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MELIA DUBIA CAV: ETHNOBOTANICAL, PHYTOCHEMICAL STUDIES, PHARMACOLOGICAL ASPECTS WITH FUTURE PROSPECTS.

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Abstract

Melia dubia, commonly known as Malabar neem, is a tree species valued for its fast growth and adaptability. This paper explores the ethnobotanical uses, phytochemical composition, pharmacological activities, and future prospects of M. dubia. The plant has been traditionally used in herbal remedies for various ailments, and its extracts have shown promising pharmacological properties such as antioxidant, antibacterial, antifungal, anti-inflammatory, antidiabetic, and anticancer activities. Phytochemical analysis has revealed the presence of alkaloids, carbohydrates, steroids, tannins, flavonoids, and other bioactive compounds. M. dubia also holds potential in green synthesis of nanoparticles with antimicrobial properties. The findings highlight the importance of M. dubia in traditional medicine, its potential as a source of therapeutic agents, and its role in sustainable forestry practices and industrial applications. Further research is warranted to unlock the full potential of this valuable tree species.

Keywords

Melia dubia, Phytochemistry, Pharmacology, Nanoparticles, Ethnobotany, Maha neem.

1. Introduction

M. dubia, a member of the Meliaceae family (Vennila & Mariyal, 2015), also called Malabar neem, is well-known for its wood in southern Indian states due to its quick development and broad tolerance to a variety of edaphic and climatic conditions. M. dubia have all been deemed extremely helpful in tree breeding projects by the world agroforestry centre (Dinesh *et al.*, 2020). M. dubia has demonstrated excellent promise for pest control in terms of secondary plant chemistry. It is a large deciduous tree variety that is indigenous to

India. The wood from it is primarily used to make furniture and farming tools. Traditional natural remedies made from the entire plant are used as anthelmintics, treatments for leprosy, eczema, asthma, malaria, fevers, and venereal illnesses (Murugesan, Senthilkumar, Rajeshkannan, & Vijayalakshmi, 2013). M. dubia is also known as Maha neem or forest neem (Khan, Khan, & Shukla, 2008). M. dubia has demonstrated excellent promise for secondary plant chemical control. Every part of the M. dubia plant is used in traditional herbal remedies to treat leprosy, eczema, asthma, malaria, fevers, and venereal disorders (Govindachari, 1992). The traditional knowledge of medicinal plants plays a significant role in the development of pharmaceuticals and plant-based therapies. The increasing cost of conventional medicine, along with the growing incidence of diseases, has driven the search for more affordable and effective treatments. Medicinal plants provide a valuable source for this pursuit (Gopal, Prakash Yoganandam, & Manju, 2015). M. dubia is found at elevation of 1,500-1,800m in the South and Central Western Ghats, Eastern Ghats, and Northeast India. It has been widely naturalised in Europe, North America, and Australia (Mabberley, 1984). It is one of the fastest growing tree species in India, Sri Lanka, Malaysia, Australia, and Angola. It grows in deciduous woods from the lowlands to 750 metres above sea level. M. dubia blooms from March to April and bears fruit in April (Khan, Khan, & Shukla, 2008). The common names of M. dubia are given in Table 1.

Table 1: Local names of M. dubia (Florido, 2010)

Philippines	Agalunga, Bagalunga, Balangago, Paraiso (Visaya), Gango, Iintana, Maliba, Maluggayan, Malunggaian Sili-Sili (Tagalog, Laguna in Luzon), Bagalnga (Mindanao), Bulibising (Bukidnon, Iloko), Mamabuaya (Chabacano)
Indonesia	Samer (Malaka in West Timor), Mindi Gede (Pandeglang), Gringging, Mindi, Cakracikri (Java), Mindi Kecil, Marambung (Renceh in Sumatera)
Malaysia	Mindi Kecil, Gringging, Marambung, Mindi, Mindi Besar
Thailand	Hian, Krian (Northern Thailand), Lian, Lian Bai Yai, Khian (Central Thailand)
Vietnam	Cây xoan, Sâ dông

