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MEDICINAL IMPORTANCE OF *MADHUCA SPS* (SAPOTACEAE) IN AYURVEDA AND MODERN SCIENCE: A REVIEW

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ABSTRACT

Madhuca sps is herbal medicine and commonly known as Mahua or Butternut tree. *Madhuca sps* is used in traditional and folklore systems of medicine widely across India, Nepal, and Sri Lanka for its various pharmacological properties. Past studies reported the presence of secondary metabolites such as saponin, sapogenin, flavonoids, triterpenoid. The whole plant of *Madhuca* sps is rich in phytoconstituent's used to treat infections such as rheumatism, burns, wounds, diabetics and many others. Several pharmacological activities proved its antimicrobial, anti-inflammatory, antioxidants, hepatoprotective, Nephroprotective, and hypoglycemic properties. A study has been carried out and showed significant responses in experimental models. Scientific investigation on various crude and isolated phytoconstituents and their efficacy on diseases proved the future use of *Madhuca sps.* Hence the potential use of *Madhuca* sps is required for assessing the phytochemistry, pharmacological and therapeutic potential is necessary for acquiring traditional knowledge and its scope in today's modern medicine.
Keywords: Sapotaceae, *Madhuca* sps, phytoconstituents, pharmacology, herbal medicine, Phytochemistry

Introduction

From the ayurvedic era, herbal medicines are considered the backbone of a traditional system of medicine, as they have potent pharmacological effects thought to be a potential source of new drug development (Grover JK *et al.,* 2002; Yadav SP *et al.,* 2004). One such herbal medicinal plant *Madhuca* sps is an economic plant growing throughout the subtropical region of Indo-Pak subcontinents with a rich phytoconstituents having therapeutic value. Scientific intervention about the plant and its derivatives shows a broad spectrum of efficacy and safety with comparatively lesser side effects than synthetic molecules. Preliminary screening of *Madhuca* sps such as pet ether, chloroform, methanol, ethanol, alkaloids and aqueous extract, among all the extract methanol and ethanol extract showed a significant response to various pharmacological activities (Triveni *et al.*, 2018). A new triterpene was isolated from *Madhuca longifolia* leaves and the isolated compound was derivative of Madhucic acid (DMA). Both methanolic extract and isolated compound of *Madhuca longifolia* have various pharmacological activities and being a significant response in experimental models (Triveni *et al.*, 2012). Screening of plant bioactive is necessary for isolation and characterization as the plant is of high medicinal value. In this review, the phytochemistry and pharmacological aspects of *Madhuca* sps highlighted.

Botanical description

In India *Madhuca* sps are medium-sized to large deciduous trees, typically 15–16 m high with clustered leaves at the end of branches. The barks are brownish to yellowish-grey. Elliptic flowers are small and cream colored produced in clusters (Padhan *et al.*, 2013). Fruits are 2-6 cm long, fleshy and greenish (Fig. 1). The taxonomy and nomenclature of the plant are presented it in Table 1.

A **B**

Fig. 1: *Madhuca* sps (**A**) Tree (**B**) Fruits

Table 1: Taxonomy and Nomenclature

Binomial Name	***Madhuca longifolia***
Kingdom	Plantae
Order	Ericales
Family	Sapotaceae
Genus	Madhuca
Species	*longifolia*

Distribution

Mahua is an essential economic plant growing throughout the subtropical region of the Indo-Pakistan subcontinent. Mahua trees are found in Nagpur, Dehradun, Chota Siwaliks, Saharanpur, Madhya Pradesh, Orissa, Uttar Pradesh, Jharkhand, Chhattisgarh, Gujarat, Andhra Pradesh, West Bengal, Maharashtra, Bihar, Deccan and Karnataka (Patel Madhumita *et al.,* 2010, Kokate *et al.,* 2008, Bina *et al.*, 2010). *Madhuca* sps known with different names in different states throughout India as presented it in Table 2.

