BIOLOGICAL ACTIVITIES OF MANGO LEAVES *(Mangifera indica)*

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Abstract

Mango leaves (*Mangifera indica*) are widely used in traditional medicine and have gained scientific attention for their broad biological activities. Rich in bioactive compounds like mangiferin, flavonoids, phenolic acids, and terpenoids, mango leaves exhibit antioxidant, anti-inflammatory, anti-diabetic, antihypertensive, antimicrobial, gastroprotective hepatoprotective, neuroprotective and other bioactivities. These activities are linked to their ability to neutralize free radicals, modulate signaling pathways, and inhibit pathogenic microorganisms. Mango leaf extracts show promise in managing metabolic disorders, skin conditions, and age-related damage. Despite promising preclinical results, further clinical studies are needed to validate their therapeutic potential and safety in humans.

Keywords: anti-diabetic, antioxidant, bioactive compounds, *Mangifera indica*, pharmacological potential

1. Introduction

Mango (*Mangifera indica*) is a tropical tree belonging to the Anacardiaceae family, famous for its edible fruit. In addition to the fruit, various parts of the mango tree, particularly its leaves, have been employed in traditional medicine for centuries. Mango leaves are a rich source of bioactive compounds such as polyphenols, flavonoids, terpenoids, and xanthones. One of the most notable compounds in mango leaves is mangiferin, which has garnered attention due to its wide range of reported biological activities, including antioxidant, anti-inflammatory, antimicrobial, anti-diabetic, and hepatoprotective effects (Ediriweera et al., 2017).

Recent studies have highlighted the potential of mango leaves as a natural remedy for various health conditions, particularly metabolic disorders, diabetes, and infections. The compounds present in the leaves contribute to their therapeutic effects, making them a promising candidate for further exploration in clinical applications. Studies have shown that mango leaf extracts exhibit significant potential in controlling blood sugar levels, reducing inflammation, protecting the liver, and combating microbial infections. As research continues to explore the full spectrum of benefits that mango leaves offer, there is growing interest in utilizing them in pharmaceutical and nutraceutical industries.

In the past two years, emerging research has expanded the application of Mangifera indica leaves beyond traditional medicinal use. For instance, the incorporation of mango leaf powder into functional food products and the green synthesis of nanoparticles using mango extracts have demonstrated promising health-promoting properties (Rana et al., 2023; Ramón-Canul et al., 2023). These advancements reflect a growing scientific interest in utilizing mango leaves as a source of bioactive compounds for modern therapeutic and nutritional interventions. This review aims to synthesize the current findings on the biological activities of mango leaves, highlighting their significance in traditional medicine and their potential as future therapeutic agents. By summarizing the emerging research, the review underscores the need for continued exploration of mango leaves in modern medicine.

2. The Role in Traditional Medicine and Phytochemical Composition of Mango Leaves (*Mangifera indica*)

Traditional medicine in Sri Lanka has long employed the leaves and flowers of the mango tree (*Mangifera indica*) to treat respiratory diseases, including lung disorders, cough, asthma, as well as gastrointestinal conditions such as diarrhea and dysentery (Jayaweera, 1980). In Cuba, the bark of the mango tree is used to treat oral ulcers, toothaches, cancer, diabetes, asthma, and gastrointestinal disorders. In Brazil, mango bark is applied in the treatment of scabies (Wauthoz et al., 2007). In Ghana, mango bark is traditionally used to treat hypertension and diabetes, while in Nigeria, mango leaves are employed in managing diabetes and malaria (Etuk et al., 2010). In Bangladesh and India, mango bark has been used for centuries in traditional medicine to treat a broad spectrum of conditions, including diarrhea, gastrointestinal disorders, asthma, mouth ulcers, liver disease, urinary tract infections, diabetes, rheumatism, pulmonary hemorrhage, neurological disorders, cough, and jaundice. The roots are applied for the treatment of ulcers, syphilis, and gonorrhea, while the leaves are used for burns and diabetes management (Parvez, 2016). In Vietnam, mango leaves have been traditionally used in folk remedies to manage symptoms of diabetes. A common preparation involves steeping 3-5 young mango leaves in 200ml of boiling water, allowing the infusion to sit overnight, and consuming it the following morning. Additionally, mature leaves are dried, ground into a fine powder, and taken with warm water twice daily before meals.

