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Ethnomedicinal and biological activities of tropical Mahua (*Madhuca* species) - A comprehensive review

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ABSTRACT

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The genus *Madhuca*, of the family Sapotaceae is a multi-functional tropical tree with the species, *Madhuca indica* (*latifolia*), *M. longifolia,* and *M. butyracea* being the most prevalent. The nutritional and health benefits of mahua are due to the richness of its anti-oxidant, vitamin, mineral, and biochemical composition. Mahua plant (flowers, fruits, roots, bark, seeds, and leaves) extracts have a variety of bioactivities and ethnomedicinal applications (antidiabetic, anti-carcinogenic, anti-inflammatory, antimicrobial, etc.). They are traditionally well-known for their ability to prevent/treat various ailments. The phytochemical constituents have a defense mechanism and therapeutic role in the treatment of disease. *Madhuca* spp. has built the linkage between ethnic people, traditional knowledge, and livelihood support of the resources. This study/literature review has been undertaken to investigate the mahua as a forest resource that can be used for building livelihood resilience among ethnic communities. This review gives an extensive overview of the scientifically evaluated mahua plant extract bioactive molecules and a possible mechanism for the therapeutic potential for treating various diseases. Further, analyses of the opportunities and scope with future openings for the development of health-giving properties/abilities are extensively summarized.

Keywords: *Madhuca*, ethnobotany, bioactive agents, therapeutic activity, health benefits

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INTRODUCTION

Mahua (*Madhuca* spp.) is a deciduous tree native to the tropical rain forests of the: Asian and Australian continents (Gupta et al 2012, Sinha et al 2017), which has three main species in India: *M. indica* (*latifolia*), *M. longifolia,* and *M. butyracea* (Ramadan and Mörsel 2019). However, *M. longifolia* Syn. *M. indica* is an important economic tree that grows throughout the Indo-Pak subtropical region, especially in India (Awasthi et al 1975, Ramadan and Mörsel 2019). These species have been well known for their wide range of applications. Since ancient times, almost every part of the tree has been used (Awasthi et al 1975) and is economically valuable (Gupta et al 2012, Mishra and Padhan 2013, Devi and Sangeetha 2016, Sangeetha and Naggapan 2016). *Madhuca* or Mahua is mentioned in ancient Sanskrit literature (Vedas, Ayurveda) (Awasthi et al 1975, Mishra and Poonia 2019) and also quoted in travelogues of foreign travelers, including its economic importance (Ibn Battuta 1334 AD). The whole mahua plant and its constituents contain various pharmacologically important macromolecules, the efficacy of which has been thoroughly proven by several biochemical and pharmacological studies (Awasthi et al 1975, Gupta et al 2012, Devi and Sangeetha 2016, Ramadan et al 2020). Due to their high sugar content (66-72% dry weight), Mahua flowers are used in folk medicine to prepare a strong intoxicating liquor (Awasthi et al 1975, Behera and Ray 2019).

A search conducted between 1938 and 2021 yielded 99 documents on *Madhuca indica* (*latifolia*)*, M. longifolia,* and *M. butyracea* species. Outstanding authors and papers of importance have been listed. The most cited documents related to the ethnomedicinal and biological activities of *Madhuca* spp. were included in this comprehensive review. Moreover, this review aims to bring together numerous studies on this plant and critically analyze topics connected to mahua ethnobotany, ethnomedicine, and ethnopharmacology. The study appraises potential *Mahua* in traditional usage and discoveries from modern bioscientific research. The bioactive compounds and their functional characteristics and health-promoting properties have been abridged.

Taxonomic Description and Distribution

Classification	Name
Botanical Name	*Madhuca indica* (*Syn. Madhuca latifolia*)
Family	Sapotaceae
Subfamily	Caesalpinioideae
Tribes	Caesalpinieae
Genus	*Madhuca*
Species	*indica* (*latifolia*)
Order	Ericaleae

Mahua (*Madhuca latifolia* L.) is a tree native to Asia and Australia that grows in mixed deciduous forests on sandy and rocky soils (Behera et al 2012, Behera et al 2016). Malaysia, Sri Lanka, Australia, New Guinea, and Thailand are also home to several other *Madhuca* species (Sunita and Sarojini 2013).

According to a survey conducted by the Indian Central Oilseeds Committee, there are approximately 8.5 million mahua trees in India (Figure 1), called mahua, mahula, mowrah, moha, mova, or mahuda locally, depending on the religion and the place. In India, five species (out of 84) can be distinguished based on their leaf structure. (Awasthi et al 1975, Ghadge and Raheman 2006, Sinha et al 2017). *M. latifolia* and *M. longifolia* are the two *Madhuca* species found almost anywhere in India. Except for the arrangement of their leaves, these two species are very similar, and this distinction has been assumed to be varietal rather than unique. These two Malaysian species have merged and are now known as *M. longifolia* var. *longifolia* and *M. longifolia* var. *latifolia* (Awasthi et al 1975, Sinha et al 2017). Uttar Pradesh, Madhya Pradesh, and Telangana are home to *M. latifolia*. *M. butyracea* can be found in the Kumaon and Gharwal regions of the Sub-Himalayas. South Karnara, Mysore, Chennai, and Mumbai are all home to *M. neriifolia*. *M. bourdillonii* and *M. longifolia* are present in Mysore and the Western Ghats, respectively (Awasthi et al 1975, Ghadge and Raheman 2006, Sinha et al 2017). Mahua trees are fast-growing, can reach a height of 20m, have a temperature range of 2-46°C, and have evergreen or semi-evergreen foliage. These trees thrive in various soils, but they prefer alluvial soil. A deep loamy or sandy-loam soil with good drainage is the best choice for increased growth and productivity. The tree's broad, spreading superficial root system keeps the soil together and prevent soil erosion (Sunita and Sarojini 2013, Kumar et al 2018).