1.1 Botanical Description

M. dubia is a huge deciduous perennial tree that grows to a height of 6 to 30 m. While young, the bark is smooth and greenish, but when mature, it becomes dark brown and cracks, generating enormous rectangular flakes. From around 8m, the wood trunk has few or no branches. Immature branchlets are scurfy tomentose and terete, becoming glabrous as they mature. Compound leaves are bipinnate to tripinnate, imparipinnate, alternating, spiral, packed, and pulvinate. The leaves fall off in December, and a new flush of leaves appears in February and March, accompanied with the flowers (Warrier, 2011). Wide spreading branches of attractive leaves. The bark is dark brown and fibrous, peeling off in broad rectangular pieces. When mature, the young branches are scurcy-tomentose, and the branchlets are terete and glabrous. Growing in deciduous woodlands and along rural roads on wastelands. Leaves fall off in December and January, and new leaves develop in February and March, along with flowers. The inflorescence is a 12-20 cm long

auxiliary panicle with tiny, greenish white, honey-scented flowers that arise in bunches with a new flush of leaves. The fruit is a drupe, ovoid or ellipsoid in shape with longitudinal ridges, pulpy and yellowish when ripe, and has a pleasant aroma. Fruit that is ripe during the cold season (October-February) and consists of 3-4 seeds (Yadav, Sahoo, & Wani, 2019). The taxonomic classification of M. dubia is shown in Table 2.

Table 2: Taxonomic classification of Melia dubia (Florido, 2010)

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Sapindales
Family	Meliaceae
Genus	Melia
Species	*dubia*
Binomial name	*Melia dubia*

1.2 Ethanobotanical Knowledge

Various parts of M. dubia have pharmacological activities such as hepatoprotective, antiulcer, antimicrobial, anti-inflammatory, anti-feedant, analgesic, anti-urolithiatic, anti-diabetic, anti-larvicidal, anticancer, and have been found to have biopesticidal properties. M. dubia is renowned for its termite and fungus-resistant wood. The majority of the timber is utilised for furniture, agricultural instruments, and home construction. Its branches serve as firewood, termite-resistant poles, and feed. It is used for the outriggers of boats in Ceylon. Carbon sequestration has been demonstrated to efficiently lower CO_2 levels in tree species (Mahalakshmi, AbiraamiValli, & Uma Gowrie, 2020).

1.3 Traditional Uses

Every part of the M. dubia plant is used in traditional herbal remedies to treat leprosy, eczema, asthma, malaria, fevers, and venereal disorders (Govindachari, 1992). In addition to cholelithiasis, acariasis, and pain (Kokwaro, 2009). M. dubia fruits are thought to be beneficial in colic and skin diseases, as well as an anthelmintic (Purushothaman, Duraiswamy, & Connolly, 1984). Philippine Islands: The fruit of the bagalunga is used to cure colic in halves. Scabies is treated in Laguna using fruit juice and sulphur (Razal & Palijon, 2009). Stem barks are used to treat skin ailments such as open wounds, while boiled leaves are used to treat stomachaches. Fruits are regarded an anthelmintic, which is why they are used to help alleviate colic in Laguna (Florido, 2010). The country of the Philippines. Locals have long utilised the leaves to promote the ripening of bananas and as a pesticide against chicken and hog pests. The leaves are burned, and the smoke acts as a natural mosquito repellent, while the seed oil acts as an insect repellent. Moreover, the

seeds are utilised to make rosary beads and bracelets (Florido, 2010). The Subanen people in Gala and Guimad villages in Ozamis City, Mindanao, the Philippines, mashed the leaves to obtain a juicy extract, mixed it with a little kerosene, and used it topically on the skin to treat problems such as allergies, acne, and ringworm (Alduhisa & Demayo, 2019). Indonesia: Native people in Malaka, West Timor, utilise stem barks as a medicine to cure malaria (Taek, Prajogo EW, & Agil, 2018).

