**Mango (*Mangifera indica L*.) Leaves: Phytochemical Profile, and Health-Promoting Bioactivities**

Alireza Farahnak1

1\_Bachelor student in microbiology , Faculty of Technical Engineering , University of Science and Arts of Yazd

**Abstract**

Mango leaves are excellent in balancing blood sugar levels in diabetic patients. Those leaves contain tannins called anthocyanidins that may help in treating early diabetes. It also contains 3beta taraxerol and ethyl acetate, which help treat hyperglycemia (increased blood sugar levels).

Mangifera indica L. belongs to the family of Anacardiaceae and is an important fruit from South and Southeast Asia. India, China, Thailand, Indonesia, Pakistan, Mexico, Brazil, Bangladesh, Nigeria, and the Philippines are among the top mango producer countries. Leaves of the mango plant have been studied for their health benefits, which are attributed to a plethora of phytochemicals such as mangiferin, followed by phenolic acids, benzophenones, and other antioxidants such as flavonoids, ascorbic acid, carotenoids, and tocopherols. The extracts from mango leaves (MLs) have been studied for their biological activities, including anti-cancer, anti-diabetic, anti-oxidant, anti-microbial, anti-obesity, lipid-lowering, hepato-protection, and anti-diarrheal. In the present review, we have elaborated on the nutritional and phytochemical profile of the MLs. Further, various bioactivities of the ML extracts are also critically discussed. Considering the phytochemical profile and beneficial effects of the MLs, they can be used as a potential ingredient for the development of functional foods and pharmaceutical drugs. However, more detailed clinical trials still needed to be conducted for establishing the actual efficacy of the ML extracts.

**Keywords:**

mango leaves, biological activities, phenolic bioactives, polysaccharides, health promoting effects

## Introduction

Mango (*Mangifera indica L*.) ascribed to the family Anacardiaceae has been adjudged as the vital traditionally significant and one of the most economically important tropical fruit crop globally [1]. Mango is an evergreen tree with a lot of traditional medicinal resources apart from its very famous fruits. Mangoes are native to the South and Southeast Asia, and in 2018, the global production of mangoes (the report includes guavas and mangosteens) was 55.4 million tonnes. The largest mango producing countries are India, China, Thailand, Indonesia, Pakistan, Mexico, Brazil, Bangladesh, Nigeria, and the Philippines. Apart from its economically important portion (fruit), large amounts of crop residues such as leaves, flowers, stem, and bark are generated during pruning, which causes complications of disposal to the farmers. Mango leaves (MLs) are the potential source of minerals, viz. nitrogen, potassium, phosphorus, iron, sodium, calcium, magnesium, and vitamins, viz. A, B, E, and C. A major bio-macromolecule present in mango leaves is protein. MLs can be utilized as an alternative source of livestock feeding in developing countries for alleviating the food shortage for livestock.

Extracts of the MLs have been utilized for traditional medicines to cure diabetes, bronchitis, diarrhea, asthma, kidney, scabies, respiratory problems, syphilis, and urinary disorders [2,3]. The most active biological constituent of MLs is mangiferin, followed by phenolic acids, benzophenones, and other antioxidants such as flavonoids, carotenoids, quercetin, isoquercetin, ascorbic acid, and tocopherols. Mangiferin is the main contributor of most of the biological activities of MLs extract. MLs have a great scope of valorization as they are recognized to possess varied phytochemical, biological, and pharmacological properties, viz. anti-microbial, antioxidant, anti-diabetic, anti-tumour, and immunomodulatory effects. ML oil (MLO) contains monoterpenes, sesquiterpenes, minor quantities of other analogues, and trace amounts of non-terpenoid hydrocarbons and oxygenated hydrocarbons. The essential oil from MLs also possesses bacteriostatic properties and contains several antimicrobial constituents such as α-gurjunene, trans-caryophyllene, α-humulene, α-selinene, and camphor. The benzophenone derivatives in MLs possess significant α-glucosidase inhibitory and immunosuppressive activities. There are several reviews that have been developed to discuss the bioactive compounds and health promoting effect of mango fruit/pulp [4,5,6,7], whereas others contain a scattered compilation of literature on mango seeds, MLs, and mango bark [8,9].

There is no critical compilation on the crucial information on MLs’ bioactives and associated bioactivities. Therefore, the current review will be focused on the nutritional and phytochemical profile of the MLs. The review also delivers important health promoting activities of the MLs extracts.

## Phytochemical Profile

## Generally, MLs are burnt or discarded, considered as an agricultural crop waste. However, the medicinal properties of MLs make them a useful ingredient in traditional folk tea preparation, and to treat diabetes and respiratory diseases in Asian and African countries. they a contain superior quality of bioactive polysaccharides, proteins, lipids, vitamins, and minerals. Bioactive phytochemicals present in MLs extracts have a high potential in terms of biological and pharmacological activities viz. antioxidant, antidiabetic, anti-inflammatory, antimicrobial, antiviral, immunomodulatory, anti-obesity, antiallergic, antifungal, antiparasitic, antidiarrheal, antipyretic, and anti-tumour activities [9,27]. Phytochemicals present in MLs can be broadly categorized as polyphenols, terpenoids, carbohydrates, sterols, carotenoids, vitamins, fatty acids, and amino acids. Among them, total phenolic compounds (TPC), including phenolic acids, xanthones, benzophenones, tannins, terpenoids, and flavonoids, are most abundant in ML. Several epidemiological studies have proved the activities of TPC against chronic diseases viz. cancer, diabetes, and cardiovascular and neurodegenerative diseases [28]. TPC modulates numerous physiological processes such as enzymatic activity, cell proliferation, signal transduction pathways, and cellular redox potential to fight against chronic pathologies [29].

##

## TPCs possess an aromatic benzenoid-ring attached to a hydroxyl group. Among all TPCs, mangiferin particularly is a potential bioactive compound in ML. In recent years, diets enriched with bioactive compounds are getting much attention due to their potential to minimize the risks of several chronic diseases’ development. Pan et al. [30] stated mangiferin (7.43%) is a major constituent in ML extract, whereas other compounds reported in higher concentration include quercetin-3-O-β-Dglucoside (0.82%), quercetin-3-O-β-D-galactoside (0.86%), and isoswertisin (1.25%). Mangiferin is a natural xanthonoid polyphenol antioxidant and plays role in ameliorating insulin resistance, modulating glucose metabolism, lowering cholesterol synthesis, and inhibiting the expression of the inducible nitric oxide synthase and TNFα [34]. TPC and total flavonoid content in crude, MeOH, and EtOAc extracts of ML was reported as 230, 99, and 186, and 131, 46, and 191 mg/g, respectively. The phytochemical investigation of MeOH, EtOAC, and crude extracts of ML using ultra high-pressure liquid chromatography (UPLC)-MS/MS identified several secondary metabolites, including eleven phenols, ten benzophenones, nine flavanols, four derivatives of gallotannins, four xanthones, and seven terpenoids. The EtOAC extract showed higher TPC and total flavonoids (TFC) compared to the MeOH extract [13]. Ouf et al. [18] identified 83 compounds in ML essential oils of five cultivars using gas chromatography–mass spectrometry (GC–MS). Among them, trans-caryophyllene (8.06–18.88%), α-selinene (4.33–16.92%), and α-humulene (8.48–25.98%) were found in the higher concentrations. Gu et al. [31] isolated and characterized four benzophenone derivatives, manindicin A, manindicin B, mangiferin, and norathyriol from ML extract by nuclear magnetic resonance (NMR) spectroscopic technique. Some of these compounds exhibited significant α-glucosidase inhibitory, immunosuppressive, and antioxidant activities. These studies proved that ML can be served as potential source of food supplement for improving human health.

