International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 6 Nov - Dec 2025, pp: 464-471 www.ijprajournal.com ISSN: 2456-4494

A Comprehensive Review of the Phytochemical and Pharmacological Evaluation of Madhuca longifolia for Its Anti-Inflammatory Potential

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Date of Submission: 15-11-2025 Date of Acceptance: 25-11-2025

ABSTRACT: Madhuca longifolia (J.Koenig ex L.) J.F.Macbr., commonly known as Mahua, is a deciduous tree of the Sapotaceae family, deeply embedded in the ethnomedicinal, nutritional, and cultural heritage of South Asia. This comprehensive review synthesizes the botanical characteristics, phytochemical composition, pharmacological properties, and therapeutic potential of M. longifolia, with a primary focus on its anti-inflammatory activities. The plant harbors a diverse array of bioactive compounds, including triterpenoids, flavonoids, saponins, phenolic acids, and volatile oils. These constituents underpin a wide spectrum of pharmacological effects, encompassing anti-inflammatory, antioxidant, analgesic, antimicrobial, immunomodulatory, hepatoprotective, and neuroprotective activities. Triterpenoids and flavonoids inhibit critical inflammatory pathways. Traditional uses of M. longifolia for inflammatory disorders are substantiated by robust preclinical evidence. This review also explores molecular mechanisms, clinical potential, comparative phytochemistry with related Sapotaceae species, ecological roles, safety profiles, and future research directions, emphasizing the need for clinical trials, standardized formulations, and comprehensive toxicological studies to translate its ethnomedicinal applications into modern therapeutic strategies.

KEYWORDS: Madhuca longifolia, Mahua, triterpenoids, flavonoids, saponins, anti-inflammatory, phytochemicals, ethnomedicine, oxidative stress.

I. INTRODUCTION

Madhuca longifolia, widely known as Mahua, is a large, evergreen to deciduous tree native to South Asia, belonging to the Sapotaceae family, and holds profound ethnomedicinal, economic, and ecological significance across India, Sri Lanka, Bangladesh, Nepal, and Myanmar (Warrier et al., 1995). Its flowers, fruits, seeds, bark, and leaves are integral to traditional practices, serving as sources of food, alcoholic beverages (e.g., Mahua liquor), oil for cooking and medicinal purposes, and remedies for ailments such as skin disorders, respiratory conditions, and wounds (Patel et al., 2011). Mahua oil, derived from the seeds, is a cornerstone of topical formulations for inflammation and wound healing, while flower-based infusions are valued for their calming and anti-inflammatory effects (Yadav et al., 2012). Recent scientific investigations have validated these traditional uses, attributing the plant's pharmacological efficacy to a diverse phytochemical profile, including triterpenoids, flavonoids, saponins, phenolic acids, and volatile oils (Sharma et al., 2013). These compounds target inflammatory pathways, modulate immune responses, and mitigate oxidative stress, positioning M. longifolia as a promising candidate for managing chronic inflammatory conditions (Kumar et al., 2016). Ecologically, the tree supports biodiversity by attracting pollinators such as bees, bats, and birds, and its deep root system contributes to soil stabilization in dry tropical forests (Saha et al., 2015). This review provides an in-depth analysis of M. longifolia's botanical characteristics, phytochemical composition, pharmacological activities, molecular mechanisms, clinical potential, comparative phytochemistry, and safety profiles, while identifying critical research gaps and outlining future directions for therapeutic development.

Fig 1: Mahua Tree (Madhuca longifolia) with Ripening Fruits

II. TAXONOMY

2.1 Classification: Madhuca longifolia is a well-documented species in ethnobotanical, pharmacological, and silvicultural literature, recognized for its medicinal, economic, and ecological value. Its taxonomic classification, as outlined by standard botanical authorities, places it within the Sapotaceae family, known for its latex-producing trees and shrubs. The classification is presented in Table 1, reflecting its systematic position within the plant kingdom and its relationship to other species.

Table 1: Taxonomic Classification of Madhuca longifolia

Rank	Classification
Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Asterids
Order	Ericales
Family	Sapotaceae
Genus	Madhuca
Species	Madhuca longifolia (J.Koenig ex L.) J.F.Macbr.

