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A Comprehensive Review on the Phytochemical Constituents, Traditional Uses, Pharmacological Activities, and Safety of *Mangifera indica leaves*

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Abstract: Mangifera indica L. (mango) belongs to the family Anacardiaceae and is widely cultivated in tropical and subtropical regions. Although the fruit is the economically important part, the leaves have been traditionally used for various medicinal purposes. Mango leaves contain diverse bioactive phytoconstituents, including mangiferin, flavonoids, phenolic compounds, tannins, terpenoids, benzophenones, sterols, saponins and alkaloids. The present review summarizes the available literature on the botanical characteristics, traditional uses, phytochemical constituents, preliminary phytochemical screening, pharmacological activities and safety aspects of M. indica leaves. Published studies reporting biological and pharmacological effects of mango leaf extracts and their major constituents were considered. The reviewed literature indicates that M. indica leaves possess several pharmacological activities, including antibacterial, antioxidant, antidiabetic, antipyretic, hepatoprotective, anticancer, analgesic and anti-inflammatory effects. Mangiferin and other phenolic and flavonoid constituents are considered important contributors to these biological activities. Experimental studies have reported significant analgesic and hypoglycaemic effects, while hepatoprotective and anticancer activities have also been investigated. Available toxicity studies suggest no marked abnormalities following acute administration and prolonged treatment at the studied doses, although some biochemical changes were observed at certain doses. Overall, M. indica leaves represent a promising natural source of bioactive compounds with potential therapeutic applications. Further studies are required to establish their mechanisms of action, standardize extracts, and confirm their efficacy and long-term safety.

INTRODUCTION

Mangifera indica L. (mango) belongs to the family Anacardiaceae and is widely cultivated in tropical and subtropical regions, particularly in South and Southeast Asia. Although the fruit is considered the economically important part of the plant, the leaves have also been traditionally used for various medicinal purposes. Mango leaves are regarded as a valuable source of diverse bioactive and nutritional constituents.

The leaves are often discarded as agricultural waste during pruning; however, their potential as a source of biologically active compounds has received considerable attention.

Mango leaves contain a wide range of phytoconstituents, including mangiferin, flavonoids, phenolic compounds, benzophenones, terpenes, tannins, saponins, glycosides, sterols, and alkaloids. Among these constituents, mangiferin is considered one of the major biologically active compounds and is predominantly reported in the leaves and twigs. Other bioactive and antioxidant constituents, including quercetin, isoquercetin, carotenoids, tocopherols, ascorbic acid, and phenolic acids such as gallic acid, sinapic acid, and vanillic acid, have also been identified in mango leaves.

In addition to phytochemicals, mango leaves have been reported to contain various nutritional constituents, including vitamins A, B, C, and E, as well as minerals such as calcium, iron, potassium, phosphorus, and magnesium. Proteins, amino acids, and organic acids have also been reported in the leaves. The presence of these diverse chemical and nutritional constituents may contribute to the biological and pharmacological potential of *M. indica* leaves.

Traditionally, mango leaf preparations have been used for the management of several health conditions, including diarrhoea, dysentery, cough, bronchitis, asthma, diabetes, respiratory disorders, wounds, and urinary disorders. In addition, *M. indica* leaves have been used in traditional medicinal practices in different geographical regions. Several pharmacological activities have been reported for mango leaf extracts, including antioxidant, antibacterial, antimicrobial, anti-inflammatory, antidiabetic, antifungal, anthelmintic, immunomodulatory, hepatoprotective, and cardioprotective activities. These reported traditional uses, phytochemical constituents, and pharmacological properties indicate that mango leaves represent a promising natural source for further pharmacological investigations.

MEDICINAL USES AND TRADITIONAL BENEFITS

In traditional medicine, dried leaves of *Mangifera indica* have been used for the management of respiratory infections and diabetes. Different parts of *M. indica* have also traditionally been used in the treatment of conditions such as fever, ulcers, gastritis, and diarrhoea. Mango leaves have particularly been used for managing diabetes and relieving respiratory ailments.

The leaves are also used as important ingredients in certain traditional Chinese medicinal formulations, including Mango Anticough Tablets and Yinhua Mango Granules. In some regions of China, particularly Guangxi Province, an aqueous extract of *M. indica* leaves has traditionally been consumed in the form of tea.