## Biological Activities of the Mango Leaves Extract

## Anticancer Activities

## Cancer is one of the most prevalent global threats after cardiovascular disease. Thus, there is an imperative need to undertake novel treatment strategies to counter this global issue. Polyphenols present in MLs like gallotannins, phenolic acids, quercetin, and mangiferin exhibit chemo-preventive effects against various cancer types due to their anti-inflammatory and antioxidant effects [35]. Antitumoral activities of MLs extract are mainly attributed to the primary bioactive xanthone glucoside, mangiferin. These compounds are demonstrated to suppress several cancers by impeding their invasion, migration, and proliferation [36]. Mangiferin is found to overturn the transition from epithelial-to-mesenchymal in MCF7 breast cancer cell lines by inhibiting Wnt/β-catenin pathway and by downregulating the expression of specific enzymes (5′Nucleotidase, γ-GT, and aryl hydrocarbon hydroxylase) in lung cancer bearing albino mice [37,38]. It also suppresses the levels of Akt phosphorylation and cyclin B1, causing spontaneous cell cycle arrest in G2/M phase. It was also found to instigate Nrf2-mediated antioxidant activities at a concentration of 50 μM, with no influence of myeloid leukaemia cell sensitivity to chemotherapeutics [39]. Mangiferin was also found to mitigate the oxidative stress and inhibit methylmercury-induced DNA damage in human neuroblastoma cell line IMR-32 [40]. The anti-invasive and antimetastatic activities of mangiferin could also be attributed to its ability to regulate the expression of metalloproteinases, which determines the cell proliferation and inhibits epithelial–mesenchymal transition, eventually causing a loss in cell adhesion.

## A study was conducted to investigate the antitumoral effects of ML extracts on (MDA-MB-231) highly and (MCF7) minimally invasive breast cancer cells and (MCF10) non-tumorigenic cells at IC50 >200 µg/mL [41]. The leaf extracts displayed protective properties against cytotoxic and oxidation effects on breast cancer cell lines and minimal damage to non-carcinogenic cells. MLs extracts with a high concentration of homo-mangiferin and methyl gallate were found more effective against MDA-MB-231 cells, while gallotannins showed cytotoxicity against MCF7 cells. In another study, ethanolic extract of mango leaves at a concentration of IC50 >200 µg/mL exhibited cytotoxic activities against lung fibroblast (ATCC CLS 300421,WI-38 VA-13 subline 2RA), skin fibroblast (ATCC CRL1947, CCD-986SK), colon adenocarcinoma (ATCC CCL227, SW 620), gastric carcinoma (ATCC HTB103, Kato-III), liver hepatoblastoma (ATCC HB8065, Hep-G2), bronchogenic carcinoma (ATCC HTB-168TB, Chago K-1), and ductal carcinoma (ATCC HTB20, BT474) [42]. Similarly, MLs extract was used to synthesize silver nanorods. These nanorods exhibited strong in vitro cytotoxicity, antioxidant, and anticancer activities at 10% w/v against colorectal carcinoma and breast cancer cell lines (HCT-116, MCF-7) [43]. Anti-cancer potential of the mangiferin is schematically depicted in Figure 2.

##

## Figure 2

## Anti-Diabetic Activity

## MLs have been widely claimed as effective ethnomedicine against DM due to their anti-diabetic bioactive constituents like benzophenones (mangiferin) and flavonoids (quercetin and its glucoside forms). One of the best effective approaches in the cure of DM is the inhibition of α-amylase and α-glucosidase enzymes, which regulate postprandial glucose absorption [47]. A comparative analysis of mangiferin and MLs extract was done to check the efficiency of each extract to inhibit α-glucosidase enzymes. MLs extracts at a concentration of 100, 250, and 500 mg/mL caused up to 77.8%, 83.4%, and 95.7% inhibition of α-glucosidase, respectively. At the same time, mangiferin at a concentration of 10, 25, and 50 resulted in 86.85%, 92.35%, and 99.11% inhibition of α-glucosidase, respectively. It can be inferred that mangiferin is an active ingredient in the inhibition of α-glucosidase enzyme activity and in managing the diabetic condition [48]. Ganogpichayagrai et al. [42] evaluated the anti-diabetic activity of mangiferin and MLs extract through the inhibition of α-glucosidase and α-amylase in vitro. Authors reported that mangiferin showed strong inhibition of rat α-glucosidase with a median inhibitory concentration IC50 of 433.3 µg/mL and MLs extract showed potent inhibition of yeast α-glucosidase with the IC50 of 50.3 µg/mL. Saleem et al. [49] evaluated the anti-diabetic potential of MLs extract (550, 750, 950 mg/kg) cv. Ratol in alloxan monohydrate (150 mg/kg) induced diabetes in albino mice. Authors found that the administration of MLs extract in chemically induced diabetic mice reduced the postprandial glucose level, prevented the surge of glucose in the blood, and improved the lipid profile along with body weight. Different bioactive compounds have been isolated from the MLs extract and demonstrated their anti-diabetic potential. Gu et al. [31] isolated and characterized four bioactive compounds as manindicins A and B, mangiferin, and norathyriol (deglycosylated mangiferin) from MLs extract. Authors revealed that norathyriol exhibited strong α-glucosidase inhibition with IC50 of 4.22 ± 0.19 μg/mL, which was four-fold effective with respect to commercial inhibitor acarbose (IC50: 16.28 ± 1.22 μg/mL), while mangiferin (IC50: 32.11 ± 2.01 μg/mL) and manindicin A (IC50: >300 μg/mL) and B (>300 μg/mL) displayed weaker α-glucosidase inhibition. The less inhibitory potential of Mangiferin may be due to its molecular size and polarity. The replacement of glucose moiety with hydrogen may weaken the steric hindrance during mangiferin–enzyme interaction and enhance the inhibitory potential of mangiferin towards α-glucosidase [31]. The anti-diabetic potential of the mangiferin is schematically shown in Figure 3. The anti-diabetic potential of mangiferin was also demonstrated, as it increases insulin sensitivity and inhibits α-glucosidase [50]. Similarly, for quercetin, α-glucosidase inhibition was substantially higher than that of its 3-O-glucoside hyperoside [51]. Bhuvaneshwari et al. [52] investigated the anti-diabetic activity of tender and mature leaves of totapuri cultivar of mango, and authors found that tender leaves extract (500 mg/kg) efficiently inhibited the α-amylase with IC50 22.01 µg/mL, while mature leaf extract (500 mg/kg) exhibited the α-glucosidase inhibition with IC50 21.03 µg/mL. Findings suggest that bioactive compounds from the ML can be effective in reducing the risk of diabetes.

