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PHARMACOLOGICAL INVESTIGATIONS OF THERAPEUTICALLY POTENT PLANT *M. PARVIFOLIA*(ROXB.) KORTH.: A REVIEW

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ABSTRACT

Plants are used for treating various ailments since time immemorial. Significant observations have been made on the efficacy and potentiality of various plant extracts as medicines. The medicinal importance of plants is associated with active compounds present in them and their related therapeutic properties. M. parvifolia(Roxb.) Korth. Commonly known as "Kaim", "Kadam", belongs to family Rubiaceae. It is highly endangered plant species of Thar desert, Rajasthan. Various oxindolic alkaloids like Mitraphylline, Isomitraphylline, Pteropodine, Isopteropodine, Speciophylline, Uncarine F from M. parvifolialeaves and indolic alkaloids like tetrahydroalstonine, hirsuteine etc. from stem-bark and roots of the tree have been reported. In Ayurveda system, plant is used as antipyretic, anti-arthritis, anticonvulsant, anthelmintic, antimicrobial, antiproliferative and antioxidant. In traditional Indian medicine system, bark and roots used to cure fevers, colic, muscular pains, stomach burning, poisoning, gynecological problems, cough, edema and as aphrodisiac. Leaves are also used to healing of wounds and ulcers and to alleviate pain.The present work has been reviewed the phytochemical, traditional and scientifically proved current studies on biological activities of M. parvifoliaplant.

Keywords: *Active Compounds, Oxindolic Alkaloids, Indolic Alkaloids, Endangered Plant, Rubiaceae.*

Introduction

*Mitragynaparvifolia*is a plant of family Rubiaceae (Coffee family) and commonly known as Kaim or Dhara Kadam. It is an endangered and medicinally potent plant of Indian Thar desert (Patel *et al*., 2020). The plant is native to India and distributed throughout the semiarid regions; however, it is facing a threat of its extinction in its natural habitat (Bidalia *et al.* 2017). It is a large deciduous tree that grows up to a height 40 to 50 feet with a branch spread over 15 feet. Stem is erect and branched. Leaves are dark green, petiolate, petiole 1-4 cm long, stipulate, stipule interpetiolar, leaves simple, opposite decussate, smooth, rounded. Bisexual flowers are in terminal heads and in ball-shaped clusters, fragrant, creamy-white or yellow, peduncle is supported by a pair of bracts like oblong leaves. Fruits are capsules, wavy, separating into two cocci. arranged in globose heads, 2 to 3 mm long, ribbed. Seeds are numerous, small, 10-ribbed. Bark is 20-25 mm thick and grey-black in colour.

Phytochemical Constituents

Various studies have been performed for the presence of numerous phytochemicals in *M. parvifolia*. These studies revealed alkaloids as main constituents in different parts of the plant. Preliminary distribution of alkaloid pattern in *M. parvifolia*in young plants grown from Ceylon seed revealed that 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 (Shellard and Houghton, 1971). A more detailed examination of all parts of a young plant grown from seed and of the seeds and seedlings showed presence of alkaloids throughout

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the plant. The leaves contain a range of indolic and oxindolic alkaloids. Out of them only six alkaloids, Mitraphylline, Isomitraphylline, Pteropodine, Isopteropodine, Speciophylline, Uncarine F are the major oxindolic alkaloids isolated from *M. parvifolia*from the Lucknow region. Root xylem and phloem contain isorhynchophylline, rhynchophylline and corynoxeine. Root phloem contains hirsutine and hirsuteine (Als-hirsutine) in addition. Rotundifoline, Rhynchophylline, Isorotundifoline, Rhynchociline, Speciociliatine, Speciofoline, Mitragynine are some other alkaloids found in the plant. In addition to alkaloids, other compounds like pyroligneous acids, aldehydes, ketones, scopoletin, thermophyllin, daucosterol, quinovic acid, β- sitosterol and methyl acetate are also reported in the plant (Shellard*et al.,* 1969). In a study total of four hetero yohimbine type oxindole alkaloids were isolated from an acid base treated chloroform fraction of ethanolic extract of *M. parvifolia*leaves. These are- 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 (Seki *et al.,* 1993). Pandey *et al.,* (2006) elucidated the structures of 1 and 2 using 1H-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 sp1, sp2, sp3, and quaternary carbon atoms.

Antimicrobial Activity

Kumar and Shreya (2011) performed the antimicrobial efficacy of *M. parvifolia*bark extracts (ethanol, methanol and water) against human pathogenic microbial strains such as two Gram positive bacteria (*Staphylococcus epidermidis, Bacillus subtilis*), two Gram negative bacteria (*Escherichia coli, Pseudomonas aeruginosa*) and two yeasts (*Saccharomyces cereviseae, Candida albicans*) by agar well diffusion assay. Out of three different extracts, maximum inhibition was exhibited by methanol extract against bacteria. Methanolic extract showed inhibition zone the range from 14 mm to 25 mm in diameter. The aqueous extracts did not show any permissible results against any of the test bacterial strains. The MIC values of bark methanol extract against test bacterial strains ranged from 6.25mg/ml to 12.5mg/ml. Antifungal activity was observed as negligible against the test yeast strains. Sanej*aet al*., (2009) found that ethanolic extract of *M. parvifolia* fruit did not show any anti-bacterial potential against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa*.