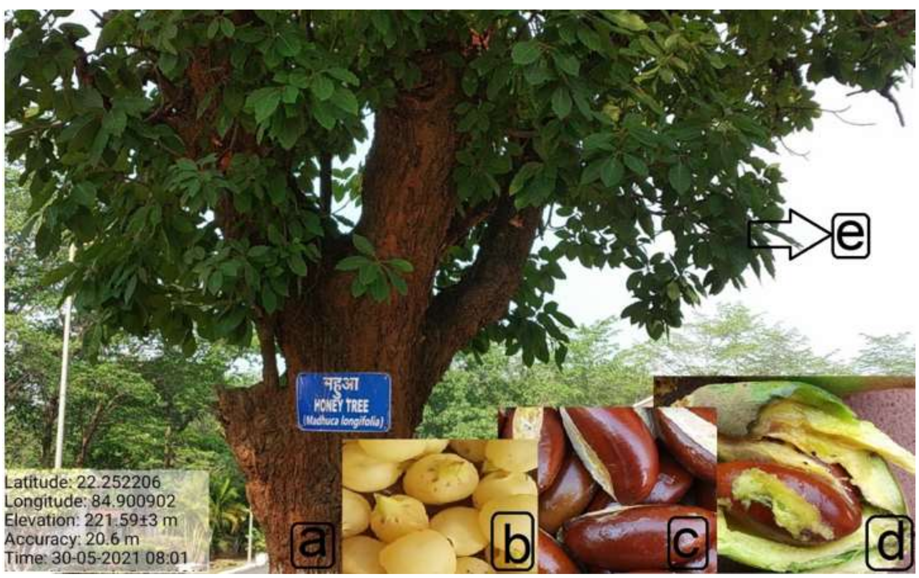

Figure 1. The photographs of whole plant (a) and its parts (leaves (e), flower (b), seeds (c) and fruit attached seed (d)).

Madhuca butyracea syn. Diploknema butyracea (family *Sapotaceae*) grows abundantly in the Sub-Himalayan tract of India at altitudes ranging from 300 to 1500m. Its bark, leaves, flowers, fruits, and seeds find various uses in the indigenous system of medicine, and the plant is often identified under the name *Madhuca* together with its sister species, *M. latifolia* (Mahua). The seed kernel is rich in saponins, and the seed fat has a unique place amongst the vegetable fats for its highest palmitic acid content (56%) ever recorded in a nut-fat (Awasthi and Mitra 1968).

Cultivation Details

The mahua tree grows from the sub-tropics to the hot tropics. It grows at heights of up to 16-20m and has a short, stout trunk (80cm in diameter). The tree is found in areas where annual daytime temperatures range from 2°-46°C, and it can also resist moderate frost. The tree thrives in climates with annual rainfall ranging from 550-1,500mm. It necessitates a sunny location. A deep loamy or sandy-loam soil with good drainage is preferred for cultivation. It also grows on calcareous, clayey, and bouldery soils. The mahua trees that have been established for a long time are drought resistant. It is a long-lived tree that starts flowering after ten years of planting (Mishra and Padhan 2013, Sangeetha and Naggapan 2016).

Conservation Status of Mahua Trees

Mahua can be regarded as a keystone species of dry deciduous forests in India because it enhances the region's biodiversity and is being protected by local communities (RLS 2002). Primarily the flowers provide a ready income of INR 60-70 per head per day of collection. Local communities have conserved the species and secured the tenure rights of each tree, mainly outside the forest area. However, due to more anthropogenic pressure, including unattainable harvesting, distress selling, and a wide fluctuation in the price of flowers, the mahua populations are facing the problem of natural regeneration despite producing a considerable quantity of viable seeds (Hegde et al 2018).

Use in Traditional Medicines

The use of mahua plants as a fundamental component of the Asian traditional healthcare system is perhaps the oldest and the most varied therapeutic approach (Gupta et al 2012). In many parts of rural India, traditional healers prescribing mahua plant parts are the most easily accessible and affordable health resource available to the local community and at times the only therapy that subsists (Puhan et al 2005, Gupta et al 2012, Sunita and Sarojini 2013, Pinakin et al 2020). Mahua flowers have been reported to provide benefit for the treatment of tonsillitis, bronchitis, helminths, pharyngitis, impotency, inflammation, eczema, skin illnesses, and eye problems (Verma et al 2014, Mishra and Usha 2019). Oleation for skin problems uses the flower extract (Soni and Dey 2013). The fresh juice extracted from the flower helps to stop bleeding. Its paste helps to prevent abscesses (Mishra and Usha 2019). Nasal administration of fresh mahua flower juice is used to treat several disorders such as headaches, eye burning, etc. To treat nerve weakness and illnesses of the neuromuscular system, dried mahua flowers are boiled in milk and given in a dose of 40-50mL. The flowers fried in ghee (clarified butter) are eaten by people suffering from piles. Mahua is use to treat diarrhea and colitis because of its astringent properties (Singh and Mani 2014, Mishra and Usha 2019).

Phytochemistry

Mahua plant is a storehouse of many phytochemicals (Ranjana et al 2018), which are used by the tribes of India to cure various ailments. Vitamins, sugars, amino acids, organic acids, enzymes, and other compounds are abundant in this plant (Verma et al 2010). For phytochemical screening of bioactive compounds, Verma et al (2010) examined the aqueous, ether, acetone, and methanolic extracts of fresh flowers and fruits of *M. indica*. Carbohydrates, proteins, flavonoids, and tannins were detected in all four extracts, while alkaloids were detected only in the aqueous and ether extracts. On the other hand, saponins were found to be positive only in the methanolic extract.