Table 2: Different Names of *Madhuca* sps used in Different Places

Common Name	**Places**
Butter Tree	English
Mahua, Mohwa, Mauwa	Hindi
Mahwa, Maul, Mahwla	Bengali
Mahwa, Mohwra	Marathi
Madhuda	Gujarath
Ippa	Telugu
Illupei, Ewpa	Tamil
Tuppe	Kannada
Poonam, Ilupa	Malyalam
Mahula,Moha,Madgn	Oriya

Nutritional Uses

Mahua tree is of high nutritional value. The seed has a high amount of fats known as Mowrah butter, mahua butter. *Madhuca* fat obtained from fruit oil is used for frying, cooking and the preparation of chocolates. It can be used as a massage oil as it's perfect for moisturizing skin. From a literature review, the flowers of mahua are of the high nutritional valve. The flowers of mahua are rich source of sugar and protein and also have essential minerals such as calcium, iron, phosphorous and potassium (Sengar *et al.,* 2009; Behl *et al.,* 2002; Variers *et al.,* 1995; The wealth of India, 2007).

Medicinal Uses

All parts of the plant have medicinal properties used to treat various ailments such as emollient, demulcent, heating, burn, stimulant, rheumatism, headache, piles, laxative, and astringent properties (Wyk Ben Erik *et al.,* 2004; Shriwastaea *et al.,* 1970).

Industrial Uses

Mahua has industrial applications other than edible and medicinal uses. It is used in manufacturing lubricants and laundry soaps (Puhan Sukumar *et al.*, 2005). Several studies reported on pesticide and insecticidal property and also mahua is used as organic manure (Shashikant *et al.*, 2008).

Sugar syrup

Several reports on Mahua flower for the preparation of sugar syrup because of its sweet property used for fermentation process (Chakma *et al.,* 2011; Srirangam *et al.*, 2010; Kumar Pavan *et al.*, 2011). Water extract of a dried flower was decolourized with a decolorizing agent like charcoal. This activated charcoal is the best agent for sugar syrup

preparation at a concentration of 2-4%. Thus, sugar obtained from the flower is used as a sweetening agent (Khan Salehin *et al.*, 2011).

Traditional Uses

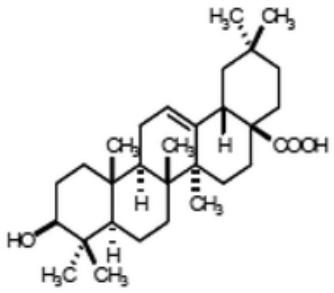
In traditional *Madhuca* plays an immense role in the prevention and cure of many diseases. All parts of the plant show traditional uses for curing many ailments. Flowers are used as a tonic and traditionally used to treat analgesic, diuretic, demulcent, helminths, acute and chronic tonsillitis, pharyngitis, aphrodisiac, and bronchitis, also used as cooling agents, astringent (Chaudhary Anu *et al.*, 2011). Fruits are astringent and primarily used as a lotion in acute and chronic tonsillitis, chronic ulcer and pharyngitis (Pawar Rahul *et al*., 2004; Shivabasavaiah *et al*., 2011). The bark of *Madhuca sps* is an excellent remedy for snake-bite, swelling, itch and fracture. It is also used to treat diabetes mellitus, chronic bronchitis, rheumatism and decoction of the bark for bleeding and spongy gums. Leaves are expectorant and mainly used to treat Cushing's disease, bronchitis, dyspepsia, rheumatism, cephalgia, haemorrhoids, verminous, gastropathy, dermatopathy (Patel Sandip *et al.*, 2011; Alexander Jan *et al.*, 2009; Sidhu *et al.*, 2009). Seeds mainly used to treat skin disease, headaches, laxatives, piles and seed fat have emulusent properties. The roots of *Madhuca sps* are used to treat inflammation, antipyretic, anti-diarrheal as an antioxidant and also used to treat phthisis and scrofula (Devi *et al.*, 2016).