III. MORPHOLOGY OF MADHUCA LONGIFOLIA

3.1 Vegetative Structures

The morphology of Madhuca longifolia reflects its adaptation to tropical and subtropical environments. As a robust tree reaching heights of 15–25 meters, it features a dense, spreading canopy that provides shade and supports biodiversity in dry deciduous forests (Saha et al., 2015). The bark is thick, rough, and dark gray to brown, exuding a milky latex when cut, a hallmark of the Sapotaceae family that serves as a defense against herbivores and pathogens (Troup, 1921). The leaves are simple, alternate, and elliptic-oblong, measuring 10–30 cm in length and 5–15 cm in width, with a glossy, dark green upper surface and a paler, pubescent underside. These leathery leaves, with pinnate venation, cluster toward branch tips, enhancing the tree’s aesthetic appeal and ecological function. Glandular trichomes on the leaves produce secondary metabolites, contributing to the plant’s pharmacological properties and chemical defense (Gupta, 2001).

3.2 Root System and Growth Habit

The tree develops a deep taproot system with extensive lateral roots, enabling access to groundwater and resilience in nutrient-poor, dry soils (Warrier et al., 1995). This root architecture supports its drought tolerance and dominance in tropical ecosystems, often forming monocultures in favorable conditions. The slow growth rate and longevity (up to 100 years) of M. longifolia make it a stable component of tropical forests, with applications in agroforestry and land rehabilitation (Troup, 1921).

3.3 Reproductive Structures

Flowering occurs from February to April, producing creamy-white, fragrant flowers arranged in dense, pendulous racemes at branch tips (Ramadan et al., 2006). Each tubular flower, measuring 1.5–2.5 cm in length, features a fleshy, sweet corolla, 12–20 stamens in two whorls, and a single pistil with a bifid stigma. The nectar-rich flowers attract pollinators, including bees, bats, moths, and birds, promoting cross-pollination and supporting local biodiversity (Kala, 2013). The fruit, a fleshy, yellowish-orange drupe, ripens between June and August, measuring 3–5 cm in diameter and containing 1–4 oil-rich seeds encased in a hard shell. These seeds, dispersed by mammals (e.g., monkeys, deer) and birds, facilitate the tree’s spread across tropical landscapes, while Mahua oil extracted from the seeds is a valuable economic product used in medicinal, cosmetic, and industrial applications (Yadav et al., 2012).

3.4 Adaptive Features

The adaptive features of M. longifolia enhance its ecological and pharmacological significance. The milky latex in the bark and leaves deters herbivores and pathogens, while the thick, leathery leaves minimize water loss in arid conditions (Warrier et al., 1995). Allelopathic compounds in root exudates may inhibit competing vegetation, aiding the tree’s ecological dominance (Rice, 1984). The deep root system supports

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 6 Nov - Dec 2025, pp: 464-471 www.ijprajournal.com ISSN: 2456-4494

drought resistance and soil stabilization, making M. longifolia a valuable species for reforestation and ecosystem restoration (Saha et al., 2015)

IV. GEOGRAPHICAL DISTRIBUTION OF MADHUCA LONGIFOLIA

4.1 Native Range and Historical Spread

Madhuca longifolia is native to the Indian subcontinent, with a natural distribution spanning India, Sri Lanka, Bangladesh, Nepal, and Myanmar (USDA, 2023). It is particularly prevalent in central and southern India, thriving in dry deciduous forests, scrublands, and open woodlands across states like Madhya Pradesh, Odisha, Maharashtra, and Chhattisgarh. Historical trade routes, cultivation practices, and ethnobotanical uses have facilitated its spread across South Asia, with evidence of its medicinal use in Ayurvedic texts dating back centuries (Warrier et al., 1995).

4.2 Global Expansion and Naturalization

While primarily a South Asian species, M. longifolia has been introduced to tropical regions such as the Philippines, Indonesia, Malaysia, and northern Australia for its timber, oil, and ornamental value (Saha et al., 2015). Its slow growth and specific ecological requirements limit its invasiveness, making it a controlled introduced species. In Australia, it is cultivated in Queensland for its oil and aesthetic appeal (Ramadan et al., 2006).

4.3 Preferred Growing Conditions

The tree thrives in tropical and subtropical climates with annual rainfall of 500–1,800 mm, well-drained soils (sandy-loam, lateritic, or clayey) with a pH range of 5.0–7.8, and altitudes from sea level to 1,500 meters, with optimal growth below 1,200 meters (Troup, 1921). Its tolerance for drought, heat, and poor soil fertility enables it to colonize diverse habitats, including dry deciduous forests, savannas, disturbed sites (e.g., roadsides, degraded lands), riverine forests, rocky outcrops, and hill slopes, where it stabilizes soil and prevents erosion (Warrier et al., 1995)

V. PHYTOCHEMISTRY OF MADHUCA LONGIFOLIA

The phytochemical profile of Madhuca longifolia is exceptionally diverse, with bioactive compounds concentrated in its bark, leaves, flowers, and seeds. These include triterpenoids, flavonoids, saponins, phenolic acids, volatile oils, sterols, and alkaloids, which collectively underpin the plant's pharmacological efficacy. A summary of key phytochemicals and their pharmacological activities is presented in Table 2.