1.4 Phytochemical Constituents

M. dubia leaf extracts contained alkaloids, carbohydrates, steroids, tannins, flavonoids, saponins, and glycosides (Valentina, Ilango, Kiruthiga, & Parimala, 2013). M. dubia leaves and seeds have yielded two novel tetranortriterpenoids, compositin and compositolide. Nagalakshmi, Thangadurai, Anuradha, & Pullaiah (2001) had reported that the leaf essential oil is mostly composed of monoterpenes (35.71%) and oxygenated monoterpenes (27.98%), with a significantly lesser proportion of alkanes (11.17%), sesquiterpene hydrocarbons (9.26%), and phenylpropanoids (3.90%). M. dubia Cav. has a bitter principle. Fruits contain salannin, which was originally discovered in *M. azadirachta* L. (De Silva, Stöcklin, & Geissman, 1969). Murugesan, Senthilkumar, Rajeshkannan, & Vijayalakshmi (2013) had reported that the unsaturated fatty acids, terpenoids (diterpenes and sesquiterpenes), antioxidants, phenolic derivatives, and lipophylic organic compounds are among the phytochemical components of *M. dubia*. Linolenic acid, palmitic acid, caryophyllene, humulene, aromadendrene, probucol, germacrene-D, phthalic acid 6-ethyl-3-octyl, butylated hydroxy toluene are some phytochemical molecules. M. dubia phytochemical research reveal three novel tetranortriterpenoids: compositin (1, 7-ditiglyl vilasinin), compositolide (photosalannin), and salannin from the leaves and seeds (Nithaniyal Stalin, 2021). The root contains a glycosyl derivative of ellagic acid. The bark contains five novel constituents, including meliastatin 1-5 and euphane-type triterpenes, methyl kulonate, kulinone, 16-hydroxybutyrospermol, kulactone, dubione A, dubione B, methyl palmitate, methyl stearate, cyclohexene, and ketorolac (Nithaniyal Stalin, 2021).

Table 3: Active constituents present in different part of M. dubia

Part	Chemicals found
Leaf	Alkaloids, Carbohydrates, Steroids, Tannins, Flavonoids, Saponins, Glycosides (Valentina, Ilango, Kiruthiga, & Parimala, 2013), Tetranortriterpenoids (Compositin, Compositolide, Salannin) (Nithaniyal Stalin, 2021),
Seed	Tetranortriterpenoids (Compositin, Compositolide, Salannin) (Nithaniyal Stalin, 2021),
Leaf Oils	Monoterpenes, Oxygenated Monoterpenes, Sesquiterpene Hydrocarbons, Phenylpropanoids (Nagalakshmi, Thangadurai, Anuradha, & Pullaiah, 2001)
Fruit	Salannin (De Silva, Stöcklin, & Geissman, 1969)
Root	Glycosyl Derivative Of Ellagic Acid (Nithaniyal Stalin, 2021),
Bark	Meliastatin 1-5 And Euphane-Type Triterpenes, Methyl Kulonate, Kulinone, 16-Hydroxybutyrospermol, Kulactone, Dubione A, Dubione B, Methyl Palmitate, Methyl Stearate, Cyclohexene, And Ketorolac (Nithaniyal Stalin, 2021)
Whole Plant	Unsaturated Fatty Acids, Terpenoids (Diterpenes And Sesquiterpenes), Antioxidants, Phenolic Derivatives, Lipophilic, Linolenic Acid, Palmitic Acid, Caryophyllene, Humulene, Aromadendrene, Probucol, Germacrene-D, Phthalic Acid 6-Ethyl-3-Octyl, Butylated Hydroxy Toluene (Murugesan, Senthilkumar, Rajeshkannan, & Vijayalakshmi, 2013)

1.5 Pharmacological Activities

1.5.1 Antioxidant activity

Valentina, Ilango, Kiruthiga, & Parimala (2013) had reported that *M. dubia* solvent extracts demonstrated high antioxidant activity using the nitric oxide radical scavenging technique, as revealed by a decreased IC50 (16.89 g/ml) value in the ethanolic extract. The results suggested that the ethanolic fraction of M. dubia Cav, which contains the maximum quantity of phenolic and flavonoids compounds, may contribute to the plant's antioxidant capacity.