In tropical Africa, *M. indica* has been traditionally used as an astringent for the management of toothache, skin diseases, internal hemorrhage, catarrh, and bronchitis. Tea prepared from the leaves has been traditionally used for the treatment of fever and diarrhoea. The leaves have also been used as antidiabetic agents in folk medicine. Furthermore, the ash obtained from burnt leaves has been traditionally applied for the management of burns and scalds, while smoke produced by burning the leaves has been inhaled for relief of throat-related ailments.

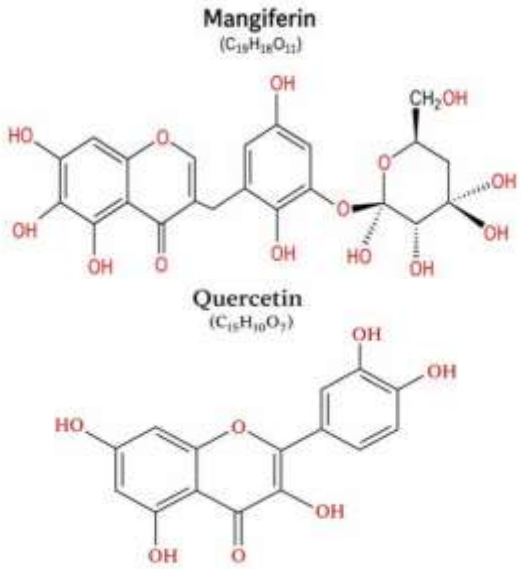
ACTIVE CONSTITUENTS AND PHYTOCHEMICAL PROFILE

The leaves of *Mangifera indica* contain a diverse range of bioactive constituents. Phytochemicals reported in mango leaves can be broadly classified into polyphenols, terpenoids, carbohydrates, sterols, carotenoids, vitamins, fatty acids, and amino acids. Among these, phenolic compounds, including phenolic acids, xanthones, benzophenones, tannins, terpenoids, and flavonoids, constitute important groups of phytochemicals reported in mango leaves.

Mangiferin is considered one of the major bioactive compounds associated with *M. indica*. Other reported constituents include flavonoids, tannins, alkaloids, terpenoids, anthraquinones, saponins, cardiac glycosides, and steroids. The presence of these diverse phytoconstituents has been associated with several reported pharmacological properties of different parts of the mango plant.

The amino acids reported in mango leaves include alanine, glycine, valine, tyrosine, leucine, and γ-aminobutyric acid. Polyphenols and phenolic acids include protocatechuic acid, gallic acid, hyperin, catechin, quercetin, mangiferin, kainic acid, ethyl digallate, ellagic acid, and shikimic acid.

Several volatile and terpenoid constituents have also been reported in mango leaves. These include α-pinene, β-pinene, δ-elemene, taraxerol, β-elemene, α-cubebene, camphene, γ-cadinene, lupeol, friedelin, linalool, β-bulnesene, α-guaiene, humulene, α-farnesene, myrcene, car-3-ene, limonene, β-ocimene, γ-terpinene, and α-terpinolene. Phenylpropene constituents such as estragole, methyleugenol, and elemicin have also been reported. Sterol constituents include α-, β-, and γ-sitosterol.



BOTANICAL DESCRIPTION AND TAXONOMY

Mangifera indica L., commonly known as mango or mango tree, belongs to the family Anacardiaceae. It is an important tropical and subtropical plant and is widely cultivated in several regions. The plant is particularly well known for its edible fruit; however, its leaves are also of considerable medicinal importance.