## Diagram  Description automatically generated

## Figure 3

## Antioxidant Activities

## Many recent studies have shown that free radicals generated during the metabolic process contribute to various degenerative diseases such as acquired immunodeficiency syndrome, ischaemic diseases, neurological disorders, and many more [53]. Antioxidant substances, on the other side, provide a high level of antioxidant activity to lessen the adverse effects of free radicals. MLs were reported to have antioxidant capacity due to the presence of phenolics and flavonoids in different studies [54]. High-performance liquid chromatography coupled to electrospray ionization and quadrupole time-of-flight mass spectrometry (HPLC-ESI-qTOF-MS/MS) analysis of MLs extract had identified neomangiferin, mangiferin, kaempferol-3-O-rutinoside, isoquercitrin, and quercetin as the main compounds and also reported that these compounds contributed directly to the antioxidant activity of MLs [55]. The 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay and superoxide dismutase (SOD)-like activity had shown that MLs serve as a moderate antioxidant with an IC50 value of ~9 and 117 μg/mL [56]. In another analysis, MLs methanol extract provided radical scavenging activity with an IC50 value of 13.37 μg/mL [57]. Fraction analysis of MLs extract with n-butanol, hexane, and ethylacetate demonstrated that ethylacetate fraction had the highest antioxidant capacity of 1226 and 2817.99 mg trilox/g estimated using DPPH and 2,2′-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid (ABTS) assay, respectively, and reducing power of 10172.59 µmol FeSO4.7H2O/g extracts analyzed through ferric reducing antioxidant power (FRAP) assay [58]. Similarly, subcritical water extracts of MLs had antioxidant activity index (AAI) values of 7.92 ± 0.16 and demonstrated superior activity to (+)-α-tocopherol (AAI = 3.65 ± 0.07) [41]. Trolox equivalent antioxidant ability (TEAC) study of MLs extracts had recorded 2.13 and 2.59 mmol TE/g DW TEAC values, respectively, for mangiferin pentoside and benzophenones [59]. The efficacy of the MLs was also studied in the chitosan-based films, and it was found that antioxidant capacity of the MLs supplemented chitosan films improved in a dose-dependent manner [60]. The antioxidant activity of hydroalcoholic MLs extract fermented with either Lactobacillus casei or effective microorganisms had higher antioxidant activity. The study also showed that fermented extracts decreased lipopolysaccharide-generated reactive oxygen species [61]. In an advanced study, MLs extract was found suitable as a green antioxidant for increasing the storage life of biodiesel [62]. In summary, many interesting results indicated the potential of MLs extract as an antioxidant with wider applicability in food, food packaging, and many more industries.

## Antimicrobial Activities

## There is immense interest in unravelling the role of bioactive compounds present in nature. Some medicinal plants with antimicrobial attributes are capable of evading the activity of multi-drug resistant (MDR) microbes, which helps in withstanding antimicrobial resistance [63]. Distinct morphological parts of the mango plant like leaves, stem, kernel, seeds, and bark have been manifested to show antimicrobial activities against microbes like Staphylococcus sp., Bacillus subtilis, Escherichia coli, Candida albicans, Proteus vulgaris, Pseudomonas fluorescens, Shigella flexneri, Klebsiella pneumoniae, and Salmonella typhi. MLs extract is the most studied part for antibacterial effects. Bharti [64] observed that hexane and hexane/ethyl acetate extracts of MLs exhibit favorable antibacterial effects against Mycobacterium tuberculosis and Enterobacter aerogenes. Antimicrobial investigation of the essential oils extracted from leaves of five Egyptian mango cultivars to be used as preservatives materials has been demonstrated by Ouf et al. [18] against Staphylococcus sp. (Minimum Inhibitory Concentration (MIC): 62.5 μg/mL), Bacillus subtilis (MIC: 125 μg/mL), Escherichia coli (MIC: 125 μg/mL), Pseudomonas aeruginosa (MIC: 500 μg/mL), Aspergillus flavus (MIC: 1000 μg/mL), and Salmonella typhi (MIC: 1000 μg/mL). The major phytochemicals responsible for the antimicrobial activity in mango leaves include phenolics, alkaloids, saponins, glycosides, terpenes, and tannins. The concentration of the aforementioned compounds were measured as follows: flavonoid content was the highest at 11.25 mg/100 g; there was 3.23 mg/100 g of saponins; phenolic content was 0.08 mg/100 g; and tannins in leaves was at 0.46 mg/100 g [24]. Polyphenols and phenolic acids present in ML extract include protocatechuic acid, gallic acid, hyperin, catechin, quercetin, kainic acid, ethyl digallate, ellagic acid, and shikimic acid, which can inhibit the growth of pathogens [8]. The mechanism of exertion of antimicrobial activity by these compounds involves depleting intracellular ATP levels, depolarization of plasma membrane, cytoplasm leakage, damaging genetic material, and declining the concentration of microbial protein [65]. Anti-microbial activity of mangiferin is schematized in Figure 4. Additionally, an adequate level of antibacterial activity of leaf extract was found against Gram positive bacteria, but no or less activity against Gram-negative bacteria was observed [66]. The study indicated that MLs extract exhibited diameter of zone of inhibition in the range of 7.0‒11.5 mm against Gram-positive bacteria like Staphylococcus and Bacillus sp., but no activity was seen against gram-negative Salmonella spp. Additionally, Mangiferin, a xanthone C-glycosyl compound extracted from MLs extract, has also shown to possess strong iron chelating activity, which favors antimicrobial activity. Furthermore, chemical analysis of MLs extract for antimicrobial activity indicated the presence of five major flavonoid compounds including epicatechin-3-O-β-glucopyranoside, 5-hydroxy-3-(4-hydroxyl phenyl) pyrano chromene-4 (8H)-one, 6-(phydroxybenzyl) taxifolin-7-O-β-D-glucoside, quercetin-3-O-α-glucopyranosyl-(1-2)-β-D-glucopyranoside, and epicatechin(2-(3,4dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol [67]. These compounds are identified to be synthesized immediately after a fungal attack, and a concentration of 1000 ppm has curtailed the growth of target fungal species like Aspergillus and Alternaria from 56‒97% [67]. A myriad of terpenes identified from MLs extract including α-pinene, β-pinene, δ-elemene, taraxerol, β-elemene, camphene, γ–cadinene, lupeol, friedelin, linalool, α-guaiene, humulene, α-farnesene, myrcene, limonene, β-ocimene, γ–terpinene, and α-terpinolene exhibit bacteriostatic and bactericidal effects against different pathogens [8]. HPLC-TOF-ESI/MS analysis of leaf extract to identify hydrolyzable tannins revealed the presence of gallatotannins. Antimicrobial properties of gallatotannins have been associated with their ability to hinder the enzymes of the pathogen, disintegrate lipid bilayer membranes, and promote chelation of metal ions [68]. The MIC of MLs extract is reported to be in the range 11–52 mg/mL [69] and the MIC values were greatest against E. coli with 36.3 mg/mL. The aforementioned phytocompounds purified from ML extract can be directly used as food additives to enhance the shelf-life of foods, and as an alternative for the synthetic antimicrobial agents, owing to their broad biological and pharmacological activities [70].