1.5.2 Anti-bacterial activity

A preliminary investigation done at Ootacamund, Tamilnadu indicated that the bark's ethanolic and aqueous extracts were shown to have considerable antibacterial action against S. aureus (Anonymous, 1999). Nagalakshmi, Thangadurai, Anuradha, & Pullaiah (2001) had reported M. dubia leaf essential oil was found to be bactericidal against Pseudomonas aeruginosa, Escherichia coli and K. Pneumoniae. Gerige & Ramjaneyulu (2007) studied the chemical constituents of M. dubia leaf volatile oil were studied using GC-MS, and it was discovered that the chemical compound "monoterpine camphene" has good antimicrobial activity, inhibiting 78% of skin isolates at 250ml concentration, whereas M. dubia leaf volatile oil, which contains 21.68% camphene as a major constituent, inhibits 88% of skin pathogens. Chanthuru, Prabhu, Aysha, & Karthik (2014) showed that, at a concentration of 60 µl, the M. dubia leaf extract demonstrated significant zone of inhibitory action against all of the bacterial pathogens examined, including E. coli, Salmonella typhi, S. paratyphi, Klebsilla peneumonia, and S. aureus (28, 20, 18, 26 and 22 mm respectively). The ethyl acetate extracts of the root showed the least action in some species, including E. coli and S. paratyphi (7 and 8 mm, respectively).

1.5.3 Antifungal Activity

Nagalakshmi, Thangadurai, Anuradha, & Pullaiah (2001) had reported M. dubia leaf essential oil was found to be fungicidal against Fusarium oxysporum, and Candida albicans.

1.5.4 Anti-inflammatory Activity

Khadse & Kakde (2014) had reported that at different doses, the anti-inflammatory efficacy of aqueous extracts and fractions of M. dubia fruits was tested *in vivo* using the carrageenan-induced rat paw edoema technique and *in vitro* using the albumin denaturation and membrane stabilisation assay. The aqueous extract was discovered to be the most active, thus it was fractionated into four main fractions and tested for anti-inflammatory efficacy. In vivo results indicated that FR-III 200 mg/kg and 400 mg/kg exhibited the most significant inhibition of edoema with 49.11% and 56.24%, respectively, as compared to the reference medication indomethacine, which showed the most significant inhibition of edoema with 60.15%. At a concentration of 200g/ml, an *in vitro* investigation of FR-III revealed 61.45% inhibition of thermally induced protein denaturation and 61.43% inhibition via membrane stabilization technique. According to the findings of this research, FR-III has substantial dose-dependent anti-inflammatory activity.

1.5.5 Anti-diabetic Activity

The fruit extract of M. dubia was investigated on mice and found to be an efficient hypoglycemic

agent (Susheela, Balaravi, Theophilus, Reddy, & Reddy, 2008). Sharma & Arya (2011) had reported that Liminoid, an active component of M. dubia, and an alcoholic extract of its fruit, at a dosage of 300mg/g, demonstrated anti-diabetic action in Streptozotocin-induced diabetic mice. However, research of Valentina, Ilango, Kiruthiga, & Parimala (2013) had clearly demonstrated that M.dubia ethanolic extract has a high potency α-amylase blocking ability, with an IC50 value of 24.82 µg/ml.

1.5.6 Anti-bacterial Activity

Chanthuru, Prabhu, Aysha, & Karthik (2014) showed that, at a concentration of 60 µl, the M. dubia leaf extract demonstrated significant zone of inhibitory action against all of the bacterial pathogens examined, including E. coli, Salmonella typhi, S. paratyphi, Klebsilla peneumonia, and Staphylococcus aureus (28, 20, 18, 26 and 22 mm respectively). The ethyl acetate extracts of the root showed the least action in some species, including E. coli and S. paratyphi (7 and 8 mm, respectively).Further, Karthikeyan, Mullai Nila, Thooyavan, & Vimalkumar (2014) confirmed Antibacterial efficacy against Bacillus subtilis, Proteas mirabilis, and Vibrio cholera.

1.5.7 Antifeedant Activity

Koul, Jain & Sharma (2000) had reported, *M. dubia* (Meliaceae) extracts were tested for their ability to suppress development and discourage *Spodoptera* litura and Helicoverpa armigera larvae. Using neonate larvae of both S. litura and H. armigera, artificial diet bioassays revealed that dichloromethane]

(DCE) and methanol (Me) extracts of M. dubia inhibited development in a dose-dependent way. In a leaf disc-choice test, DCE and Me-SII components deterred S. litura larvae by 50% at doses of 22.5 and 16.8 µl/cm^2, respectively.