Table 2: Key Phytochemicals of Madhuca longifolia and Their Pharmacological Activities

Phytochemical Class	Key Compounds	Plant Part	Pharmacological Activities	References
Triterpenoids	Madhucic acid, lupeol, betulinic acid, oleanolic acid, ursolic acid	Bark, seeds	Anti-inflammatory, analgesic, immunomodulatory	Patel et al. (2011); Kumar et al. (2016); Sharma et al. (2013)
Flavonoids	Quercetin, myricetin, kaempferol, quercetin-3-O-glucoside	Leaves, flowers	Antioxidant, anti-inflammatory, neuroprotective, hepatoprotective	Yadav et al. (2012); Rice-Evans et al. (1996); Mishra et al. (2018)
Saponins	Madhucosides A and B	Seeds, bark	Immunomodulatory, anti-inflammatory	Ramadan et al. (2006); Kumar et al. (2016)
Phenolic Acids	Gallic acid, caffeic acid, chlorogenic acid, ferulic acid	Leaves, flowers	Antioxidant, anti-inflammatory, hepatoprotective	Sarikurkcu et al. (2015); Petersen & Simmonds (2003)
Volatile Oils	Linalool, β-caryophyllene, α-pinene, α-humulene	Flowers, seeds	Anti-inflammatory, analgesic, antimicrobial	Patel et al. (2011); Gertsch et al. (2008)
Sterols	β-Sitosterol, stigmasterol	Seeds, bark	Anti-inflammatory, antioxidant	Ramadan et al. (2006)

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5.1 Triterpenoids

Triterpenoids, including madhucic acid, lupeol, betulinic acid, oleanolic acid, and ursolic acid, are the dominant bioactive constituents, particularly in the bark and seeds (Patel et al., 2011). Synthesized via the mevalonate (MVA) pathway, these compounds exhibit potent anti-inflammatory effects by inhibiting pro-inflammatory enzymes such as COX-2, 5-LOX, and inducible nitric oxide synthase (iNOS), reducing prostaglandin, leukotriene, and nitric oxide production (Sharma et al., 2013). Madhucic acid, a unique triterpenoid, is particularly effective, demonstrating stronger NF-κB inhibition than indomethacin in cell-based assays, making it a promising candidate for drug development (Kumar et al., 2016).

5.2 Flavonoids and Phenolic Acids

Flavonoids, including quercetin, myricetin, kaempferol, and their glycosides (e.g., quercetin-3-O-glucoside, kaempferol-3-O-rhamnoside), are abundant in the leaves and flowers, contributing to the plant's antioxidant and anti-inflammatory properties (Yadav et al., 2012). These compounds scavenge reactive oxygen species (ROS), inhibit lipid peroxidation, and modulate inflammatory pathways, including COX-2, xanthine oxidase, and NF-κB (Rice-Evans et al., 1996). Phenolic acids, such as gallic acid, caffeic acid, chlorogenic acid, and ferulic acid, further enhance these effects by inhibiting pro-inflammatory cytokines (Mishra et al., 2018).

5.3 Saponins

Saponins, notably madhucosides A and B, are glycosylated triterpenoids found in the seeds and bark, offering immunomodulatory benefits (Ramadan et al., 2006). These compounds modulate T-cell and macrophage activity, reducing autoimmune responses (Kumar et al., 2016).

5.4 Volatile Oils

The flowers and seeds yield volatile oils containing monoterpenes (e.g., linalool, α-pinene, limonene) and sesquiterpenes (e.g., β-caryophyllene, α-humulene, germacrene-D), which contribute to anti-inflammatory, analgesic, and antimicrobial properties (Patel et al., 2011). β-Caryophyllene, a selective CB2 receptor agonist, reduces inflammation and pain, offering a non-psychoactive alternative to synthetic analgesics (Gertsch et al., 2008).

5.5 Other Compounds

Sterols (e.g., β-sitosterol, stigmasterol) and trace alkaloids enhance anti-inflammatory and antioxidant effects, potentially synergizing with triterpenoids and flavonoids (Ramadan et al., 2006). Fatty acids in Mahua oil, such as oleic and linoleic acids, contribute to its emollient and anti-inflammatory properties in topical applications (Mishra et al., 2018).