Botanical Name and Family

- Botanical name: *Mangifera indica* L.
- Common name: Mango or Mango tree
- Family: Anacardiaceae
- Genus: *Mangifera*

- Species: *indica*

Taxonomical Classification

The taxonomical classification of *Mangifera indica* is given below:

Kingdom	**Plantae**
Phylum	Mangoliophyta
Class	Magnoliopsida
Order	Sapindales
Family	Anacardiaceae
Genus	*Mangifera*
Species	*Mangifera indica*

Species of *Mangifera*

Several species are reported under the genus *Mangifera*. Some of the species include:

- *Mangifera altissima*
- *Mangifera caesia*
- *Mangifera persiciformis*
- *Mangifera similis*
- *Mangifera casturi*

MORPHOLOGICAL DESCRIPTION OF *MANGIFERA INDICA* LEAVES

The leaves of *Mangifera indica* are simple, symmetrical, and generally oblong-elliptic to lanceolate in shape. The leaf blade is characterized by an acute apex and an acute base, with an entire and slightly undulate margin. The leaves possess a thick and coriaceous texture and are generally observed in a flat posture. The adaxial surface is dark green, whereas the abaxial surface is light green.

The reported leaf length ranges approximately from 17.5 ± 1.8 to 35.0 ± 3.5 cm, while the leaf width ranges from 3.5 ± 0.3 to 9.5 ± 0.3 cm. In another morphological description, an average leaf length of approximately 15–20 cm and a width of 4.5–5.5 cm has been reported. Variation in leaf dimensions may occur among different varieties.

The petiole is short to long, with the basal portion being relatively thick. Reported petiole length ranges approximately from 1.75 ± 0.2 to 6.0 ± 0.7 cm, while another description reports a petiole length of approximately 1.5–3 cm. The leaf blade shape may be assessed based on the ratio of leaf length to width. Most varieties have been described as narrowly elliptic or lanceolate, whereas a falcate blade shape has been reported in the Ramkela variety. The venation of the leaves is pinnate and has been described as simple craspedodromous or eucamptodromous in different morphological descriptions. A single, stout, and straight primary vein is present and becomes thicker towards the basal region. Approximately 20–22 pairs of moderate secondary veins may be observed at intervals of about 0.5–1.5 cm. These secondary veins are generally arranged alternately and may rarely occur oppositely or become branched. They exhibit an angle of divergence of approximately 45°–65° and are uniformly curved upwards, joining the adjacent secondary veins. Inter-secondary veins are present and are frequently composite, with occasional connections to the secondary veins. Intra-secondary veins are generally absent. Moderate tertiary veins are also present, with a predominantly percurrent course. These veins may be straight to sinuous and can be branched or curved near the midrib. They are generally oblique to the midvein and are predominantly alternate and closely arranged. Well-developed areoles consisting of third-, fourth-, and fifth-order veins are present and contain free-ending veinlets.

Overall, the leaves of *M. indica* exhibit characteristic simple leaf morphology with a coriaceous texture, entire to undulate margin, distinct pinnate venation, and a prominent primary midrib. These morphological characteristics can be useful in the botanical identification and characterization of *M. indica* leaves.

PRELIMINARY PHYTOCHEMICAL SCREENING

Preliminary phytochemical screening of the ethanol extract of *Mangifera indica* L. leaves was carried out using standard qualitative methods to identify the major classes of phytoconstituents. The screening indicated the presence of **alkaloids, flavonoids, tannins, phenolic compounds, and quinones**.

- Alkaloids were identified using Dragendorff's reagent by the formation of a pale-yellow precipitate.
- Flavonoids were detected by Shinoda's test, which produced red coloration.
- Tannins showed a blue-black coloration upon treatment with ferric chloride.
- Phenolic compounds were indicated by dark blue to black coloration with ferric chloride and a creamy-white precipitate with lead acetate.
- Quinones were indicated by the development of yellow coloration or a yellow precipitate following treatment with concentrated hydrochloric acid.

PHARMACOLOGICAL FINDINGS

Antibacterial Activity

Mangifera indica L. has traditionally been used for the treatment of infectious diseases, and its leaves have been reported to contain several phytoconstituents associated with antibacterial activity. The glucoside mangiferin has been reported to be present in the leaves, along with saponins, glycosides, unsaturated sterols, polyphenols, euxanthin acid, mangiferine, mangin, and gallic tannins. Leaf extracts have also been traditionally used as antiseptic agents for the management of burns, scalds, sores, wounds, abscesses, and other infections in humans and animals.

The antibacterial activity of *M. indica* leaf extracts has been investigated against *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853), and *Staphylococcus aureus* (ATCC 25923). The phytochemical classes present in the different extracts were also determined. These findings support the traditional use of *M. indica* leaves and indicate their potential as a source of antibacterial phytoconstituents.