1.5.8 Anticancer Activity

Silver nanoparticles were made and analyzed using UV-visible, XRD, and SEM-EDS on M. dubia plant extract. The impact of silver nanoparticles on human breast cancer (KB) cell lines has been investigated. Silver nanoparticles demonstrated exceptional killing action against the KB cell line, indicating a high therapeutic index value. Many other studies have found that M. dubia plant preparation has anticancer effects (Goswami, Bhagta, & Sharma, 2020).

1.5.9 Biopesticidal Activity

Importantly, numerous pesticidal chemicals are found in various sections of M. dubia. As a result, many extracts of different sections of this plant have pesticidal qualities. Refined bark contains 60-70% toosandanin, which can be used to regulate *Helicoverpa armigera* and is an effective antifeedant and development suppressant for *Pieris rapae* larvae. Meliaceae limonoids have the ability to successfully control a wide range of insect pests while causing no damage to the ecosystem. Several M. dubia preparations contain ovicides, larvicides, growth inhibitors, antifeedants, stomach toxins, and induce moulting disorders and morphological abnormalities in a variety of pests. The pest-controlling ability of two M. dubia leaf extracts, namely aqueous extract and aqueous formulation made using the methanol extract to control pests such as thrips, mealy bugs, scale insects and caterpillars, was examined by scientists. To manage thrips, mealy bugs, and caterpillars, methanol extract of M. dubia leaves is far more efficient than aqueous

extract. The aqueous mixture made from the methanol extract of M. dubia leaves significantly reduces the harm caused by caterpillars in agricultural cultivations. Therefore, the yield can be ensured as it stops the decrease of the leaf area through decreasing the number of caterpillars. When M. dubia aqueous formulation was applied to cabbage seedlings, the output was considerably greater than the control (Goswami, Bhagta, & Sharma, 2020).

Table 4: Pharmacological activities from different part of M. dubia

Tree Part Used	Pharmacological Activities
Leaf	Antioxidant Activity (Valentina, Ilango, Kiruthiga, & Parimala, 2013), Anti-cancer activity (Goswami, Bhagta, & Sharma, 2020), Anti-bacterial activity (Chanthuru, Prabhu, Aysha, & Karthik, 2014), Antidiabetic Action (Valentina, Ilango, Kiruthiga, & Parimala, 2013), Antifeedant activity (Koul, Jain, & Sharma, 2000), Biopesticidal activity (Goswami, Bhagta, & Sharma, 2020), Larvicidal activity (Karthikeyan, Mullai Nila, Thooyavan, & Vimalkumar, 2014) (Chanthuru, Prabhu, Aysha, & Karthik, 2014).
Fruit	Anti-inflammatory activity (Khadse & Kakde, 2014), Antidiabetic Action (Susheela, Balaravi, Theophilus, Reddy, & Reddy, 2008).
Bark	Anti-bacterial activity (Anonymous, 1999), Biopesticidal activity (Goswami, Bhagta, & Sharma, 2020).
Leaf oil	Anti-bacterial activity (Nagalakshmi, Thangadurai, Anuradha, & Pullaiah, 2001), Antifungal activity (Nagalakshmi, Thangadurai, Anuradha, & Pullaiah, 2001)
Leaf volatile oil	Anti-bacterial activity (Gerige & Ramjaneyulu, 2007).
Root	Anti-bacterial activity (Chanthuru, Prabhu, Aysha, & Karthik, 2014).
Leaf nanoparticles	Anti-bacterial activity (Karthikeyan, Mullai Nila, Thooyavan, & Vimalkumar, 2014).

1.5.10 Larvicidal Activity

Karthikeyan, Mullai Nila, Thooyavan, & Vimalkumar (2014) had reported that the larvicidal efficacy of crude aqueous leaf preparations of M. dubia and silver nanoparticles made from M. dubia leaves was evaluated against filarial vector Culex quienquefasciatus 4th instar larvae. The findings showed that when compared to pure aqueous leaf preparations of M. dubia, the synthesised silver nanoparticles had the greatest mortality of filarial vectors. Chanthuru, Prabhu, Aysha, & Karthik (2014) confirmed that this Plant material showed considerable activity against Culex quienquefasciatus and could thus be deemed a powerful natural larvicidal agent.