Numerous phytochemical investigations have confirmed that mango leaves (*Mangifera indica*) are rich in a wide array of bioactive compounds, which underlie their therapeutic efficacy. These include amino acids, polyphenols, phenolic acids, terpenoids, phenylpropenes, sterols, vitamins, and carotenoids (Shah et al., 2010; Sferrazzo et al., 2022). The amino acid profile of mango leaves comprises alanine, glycine, valine, tyrosine, leucine, and γ-aminobutyric acid. Polyphenolic and phenolic constituents are especially abundant, with key compounds such as mangiferin, protocatechuic acid, gallic acid, hyperin, catechin, quercetin, kainic acid, ethyl digallate, ellagic acid, and shikimic acid. Among these, mangiferin, a major C-glucosyl xanthone, has been widely studied for its diverse pharmacological activities, including antioxidant, anti-inflammatory, antidiabetic, and anticancer effects. The terpenoid content includes α-pinene, β-pinene, δ-elemene, taraxerol, lupeol, linalool, humulene, myrcene, and limonene. Notably, lupeol is associated with anti-inflammatory and anticancer activities. Mango leaves also contain phenylpropenes such as estragole, methyleugenol, and elemicin, as well as plant sterols including α-, β-, and γ-sitosterol, which contribute to lipid-lowering and anti-inflammatory properties. In addition to secondary metabolites, mango leaves possess essential nutrients such as vitamins A and C and various carotenoids, further enhancing their antioxidant potential (Sferrazzo et al., 2022). Collectively, the rich phytochemical composition of mango leaves supports their broad pharmacological applications in traditional and modern medicine.

3. Biological Activities of Mango Leaves

3.1. Antioxidant Activity

In Vietnam, research on Mangifera indica has traditionally concentrated on agricultural aspects such as improving yield, developing new varieties, refining cultivation techniques, and enhancing care and breeding practices. In contrast, the medicinal properties of the mango tree - particularly its leaves - have received comparatively limited scientific attention. Only in recent years have Vietnamese researchers begun to investigate the extraction of bioactive compounds and conduct preliminary evaluations of the biological activities of mango leaves. In particular, Loan (2018) optimized the extraction of mangiferin using ethanol solvent, finding that the ultrasound-assisted extraction method yielded 1.3 times more mangiferin than the traditional Soxhlet method. Moreover, the antioxidant activity of the extract obtained via ultrasound was 11.3% higher, underscoring the method’s potential for enhancing extract quality.

Globally, research on Mangifera indica and its antioxidant potential has evolved significantly over the past decades. As early as 2002, Nunez-Selles et al. investigated the isolation and quantification of phenolic antioxidants, free sugars, and polyols from mango bark, peel, and seeds used in Cuba as dietary supplements. Their study emphasized the strong antioxidant and anticancer potential of polyphenolic compounds, such as catechins and galloyl esters, which play critical roles in modulating enzymes linked to human antioxidant defense systems like superoxide dismutase (SOD) and glutathione peroxidase (GPx).

Subsequent research further reinforced these findings. In 2008, Barreto et al. characterized and quantified polyphenolic compounds in various parts of the mango plant—including bark, kernels, leaves, and peels-highlighting their potent antioxidant properties due to high phenolic content. That same year, Masibo and Qian (2008) provided a comprehensive review of major mango polyphenols and their relevance to human health. Ribeiro et al. (2008) also explored the phenolic profile of Brazilian mango varieties, identifying 12 flavonoids and xanthones, particularly in the Ubá variety, and proposing its industrial potential despite limited commercial use.

Continuing this trajectory, Manthey and Perkins-Veazie (2009) examined the effects of harvest timing and geographic location on the antioxidant profile of five commercial mango varieties. Their findings demonstrated minor variations in β-carotene, ascorbic acid, and total phenolics, suggesting relatively stable antioxidant capacity across cultivars.

By 2012, Fernández-Ponce et al. advanced the field further by employing green technologies to extract antioxidant compounds from mango leaves. Their study confirmed that aqueous extracts not only yielded high concentrations of phenolic compounds but also retained strong antioxidant activity. This positioned mango leaves as a promising raw material for applications in the food, cosmetic, and pharmaceutical industries.