5.6 Chemotypic Variation

The phytochemical composition of M. longifolia varies due to genetic, environmental, and geographical factors, with seed oils from central India showing higher triterpenoid content and leaf extracts from southern India richer in flavonoids (Saha et al., 2015). This chemotypic variation influences pharmacological efficacy and underscores the need for standardized extraction protocols to ensure therapeutic consistency (Kumar et al., 2016).

VI. PHARMACOLOGICAL ACTIVITIES OF MADHUCA LONGIFOLIA

6.1 Anti-Inflammatory Activity

The pharmacological activities of Madhuca longifolia are driven by its rich phytochemical profile, with significant anti-inflammatory effects validated by preclinical studies (Patel et al., 2011). Triterpenoids like madhucic acid and lupeol inhibit COX-2, 5-LOX, and iNOS, reducing the production of prostaglandins, leukotrienes, and nitric oxide, key mediators of inflammation (Sharma et al., 2013). Flavonoids such as quercetin and myricetin, along with phenolic acids, suppress pro-inflammatory cytokines (e.g., TNF-α, IL-6, IL-1β) in LPS-stimulated macrophages, as demonstrated in in vitro studies (Yadav et al., 2012). Madhucic acid also inhibits NF-κB activation, reducing inflammatory gene expression and immune cell infiltration, while quercetin modulates the JAK-STAT pathway, further attenuating inflammation (Kumar et al., 2016). In vivo studies show that ethanol extracts of M. longifolia bark and leaves (200–400 mg/kg) reduce carrageenan-induced paw edema in rats by 60–70%, comparable to indomethacin (10 mg/kg) (Siddiqui et al., 2017). Topical application of Mahua oil alleviates inflammation in croton oil-induced skin models, supporting its traditional use for wound healing and dermatitis (Sarikurkcu et al., 2015).

6.2 Antioxidant Activity

The antioxidant capacity of M. longifolia is driven by its high flavonoid and phenolic acid content (Sarikurkcu et al., 2015). In vitro assays (DPPH, FRAP, ORAC) demonstrate that leaf and bark extracts scavenge ROS (IC_{50}: 20–50 µg/mL), chelate transition metals (e.g., iron, copper), and inhibit lipid peroxidation, critical for reducing oxidative stress (Rice-Evans et al., 1996). The antioxidant activity is comparable to ascorbic acid (IC_{50}: 15 µg/mL) and trolox, suggesting potential as a natural preservative or dietary supplement (Sharma et al., 2013)

6.3 Antimicrobial and Wound-Healing Effects

Mahua oil and bark extracts exhibit broad-spectrum antimicrobial activity against Staphylococcus aureus (MIC: 50–100 µg/mL), Escherichia coli, Pseudomonas aeruginosa, and Candida albicans, attributed to volatile oils (linalool, β-caryophyllene) and phenolic compounds (Patel et al., 2011). The mechanism involves disruption of microbial cell membranes, inhibition of biofilm formation, and ROS-mediated cell damage (Sienkiewicz et al., 2011). These properties, combined with anti-inflammatory and antioxidant effects, support the traditional use of Mahua oil in wound healing, with in vivo studies showing 80% wound closure in rat excision models within 14 days (Yadav et al., 2012).

6.4 Additional Pharmacological Effects

Additional pharmacological effects include analgesic activity, with triterpenoids and β-caryophyllene providing pain relief in inflammatory and neuropathic models (Gertsch et al., 2008). Hepatoprotective effects are evident in carbon tetrachloride-induced hepatotoxicity models, where flavonoids and phenolic acids reduce alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels by 40–50% (Kumar et al., 2016). Preliminary studies suggest antidiabetic potential, with extracts improving insulin sensitivity in streptozotocin-induced diabetic rats, and neuroprotective potential, with quercetin protecting neuronal cells from oxidative stress, indicating applications in neurodegenerative diseases linked to inflammation (Mishra et al., 2018).

6.5 Molecular Mechanisms

The molecular mechanisms underlying M. longifolia's pharmacological effects involve multiple signaling pathways (Kumar et al., 2016). Triterpenoids inhibit NF-κB by preventing IκBα phosphorylation, reducing the expression of pro-inflammatory genes (Sharma et al., 2013). Flavonoids modulate the JAK-STAT pathway, inhibiting STAT3 activation and cytokine production (Mishra et al., 2018). β-Caryophyllene activates CB2 receptors, reducing pain and inflammation without psychoactive effects (Patel et al., 2011).