In contrast, sterol was found to be positive in the ether, acetone, and methanol extracts, and lipid was positive in the aqueous, ether, and methanolic extracts. In another study, Annalakshmi et al (2013) investigated the Gas Chromatography-Mass Spectrometry (GC–MS) and High-Performance Thin-Layer Chromatography *(*HPTLC) analyses for identification of phytochemical contents found in the leaves of *M. longifolia* (Koenig) Linn. *M. longifolia* shade-dried leaves were extracted with ethanol, and the concentrated ethanolic extracts were then submitted for GC–MS analysis. The powdered dried leaves were soaked in 50% aqueous alcohol, then refluxed, filtered, and dried before being used for HPTLC analysis. GC–MS research revealed the presence of phenolic acids, ketones, aldehydes, polysaccharides, heterocyclic compounds, and hydrocarbons, among other bioactive substances. Ranjana et al (2018) studied the GC-MS analysis to identify the important phytochemicals in the bark, flower, leaf, and seed, which might lead to the formulation and addition of many future drugs. The GC-MS analysis of the methanol extract of bark, flower, leaf, and seed revealed the presence of 42, 38, 46, and 39 phytochemicals, respectively. Their study forms the basis for the biological depiction and prominence of the compounds identified (Ranjana et al 2018*)*. The primary phytochemicals of *M. longifolia* are starch, terpenoids, proteins, mucilage, anthraquinone glycosides, cardiac glycosides, saponins, and tannins (Yoshikawa et al 2000, Ramadan et al 2020). The findings of several studies supported the traditional use of *M. longifolia*, which contains a number of recognized and unknown bioactive chemicals that could be utilized to treat various ailments (Annalakshmi et al 2013, Ranjana et al 2018, Ramadan et al 2020).

A new triterpenoid sapogenin, butyric acid, 2β, 3β, 6α, 23-tetrahydroxyolean-12-en-28-oic acid, has been isolated from *M. butyracea* leaves in addition to six known compounds (hentriacontane, hexacosanol, α-spinasterone, β-amyrin acetate, α-spinasterol, and myricetin-3-O-L-rhamnoside). The structure of these compounds has been established by spectral data and chemical reactions (Banerji et al 1985). *M. butyracea* is found to consist of about 62% "oleo"-dipalmitins, about 23%, palmitodi-oleins eight percent of tripalmitin, and seven percent of "oleo"-palmitostearins (Bushell and Hilditce 1938). Further, investigation of the seeds of *M. butyrocea* has yielded two new triterpenoid saponins, namely butyrosides C and D, whose structures were established using chemical and spectral analyses (Li et al 1994). Lalitha and Venkataraman (1987) studied the isolation of saponins from the seed cake of *M. butyracea* and their characteristics properties. The chemical composition of defatted seed flour of *M. butyracea* was also studied. The flour contains carbohydrates (45.7%), proteins (27.4%), and saponins (10.4%) as major constituents. The dried bark of *D. butyracea* (25g) revealed the presence of different phytoconstituents such as flavonoids, tannins, glycosides, terpenoids, and carbohydrates, together with a considerable amount of phenolic compounds (Chhetri et al 2020).

Biochemical Composition of the Flowers

The biochemical study revealed that Mahua flowers contained moisture (10-15%), sugar (64-68%), reducing sugars (50-55%), invert sugars (10-14%), ash (2-4%), crude protein (4-5%), crude fat (0.8-1%), Fe^{2+}, and Ca^{2+} (Banerjee and Samanta 2018). In addition, the phenolic compounds ascorbic acid, gallic acid (GA), quercetin, and myrcetin were detected and quantified in mahua flower and fruit extracts (Singh et al 2020). Recently, Singh et al (2020) reported that minerals such as Na, K, Mg, and Ca were found in Mahua flower and fruit extracts.

Biochemical Composition of Seeds/Seed Oil

Significant variations in oil content were found between agro-climatic zones (50.07-53.85%) (Yadav et al 2011, Munasinghe and Wansapala 2015). Yadav et al (2011) investigated the variation in oil content of mahua seed collected from various locations in Tamil Nadu, India. Oil parameters such as kernel oil percent, palmitic acid, stearic acid, oleic acid, and linoleic acid showed significant differences. The saturated fatty acids, palmitic acid, and stearic acid ranged from 11.7-25.9% to 19.1-32.2% in kernel oil, respectively. The percentages of oleic acid and linoleic acid, on the other hand, ranged from 32.9 to 48.7% and 9.4 to 15.4%, respectively. Many of the traits tested had high heritability. Munasinghe and Wansapala (2015) investigated seed morphology, seed oil content, and fatty acid profile of *M. longifolia*. They determined the relationship between oil content, fatty acid composition, and environmental conditions. The oil from the seed kernel was extracted using the Soxhlet method (n-Hexane, 65-70°C), and the fatty acid profile was calculated using the GC-MS technique. The saturated fatty acid content (oleic, linoleic, palmitic and stearic) was claimed to range from 40.87 to 47.20%. The total unsaturated fatty acid (monounsaturated fatty acids + polyunsaturated fatty acids) content, on the other hand, was between 49.6 and 53.86%.

Biological Activities

The roots, wood, bark, flowers, fruits, and seeds of the mahua tree can produce a variety of biological activities (Yadav et al 2012, Patel et al 2019). Furthermore, *M. longifolia* is used in traditional and folklore systems of medicine due to its various pharmacological properties (Panghal et al 2010). Therefore, it is also termed the panacea of ayurvedic medicine (Puhan et al 2005, Gupta et al 2012, Sunita and Sarojini 2013, Pinakin et al 2020). In addition, *mahua* is known to have antimicrobial, anti-ulcer, hepatoprotective, antidiabetic, anti-inflammatory, and analgesic activity (Pinakin et al 2020). Traditional medicinal uses of mahua tree components are described in Table 1.