Building on earlier studies, Mohan et al. (2013) assessed the antioxidant potential of methanol extracts and their fractions from mango leaves using the DPPH assay. Notably, the ethyl acetate fraction showed an IC_{50} of 3.55µg/mL - comparable to gallic acid - demonstrating its remarkable antioxidant efficiency.

Most recently, Maharaj et al. (2022) evaluated the seasonal variation in antioxidant activity of methanolic mango leaf extracts, with IC50 values ranging from 12.71 to 14.35µg/mL. These results, consistent with earlier findings by Kabir et al., reaffirmed the high antioxidant potential of mango leaf extracts across different conditions.

This chronological progression illustrates a clear evolution in global research - from basic characterization of antioxidant compounds to the application of advanced extraction techniques -underscoring a growing emphasis on technological innovation and commercial application. In contrast, Vietnamese research remains relatively nascent, with recent efforts only beginning to explore similar directions in bioactive compound extraction and preliminary biological evaluation.

3.2. Anti-inflammatory Activity

Jiang et al. (2012) investigated the anti-inflammatory effects of ethanolic mango leaf extract in an arthritis-induced mouse model. Mice were given monosodium urate to induce inflammation, followed by oral administration of mango leaf extract (50, 100, 200mg/kg) for nine days. Results showed significant reduction in ankle swelling and downregulation of TNF-α and IL-1β at both the protein and mRNA levels, confirming the extract's anti-inflammatory potential.

In 2013, Khu and colleagues (2013) studied the acute toxicity and anti-inflammatory effects of the liquid extract of Yên Châu round mango leaves from Sơn La. The results indicated that the liquid extract of Yên Châu round mango leaves administered orally did not exhibit acute toxicity in white rats at a dose corresponding to 490.10 g of raw material/kg, more than 81 times the estimated human dose. The liquid extract at doses of 8g, 16g, and 32g of raw material/kg/day, administered for four consecutive days, demonstrated anti-inflammatory effects in two experimental acute inflammation models, comparable to aspirin at a dose of 200mg/kg.

3.3. Antidiabetic Activity

Many studies have highlighted the antidiabetic potential of mango leaves. The ethanol extract of Mangifera indica exhibited significant alpha-amylase inhibitory activity with an IC50 value of 37.86 ± 0.32µg/mL, which is notably lower than the IC50 value of acarbose (83.33 ± 0.75µg/mL). This indicates that Mangifera indica may be more effective in inhibiting alpha-amylase activity and could serve as a promising natural alternative for managing postprandial hyperglycemia in type 2 diabetes (Dineshkumar et al., 2010).

The study by Aderibigbe et al. (1999) found that the aqueous extract of Mangifera indica leaves (1g/kg) had no effect on blood glucose levels in normoglycaemic or streptozotocin (STZ)-induced diabetic rats. However, the extract demonstrated significant hypoglycaemic effects in glucose-induced hyperglycemia when administered either simultaneously with glucose or 60 minutes prior, with results comparable to chlorpropamide (200mg/kg). In a separate study, Miura et al. (2001) investigated the antidiabetic properties of mangiferin, a xanthone compound from Mangifera indica, which exhibited potent α-glucosidase inhibitory activity. This inhibition results in reduced postprandial glucose levels, making mangiferin a promising candidate for diabetes management.

Gondi and Rao (2015) examined the ethanol extract of mango peel (*Mangifera indica L.*) for its inhibition of α-amylase and α-glucosidase activities and its improvement of diabetes-related biochemical parameters in streptozotocin (STZ)-induced diabetic rats. The beneficial effects of the peel extract may be through various mechanisms, such as increasing plasma insulin levels, reducing oxidative stress, and inhibiting carbohydrate-hydrolyzing enzyme activities by its bioactive compounds.

Ganogpichayagrai et al. (2017) investigated the antidiabetic and anticancer activities of mango leaves, showing that mango leaf extract and its active compound, mangiferin, exhibited in vitro inhibitory potential on key enzymes involved in glucose metabolism, namely α-amylase and α-glucosidase. Mango leaf extract (≥200µg/ml) demonstrated cytotoxic effects against tested cancer cell lines. Both mango leaf extract and mangiferin increased the survival rate of skin fibroblasts.

