] Leaf alkaloids - The leaves of plant mitragynaparvifolia have affordable two alkaloids 16, 17 – dihydro – 17 β hydroxyl isomitraphylline and 16, 17, dihydro – 17 β hydroxyl mitraphylline together. Mitraphylline was main alkaloid constituents. [20] The ariel parts, stem, bark and roots of the tree contains indolic (tetrahydroalstonine, akkyamigine, hirsuteine etc.) and oxiindollic alkaloids. [21]

Pharmacological Activity or Review:

i. Antibacterial And Antifungal Activity:

The extract in different concentration Tested for antibacterial activity using agar well diffusion method. The extract significantly inhibited 5 aureus and showed some degree of inhibition against Paeruginosa and E. coli (A) Plant

extract did not exhibit by antibacterial potential against staphylococcus aureus, Bacillus subtilis, Escherichia coli and pseudomonas aeruginosa. [22], [38]

ii. Analgesic, Antimicrobial and Anti-inflammatory Activity:

The analgesic activity was carried out on swiss albino male mice by Eddy's hot plate and acetic acid induced writhing test, all the test does while extract at dose of 500 mg/Kg ($P < 0.01$) showed strong analgesic activity comparable to standard drug Diclofenac sodium (50 mg/Kg) in hot plate method.

Ethanol extract of M. P. evaluated for anti-inflammatory, analgesic and antimicrobial activities. [23]

iii. Anticancer Activity:

Anticancer potential of Dichloromethane extract of MitragynaParvifolia stem bark using MTTT assay and molecular docking studies. MTT assay was performed on MCFT A549 and Hep G2 cell lines. IC50 Values were found to be 402.8 $\mu\text{g/ml}$, 207.4 $\mu\text{g/ml}$, and 104.4 $\mu\text{g/ml}$, respectively. phytoconstituents of extract were determined by GC – MS analysis. Most probable structure were identified a named using NTST library. A molecular docking study was conducted on selected compound by choosing respective anticancer drug target proteins, VEGFR2, Kinase (Lung cancer), (breast cancer) and EGFR Kinase (liver cancer) using autodockvina. In the docking study, the binding energy and interactions of steroidal derivatives were comparable to those of standards (Sorafenib, SYR and Erlotinib) indicating remarkable anticancer activity of Extract. [24]

iv. Anticonvulsant Activity:

The anticonvulsant effect of ethanolic extract form leaves of MitragynaParvifolia. Was investigated by studying the effect of seizure's induced by phenylenetetrazole (PTZ) and maximal electroshock convulsive methods in mice. The extract was administered orally in mice at three doses (100, 250 & 500 mg/Kg) the exhibited protector effect only at 500 mg/Kg. Thus, result showed dose – dependent in both model [25]

v. Anthelmintic activity:

The effect of ethanolic and aqueous extract of leaves from MitragynaParvifolia was examined for their anthelmintic activity against pheritimaphostuma, demonstrating significant paralysis of worms at higher concentrations of 50 mg/ml as compared with albendazole (10 mg/ml) as standard reference. (Sahu et al 2009). Methanolic extract of dried stem bark at conc. Of 100 mg/ml produced significant anthelmintic activity evaluated by observing paralysis time and death time of earthworms and were found to be dose dependent a 20 mg/ml lower concentration did not produce result. [26] The result of anthelmintic activity of methanolic and ethanolic extract of M. Parvifolia fruit produced compared with piperazine citrate standard observing paralysis time and death time of earthworms and were found to be dose dependent. [27]

vi. Antiinflammatory and Anti Nociceptive Activity:

The maximum antiinflammatory effect of an ethanolic extract of dried leaves of MitragynaParvifolia showed in carrageenan induced paw edema model was equivalent to phenylbutazone (PBZ) (80 mg/Kg orally) ($P < 0.05$). The extract also exhibited marked antinociceptive activity was comparable with standard drug Ibuprofen [28]

vii. Antimicrobial Activity:

MitragynaParvifolia. (barks) and Butea Monospema (leaves) against human pathogenic microbial strains such as two Gram positive (Staphylococcus epidermis, Bacillus Substillis), two Gram negative (Escherichia coli, Psudomonas aeruginosa) and two yeast (saccharomyces cereviseae, candida albicans) assayed by using agar well diffusion assay. Three different extracts (ethanol, methanol water) of MitragynaParvifolia showed better activity than Butea Monosperma extract. [29]

viii. Anxiolytic Activity:

Various extracts of stem bark of MitragynaParvifolia 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 effects. The anxiolytic activities were mediated via GAB allergic system (VIII) C.MC is used for treating pain, fever, skin, infection and as a mild anxiolytic. [30]

ix. Antiproliferative and Antioxidant Activity:

MitragynaParvifolia (Roxb.) Korth bark and leaves were evaluated for total phenolic content, total flavanoid content, antioxidant potential lipid peroxidation and antiproliferative effect on HeLa cell lines. Antioxidant potential and flavanoids estimation were investigated using DPPH radical scavenging activity and aluminium chloride method respectively. Further lipid peroxidation and antiproliferative effect were observed using TBARS and MTT assay, followed by cell morphology using Giemsa and Acridine orange staining [31]

x. Antiarthritic and Antipyretic Activity:

The methanolic extract of *M. P.* (MEMP) leaves were investigated for its antiarthritic activity using Acetic Acid induced vascular permeability in mice and Freund's adjuvant induced arthritis in rats, and antipyretic activity was analysed using yeast induced pyrexia in rats MEMP was administered orally at 125, 250 and 500 mg/Kg and showed significant antiarthritic and antipyretic effect. [32]

xi. Immunosuppressive Activity:

The flavanoids from the leaves of the three medicinal plants are evaluated in vitro effect on human peripheral blood mononuclear cells (PBMC) using hepatitis B vaccine containing surface antigen (HBs, Ag,) 20 µg/ml; 10 µg/ml and determined its HBs, Ag proliferation, nitric oxide production and CD 14 monocyte surface marker. The results showed that flavanoids at higher doses (25 µg/ml ; 50 µg/ml) inhibited HBsAg stimulated proliferation of human PBMC cells as well as nitric oxide production and also blocked the activation of CD-14 monocyte surface marker, which are necessary for T cell activation. The result reporting the immunosuppressive activity and it also acts as an cytotoxic agent. [33]

xii. Anti-Hypertensive Activity:

The anti-hypertensive activity and vasorelaxant potential of alcohol extract *MitragynaParvifolia* root. Hypertension was induced by uninephrectomy followed by administration of 11 % w/v sodium chloride solution with drinking water and S. C. injection of desoxy corticosterone acetate (20 mg/Kg). The alcohol extract of *M. P.* roots was administered at doses 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 contractions on isolated tissue. [34]

xiii. Antimicrobial Activity:

The green synthesized copper nanoparticles proved to be potential candidates for medical applications where antimicrobial activity is highly essential. *Mitragynaparvifolia* plant bark used to prepare aqueous extract which provides, cost – effective, ecofriendly process, less time consuming, an environmentally benign easy and proficient way for the synthesis of copper nano – particles. Colour change of solution dark brown from pale yellow colour confirms formation of copper nanoparticles. [35]

xiv. Antiviral Activity:

Mitragynaparvifolia extract screened against bovine herpes virus type – 1, causing infectious bovine rhinotracheitis disease, abortion in 5-7 month of pregnancy in bovines and leading to high economic loss. The in vitro antiviral potential of these plants extracts BHV – 1 were tested by cytopathic inhibition test using MDBK cell line. MDBK cell line were determined by microculture tetrazolium assay (MTT) assay. [36]

xv. Anti – Diabetic Activity:

DHIM is an indole alkaloid isolated from *M. Parvifolia*. DHIM exhibited marked inhibition of DPP IV. In an In vivo study on neonatal wistar albino rats treated with STZ, Chronic administration of DHIM markedly 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 reduced pancreatic cell and increase the formation of β – cells. [37].

II. Conclusion

Medical treatment, using plant-based sources have been studied extensively. Future research is required to establish safety and toxicology limits, medicinal chemistry parameters and potential role of traditional medicinal plants for the different physiological response among varying genetic population to support regulatory requirements for fighting pandemics. *MitragynaParvifolia* have already been identified to have potential for therapeutic applications due to its potential health benefits.

This paper is reviewed the potential use of traditional medicinal plant *MitragynaParvifolia* (RoxB) Korth Species belonging to family Rubiaceae reference to botany and known chemistry in order to highlight areas plant Science contribution to fighting Viral pandemics covid 19 as a case study as the fruit of Kadamba which now looks like corona virus.

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