##

## Figure 4

## Hepatoprotective Properties

## Hepato steatosis or fatty liver disease (FLD) is mainly caused by an imbalance in production and metabolization of fat in the body. Higher consumption of fat also negatively affects oxidation of fatty acid in the liver and enhanced deposition in the chief functional cells of the liver (hepatocytes), which causes oxidative stress and hepatic steatosis. A very high fat cell deposition alters the signaling pathways. The peroxisome proliferator-activated receptor (PPAR) and nuclear factor kappa B (NF-kB) pathways are involved in the obesity inflammation process. The progression of liver damage may result in subclinical icteric hepatitis to necro-inflammatory hepatitis, cirrhosis, and carcinoma [71]. Therefore, the compounds having a role as an antioxidant and inhibitor of lipid peroxidation and their free radical scavenging capacity may show the hepatoprotective properties. MLs tea was prepared using Ubá variety leaves [72]. This MLs tea contains about 0.72 mg/mL mangiferin, 1.59 mg GAE/mL total phenolic content, 80% of radical scavenging activity, and 0.007 µg/µL EC50 value. The 25 mL/day dose of MLs tea was given to fat obese rats and the effects were evaluated. The rats consuming a high-fat diet activated hepatic steatosis and increased accumulation of cell fat by 46% compared to control. Treatment of rats consuming a high fat diet with MLs tea increases the nucleus, cytoplasm blood vessels percentages, and reduced accumulation of fat droplets, consequently reducing the incidence of FLD. These hepatoprotective activities of MLs tea were mainly due to gene expression. It is reported that increased expression of PPAR-α enhances oxidative stress, inflammation, and lipid metabolism in obese mice, whereas negative modulation of PPAR-α and adiponectin receptor II (AdipoR2) results in FLD [73]. High fat diet decreases the expression of mRNA of PPAR-α and AdipoR2, while MLs tea up-regulates the gene expression of PPAR-α and AdipoR2, attenuating FLD. At the same time, the expressions of NF-κB p65 and sterol regulatory element-binding proteins (SREBP1c) genes were reduced in cells of liver. It was also concluded that MLs tea improves the situation of FLD by acting as an anti-inflammatory agent via PPAR-α activation and NF-κB modulation [74]. Therefore, MLs products can be used as hepatoprotective and alternative for the treatment of fatty diet induced FLD or hepatic steatosis.

## Toxicological/Allergenicity Evaluation of MLs

## Numerous studies have pointed out the various beneficial effects of mango leaves extract against cancer, diabetes, cardiovascular, and neurodegenerative diseases. These positive effects are due to the presence of a plethora of phytochemicals such as mangiferin followed by phenolic acids, benzophenones, and other antioxidants such as flavonoids, ascorbic acid, carotenoids, and tocopherols (20). Few studies also reported the toxic effects of MLE attributed to the presence of allergens. Mango allergy can occur in two ways: either the immediate hypersensitivity reaction as wheezing dyspnoea, anaphylaxis, erythema, urticaria, and angioedema, or the late reaction presenting as contact dermatitis and periorbital oedema [93]. Transcriptome analysis using high-throughput llumina sequencing of leaf and fruit reported the presence of 66 potential allergen genes mainly belonging to pollen allergen, pathogenesis-related protein Bet v I family and NADPH-dependent flavin mononucleotide (FMN) reductase [94]. A long-term study (three consecutive months) on Sprague Dawley rats at various doses (100, 300, and 900 mg/kg) of MLs revealed the slight body weight increase and higher fat weight, the serum thyroglobulin and cholesterol levels, and the slight increase in epididymis weight of male rats compared with the control group. The study also revealed no abnormalities on short-term exposure (14 days). The study concluded that MLs extract was safe at the maximum dose of 18.4 g/kg weight of mice [95]. In an independent study, MLs extract containing 60% mangiferin was evaluated in Han:Wist male and female rats in a 90 day study, and it was concluded that ML extracts demonstrated no observed adverse effect at the highest dose tested (2000 mg/kg body weight per day) [96]. Urushiol, a hapten to skin proteins that induces a type IV hypersensitivity response, is an allergenic substance found in the Anacardiaceae family, most commonly known for poison ivy (Toxicodendron radicans) and poison oak (T. diversilobum). Hershko et al. [97] reported the fact the individual with prior exposure to poison ivy/oak allergy may develop allergic contact dermatitis from mango on first exposure. Cross-sensitization of these plants with mango is known to be secondary to a superposition of urushiol antigen and 5-resorcinol, primarily found in mango peels [98]. These studies overall suggest that mango has some allergic responses, but those reactions have been limited to mango latex, pollen allergen, or prior urushiol exposure [99].

## Conclusions

## MLs exhibit exceptional biological, medicinal, and metabolic properties. MLs are otherwise considered as a waste material generated mainly through the pruning of mango plants; in reality, they are a most significant resource containing a wide variety of bioactive compounds (phenolics and essential oils), crude protein, dietary fiber, minerals, and vitamins. The various bioactive compounds present in the MLs include phenolic compounds, flavonoids, benzophenones, sesquiterpenes, saponins, xanthones, tannins, terpenoids, and alkaloids. MLs extract is found useful for the treatment of common diseases like diarrhea, chronic ailments like diabetes, and fatty liver disease. MLs extract possessed strong anti-proliferative activity against pancreatic, breast, human colon carcinoma, and other types of cancers. The extracts of MLs are also crucial in as an anti-obesity agent and demonstrate hepatoprotective action. There are numerous vital chemical compounds present in mango leaves, which are instrumental to performing various metabolic, bacteriostatic, and antimicrobial activities. Some of these include gurjunene, trans-caryophyllene, humulene, selinene, and so on. Mangiferin present in MLs was also found to mitigate the oxidative stress involved in the treatment of numerous pathologies. MLs are thus a potential source of cost-effective food supplements and nutritive ingredients for improving human health and curing acute and chronic diseases.

## References

## 1. Barreto J.C., Trevisan M.T.S., Hull W.E., Erben G., De Brito E.S., Pfundstein B., Würtele G., Spiegelhalder B., Owen R.W. Characterization and Quantitation of Polyphenolic Compounds in Bark, Kernel, Leaves, and Peel of Mango (Mangifera indica L.) J. Agric. Food Chem. 2008;56:5599–5610. doi: 10.1021/jf800738r.

## 2. Shah K.A., Patel M.B., Patel R.J., Parmar P.K. Mangifera indica (Mango) Pharmacogn. Rev. 2010;4:42–48. doi: 10.4103/0973-7847.65325

## 3. Kulkarni V.M., Rathod V.K. Extraction of mangiferin from Mangifera indica leaves using three phase partitioning coupled with ultrasound. Ind. Crop. Prod. 2014;52:292–297. doi: 10.1016/j.indcrop.2013.10.032.

## 4. Ribeiro S.M.R., Schieber A. Bioactive Foods in Promoting Health. Elsevier BV; Oxford, UK: 2010. Bioactive Compounds in Mango (Mangifera indica L.) pp. 507–523.

## 5. Lauricella M., Emanuele S., Calvaruso G., Giuliano M., D’Anneo A. Multifaceted Health Benefits of Mangifera indica L. (Mango): The Inestimable Value of Orchards Recently Planted in Sicilian Rural Areas. Nutrients. 2017;9:525. doi: 10.3390/nu9050525.