Table 1. An overview of biological activities or ethnomedicinal properties of *Madhuca* species

Bioactivity	*Madhuca* species	Preparation	Remarks	References
Anti-oxidant activity	*Madhuca longifolia*	Ethanoic bark extract (70 %)	CCl_4-induced hepatic injury in rats: in vitro and in vivo studies	Odili et al (2010)
	M. longifolia	Ethanoic extract of leaves (90%)	Acetaminophen induced toxicity in rats	Palani et al (2010)
	-	Flower extract	Ferric reducing anti-oxidant power	Indu and Annika (2014)
	M. longifolia	Ethanol, acetone, methanol, and water of flowers and fruit	Anti-oxidant activity higher in the acetone extract	Singh (2017), Singh et al (2020)
Antibacterial activity	*M. indica*	Aqueous and methanoic extract of flower	Antibacterial activity against *Bacillus subtilis* and *Klebsiella pneumonia*	Verma et al (2010)
	M. longifolia	AgNPs from flower extract	Antibacterial activity against Gram-positive and Gram-negative bacteria	Patil et al (2018)
	-	Ethyl alcohol extract	High sensitivity of *Staphylococcus aureus*	Bains et al (2020)
Anti-fertility activity	-	Alcoholic extract	Anti-fertility effects in male Swiss albino rats	Ram et al (2011)
		Seed powder in 1% gum acacia	An effective anti-fertility drug in male albino rats	Gopalkrishnan and Shimpi (2011)
Anti-ulcer ability	*M. longifolia*	Ethanolic extract of flowers	Suppression of gastric fluid volume, free acidity, and total acidity	Shrivastava 2018, Patel et al (2019)
Analgesic activity	*M. longifolia*	Aqueous and alcoholic extract flower	Analgesic properties	Dinesh (2001)
	Methanolic extract of *M. indica*	Methanolic extract	Peripheral analgesic efficacy	Shekhawat and Vijayvergia (2010)

Table 1. continued

Bioactivity	*Madhuca* species	Preparation	Remarks	References
Wound healing activity	*M. longifolia*	Ether-benzene-(95%) ethanol extract of leaves	Increased the rate of wound closure and epithelization in rats	Sharma et al (2010)
Hepatoprotective activity	*M. longifolia*	Ethanolic extract of bark	Hepatoprotective against D-GalN* induced hepatotoxicity in rats	Roy et al (2015)
	M. longifolia	Methanolic extract of flowers	Protective action against paracetamol-induced hepatotoxicity in rats	Umadevi et al (2011)
	M. longifolia	Aqueous extract of leaves	Normalize the changes caused by DFC-induced toxicity in rats	Simon and Evan Prince (2018)
	M. longifolia	Ethanolic and methanolic leaf extracts	Potential effect against diclofenac-induced toxicity in rats	Simon et al (2019)
Nephroprotective activity	*M. longifolia*	Aqueous leaf extract	Beneficial effect against DFC-induced renal toxicity in female Wistar albino rats	Prince (2018)

*D-GalN:D-galactosamine; DFC:Diclofenac

Anti-oxidant Activity

Commonly used medicinal plant extracts with standardized polyphenols content were investigated for their anti-oxidant activity (Quassinti et al 2016, Singh et al 2020). The extracts of mahua are known to have natural anti-oxidant properties due to hydroxyl groups, which can serve as hydrogen donors, and the reducing ability of a compound can be an important measure of its potential anti-oxidant activity (Pawar and Bhutani 2004, Verma et al 2014, Singh et al 2020). Free radical scavenging activity using 1, 1-diphenyl-2-picryl hydrazine (BPPH), reducing power assay, and superoxide scavenging activity (Erlinda et al 2020) was used to assess the ethanoic extract of Mahua plants' bark, leaves, or flowers (Prashanth et al 2010, Indu and Annika 2014). The result of the assay was then compared and found to be as potent as the natural anti-oxidant substance ascorbic acid (Prashanth et al 2010). In a study, Odili et al (2010) examined the anti-oxidant properties of the bark extract (70% ethanol) of *M. longifolia*. Reducing power and free radical (hydroxyl and superoxide) scavenging assay was used to test the ethanolic bark extract (in vitro) of the Mahua tree. The tissue glutathione (GSH) and lipid peroxidation levels were used to evaluate in vivo anti-oxidant activity (Odili et al 2010). The test extract has shown dose-dependent anti-oxidant activity in all the models. The anti-oxidant potential of *M. indica* flowers was recorded in a study by Indu and Annika (2014).

They claimed that the extract of *M. indica* flowers showed positive responses attributable to its major nutritional component, such as ascorbic acid. The reducing property of ethanolic bark extract of *M. indica* implies the donating of hydrogen atoms is dose-dependent (Pawar and Bhutani 2004, Palani et al 2010).

Chaudhary et al (2012) investigated the anti-oxidant and free-radical scavenging activity of methanolic extract of *M. indica* bark in various systems. DPPH radical, superoxide anion radical, nitric oxide radical, hydroxyl radical, lipid peroxidation, and total phenolic content assays were carried out to evaluate the anti-oxidant potential of the extract. The percentage inhibition of 40µg mL^{-1} concentration of methimazole (MMI), in a DPPH radical scavenging model was found to be 74.1%. The scavenging of nitric oxide by the plant extract was concentration-dependent, and the IC_{50} value of rutin was 161.7µg mL^{-1}. MMI elicited significant and concentration-dependent superoxide radical scavenging effect with MMI and standard curcumin, which exhibited IC_{50} values of 38.1 and 5.84µg mL^{-1}, respectively. MMI demonstrated significant scavenging activity of OH^- radicals generated from Fe^{2+}-ascorbate-EDTA-H_2O_2 in a concentration-dependent manner. The extract showed a significant dose-dependent free radical scavenging activity in all the models. The extract showed the presence of high phenolic content corresponding to 98.48µg equivalent of gallic acid, and the anti-oxidant activity could be attributed to this.