Antidiabetic Activity

The antidiabetic activity of *M. indica* leaves has been investigated using different experimental diabetic animal models. A significant ($P<0.05$) increase in fasting blood glucose concentration was observed in alloxan-induced diabetic rats. Following treatment with the ethanol leaf extract of *M. indica*, a significant ($P<0.05$) reduction in fasting blood glucose levels was observed compared with untreated diabetic rats.

The aqueous extract of *M. indica* leaves was also reported to reduce blood glucose levels in diabetic rats. A significant ($P<0.05$) reduction in blood glucose levels was observed at a dose of 400 mg/kg body weight. However, the mechanism responsible for this activity was not established. A significant reduction in serum cholesterol levels was also observed in diabetic rats treated with the extract.

Long-term administration for 21 days of methanolic and aqueous extracts of *M. indica* resulted in a reduction in blood glucose levels and normalization of other biochemical parameters in diabetic rats. However, no hypoglycaemic effect was observed following single-dose administration of the extracts in normal rats. Further studies were suggested to identify the active principles responsible for the antidiabetic activity.

The **hypoglycemic**- or antihyperglycemic activity of *M. indica* leaf and stem-bark extracts was also investigated in non-diabetic, type 1 diabetic, and type 2 diabetic model rats. Significant antihyperglycemic effects were observed with both leaf and stem-bark extracts in type 2 diabetic model rats when the extracts were administered simultaneously with glucose. A single oral dose of 250 mg/kg body weight was reported to produce a potent hypoglycaemic effect in type 2 diabetic rats.

Furthermore, the antidiabetic activity of *M. indica* leaf extract was investigated using normoglycaemic, glucose-induced hyperglycaemic, and streptozotocin (STZ)-induced diabetic mice. Hypoglycaemic activity was demonstrated by the aqueous leaf extract in these experimental models. Overall, the available findings indicate that *M. indica* leaves possess promising hypoglycaemic and antihyperglycemic potential. However, further investigations are required to identify the active constituents and clarify the mechanisms responsible for these effects.

Antipyretic Activity

Mangifera indica L. has traditionally been used for the management of fever and other health conditions. The plant belongs to the family Anacardiaceae and is an evergreen tree widely distributed throughout tropical and subtropical regions. In the Meru community, *M. indica* is locally known as 'Muembe'. The

plant is believed to have originated in Asia and is now widely distributed throughout tropical and subtropical regions.

In traditional medicine, the bark of *M. indica* has been used by the Meru community for the treatment of conditions including pneumonia, toothache, stomach-ache, cough, chest pain, and wounds. Based on its traditional use, the antipyretic activity of the methanolic stem-bark extract of *M. indica* was evaluated to investigate its potential as an alternative antipyretic agent.

Hepatoprotective Activity

Hepatoprotective activity has been reported for *Mangifera indica* leaves and has been mainly associated with their antioxidant and free-radical scavenging properties. The hepatoprotective potential of *M. indica* leaf extract against heavy-metal-induced toxicity has also been investigated. Ethanolic and methanolic *M. indica* leaf extracts were evaluated for their possible hepatoprotective effects against mercuric chloride-induced oxidative stress in mice.

Mango leaf tea containing mangiferin and phenolic compounds was reported to reduce hepatic fat accumulation and improve liver alterations in high-fat diet-induced obese rats. The protective effect was associated with upregulation of PPAR-α and AdipoR2 expression and reduction of NF-κB p65 and SREBP1c expression. These findings suggest that mango leaves may provide protective effects against fatty liver disease through antioxidant and anti-inflammatory mechanisms.

Anticancer Activity

Anticancer activity has been reported for *Mangifera indica* leaves and has been mainly attributed to polyphenols such as gallotannins, phenolic acids, quercetin, and mangiferin. Leaf extracts have been shown to inhibit cancer cell proliferation, invasion, and migration.

Mangiferin has been reported to suppress the Wnt/β-catenin pathway and induce cell-cycle arrest. Cytotoxic and protective effects have also been demonstrated against various breast, lung, colon, gastric, and liver cancer cell lines. The anticancer effects have been associated with the antioxidant, anti-inflammatory, and antimetastatic properties of the leaf constituents.