## 6. Masud Parvez G.M. Pharmacological activities of mango (Mangifera indica): A review. J. Pharmacogn. Phytochem. 2016;5:1–7.

## 7. Kabir Y., Shekhar H.U., Sidhu J.S. Handbook of Mango Fruit. Wiley; Hoboken, NJ, USA: 2017. Phytochemical Compounds in Functional Properties of Mangoes; pp. 237–254.

## 8. Ediriweera M.K., Tennekoon K.H., Samarakoon S.R. A Review on Ethnopharmacological Applications, Pharmacological Activities, and Bioactive Compounds of Mangifera indica (Mango) Evid. Based Complement. Altern. Med. 2017;2017:1–24. doi: 10.1155/2017/6949835.

## 9. Batool N., Ilyas N., Shabir S., Saeed M., Mazhar R. Mini-Review- A mini-review of therapeutic potential of Mangifera indica L. Pak. J. Pharm. Sci. 2018;31:1441–1448.

## 10. Alberts B., Johnson A., Lewis J., Raff M., Roberts K., Walter P. Molecular Biology of the Cell. Garland Science; New York, NY, USA: 2002. Protein Function.

## 11. Fafiolu A., Odugunawa O., Bambose A., Oso A., Isah O., Olantanji J., Jegede A. Feeding value mango leaf (Mangifera indica) for growing rabbits. J. Anim. Vet. Adv. 2006;5:800–804.

## 12. Akbar M., Alam M. Effects of feeding mango (Mangifera indica) and shaora (Streblus asper) tree leaves to Black Bengal goats of Bangladesh. Small Rumin. Res. 1991;6:25–30. doi: 10.1016/0921-4488(91)90004-A.

## 13. Laulloo S.J., Bhowon M.G., Soyfoo S., Chua L.S. Nutritional and Biological Evaluation of Leaves of Mangifera indica from Mauritius. J. Chem. 2018;2018:1–9. doi: 10.1155/2018/6869294.

## 14. Dayal V., Dubey A., Singh S., Sharma R., Dahuja A., Kaur C. Growth, yield and physiology of mango (Mangifera indica L.) cultivars as affected by polyembryonic rootstocks. Sci. Hortic. 2016;199:186–197. doi: 10.1016/j.scienta.2015.12.042.

## 15. Wetungu M., Tarus P., Segor F., Cheseto X., Omolo M. Essential oil chemistry of some Mangifera indica varieties from Kenya. Am. J. Essent. Oils Nat. Prod. 2015;3:1–6.

## 16. D[Zbreve]Amić A.M., Marin P.D., Gbolade A.A., Ristić M.S. Chemical Composition of Mangifera indica Essential Oil from Nigeria. J. Essent. Oil Res. 2010;22:123–125. doi: 10.1080/10412905.2010.9700279.

## 17. Fontenelle R.O.D.S., Sobrinho A.C.N., Soares B.V., De Aguiar F.L.L., De Brito E.H.S., Cavalcante C.S.D.P., Rocha M.F.G., De Morais S.M. Effect of essential oils from Mangifera indica L. cultivars on the antifungal susceptibility of Candida spp. strains isolated from dogs. Rev. Bras. Saúde Produção Anim. 2017;18:337–346. doi: 10.1590/s1519-99402017000200012.

## 18. Ouf S.A., Galal A.M.F., Ibrahim H.S., Hassan A.Z., Mekhael M.K.G., El-Yasergy K.F., El-Ghany M.N.A., Rizk M.A., Hanna A.G. Phytochemical and antimicrobial investigation of the leaves of five Egyptian mango cultivars and evaluation of their essential oils as preservatives materials. J. Food Sci. Technol. 2020:1–13. doi: 10.1007/s13197-020-04816-5.

## 19. Gebara S.S., Ferreira W.D.O., Ré-Poppi N., Simionatto E., Carasek E. Volatile compounds of leaves and fruits of Mangifera indica var. coquinho (Anacardiaceae) obtained using solid phase microextraction and hydrodistillation. Food Chem. 2011;127:689–693. doi: 10.1016/j.foodchem.2010.12.123.

## 20. Ali B.A., Alfa A.A., Tijani K.B., Idris E.T., Unoyiza U.S., Junaidu Y. Nutritional Health Benefits and Bioactive Compounds of Mangifera indica L (Mango) Leaves Methanolic Extracts. Asian Plant Res. J. 2020;6:41–51. doi: 10.9734/aprj/2020/v6i230126.

## 21. Princwill-Ogbonna I., Ogbonna P., Ogujiofor I. Proximate Composition, Vitamin, Mineral and biologically Active Compounds Levels in Leaves of Mangifera indica (Mango), Persea americana (Avocado pea), and Annona muricata (Sour sop) J. Appl. Sci. Environ. Manag. 2019;23:65. doi: 10.4314/jasem.v23i1.11.

## 22. Rymbai H., Srivastav M., Sharma R.R., Patel C.R., Singh A.K. Bio-active compounds in mango (Mangifera indica L.) and their roles in human health and plant defence—A review. J. Hortic. Sci. Biotechnol. 2013;88:369–379. doi: 10.1080/14620316.2013.11512978.

## 23. Abou-Awad B.A., Al-Azzazy M.M., Afia S.I. Effect of the leaf coating miteCisaberoptus kenyaeKeifer (Acari: Eriophyidae) on the mineral content of the host mango plantMangiferae indicaL. Arch. Phytopathol. Plant Prot. 2012;45:16–21. doi: 10.1080/03235400903309030.

## 24. Okwu D.E., Ezenagu V.I.T.U.S. Evaluation of the phytochemical composition of mango (Mangifera indica Linn) stem bark and leaves. Int. J. Chem. Sci. 2008;6:705–716.

## 25. Akram M., Munir N., Daniyal M., Egbuna C., Găman M.-A., Onyekere P.F., Olatunde A. Functional Foods and Nutraceuticals. Springer International Publishing; New York, NY, USA: 2020. Vitamins and Minerals: Types, Sources and their Functions; pp. 149–172.

## 26. Zhang Y., Chen Q., Liu M.-Y., Ruan J.-Y., Yu H.-Y., Li J., Wang T. Effects of Benzophenones from Mango Leaves on Lipid Metabolism. Chem. Pharm. Bull. 2019;67:634–639. doi: 10.1248/cpb.c18-00905.

## 27. Mirza B., Croley C.R., Ahmad M., Pumarol J., Das N., Sethi G., Bishayee A. Mango (Mangifera indica L.): A magnificent plant with cancer preventive and anticancer therapeutic potential. Crit. Rev. Food Sci. Nutr. 2020:1–27. doi: 10.1080/10408398.2020.1771678.

## 28. Rasouli H., Farzaei M.H., Khodarahmi R. Polyphenols and their benefits: A review. Int. J. Food Prop. 2017;20:1–42. doi: 10.1080/10942912.2017.1354017.

## 29. Luca S.V., Macovei I., Bujor A., Miron A., Skalicka-Woźniak K., Aprotosoaie A.C., Trifan A. Bioactivity of dietary polyphenols: The role of metabolites. Crit. Rev. Food Sci. Nutr. 2020;60:626–659. doi: 10.1080/10408398.2018.1546669.