The leaves and bark of *M. indica* showed significant anti-oxidant activity with IC_{50} value of 61.832µg mL^{-1} and 66.342µg mL^{-1} respectively (Bulbul and Begum 2014). Furthermore, the phenolic content in leaf was 62.43mg of Gallic acid equivalent (GAE) gm^{-1} of extractives. The phenolic content was 61.08mg of GAE gm^{-1} of extractives for bark, which correlated with good anti-oxidant potentiality (Bulbul and Begum 2014).

The more significant amount of ascorbic acid leads to a more potent radical-scavenging effect, as shown by *M. indica* extract (Indu and Annika 2014, Singh et al 2020). Phenolic compounds are the most common type of natural anti-oxidant found in plants, and they can act as reducing agents, free radical scavengers, and possible pro-oxidant complexers (Singh 2017). The study by Singh (2017) reported that ethanol, acetone, methanol, and water extracts of fresh *M. longifolia* flowers and fruit had anti-oxidant activity. The anti-oxidant activity of Mahua flowers and fruit was higher in the acetone extract than in the other solvent extracts (acetone extract>methanol extract>ethanol extract>water extract) as measured by several experiments. The results indicated that the flowers and fruit of Mahua are good sources of polyphenols and natural anti-oxidants. Therefore, they could be useful as functional food ingredients beneficial for human health (Singh 2017, Singh et al 2020).

Antibacterial Activity

In a study by Verma et al (2010) it was reported that the flowers of *M. indica* (aqueous and methanolic extract) showed antibacterial activity against *Bacillus subtilis* and *Klebsiella pneumonia*. For both bacteria, the aqueous extract was more active than methanolic extract [Vasquez et al (2004), Rigano et al (2007), Kaushil et al (2010); Verma et al (2010)]. Patil et al (2018) used the flower extract of *M. longifolia* to reduce silver nitrate into silver nanoparticles (AgNPs), with phytochemicals from the flower extract as a reducing and stabilizing agent. Using the agar-well diffusion method, the antibacterial activity of green synthesized

AgNPs (100-400g mL^{-1}) against diverse pathogenic organisms (*Bacillus cereus*, *Staphylococcus saprophyticus*, *Escherichia coli*, and *S. Typhimurium*) was examined. The synthesized AgNPs have shown potential antibacterial activity against Gram-positive (*B. cereus, S. saprophyticus*) pathogens and Gram-negative (*E. coli*, *S. Typhimurium*) pathogens. The *M. longifolia* flower is a good source for AgNPs synthesis, and synthesized AgNPs is an antibacterial agent in therapeutics (Patil et al 2018, Bains et al 2020, Johar and Kumar 2020). The antibacterial sensitivity profiles of mahua extract (in ethyl alcohol) against two antibacterial strains (*E. coli* and *Staphylococcus aureus*) were performed (Vasquez et al 2004, Bains et al 2020). The results claimed that *S. aureus* showed a high sensitivity to the mahua extract in ethyl alcohol with a significant inhibitory zone (18.00mm). The most dramatic inhibitory zone activity was found in *E. coli* (14mm) with the ethyl alcohol extract of Mahua (Bains et al 2020).

Antifungal Activity

The antifungal activity (antimycotic agents) of saponins isolated as a byproduct from the defatted cake of *M. butyracea* oilseed was reported by Lalitha and Venkataraman (1991). The inhibitory concentrations against plant pathogenic fungi ranged from 500 to 2000ppm. Maximum sensitivity to saponins was shown by *Penicillium expansum*, *Cephalosporium acrimonium*, *Helminthosporium oryzae,* and *Trichoderma viride*. In addition, the saponins caused leakage of cell components and underwent degradation by fungus *T. viride*.

Hepatoprotective Effect

The protective action of *M. longifolia* against paracetamol-induced hepatotoxicity validates the traditional uses of the herb for liver disorders (Kim et al 2011, Ma et al 2016). In a study, Odili et al (2010) reported the hepatoprotective effects of an ethanolic extract (70%) of *M. longifolia* bark. Mahua bark extract (at doses of 200 and 400mg kg^{-1}) and silymarin (at 100mg kg^{-1}) were given/administered in CCl_4-induced hepatotoxicity in rats. The ethanolic extract of mahua bark restored the altered biochemical and physical markers in the CCl_4-induced rats to near-normal levels in a dose-dependent manner. Paracetamol-induced liver damage in Wistar albino rats was used by Umadevi et al (2011) to assess the hepatoprotective function of methanoic extract of *M. longifolia* flowers. The animals with hepatotoxicity caused by paracetamol (2mg kg^{-1}) were given two doses of methanolic extract of *M. longifolia* (100 and 200mg kg^{-1}). The typical cellular architecture was preserved in the liver sections of rats treated with *M. longifolia* extract (intoxicated with paracetamol), confirming the protective effect of the extract. The study demonstrated the protective action of *M. longifolia* against paracetamol-induced hepatotoxicity and validates the traditional uses of the herb for liver disorders. In a similar study, the ethanolic extract of *M. longifolia* bark was tested for hepatoprotective activity against D-galactosamine (d-GalN) mediated hepatotoxicity in rats by Roy et al (2015). In rats, hepatotoxicity was achieved by injecting 400mg kg^{-1} of d-GalN intraperitoneally for five days. Silymarin (100mg kg^{-1}) was used as a reference norm. Serum biochemical parameters such as SGPT (serum alkaline phosphatase), SGOT (serum glutamine oxaloacetate transaminase), ALP (alkaline phosphatase), total cholesterol, and bilirubin (Total and Direct) were used to assess the degree of defense against liver toxicity. The results

The results claimed that the extract of *M. longifolia* bark has hepatoprotective activity against D-GalN mediated hepatotoxicity in rats.