Chemical Constituents

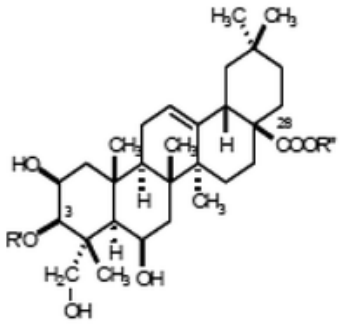
Phytoconstituents *of Madhuca* Sps have been isolated from various plant parts and presented it in Table 3. The bioactive from all parts of the plant were screened for isolation and characterization as per standard protocol. These bioactive showed significant medicinal properties. The mahua tree contains sapogenin, triterpenoids, saponin, alkaloids, flavonoids and glycosides. A new pentacyclic triterpene isolated from leaves namely madhushazone, four new oleanane type triterpene glycosides and madhucoside A and B (Fig.2). Polysaccharides on hydrolysis give D-Glucose, L-Araninose, D-Galactose, L-Rhamose, D-Xylose, and D-Glucuronic acid. Derivative of Madhucic Acid a triterpene isolated from *Madhuca longifolia* Leaves (Fig.3).

Table 3: Phytoconstituents of *Madhuca* Species

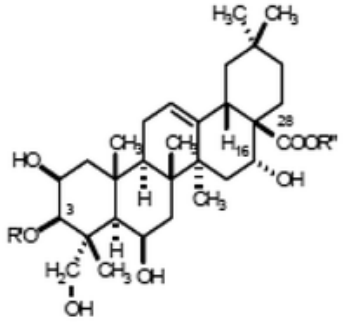
Sl. No	Plant Parts	Phytoconstituents	References
1	Flowers	Vitamin A and vitamin C	30 Patel *et al.*, 2010
2	Bark	Oleanic acids, α-spinasterol, α-amyrin acetate, erythrodiol monocaprylate betulinic acid, α-terpeniol, and sesquiterene alcohol	Awasthi *et al.*, 1968
3	Fruits	Quercetin, dihydroquecertin, β-sitosterol, α and β amyrin acetates	Awasthi *et al.*, 1967; Siddiqui *et al.*, 2004
4	Seeds	Amino acids like glycine, alanine, cysteine, leucine, and isoleucine. Arachidic, oleic, linoleic, myristic, palmitic and stearic acids. Quercetin, Misaponin A and B	Khaleque *et al.*, 1969; Kazuko *et al.*, 2000; Kitagawa *et al.*, 1978; Kaul *et al.*, 1978; Awasthi *et al.*, 1975
5	Leaves	Sitosterol, quercetin, 3-O-Lrhamnoside, stigmasterol, n-hexacosanol, n-octacosanol, myricitin, erthrodiol, β-D-glucoside, β-sitosterol, carotene, 3-O-arabinoside3-β-caproxyolcan-12-en-28-ol,3-galactoside, xanthophylls and new triterpene derivative of Madhucic Acid	Bhatnagar *et al*, 1972; Bhatnagar *et al*, 1972; Iqbal Azhar-khan *et al.*, 1993; Niranjan Reddy *et al.*, 2002; Triveni *et al.*, 2012.