## 30. Pan J., Yi X., Zhang S., Cheng J., Wang Y., Liu C., He X. Bioactive phenolics from mango leaves (Mangifera indica L.) Ind. Crop. Prod. 2018;111:400–406. doi: 10.1016/j.indcrop.2017.10.057.

## 31. Gu C., Yang M., Zhou Z., Khan A., Cao J., Cheng G. Purification and characterization of four benzophenone derivatives from Mangifera indica L. leaves and their antioxidant, immunosuppressive and α-glucosidase inhibitory activities. J. Funct. Foods. 2019;52:709–714. doi: 10.1016/j.jff.2018.11.045.

## 32. Martínez-Bernett D., Silva-Granados A., Correa-Torres S.N., Herrera A. Chromatographic analysis of phytochemicals components present in Mangifera indica leaves for the synthesis of silver nanoparticles by AgNO3 reduction. J. Phys. Conf. Ser. 2016;687:12033. doi: 10.1088/1742-6596/687/1/012033.

## 33. Ronchi S.N., Brasil G.A., Nascimento A.M.D., De Lima E.M., Scherer R., Costa H.B., Romão W., Boëchat G.A.P., Lenz D., Fronza M., et al. Phytochemical and in vitro and in vivo biological investigation on the antihypertensive activity of mango leaves (Mangifera indica L.) Ther. Adv. Cardiovasc. Dis. 2015;9:244–256. doi: 10.1177/1753944715572958.

## 34. Swaroop A., Stohs S.J., Bagchi M., Moriyama H., Bagchi D. Mango (Mangifera indica Linn) and Anti-Inflammatory Benefits: Versatile Roles in Mitochondrial Bio-Energetics and Exercise Physiology. Funct. Foods Heal. Dis. 2018;8:267. doi: 10.31989/ffhd.v8i5.526.

## 35. Jung J.-S., Jung K., Kim N.-H., Kim H.-S. Selective inhibition of MMP-9 gene expression by mangiferin in PMA-stimulated human astroglioma cells: Involvement of PI3K/Akt and MAPK signaling pathways. Pharmacol. Res. 2012;66:95–103. doi: 10.1016/j.phrs.2012.02.013.

## 36. Klein-Júnior L.C., Campos A., Niero R., Corrêa R., Heyden Y.V., Filho V.C. Xanthones and Cancer: From Natural Sources to Mechanisms of Action. Chem. Biodivers. 2019;17:e1900499. doi: 10.1002/cbdv.201900499.

## 37. Li H., Huang J., Yang B., Xiang T., Yin X., Peng W., Cheng W., Wan J., Luo F., Li H., et al. Mangiferin exerts antitumor activity in breast cancer cells by regulating matrix metalloproteinases, epithelial to mesenchymal transition, and β-catenin signaling pathway. Toxicol. Appl. Pharmacol. 2013;272:180–190. doi: 10.1016/j.taap.2013.05.011.

## 38. Sakthisekaran D., Rajendran P., Rengarajan T., Nishigaki I., Ekambaram G. Potent chemopreventive effect of mangiferin on lung carcinogenesis in experimental Swiss albino mice. J. Cancer Res. Ther. 2014;10:1033–1039. doi: 10.4103/0973-1482.137966.

## 39. Zhang B.-P., Zhao J., Li S.-S., Yang L.-J., Zeng L.-L., Chen Y., Fang J. Mangiferin activates Nrf2-antioxidant response element signaling without reducing the sensitivity to etoposide of human myeloid leukemia cells in vitro. Acta Pharmacol. Sin. 2013;35:257–266. doi: 10.1038/aps.2013.165.

## 40. Das S., Rao B.N. Mangiferin attenuates methylmercury induced cytotoxicity against IMR-32, human neuroblastoma cells by the inhibition of oxidative stress and free radical scavenging potential. Chem. Interact. 2011;193:129–140. doi: 10.1016/j.cbi.2011.06.002.

## 41. Fernández-Ponce M.T., López-Biedma A., Sánchez-Quesada C., Casas L., Mantell C., Gaforio J.J., De La Ossa E.J.M. Selective antitumoural action of pressurized mango leaf extracts against minimally and highly invasive breast cancer. Food Funct. 2017;8:3610–3620. doi: 10.1039/C7FO00877E.

## 42. Palanuvej C., Ganogpichayagrai A., Ruangrungsi N. Antidiabetic and anticancer activities of Mangifera indica cv. Okrong leaves. J. Adv. Pharm. Technol. Res. 2017;8:19–24. doi: 10.4103/2231-4040.197371.

## 43. Anoop N.V., Jacob R., Paulson J.M., Dineshkumar B., Narayana C.R. Mango leaf extract synthesized silver nanorods exert anticancer activity on breast cancer and colorectal carcinoma cells. J. Drug Deliv. Sci. Technol. 2018;44:8–12. doi: 10.1016/j.jddst.2017.11.023.

## 44. Singab A.N., Youssef F.S., Ashour M.L. Medicinal Plants with Potential Antidiabetic Activity and their Assessment. Med. Aromat. Plants. 2014;3:151. doi: 10.4172/2167-0412.1000151.

## 45. Iid I.I., Kumar S., Shukla S., Kumar V., Sharma R. Putative antidiabetic herbal food ingredients: Nutra/functional properties, bioavailability and effect on metabolic pathways. Trends Food Sci. Technol. 2020;97:317–340. doi: 10.1016/j.tifs.2020.01.017.

## 46. Al-Malki A.L., El Rabey H.A. The Antidiabetic Effect of Low Doses ofMoringa oleiferaLam. Seeds on Streptozotocin Induced Diabetes and Diabetic Nephropathy in Male Rats. BioMed Res. Int. 2015;2015:1–13. doi: 10.1155/2015/381040.

## 47. Nair S.S., Kavrekar V., Mishra A. In vitro studies on alpha amylase and alpha glucosidase inhibitory activities of selected plant extracts. Eur. J. Exp. Biol. 2013;3:128–132.

## 48. Kulkarni V.M., Rathod V.K. Exploring the potential of Mangifera indica leaves extract versus mangiferin for therapeutic application. Agric. Nat. Resour. 2018;52:155–161. doi: 10.1016/j.anres.2018.07.001.

## 49. Saleem M., Tanvir M., Akhtar M.F., Iqbal M., Saleem A. Antidiabetic Potential of Mangifera indica L. cv. Anwar Ratol Leaves: Medicinal Application of Food Wastes. Medicina. 2019;55:353. doi: 10.3390/medicina55070353.

## 50. Gupta R. Active phytoconstituents for diabetes management: A review. J. Complement. Integr. Med. 2018;15:15. doi: 10.1515/jcim-2017-0123.

## 51. Islam N., Jung H.A., Sohn H.S., Kim H.M., Choi J.S. Potent α-glucosidase and protein tyrosine phosphatase 1B inhibitors from Artemisia capillaris. Arch. Pharmacal Res. 2013;36:542–552. doi: 10.1007/s12272-013-0069-7.

## 52. Bhuvaneshwari J., Khanam S., Devi K. In-vitro enzyme inhibition studies for antidiabetic activity of mature and tender leaves of Mangifera indica var. Totapuri. Res. Rev. J. Microbiol. Biotechnol. 2014;3:36–41.