Diclofenac (DFC) is a non-steroidal anti-inflammatory drug used as an analgesic. Overdosing and long-term use has been linked to causing hepatotoxicity (Simon and Evan Prince 2018). Simon and Evan Prince (2018) studied the protective effect of *M. longifolia* aqueous leaf extract against diclofenac-induced toxicity in rats. Aqueous *M. longifolia* leaves extract could normalize the changes caused by diclofenac. The aqueous leaves extract of *M. longifolia* was found to have a protective effect against diclofenac-induced toxicity. Long-term use of diclofenac, as well as overdose, has been linked to side effects such as drug-induced liver damage, gastrointestinal and renal toxicity (Simon et al 2019). The possible impact of ethanolic and methanolic leaf extracts of *M. longifolia* against diclofenac-induced toxicity was investigated by Simon et al (2019). The liver and renal markers, anti-oxidants, and histopathological changes in female Wistar albino rats were tested. The study claimed that the leaf extract of *M. longifolia* (ethanolic and methanolic) had a beneficial effect (hepatic, renal, and gastro toxicity) against diclofenac-induced toxicity, ethanolic leaf extract outperforming methanolic leaf extract. This needs to be researched further to learn more about how the extract affects this type of toxicity.

Antidiabetic Activity

Diabetes is a chronic metabolic condition marked by hyperglycemia that affects about 6% of the world's adult population. There are many allopathic medicines available to treat diabetes, but they come with a slew of side effects, necessitating natural drugs instead (Dahake et al 2010, Jebaseelan and Ramasubramanian 2014, Jimoh 2018, Semwal et al 2020). In a study, Dahake et al (2010) assessed the antihyperglycemic effects of a methanolic extract of *M. longifolia* bark in natural, glucose-loaded, and streptozotocin-induced diabetic rats. The methanolic extract of *M. longifolia* was given to all three animal groups at doses of 100 and 200mg kg^{-1} body weight and the standard drug glibenclamide at a dose of 500mg kg^{-1}. The level of glucose in the blood was measured on days 0, 7, 14, and 21 of treatment. Compared to the regular antidiabetic drug glibenclamide, the extract showed dose-dependent hypoglycemic activity in all three animal models. In alloxan-induced male diabetic Wistar rats, Jebaseelan and Ramasubramanian (2014) investigated the antidiabetic function of *M. indica* leaf extracts. The leaves of *M. indica* were extracted using ethanol, petroleum ether, chloroform, and water, among other solvents. The study revealed that the active constituents were found in both the ethanolic and aqueous extracts. Hyperglycemic and normoglycemic rats were given the ethanolic and aqueous extracts at a 500mg kg^{-1} dosage for 7 days. The plasma glucose concentration was significantly decreased by both the extracts when compared with the control. The study indicated that the methanolic extract of *M. longifolia* was found to be a possible antidiabetic agent, adding scientific support to its use in traditional medicine (Dahake et al 2010, Jebaseelan and Ramasubramanian 2014).

Nephroprotective Activity

Diclofenac, one of the most regularly used non-steroidal anti-inflammatory medicines, has serious adverse effects on the kidney (Yadav 2015). The beneficial effect of aqueous leaf extract of *M. longifolia* against diclofenac-induced renal toxicity in female Wistar albino rats was documented by Prince (2018). Furthermore, the aqueous leaf extract of *M. longifolia* was more effective in normalizing diclofenac toxicity and renal function by restoring anti-oxidants and preventing cellular damage (Badukale et al 2021).

Anti-fertility Activity

Recent scientific research revealed that various herbal medicinal plants had exhibited anti-fertility action in both males and females. Herbal contraceptives are not as effective as pills, but they can be used as a safer option (Solakhia et al 2019). The crude mahua extract possesses anti-fertility action when administered to male albino rats due to a bioactive entity (Jha and Mazumder 2018). Ram et al (2011) evaluated the anti-fertility effect of an alcoholic extract of leaves (200mg kg^{-1} body weight) in male albino rats that was administered orally for 20 days. The transverse section of testes of treated animals showed regressed seminiferous tubules and fewer sperm in the lumen of lobules. The results showed that the alcoholic extract of *M. indica* leaves has anti-fertility effects in male Swiss albino rats. Gopalkrishnan and Shimpi (2011) conducted a study on male albino rats to prove the folklore claims of *M. latifolia* seed as a male contraceptive and anti-fertility agent. Male albino rats were given an aqueous powdered drug (2g kg^{-1} body weight) that proved to be an effective anti-fertility drug. The activity was confirmed by significant reductions in sperm count, biochemical assays, and histopathological investigations. As a result, after the requisite clinical trials, *M. latifolia* seeds could be a reliable herbal alternative (Solakhia et al 2019, Badukale et al 2021).

Pain Relief

Mahua oil has several medicinal properties and is used in rheumatism, headache, and skin diseases (Soni and Dey 2013). However, mahua oil cake is used as an ointment to prevent winter skin cracks. In addition, mahua seed paste is applied to cure muscle fatigue and relieve pain in the muscles and joints. The application also improves the texture and vigor of the skin (Patel et al 2019).

Wound Healing

The wound healing function of ethanolic extracts of *M. longifolia* leaves and bark was investigated by Sharma et al (2010). In the form of a 5%(w/w) ointment, an ethanolic extract of *M. longifolia* leaves and bark was tested for wound healing potential in experimental animals' dorsal excision wounds. The findings were comparable to the standard drug betadine (5%w/w). The antibacterial activity of the plant's ethanolic extract was also tested as proof of its wound-healing ability (Das et al 2016, Das et al 2017). The leaves and bark of *M. longifolia* significantly improved the rate of wound closure and epithelization in rats.