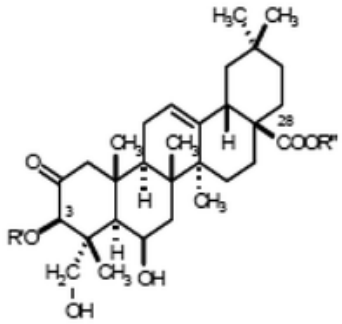
oleanolic acid



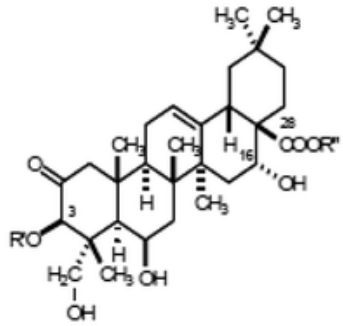
R' = R'' = H: protobassic acid



R' = R'' = H: 16α-hydroxyprotobassic acid



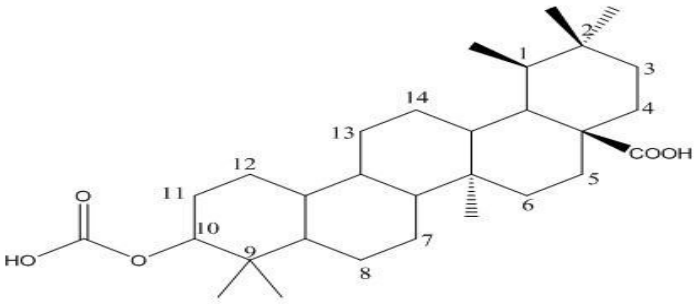
R' = R'' = H: 6β,28-dihydroxy-2-oxooleanolic acid



R' = R'' = H: 6β,16α,28-dihydroxy-2-oxooleanolic acid

Fig. 2: Structure of Phytoconstituents of *Madhuca* sps

10-(carboxyoxy)-1,2,2,6a,9,9-hexamethyldocosahydropicene-4a-carboxylic acid



Derivative of Madhucic Acid

Fig. 3: Major phytoconstituents of *Madhuca longifolia*

Pharmacological Activities

Scientific investigation and authentication of *Madhuca* sps revealed the presence of bioactive compounds like saponin, alkaloids, triterpene and flavonoids proposed to various pharmacological activities. Extensive work was carried out from the bark and leaves of *Madhuca* sps. The experimental studies of different plant parts showed pharmacological activities and are presented it in Table 4.

Table 4: Pharmacological activities of *Madhuca* Species

Plant part	Extract	Pharmacological activity	References
Flower	Methanol and Ethanol	Analgesic, Antiulcer and hepatoprotective	Patel *et al.*, 2011; Banerji *et al.*, 1996; Akshatha *et al.*, 2013
Bark	Methanol and Ethanol	Anti-ulcer, wound healing, hepato-protective, antidiabetic, antioxidant, antimicrobial and anti-inflammatory	Ghosh *et al.*, 2009; Palani *et al.*, 2010, Roy *et al.*, 2015; Tamai *et al.*, 1998; Dahake *et al.*, 2010.
Leaves	Methanol, Acetone, Ethanol, hydroethanolic and chloroform	Anxiolytic, cytotoxic, hepato-protective, neuroprotective, wound healing, antioxidant, anti-hyperglycaemic, antimicrobial	Dhruv Jha *et al.*, 2018; Devi *et al.*, 1995; Harpreet Singh *et al.*, 2014; Israt Jahan Bulbul *et al.*, 2014; Saluja *et al.*, 2011.
Seeds	Methanol, Ethanol and Aqueous	Anti-helminthic, neuropharmacological, antiulcer, anticancer, antifertility, anti-inflammatory, antioxidant	Smeeta *et al.*, 2011; Kalaivani *et al.*, 2013; Shivabasavaiah *et al.*, 2011; Gopalkrishnan *et al.*, 2011
Fruits	Ethanol	Asthma and phthisis	Patel *et al.*, 2011
Roots	Alcoholic	Anti-inflammatory, antidiarrheal, antipyretic and antioxidant	Sunita *et al.*, 2013; Khare 2000

Antimicrobial activity

The methanolic extract of *Madhuca* sps possesses antibacterial activity against *P. aeruginosa, P. vulgaris* and *S. typhi*. The alcoholic extract screened for antimicrobial activity against *E. coli, B. subtilis, M. aureus, A. oryzae, A. niger* has confirmed and revealed significant antimicrobial activities against test microbes (Dahake *et al*, 2010).

Anxiolytic activity

Hydroalcoholic leaves extract of *Madhuca* sps was investigated for anxiolytic activity by closed field test shows a significant decrease in several rearing, assisted rearing and number of squares travelled compared to control group after administration of hydroalcoholic extract of *Madhuca* sps (Dhruv Jha *et al.*, 2018).