2. Green Synthesis of Nanoparticles

2.1 Silver nanoparticles synthesized from M. dubia –

Silver nanoparticles (AgNPs) were synthesized using M. dubia leaf extract through a green synthesis method. A 0.01 M aqueous solution of silver nitrate was mixed with varying concentrations of the leaf extract (1-4 ml) at 28°C. The formation of AgNPs was indicated by a color change to dark brown after 15 minutes. Increasing the leaf extract concentration resulted in smaller nanoparticles, with the 4 ml extract producing the smallest particles. The purified nanoparticles were then tested on MCF-7 breast cancer cells. Results showed that the AgNPs were highly effective, with 50% of cancer cells killed at an IC50 concentration of 31.2 µg/ml, demonstrating promising anticancer potential (Kathiravan, Ravi, &

Ashokkumar, 2014). Silver nanoparticles (AgNPs) were synthesized by adding 25 mL of M. dubia leaf extract to a 3 mM silver nitrate ($AgNO_3$) solution and stirring the mixture for 5 hours. During this time, the solution's color changed from light to yellowish brown, reddish brown, and finally colloidal brown, indicating nanoparticle formation, which was confirmed by UV-visible spectrophotometry. The synthesized AgNPs were then tested for antibacterial activity against *Vibrio cholerae*, *Escherichia coli*, *Staphylococcus aureus*, and *Klebsiella pneumoniae*, showing strong antibacterial effects against all pathogens (Vimala, Sheela, Dayana Jeya Leela, & Monisha, 2016).

2.2 Zinc oxide nanoparticles synthesized from M. dubia –

For the Green Synthesis of Zinc Oxide Nanoparticles (ZnO NPs), 0.1 M zinc acetate dihydrate was used as a precursor, and M. dubia leaf extract was added at a 2:1 ratio to the zinc acetate solution under constant stirring at 600 rpm. The extract was added at 10 drops/min, with stirring continued for 14 hours to convert zinc acetate to ZnO. The solution was left undisturbed for 72 hours for precipitation, after which the particles were dried at 60°C and crushed into fine powder. The ZnO NPs were split into uncalcined and calcined (200°C) samples. The antibacterial activity of the leaf extract, uncalcined, and calcined ZnO NPs was tested against *Staphylococcus aureus* and *Escherichia coli*. The leaf extract was effective against *S. aureus* but not *E. coli* due to its dense cell wall. The uncalcined ZnO NPs showed good activity against *E. coli*, but calcination reduced their effectiveness. Both uncalcined and calcined samples were equally effective against *S. aureus*, matching the performance of chemically prepared ZnO NPs (Prabhu, Vaideki, Anitha, & Rajendran, 2017)

3. Conclusion

In conclusion, Melia dubia (Malabar neem) stands as a significant tree species with diverse applications in traditional medicine, forestry, and industrial sectors. The plant possesses a rich ethnobotanical heritage, with various parts utilized for their therapeutic properties in treating ailments such as leprosy, asthma, malaria, and fevers. Extensive phytochemical studies have identified bioactive compounds, including alkaloids, flavonoids, steroids, and tannins, contributing to the plant's pharmacological activities. The pharmacological investigations have demonstrated the potential of M. dubia extracts and essential oils in exhibiting antioxidant, antibacterial, antifungal, anti-inflammatory, antidiabetic, and anticancer properties. These findings support the traditional use of M. dubia and provide a scientific basis for its therapeutic applications. Additionally, the green synthesis of nanoparticles using M. dubia extracts has shown antimicrobial efficacy, opening avenues for novel applications in nanotechnology. Looking ahead, M. dubia holds promising prospects for sustainable forestry practices, industrial applications such as furniture, plywood, and paper production, and the development of plant-based therapeutic agents. Further research is needed to explore the full range of its phytochemical constituents, elucidate their mechanisms of action, and conduct clinical trials to validate their efficacy and safety. This would enable the integration of M. dubia into mainstream medicine and contribute to the development of cost-effective and accessible healthcare solutions. In summary, *Melia dubia* represents a valuable

botanical resource with immense potential in traditional medicine, pharmacology, and various industries. Its ethnobotanical significance, phytochemical composition, pharmacological activities, and green synthesis capabilities pave the way for further exploration and utilization of this remarkable plant species.

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