In vivo Acute and Sub-acute Toxicity

The acute and sub-acute toxicity of *M. longifolia* leaf extract on experimental rats was studied by Devi and Sangeetha (2019) using selected hematological, biochemical, and histopathological changes as toxicity indices. At a limit dose of 2000mg kg^{-1} body weight, no morbidity or mortality was observed in the acute sample, proving that the hydrochloric extract of *M. longifolia* was non-toxic and safe to use within range. Furthermore, leaf extract had no impact on general behavior, body weight, food and water intake, or biochemical parameters in sub-acute care, indicating no toxic effect.

Anticancer Activity

Cancer is a public health problem that affects people all over the world. Anticancer activity has been demonstrated in many plants and their isolated constituents (Bhaumik et al 2014, Ebuehi et al 2019). In vitro cytotoxicity of an ethanolic whole plant extract of *M. indica* against lung, neuroblastoma, and colon cancer cell lines was demonstrated by Shaban et al (2012). There was no evidence of growth inhibition in the liver cancer cell line. For the in vitro cytotoxicity test, the Sulforhodamine B dye (SRB) assay was used. Five human cancer cell lines, including lung (A-549), liver (Hep-2), colon (502713 HT-29), and neuroblastoma (IMR-32), were tested in vitro for cytotoxicity. The extract was used at a 100g mL^{-1} concentration for the activity. Plant extract inhibited the development of the lung (A-549) cell line by 83%. The liver (Hep-2) displayed no activity, while the colon 502713 cell line plant extract showed the highest activity level. Plant extract demonstrated 99% activity in the HT-29 liver human cancer cell line and 98% activity in the IMR-32 neuroblastoma cell line, respectively. Via preliminary cytotoxic research, Indu and Annika (2014) confirmed the anti-tumor potential of *M. indica* flowers in a sample. The cytotoxic potential of a methanol extract of *M. indica* flowers was assessed using a cell viability assay on a chicken liver cell line, yielding positive results for cytotoxic activities.

Analgesic Activity

Analgesics are pain relievers that work without disrupting consciousness or interfering with other activities (Shekhawat and Vijayvergia 2010). *M. longifolia* flower extracts, both aqueous and alcoholic, have analgesic properties. The analgesic efficacy of *M. longifolia* was tested using the tail-flick test, hot plate test, and intramuscular administration of aqueous and alcoholic extract doses of 4 to 64mg kg^{-1} body weight for three days on rats or mice (Dinesh 2001, Jha and Mazumder 2018). In a study, Shekhawat and Vijayvergia (2010) evaluated the analgesic activity of the *M. indica* by using another evaluation method like the tail-flick method or hot plate method in rats. The methanolic extract at a dose of 50–200mg kg^{-1} given intraperitonally significantly reduced acetic acid-induced pain in a dose-dependent manner, showing that the extract possessed peripheral analgesic efficacy (Jha and Mazumder 2018).

Anti-ulcer Activity

Gastrointestinal ulcers are a common gastrointestinal condition. The ulcer is caused by misalignments of the gastrointestinal tract (GIT)'s defense and attacking components (Pereira et al 2013, Sofidiya and Awolesi 2015). An ulcer is a local flaw or excavation of the upper section of an organ's or tissue's surface (Devi and Sangeetha 2016). The anti-ulcer action of the *M. indica* plant was demonstrated in male vistar rats. The animal is first made to generate an ulcer using any suitable method, such as a stress-induced ulcer or carrageen-produced ulcer, and then treated with the extract of the tested plant components. The results claimed that the test *Mahua* extract showed active anti-ulcer activity (Seshagiri and Gaikwad 2007).

Furthermore, the anti-ulcer efficacy of an ethanolic extract of *M. longifolia* flowers was tested in albino rats with pylorus ligated ulceration. The presence of phytochemicals in the ethanolic extract of *M. longifolia* flowers at doses of 100, 200, 300mg kg^{-1} body weight resulted in considerable suppression of gastric fluid volume, free acidity, and total acidity, resulting in anti-ulcer characteristics of the extract (Shrivastava 2018, Patel et al 2019). More recently, Simon and Evan Prince (2021) studied the effect of *M. longifolia* aq. leaf extract on rat stomach and intestine against diclofenac-administered toxicity. The tissue samples were examined for anti-oxidant, cytokine, protein expression, and histopathological alterations. The diclofenac-treated rats displayed substantial changes in anti-oxidants, cytokines, protein expression, and pathological abnormalities compared to *M. longifolia*-treated rats.

Other Beneficial Properties

The Indian Pharmaceutical Codex (IPC) classifies the leaves, bark, bulbs, and seeds of *M. latifolia*, *M. longifolia*, and *M. butyracea* as *Madhuca* (Awasthi et al 1975). *Madhuca* is said to be astringent, stimulant, emollient, demulcent, and nutritive in the Ayurvedic system of medicine (Awasthi et al 1975). *M. longifolia* is an ancient plant used to treat wound healing, astringent, stimulant, demulcent, rheumatism, piles, gastropathy, bronchitis, and hemorrhoids in India, Nepal, and Ceylon (Saluja et al 2011, Verma et al 2014). Different parts of *M. longifolia* have shown efficacy in treating epilepsy, diabetes, inflammation, bronchitis, ulcer, and other diseases (Akshatha et al 2013, Roxanne et al 2021). *Madhuca* oil extracted from the seed is used as biofuel, edible fats and has shown good anti-oxidant and antimicrobial properties (Patel and Naik 2010, Khare et al 2018). The flowers are well known for their reducing sugar content and have been used as a cooling agent, astringent, demulcent. Clinical study proves its activity in decreasing the sperm count (Sikarwar and Kumar 2005, Inganakal and Swamy 2013). Leaves of *M. longifolia* are used in Cushing's disease and bronchitis and have anti-oxidant properties (Inganakal and Swamy 2013). The bark has shown remedies for itching, swelling, snake poisoning, and diabetes (Dahake et al 2010, Sunita and Sarojini 2013). The fruit is used as a cure for bronchitis, consumption, and blood diseases. Root paste in mahua liquor is continuously given at bedtime for 3-5 days to expel intestinal worms (Tomar 2009, Dambhare et al 2020). Lalitha and Venkataraman (1987) studied the usefulness of saponins in piscicidal preparations. The saponins were extracted with 80% (v/v) ethanol and were resolved into five components on thin-layer chromatography. Resolution of the total saponins on silica gel column using increasing ratios of methanol in chloroform resulted in the isolation of two compounds, saponins A and B. the LD_{50} and LD_{90} values, to guppy fish (*Lebistes reticulatus*) were 11 and 14ppm, respectively.