Anthelmintic Activity

Badgujar and Surana (2010) examined in vitro anthelmintic activity of *M. parvifolia*stem bark against adult earthworm (*Pheretimaposthuma*) due 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 significant anthelmintic activity of methanolic extract of *M. parvifolia*stem bark was found at the concentration of 100 mg/ml, whereas 20 mg/ml lower concentration did not show significant results when compared with standard ($P<0.01$). Similar studies were conducted by Sahu *et al*., (2009) in ethanolic and aqueous extracts of leaves from Mitragynaparvifolia using different concentrations (10mg/ml, 25mg/ml and 50 mg/ml). The result of anthelmintic activity of methanolic extract was dose dependent and exhibited as paralysis time as well as death time of earthworms. The results suggest that the ethanolic and aqueous extracts significantly demonstrated paralysis and also caused death of worms especially at higher concentration of 50 mg/ml, as compared to standard reference, Albendazole (10 mg/ml).

Anti-inflammatory Activity and Antinociceptive Activity

Gupta *et al*., 2009 evaluated the ethanolic extract of dried leaves of *M. parvifolia*(MPEE) at various dose levels for both anti-inflammatory and antinociceptive activity, using the Carrageenan-induced paw edema method in rats and Tail-flick method in mice respectively. The highest anti-inflammatory effect was found at 300 mg/kg dose in carrageenan test which was equivalent to phenylbutazone (PBZ) (80 mg/kg, orally). The extract also revealed marked antinociceptive activity at a dose of 300 mg/kg which was comparable to that of standard drug, Ibuprofen (100 mg/kg orally).

Antiproliferative Activity and Antioxidant Activity

Ghatak*et al*., 2014 demonstrated that among the different parts of *M. parvifolia*used, the acetone extract of bark (57.08 ± 6.16 mg/mL) and leaf (60.1 ± 3.74 mg/mL) showed highest phenolic content. Antioxidant potential was maximum in distilled water extracts of bark (94 ± 0.05%) and leaf (95.63 ± 0.34%). Percent protection was found to be maximum in acetone extracts of bark (19.04±0.02%) and leaf (25.11±0.09%). Total flavonoid content was observed maximum in distilled water leaf extract (0.869±0.001 mg/mL). High cytotoxic effect was found in acetone extracts on HeLa cells compared to other extracts with very minimal or no cytotoxicity in comparison to positive control of 5% ricin.

Kaushik *et al*., 2009 screened ethanolic leaves extract of *M. parvifolia*for anti-inflammatory activity using Carrageenan-induced paw edema at different doses (100, 250 and 500 mg/kg) and the results were analysed with standard drug Diclofenac sodium (50 mg/kg). Marked significant activity was found at 250 and 500 mg/kg ($p < 0.01$). The extract was also screened for antioxidant and free radical scavenging effects at various concentrations (100, 300 and 500 µg/ml) by reducing power assay, superoxide radical and DPPH free radical scavenging method. All these antioxidant activities were concentration dependent which were compared with standard antioxidants such as BHA and ascorbic acid. The antioxidant activity was found to be maximum in *M. parvifolia*leaves extract at a concentration of 500µg/ml.

Sanejae*t al*., (2009) evaluated ethanolic extract of the *M. parvifolia*fruit for antiinflammatory, analgesic and antimicrobial activities. The extract showed marked analgesic and anti-inflammatory potential. The significant analgesic activity was found at the dose of 500 mg/kg ($P< 0.01$) as compare to the doses of 250 and 100 mg/kg. While screening the extract for antiinflamatory activity, it was observed that at the dose of 500 mg/Kg extract showed very high % inhibition in edema volume comparable to standard drug Diclofenac sodium (50 mg/Kg).

Anticonvulsant Activity

Kaushik et al., (2009) performed anticonvulsant activity using ethanolic extract of *M. parvifolia*leaves by pentylenetetrazole (PTZ) and maximal electroshock induce convulsion in mice. The three doses (100, 250 and 500 mg/kg) extract were administered orally in micet. 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 was compare to controls 60.0% ($p<0.05$).

Antiarthritic and Antipyretic Activity

According to Jain et al. (2009) potential antiarthritic and antipyretic activity were found in methanolic extract of *M. parvifolia* (MEMP) leaves in rodent. The antiarthritic activity was performed 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 rat. MEMP was administered orally at 125, 250 and 500 mg/kg which showed significant antiarthritic, antipyretic effect ($p < 0.05$- 0.01).

Anxiolytic Activity

Badgujar and Surana (2009) investigated anxiolytic activity of methanolic, ethyl acetate extract and alkaloid rich fraction prepared from the stem-bark of *M. parvifolia* (Roxb.) Korth (Rubiaceae) using the 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 that was comparable to that of negative control group treated with 0.5 % CMC and positive control of the standard benzodiazepine diazepam (1.0 mg/kg p.o.). 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 showed 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 tests.

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