Cytotoxic activity

The screening of cytotoxic activity of crude extract of leaves and bark of *Madhuca* sps were investigated by brine shrimp lethality using vincristine sulfate as standard and the result showed significant toxicity for both natural extract of leaves and bark extract (Israt Jahan Bulbul *et al.*, 2014; Saluja *et al.*, 2011).

Wound healing activity

The ethanolic extract of leaves and bark of *M. longifolia* treated animal showed a significant reduction in wound area and period of epithelisation. This potent wound healing activity compared with standard drug betadine (Smita Sharma *et al.*, 2010; Sharma *et al.*, 2010).

Antiulcer activity

Madhuca sps of methanolic and ethanolic extract studied for antiulcer activity using pyrolus ligation and naproxen induced gastric ulcer models in rats. Both the sections possess high antiulcer activity. As per study revealed that inhibition of gastric fluid volume, free acidity and total acidity is due to increase in the protective layer of mucin and decrease the damage or digestive effects of pepsin and acid content (Smeeta *et al.*, 2011; Kalaivani *et al.*, 2013).

Anti-analgesic activity

The nociceptive activity was evaluated using a hot plate and tail flick method to screen the analgesic effect of aqueous and alcoholic extract of *Madhuca*

longfolia flowers possess significance against nociceptive. The aerial parts of *M. indica* have analgesic activity using acetic-induced nociception response (Chandra *et al.*, 2001).

Anti-helminthic Activity

Madhuca Longifolia leaf extract was evaluated for anthelmintic activity and the result was found to be better with methanolic and aqueous extract than standard drug Albendazole (Akhil *et al.*, 2014).

Anticancer activity

Four different solvent extracts such as methanol, acetate, chloroform and ethanol of seeds and fruits of *M. longifolia* used to analyse *in vitro* cancer studies against human cancer cell line (HeLa) and MTT assay for cell growth inhibition. From the investigation all the four extracts showed moderate anticancer activity (Sangameswaran *et al.*, 2012). The acetone and ethanolic extract of *M. longifolia* leaves were assessed to perform a study against carcinoma in mice. The parameter was assessed for survival time, tumor volume, tumor weight, tumor cell count, and body weight hematological studies and *invitro* cytotoxicity. Oral dose administration in mice showed there is increase in survival time, tumor weight, body weight and tumor volume and tumor cell count were significantly reduced and the result was compared with standard drug 5-Flurouracil (Balakrishnan *et al.*, 2012; Asish Baume *et al.*, 2016).

Antioxidant activity

The methanolic and ethanolic extract of *M. longifolia* bark was evaluated for free radical scavenging activity using DPPH, reducing power assay, super oxide scavenging assay. The result found that both the bark extract possesses significant scavenging activity when compared with natural antioxidant gallic acid and ascorbic acid. The *M. longifolia* methanolic extract and isolated compound triterpene for free radicle scavenging showed considerable results compared with the standard the methanolic extract and isolated compound present in the leaves, not only scavenges but also inhibit the generation of free radicals (Triveni *et al.*, 2013). Triterpene antioxidant activity and the section of many plant species showed a positive relationship, according to many reports (Roy *et al.*, 2010; Odili *et al.*, 2010). *In vivo* antioxidant activity of both methanolic extract and isolated compound of *M. longifolia* leaves were studied by screening glutathione (GSH) and lipid peroxidation. Methanolic extract and isolated compound showed statistically significant inhibition of lipid peroxidation by reducing hepatic malonaldhyde (MDA) level, and efficacy was found better than that of CCL_4 induced rats. Methanolic extract and isolated compound of *Madhuca longifolia* leaves increase hepatic glutathione level compared with standard silymarin-induced oxidative stress. The results clearly demonstrated that both extract and isolated blend of *M longifolia* leaves have a protective role against oxidative damage. Evaluation of *In vivo* antioxidant activity of a triterpene isolated from *Madhuca longifolia* L leaves (Triveni SI *et al.*, 2018).

Anticonvulsant activity

The fruit-seeds extract of *Madhuca longifolia* was used to study anticonvulsant activity. The extracts showed protection against seizures and significant reduction in the duration of tonic hind leg extension compared with the standard phenytoin (Mahendar Boddupally *et al.*, 2015).