Analgesic and Anti-inflammatory Activities

The analgesic and anti-inflammatory activities of ethanol extract of *Mangifera indica* leaves were investigated using experimental animal models. The analgesic activity was evaluated using the acetic acid-induced writhing response model in Swiss albino mice, while the anti-inflammatory activity was assessed using the carrageenan-induced paw edema model in Wistar albino rats. The effects of the leaf extract were compared with diclofenac sodium as the standard drug.

Oral administration of the ethanol leaf extract significantly ($P < 0.01$) reduced the writhing response in the analgesic model. The extract produced 55.8% inhibition of writhing, whereas diclofenac sodium produced 75.28% inhibition.

In the carrageenan-induced paw edema model, the ethanol leaf extract showed a reduction in paw edema; however, the observed effect was not statistically significant.

Overall, the study demonstrated significant analgesic activity of the ethanol extract of *M. indica* leaves, while the anti-inflammatory effect showed a reduction in paw edema without statistical significance.

SAFETY AND TOXICITY EVALUATION

The safety and toxicity of *Mangifera indica* leaf extract (MLE) were evaluated in ICR mice and Sprague–Dawley rats. In the acute toxicity study, ICR mice received MLE at a maximal dose of 18.4 g/kg by oral administration and were observed for toxic reactions and mortality for 14 days. No abnormal responses or distinct lesions in major organs were observed during the study.

Long-term toxicity was evaluated in Sprague–Dawley rats following oral administration of MLE at doses of 100, 300, and 900 mg/kg for three consecutive months. General symptoms, body weight, food consumption, haematological and coagulation parameters, biochemical parameters, and relative organ weights were evaluated. No marked abnormalities were observed during the treatment period, and the effects on body weight and food consumption were not obvious.

Some changes were observed in specific parameters following long-term administration. In male rats, serum triglyceride and cholesterol levels were significantly increased at the high dose, while certain haematological parameters showed significant changes. In female rats, a lower serum potassium level and

some changes in liver, kidney, and adrenal gland weights were observed. However, the study reported no obvious toxicological significance for the changes in AST and TBIL, and no obvious influence on haematology and coagulation function.

Overall, the study reported no obvious abnormalities following acute administration of MLE and no marked abnormalities after three months of long-term administration, although some changes in biochemical parameters and organ weights were observed at certain doses.

FUTURE PERSPECTIVES

Further research on *Mangifera indica* leaves is required to explore their full pharmacological potential. Future studies should focus on the identification and characterization of the specific bioactive constituents responsible for the reported biological activities. More detailed investigations are also required to clarify the mechanisms underlying the observed pharmacological effects.

Further preclinical studies using suitable experimental models may help to establish the efficacy and safety of *M. indica* leaf extracts. Standardization of leaf extracts based on their major bioactive constituents may also improve the consistency and reproducibility of future studies. In addition, further evaluation of the long-term safety and toxicity of the extracts is required before considering their broader therapeutic application.

Overall, systematic investigation of the bioactive constituents, pharmacological mechanisms, efficacy, and safety of *M. indica* leaves may support their potential development as a source of natural therapeutic agents.

CONCLUSION

Mangifera indica L. leaves contain a diverse range of bioactive phytoconstituents and have been traditionally used for various medicinal purposes. The presence of compounds such as mangiferin, flavonoids, phenolic compounds, tannins, terpenoids, and other phytoconstituents may contribute to the reported biological activities of the leaves.

Various pharmacological activities of *M. indica* leaves have been reported, including antibacterial, antidiabetic, hepatoprotective, and anticancer activities. The available findings indicate that mango leaves possess considerable pharmacological potential. Safety and toxicity studies have also reported no marked abnormalities following acute administration and long-term administration at the studied doses, although some biochemical and organ-weight changes were observed at certain doses.

Overall, *M. indica* leaves represent a promising natural source of bioactive constituents with potential therapeutic applications. However, further systematic studies are required to establish their pharmacological mechanisms, efficacy, standardization, and long-term safety and to support their future development as natural therapeutic agents.

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