Basic Mechanism of Action and Therapeutic Potential

For an extended period, hyperglycemia is the most common cause of diabetes complications. The link between chronic hyperglycemia and tissue damage, on the other hand, is not known. Several processes have been hypothesized, but the significance of protein glycation and the buildup of tissue-advanced glycation endproducts (AGEs) is one of the most intriguing factors (Elosta et al 2012, Badukale et al 2021). Oxidation processes frequently follow the glycation of proteins. This radical simultaneously reduces molecular oxygen to produce oxidizing intermediates/relative oxygen species (ROS), such as $O_2^{\cdot}$, $OH^{\cdot}$, H_2O_2 and α-ketoaldehydes. Biomolecules such as proteins, lipids, and nucleic acids can be harmed by reactive oxygen species (Elosta et al 2012, Devi and Sangeetha 2019). Therefore, the anti-oxidant nutrients in mahua may be a safe and simple complement to traditional therapies targeting diabetic complications. It is now believed that several pharmacological compounds in mahua extract have been investigated for their ability to inhibit glycation and AGEs formation. The hypoglycemia produced by the mahua extract may be due to enhanced glucose uptake at the tissue level (adipocytes), decreased glucose production in the liver, and improved pancreatic-cell efficiency. In addition, it could be due to inhibition of intestinal glucose absorption (Figure 2).

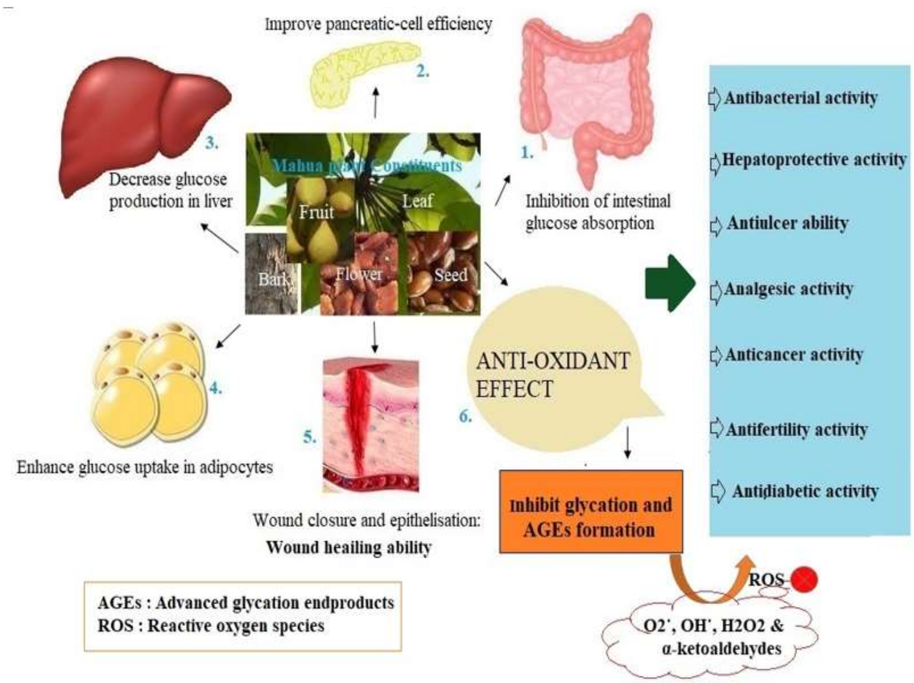

Figure 2. Possible mechanism on applications of mahua plant extract and botanical activities. 1. Mahua extract could cause a blockage of glucose absorption in the intestine; 2. Improve pancreatic-cell efficiency; 3. Decrease glucose production in the liver; 4. Enhance glucose uptake at the tissue level (adipocytes) 5. The leaves and bark of mahua significantly improve the rate of wound closure and epithelization; 6. Mahua is known to have natural anti-oxidant properties.

CONCLUSION AND FUTURE PERSPECTIVES

Mahua plant has medicinal properties, which have been vital for the healthcare of many cultures. The phytochemical analyses found high amounts of saponins, flavonoids, cardiac glycosides, and tannins. Saponins and flavonoids may have been linked to induced peripheral analgesia. Anti-oxidants in mahua extract can scavenge free radicals, prevent undesirable reactions, and suppress oxidative stress diseases. Bioprospecting the mahua trees optimally will improve the economic indices of forest resources development and improve the socio-economical status of the local or tribal people, as well as producing revenue for the government. The biological activities of mahua extract and derived phytochemicals and their applications as pharmacological agents in traditional and modern research are possible. Still, they will first require clinical trials and product development. Moreover, the education of the public for the promotion of mahua for its popularization as a prospective source of enhanced pharmaceutical properties should be globally inspired.

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