## 53. Schraml E., Grillari J. From cellular senescence to age-associated diseases: The miRNA connection. Longev. Health. 2012;1:10. doi: 10.1186/2046-2395-1-10.

## 54. Kumar Y., Kumar V. Sangeeta Comparative antioxidant capacity of plant leaves and herbs with their antioxidative potential in meat system under accelerated oxidation conditions. J. Food Meas. Charact. 2020;14:3250–3262. doi: 10.1007/s11694-020-00571-5.

## 55. Wu L., Wu W., Cai Y., Li C., Wang L. HPLC fingerprinting-based multivariate analysis of phenolic compounds in mango leaves varieties: Correlation to their antioxidant activity and in silico α-glucoidase inhibitory ability. J. Pharm. Biomed. Anal. 2020;191:113616. doi: 10.1016/j.jpba.2020.113616.

## 56. Itoh K., Matsukawa T., Okamoto M., Minami K., Tomohiro N., Shimizu K., Kajiyama S., Endo Y., Matsuda H., Shigeoka S. In vitro Antioxidant Activity of Mangifera indica Leaf Extracts. J. Plant Stud. 2020;9:39. doi: 10.5539/jps.v9n2p39.

## 57. Mohan C.G., Deepak M., Viswanatha G.L., Savinay G., Hanumantharaju V., E Rajendra C., Halemani P.D. Anti-oxidant and anti-inflammatory activity of leaf extracts and fractions of Mangifera indica. Asian Pac. J. Trop. Med. 2013;6:311–314. doi: 10.1016/S1995-7645(13)60062-0.

## 58. Kitbumrungsart P., Suntornwat O., Rayanil K. Mangiferin and antioxidant capacity from mango (Mangifera indica L.) leaves extracts. Thai J. Agric. Sci. 2011;44:62–66.

## 59. Prommajak T., Kim S.M., Pan C.-H., Kim S.M., Surawang S., Rattanapanone N. Identification of Antioxidants in Young Mango Leaves by LC-ABTS and LC-MS. Chiang Mai Univ. J. Nat. Sci. 2014;13:317–330. doi: 10.12982/CMUJNS.2014.0038.

## 60. Rambabu K., Bharath G., Banat F., Show P.L., Cocoletzi H.H. Mango leaf extract incorporated chitosan antioxidant film for active food packaging. Int. J. Biol. Macromol. 2019;126:1234–1243. doi: 10.1016/j.ijbiomac.2018.12.196.

## 61. Park A., Ku T., Yoo I. Antioxidant properties of fermented mango leaf extracts. J. Cosmet. Sci. 2015;66:1–13.

## 62. Neuana N.F., Barboza J.C.D.S., Dos Santos E.P., Da Silva M.L.C.P. A novel application of Mangifera indica L and Eugenia uniflora L extracts as antioxidants to control biodiesel oxidation stability. Environ. Prog. Sustain. Energy. 2020 doi: 10.1002/ep.13540.

## 63. Dzotam J.K., Kuete V. Antibacterial and Antibiotic-Modifying Activity of Methanol Extracts from Six Cameroonian Food Plants against Multidrug-Resistant Enteric Bacteria. BioMed Res. Int. 2017;2017:1–19. doi: 10.1155/2017/1583510.

## 64. Bharti R.P. Studies on antimicrobial activity and phytochemical profile of Mangifera indica leaf extract. IOSR J. Environ. Sci. Toxicol. Food Technol. 2013;7:74–78.

## 65. Guo L., Gong S., Wang Y., Sun Q., Duo K., Fei P. Antibacterial Activity of Olive Oil Polyphenol Extract Against Salmonella Typhimurium and Staphylococcus aureus: Possible Mechanisms. Foodborne Pathog. Dis. 2020;17:396–403. doi: 10.1089/fpd.2019.2713.

## 66. Islam M.R., Mannan M.A., Kabir M., Olival K. Analgesic, anti-inflammatory and antimicrobial effects of ethanol extracts of mango leaves. J. Bangladesh Agric. Univ. 2010;8:239–244. doi: 10.3329/jbau.v8i2.7932.

## 67. Kanwal Q., Hussain I., Siddiqui H.L., Javaid A. Antifungal activity of flavonoids isolated from mango (Mangifera indicaL.) leaves. Nat. Prod. Res. 2010;24:1907–1914. doi: 10.1080/14786419.2010.488628.

## 68. Konishi K., Adachi H., Ishigaki N., Kanamura Y., Adachi I., Tanaka T., Nishioka I., Nonaka G.-I., Horikoshi I. Inhibitory Effects of Tannins on NADH Dehydrogenases of Various Organisms. Biol. Pharm. Bull. 1993;16:716–718. doi: 10.1248/bpb.16.716.

## 69. Hannan A., Asghar S., Naeem T., Ullah M.I., Ahmed I., Aneela S., Hussain S. Antibacterial effect of mango (Mangifera indica Linn.) leaf extract against antibiotic sensitive and multi-drug resistant Salmonella typhi. Pak. J. Pharm. Sci. 2013;26:715–719.

## 70. M G., U V.N., S M.S., R A.K. Antimicrobial Activity of Some Medicinal Herbals. Int. J. Biotech Trends Technol. 2020;10:56–59. doi: 10.14445/22490183/IJBTT-V10I1P609.

## 71. Pourahmad J., Eskandari M.R., Shakibaei R., Kamalinejad M. A Search for Hepatoprotective Activity of Fruit Extract of Mangifera indica L. Against Oxidative Stress Cytotoxicity. Plant Foods Hum. Nutr. 2010;65:83–89. doi: 10.1007/s11130-010-0161-9.

## 72. Ramírez N.M., Farias L.M., Santana F.A., Leite J.P.V., Dantas M.I.D.S., Toledo R.C.L., De Queiroz J.H., Martino H.S.D., Ribeiro S.M.R. Extraction of Mangiferin and Chemical Characterization and Sensorial Analysis of Teas from Mangifera indica L. Leaves of the Ubá Variety. Beverages. 2016;2:33. doi: 10.3390/beverages2040033.

## 73. Peng Y., Rideout D., Rakita S., Sajan M., Farese R., You M., Murr M.M. Downregulation of Adiponectin/AdipoR2 is Associated with Steatohepatitis in Obese Mice. J. Gastrointest. Surg. 2009;13:2043–2049. doi: 10.1007/s11605-009-1032-2.

## 74. Ramírez N.M., De Queiróz J.H., Ribeiro S.M.R., Toledo R.C.L., Moreira M.E.C., Mafra C.L., Benjamin L.D.A., Coelho C.D.M., Veloso M.P., Martino H.S.D. Mango leaf tea promotes hepatoprotective effects in obese rats. J. Funct. Foods. 2018;49:437–446. doi: 10.1016/j.jff.2018.09.010.

## 75. Gururaja G.M., Mundkinajeddu D., Dethe S.M., Sangli G.K., Abhilash K., Agarwal A. Cholesterol esterase inhibitory activity of bioactives from leaves of Mangifera indica L. Pharmacogn. Res. 2015;7:355–362. doi: 10.4103/0974-8490.159578.