Neuroprotective activity

Anxiety and depression are most frequently psychiatric conditions commonly found in the person and suffer during their life. Terpenoids have been found to prevent and treat several diseases, including cancer and anti-inflammatory properties (Masur *et al.*, 1980; Ozturk *et al.*, 1996). The methanolic and isolated compound of *Madhuca longifolia* leaves showed alteration in reduction of spontaneous motor activity, marble burying activity and phenobarbitone induced sleep time. Both the compounds showed marked sedative effect by reduction in gross behavior and potential of phenobarbitone induced sleeping time because of metabolic inhibition or action on CNS involved in sleep regulation. Motor activity is a measure level of excitability of CNS; this decrease is due to sedation resulting in depression of CNS. *Madhuca longifolia* enhances barbital hypnosis, which is a good index of CNS depressant activity (Triveni *et al.*, 2012).

Hepatoprotective activity

Invitro and *Invivo* hepatoprotective activity of methanolic extract and isolated compound was investigated for histopathological changes and were observed the protective nature of both compound of *Madhuca longifolia* leaves against necrotic damage of hepato and renal tissue. Blend with different doses and standard silymarin on wet liver weight, liver volume and serum biomarkers such as SGOT, SGPT, ALP, direct and total bilirubin were significantly potential against hepatoprotective (Triveni *et al.*, 2018).

Anti-inflammatory activity

The ethanolic extract and crude alkaloid extract of *Madhuca longifolia* seed cake on experimental models was investigated. Both the section showed inhibitory

effect on carrageenan-induced edema by inhibiting prostaglandin synthesis. Acute, sub-acute and chronic models were used to study the anti-inflammatory effect in saponin and ethanolic extract of *M longifolia* found more valuable response than reference drug diclofenac sodium (Neha Shekhawat *et al.*, 2010; Seshagiri *et al.*, 2007; Ramchandra *et al.*, 2009).

Antihyperglycemic activity

The methanolic extract of *Madhuca longifolia* bark has a potential antidiabetic agent, lending scientific support for its use in folk medicine. The ethanolic extract of *M. longifolia* seed effectively reduced plasma glucose levels in experimental animals producing hypoglycemic effects by stimulating the release of insulin from beta cells (Akash P Dahake *et al.*, 2010).

Anti-fertility activity

The crude seed extract of *Madhuca sps* possess an antifertility effect with marked changes observed and proved its effectiveness upon administration to male albino rats. The above study showed a decrease in testis weight, Seminal vesical, epididymis, vasa deferens, and ventral prostrate this may be due to low plasma of testosterone. Drop in the importance of accessory sex organs resulting in a reduced level of testosterone. Thus seed extract of *Madhuca* has a potential antifertility effect in male albino rats (Shivabasavaiah *et al.*, 2011; Gopalkrishnan *et al.*, 2011).

Spermicidal Activity

The presence of steroids and triterpenoid saponin compounds of *Madhuca* seeds showed marked spermicidal activity reported in several studies (Benerji *et al.*, 2010).

Larvicidal and Ovicidal activity

The plant grows in a dry tropical climate. The aqueous extract of mahua oil cakes was significant against larval growth from egg-sacs of cyst nematodes. The oil cake showed effective against Meloidogyne incognita and proved for larvicidal and ovicidal activities (Ekka *et al.*, 2014).

Insecticidal and pesticidal activity

Mahua cake showed good insecticidal and pesticidal activity against Phyto nematodes and tetranychusurticae (Mani *et al.*, 2003).

Conclusion

Madhuca sps has potential and be validated scientifically to heal a variety of ailments. All parts of *Madhuca* sps showing significant responses against various pharmacological activities. Therefore, *Madhuca* sps is called has "Panacea in ayurvedic medicine or paradise tree". Furthermore, research is essential on its isolation, purification and characterization of bioactive compounds for the depth of traditional knowledge and convincing support for its clinical use as modern medicine.

Conflict of interest: Conflict of interest declared none.

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