Notably, Nguyen & Dai (2018) conducted a study on the hypoglycemic, lipid-regulating, and antithrombotic effects of mango leaves in diabetic rats. The results showed that the extract had the ability to lower blood glucose levels in diabetic rats at doses of 150, 300, and 450mg/kg without causing acute toxicity. In addition, the extract significantly reduced total cholesterol, triglycerides, and LDL levels, while markedly increasing HDL levels in diabetic rats compared to the pathological control group. These findings suggest the beneficial role of mango leaves in reducing blood glucose levels in individuals with diabetes.

3.4. Antihypertensive Activity

Gururaja et al. (2017) demonstrated that methanol mango leaf extract significantly reduced blood pressure in mice by lowering cholesterol levels and aqueous extract has also been shown to have antihypertensive effect (Morsi et al., 2010). Ronchi et al. (2015) explored the antihypertensive effects of Mangifera indica leaves using in vitro and in vivo assays. The ethanol extract of mango leaves was fractionated into dichloromethane, n-butyl alcohol, and aqueous fractions. The dichloromethane fraction exhibited the highest levels of flavonoids and total phenolic content, along with significant antioxidant activity. In vitro, this fraction demonstrated angiotensin-converting enzyme (ACE) inhibitory activity comparable to captopril. Chronic administration of this fraction to spontaneously hypertensive rats (SHRs) resulted in a reduction of mean arterial pressure (MAP) and normalized baroreflex sensitivity, similar to the effects observed with enalapril treatment. Additionally, the dichloromethane fraction reduced cardiac hypertrophy in these rats. Phytochemical analysis identified compounds such as quercetin, gallic acid, ferulic acid, and apigenin in the dichloromethane fraction, which are known for their cardiovascular benefits.

Ramón-Canul et al. (2023) evaluated the antihypertensive potential of cookies formulated with ground Mangifera indica leaves. The cookies containing 10% and 15% ground mango leaves exhibited increased crude fiber content and demonstrated antioxidant activity through DPPH, ABTS, and FRAP assays. While the study primarily focused on antioxidant and antidiabetic properties, the inclusion of mango leaf powder suggests a potential avenue for incorporating antihypertensive agents into functional foods.

3.5. Antibacterial Activity

Diso et al. (2017) demonstrated that chloroform and aqueous extracts effectively inhibited *Staphylococcus aureus*. Methanol and acetone extracts also showed broad-spectrum antibacterial activity against *Shigella flexneri, E. coli, S. aureus, Streptococcus pyogenes,* *Bacillus cereus, P. aeruginosa, S. pneumoniae, Proteus mirabilis,* and *Salmonella typhi* (Doughariand & Manzara, 2008; Islam et al. 2010). Notably, acetone extract was effective against drug-resistant *S. typhi* (Hannan et al., 2013), and ethanol extract suppressed *Streptococcus mutans* growth (Chandrashekar et al., 2016). Madduluri and colleagues (2013) reported the inhibitory effects of ethanol and methanol extracts against bacterial strains such as *Klebsiella pneumoniae, Salmonella typhimurium, S. aureus,* and *B. cereus*.

3.6. Antifungal Activity

Many studies have shown the antifungal properties of mango leaf extract. Kanwal et al. (2010) evaluated the antifungal activity of five flavonoids isolated from mango leaf extracts against five fungal species: *Alternaria alternata, Aspergillus fumigatus, Aspergillus niger, Macrophomina phaseolina,* and *Penicillium citrii*. The results indicated that all five flavonoids significantly suppressed fungal growth, with the highest concentration (1000 ppm) reducing the growth of different target fungal species by 63-97%, 56-96%, 76-99%, 76-98%, and 82-96%, respectively. This study highlights the potential of mango leaf-derived flavonoids as natural antifungal agents.

Rana et al. (2023) explored the use of green-synthesized silver nanoparticles derived from both *Azadirachta indica* and *Mangifera indica* extracts. The nanoparticles were tested for antimicrobial efficacy against various plant pathogens. The study demonstrated that *Mangifera indica*-mediated nanoparticles had notable inhibitory effects on a range of fungal and bacterial phytopathogens. The antimicrobial activity is likely attributed to the bioactive compounds in the leaf extract, which facilitate nanoparticle synthesis and enhance their biological effectiveness.