## 76. Ramírez N.M., Toledo R.C.L., Moreira M.E.C., Martino H.S.D., Benjamin L.D.A., De Queiroz J.H., Ribeiro A.Q., Ribeiro S.M.R. Anti-obesity effects of tea from Mangifera indica L. leaves of the Ubá variety in high-fat diet-induced obese rats. Biomed. Pharmacother. 2017;91:938–945. doi: 10.1016/j.biopha.2017.05.015.

## 77. Dethe S.M., Gururaja G.M., Mundkinajeddu D., Kumar A.S., Allan J.J., Agarwal A. Evaluation of cholesterol-lowering activity of standardized extract of Mangifera indica in albino Wistar rats. Pharmacogn. Res. 2017;9:21–26. doi: 10.4103/0974-8490.199770.

## 78. Sandoval-Gallegos E.M., Ramírez-Moreno E., De Lucio J.G., Arias-Rico J., Cruz-Cansino N., Ortiz M.I., Cariño-Cortés R. In Vitro Bioaccessibility and Effect of Mangifera indica (Ataulfo) Leaf Extract on Induced Dyslipidemia. J. Med. Food. 2018;21:47–56. doi: 10.1089/jmf.2017.0042.

## 79. Lopez A.D., Mathers C.D. Measuring the global burden of disease and epidemiological transitions: 2002–2030. Ann. Trop. Med. Parasitol. 2006;100:481–499. doi: 10.1179/136485906X97417.

## 80. Mehesare S.S., Waghmare S.P., Thorat M.G., Hajare S.W., Itankar P.R. Evaluation of antidiarrheal activity of polyherbal preparation. J. Pharmacogn. Phytochem. 2017;6:723–725.

## 81. Mokomane M., Kasvosve I., De Melo E., Pernica J.M., Goldfarb D.M. The global problem of childhood diarrhoeal diseases: Emerging strategies in prevention and management. Ther. Adv. Infect. Dis. 2017;5:29–43. doi: 10.1177/2049936117744429.

## 82. Thiagarajah J.R., Kamin D.S., Acra S., Goldsmith J.D., Roland J.T., Lencer W.I., Muise A.M., Goldenring J.R., Avitzur Y., Martín M.G. Advances in Evaluation of Chronic Diarrhea in Infants. Gastroenterology. 2018;154:2045–2059. doi: 10.1053/j.gastro.2018.03.067.

## 83. Kassaye K., Amberbir A., Getachew B., Mussema Y. A historical overview of traditional medicine practices and policy in Ethiopia. Ethiop. J. Heal. Dev. 2007;20:127–134. doi: 10.4314/ejhd.v20i2.10023.

## 84. Mekonnen B., Asrie A.B., Wubneh Z.B. Antidiarrheal Activity of 80% Methanolic Leaf Extract of Justicia schimperiana. Evid. Based Complement. Altern. Med. 2018;2018:1–10. doi: 10.1155/2018/3037120.

## 85. De P.K., Pal A., Roy B.C. Effects of aqueous young leaves extract of Mangifera indica on GM (-) microorganisms causing gastro-intestinal disorders. Asian J. Plant Sci. Res. 2014;4:23–27.

## 86. Yakubu M., Salimon S. Antidiarrhoeal activity of aqueous extract of Mangifera indica L. leaves in female albino rats. J. Ethnopharmacol. 2015;163:135–141. doi: 10.1016/j.jep.2014.12.060.

## 87. Pan J., Yi X., Wang Y., Chen G., He X. Benzophenones from Mango Leaves Exhibit α-Glucosidase and NO Inhibitory Activities. J. Agric. Food Chem. 2016;64:7475–7480. doi: 10.1021/acs.jafc.6b02404.

## 88. Sanchez-Sanchez J., Fernández-Ponce M., Casas L., Mantell C., De La Ossa E.M. Impregnation of mango leaf extract into a polyester textile using supercritical carbon dioxide. J. Supercrit. Fluids. 2017;128:208–217. doi: 10.1016/j.supflu.2017.05.033.

## 89. Diso S.U., Ali M., Mukhtar S.I., Garba M. Antibacterial Activity and Phytochemical Screening of Mangifera indica (Mango) Stem and Leaf Extracts on Clinical Isolates of Methicillin Resistant Staphylococcus aureus. J. Adv. Med. Pharm. Sci. 2017;13:1–6. doi: 10.9734/JAMPS/2017/31127.

## 90. Cardenas V., Mendoza R., Chiong L., Del Aguila E. Comparison of the Antibacterial Activity of the Ethanol Extract vs Hydroalcoholic Extract of the Leaves of Mangifera indica L. (Mango) in Different Concentrations: An In Vitro Study. J. Contemp. Dent. Pract. 2020;21:202–206. doi: 10.5005/jp-journals-10024-2763.

## 91. Mustapha A.A., Enemali M.O., Olose M., Owuna G., Ogaji J.O., Idris M.M., Aboh V.O., Ogaji O., Idris M. Phytoconstituents and Antibacterial efficacy of Mango (Mangifera indica) leave extracts. J. Med. Plants Stud. 2014;2:19–23.

## 92. Oseghale F., Fasina K., Ohifueme A., Omoruyi J. Biocontrol of Food Spoilage Microorganisms using Leaf extracts from Magnifera indica (Mango) and Psidium guajava (Guava) J. Chem. Soc. Niger. 2020;45:712–723. doi: 10.46602/jcsn.v45i4.496.

## 93. Sareen R., Shah A. Hypersensitivity manifestations to the fruit mango. Asia Pac. Allergy. 2011;1:43–49. doi: 10.5415/apallergy.2011.1.1.43.

## 94. Xiaolong H., Huiqing Y., Wu Z., Yin Y. Putative allergens identified in mango (Mangifera indica Linn) leaf and fruit with transcriptome analysis. J. Food Sci. Technol. 2020;5:98–110. doi: 10.25177/JFST.5.2.RA.10636.

## 95. Zhang Y., Li J., Wu Z., Liu E., Shi P., Han L., Guo L., Gao X., Wang T. Acute and Long-Term Toxicity of Mango Leaves Extract in Mice and Rats. Evid. Based Complement. Altern. Med. 2014;2014:1–8. doi: 10.1155/2014/691574.

## 96. Reddeman R.A., Glávits R., Endres J.R., Clewell A.E., Hirka G., Vértesi A., Béres E., Szakonyiné I.P. A Toxicological Evaluation of Mango Leaf Extract (Mangifera indica) Containing 60% Mangiferin. J. Toxicol. 2019;2019:1–14. doi: 10.1155/2019/4763015.

## 97. Hershko K., Weinberg I., Ingber A. Exploring the mango-poison ivy connection: The riddle of discriminative plant dermatitis. Contact Dermat. 2005;52:3–5. doi: 10.1111/j.0105-1873.2005.00454.x.

## 98. Yoo M.J., Carius B.M. Mango Dermatitis After Urushiol Sensitization. Clin. Pract. Cases Emerg. Med. 2019;3:361–363. doi: 10.5811/cpcem.2019.6.43196.

## 99. Goldstein N. The ubiquitous urushiols Contact dermatitis from mango, poison ivy, and other “poison” plants. 1968. Hawaii Med. J. 2004;63:231–235.