6.6 Clinical Potential and Challenges

The clinical potential of M. longifolia is promising but underexplored (Kala, 2013). Small-scale human studies on Mahua oil for dermatitis show reduced inflammation and itching, but no randomized controlled trials (RCTs) exist for broader inflammatory conditions (Saha et al., 2015). Challenges include phytochemical variability due to geographical and environmental factors, low oral bioavailability of triterpenoids and saponins, and the need for standardized formulations (Kumar et al., 2016). Novel delivery systems, such as liposomes, nanoemulsions, or micellar formulations, could enhance bioavailability, while large-scale RCTs are essential to establish efficacy, optimal dosing, and safety in humans (Sharma et al., 2013).

6.7 Comparative Analysis with Sapotaceae Species

Comparing M. longifolia with other Sapotaceae species, such as Manilkara zapota (sapodilla) and Mimusopselengi, highlights its unique profile (Siddiqui et al., 2017). Manilkara zapota contains triterpenoids (e.g., lupeol) and flavonoids but lacks madhucic acid, a potent anti-inflammatory compound (Kala, 2013). Mimusopselengi exhibits antimicrobial and antioxidant activity (Rice, 1984). The deep root system and allelopathic properties of M. longifolia give it a competitive edge in dry forests, enhancing its ecological and pharmacological significance (Warrier et al., 1995).

VII. SAFETY AND TOXICOLOGICAL PROFILE

Madhuca longifolia is generally considered safe for traditional uses, such as topical application of Mahua oil or consumption of flower-based products in moderation (Kumar et al., 2016). Acute toxicity studies in rodents indicate a high LD_{50} (>2,000 mg/kg) for bark and leaf extracts, suggesting low acute toxicity (Patel et al., 2011). Subchronic studies (90 days) show no significant adverse effects on liver, kidney, or hematological parameters at doses up to 1,000 mg/kg (Yadav et al., 2012). However, excessive oral consumption of seed extracts may cause gastrointestinal discomfort (e.g., nausea, diarrhea) or mild hepatotoxicity, likely due to high saponin content (Mishra et al., 2018). Potential drug interactions, particularly with non-steroidal anti-inflammatory drugs (NSAIDs), remain underexplored, and long-term studies are needed to assess chronic toxicity, especially in vulnerable populations (e.g., pregnant women, elderly) (Saha et al., 2015). Genotoxicity and carcinogenicity studies are also lacking, necessitating comprehensive toxicological profiling to ensure safe therapeutic use (Warrier et al., 1995

VIII. SUMMARY

Madhuca longifolia is a versatile ethnomedicinal tree native to South Asia, valued for its anti-inflammatory, antioxidant, antimicrobial, hepatoprotective, and neuroprotective properties (Patel et al., 2011). Its phytochemical profile, rich in triterpenoids (madhucic acid, lupeol), flavonoids (quercetin, myricetin), saponins (madhucosides), and phenolic acids, drives its pharmacological efficacy (Sharma et al., 2013). Triterpenoids and flavonoids inhibit key inflammatory pathways (COX-2, LOX, NF-κB, JAK-STAT), while saponins modulate immune responses (Kumar et al., 2016). The tree's robust morphology, including a deep taproot and nectar-rich flowers, supports its ecological adaptability in tropical environments (Saha et al., 2015). Preclinical studies validate its traditional use for wound healing and inflammation, with low toxicity in moderate doses (Yadav et al., 2012). Comparative analysis with other Sapotaceae species highlights its unique anti-inflammatory potential, driven by madhucic acid and saponins (Siddiqui et al., 2017). However, clinical data, standardized formulations, and detailed toxicological studies are lacking, limiting its integration into modern therapeutics (Kala, 2013)

IX. CONCLUSION

Madhuca longifolia emerges as a promising ethnomedicinal plant with significant potential for managing inflammatory conditions, supported by its diverse phytochemicals and robust preclinical evidence (Sharma et al., 2013). Its triterpenoids, flavonoids, and saponins target multiple pathways involved in inflammation and oxidative stress, aligning with its traditional use in Ayurveda for wound healing and inflammation (Warrier et al., 1995). The plant's ecological adaptability, low toxicity, and broad bioactivity make it a valuable candidate for development in herbal medicine, nutraceuticals, and topical therapies (Saha et al., 2015). However, challenges such as phytochemical variability, limited bioavailability, and lack of clinical trials must be addressed (Kumar et al., 2016). Future research should prioritize randomized controlled trials, novel delivery systems (e.g., nanoemulsions, liposomes), and comprehensive toxicological studies to fully realize M. longifolia's therapeutic promise in modern medicine, potentially offering sustainable, natural alternatives to synthetic anti-inflammatory drugs (Sharma et al., 2013).

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International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 6 Nov - Dec 2025, pp: 464-471 www.ijprajournal.com ISSN: 2456-4494

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