3.7. Antiparasitic Activity

Bidla et al. (2004) reported that mango leaf extract (methanol/chloroform) inhibited the growth of *Plasmodium falciparum*, the parasite responsible for malaria. Malann et al. (2014) assessed the antiplasmodial activity of various extracts and fractions of *Mangifera indica*. The dichloromethane extract produced the highest survival time in infected animals and significantly reduced parasitemia, suggesting its potential as an antimalarial agent. Alea and colleagues (2019) investigated the anthelmintic properties of *Mangifera indica* leaf extract against *Ascaris suum* (roundworms). The extract caused paralysis and death of the worms in a dose-dependent manner, outperforming the synthetic anthelmintic drug mebendazole in efficacy.

3.8. Gastroprotective Activity

Severi et al. (2009) demonstrated that oral administration of *Mangifera indica* leaf decoction (AD) at doses up to 5g/kg caused no toxicity and significantly reduced gastric lesions induced by HCl/ethanol, absolute ethanol, non-steroidal anti-inflammatory drug and stress in rodents, with effective doses at 250, 500, and 1000mg/kg. Phytochemical analysis revealed that AD contains 57.3% total phenolic compounds, including mangiferin and C-glucosyl-benzophenone, which may contribute to its gastroprotective effects. Hydroalcoholic extracts of mango peel (LPe, 30mg/kg) and pulp (LPu, 10mg/kg) significantly reduced gastric damage in naproxen-induced gastric injury in rats by decreasing malondialdehyde (MDA) levels and myeloperoxidase (MPO) activity (Ferreira Gomes et al., 2022). The extracts also restored glutathione (GSH) content to normal levels and were rich in phenolics (69.50-5287.70mg GAE/100g), carotenoids (651.30-665.50µg/100 g), and vitamin C (21.59-108.19mg/100g), contributing to their antioxidant and gastroprotective effects.

3.9. Hepatoprotective Activity

Ebeid et al. (2015) investigated the hepatoprotective and antioxidant properties of wheat, carrot, and mango when used as nutraceutical agents in a rat model of carbon tetrachloride (CCl_4)-induced liver toxicity. The study demonstrated that supplementation with these natural products significantly reduced oxidative stress markers and improved liver histopathology. Among the tested agents, mango exhibited notable efficacy in mitigating hepatocellular damage, suggesting its potential therapeutic role in liver protection.

3.10. Neuroprotective Activity

Kawpoomhae et al. (2010) evaluated the antioxidant and neuroprotective properties of standardized extracts from *Mangifera indica* (mango) leaves. The study found that the extracts exhibited strong free radical scavenging activity and effectively protected neuronal cells from oxidative stress-induced damage. These findings highlight the potential of mango leaf extract as a natural neuroprotective agent for preventing or mitigating neurodegenerative conditions.

3.11. Immunostimulatory Activity

Shailajan et al. (2016) explored the antimycobacterial and immunomodulatory effects of a standardized extract derived from *Mangifera indica* leaves. Their findings revealed that the extract exhibited notable inhibitory activity against *Mycobacterium tuberculosis* strains, along with the ability to modulate key immune responses. These results suggest that mango leaf extract holds promise as a complementary therapeutic agent in managing tuberculosis and immune-related conditions.

3.12. Analgesic Activity

Islam et al. (2010) investigated the analgesic, anti-inflammatory, and antimicrobial properties of ethanol extracts from mango leaves. The study specifically highlighted that the mango leaf extract exhibited significant pain-relieving effects in animal models, comparable to standard analgesics. These findings support the potential use of mango leaves as a natural alternative for managing pain and inflammation.

4. Conclusion

Mangifera indica leaves hold significant promise for future therapeutic applications due to their rich content of bioactive compounds, including mangiferin, flavonoids, and phenolic acids. Their potent antioxidant, anti-inflammatory, antidiabetic, and antimicrobial properties make them strong candidates for the development of treatments targeting chronic diseases such as diabetes, cardiovascular disorders, neurodegenerative conditions, and infections. Furthermore, the immunomodulatory and hepatoprotective effects of mango leaf extracts suggest potential use in managing inflammatory liver diseases and boosting immune health. In addition to pharmaceuticals, mango leaves may serve as active ingredients in nutraceuticals and functional foods aimed at health maintenance and disease prevention. Their skin-protective and anti-aging effects also open opportunities in the cosmetic and dermatological industries. However, further research is necessary to clarify the molecular mechanisms underlying these effects and to validate their safety and therapeutic efficacy through rigorous clinical studies.

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