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Pharmacological Activities of Mango (*Mangifera Indica*): A Review

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Abstract
Mangoes (*Mangifera indica*) belong to genus Mangifera which consists of about 30 species of tropical fruiting trees in the flowering plant family Anacardiaceae. It is cultivated on an area of approximately 3.7 million ha worldwide and conquers the second position as a tropical crop, in terms of production. According to ayurveda, varied medicinal properties are attributed to different parts of mango tree. Mango possesses anti-diabetic, anti-oxidant, anti-viral, anti-inflammatory properties. Various effects like antibacterial, anti-fungal, anthelmintic, anti- parasitic, anticancer, anti HIV, antibone resorption, antispasmodic, antipyretic, antidiarrheal, immunomodulation, hypolipidemic, anti-microbial, hepatoprotective, gastro protective have also been studied.

Keywords: Mango, anticancer, antidiabetic, antimicrobial, antimalarial.

Introduction
In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter [1]. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world [2]. At present nearly 30% or more of the modern pharmacological drugs are derived directly or indirectly form plants [3].
Mango (*Mangifera indica* L.) is a juicy stone fruit belongs to the family of Anacardiaceae in the order of Sapindales and is grown in many parts of the world, particularly in tropical countries. It is the national fruit of India and Philippines and the national tree of Bangladesh. Over 1000 mango varieties are available worldwide. Of the available varieties, only a few are grown on commercial scales and traded [4]. Mango is now commercially grown in more than 87 countries [5]. Currently, mango is cultivated on an area of approximately 3.7 million ha worldwide. Mango fruit conquers the 2nd position as a tropical crop, behind only bananas in terms of production and acreage used [6]. It has been well documented that mango fruits are an important source of micronutrients, vitamins and other phytochemicals. Moreover, mango fruits provide energy, dietary fibre, carbohydrates, proteins, fats and phenolic compounds [5], which are vital to normal human growth, development and health [7].

2. Common names
The common names of *Mangifera indica* include:

- Arab : Mabaz
- Bengali : Am (Um)
- Chinese: Mi wang
- Danish: Mango, Mangofrugt, Mangotrae
- Dutch: Manga, Mangga, Manja, Mangoestanboom
- English: Mango
- Finnish: Mango, Mangopuu
- French: Mangue, Manguier
- German: Indischer Mangobaum, Mango
- Greek: Magko, Mangko
- Hindi: Am, Ambi, Amia
- Japanese: Anchaa, Mangoo, Mangou

- Persian: Amb
- Sanskrit: Aamra, Ambrah
- Sinhalese: Amba
- Tamil: Mangas, Mau, Mampalam

3. Taxonomical Classification

- Kingdom: Plantae
- Subkingdom: Tracheobionta
- Superdivision: Spermatophyta
- Division: Magnoliophyta
- Class: Magnoliopsida
- Subclass: Rosidae
- Order: Sapindales
- Family: Anacardiaceae
- Genus: Mangifera
- Species: *M. indica*

4. Plant description

Tree is medium to large (10-40 m in height), evergreen with symmetrical, rounded canopy ranging from low and dense to upright and open. Bark is usually dark grey-brown to black, rather smooth, superficially cracked or inconspicuously fissured, peeling off in irregular, rather thick pieces. The tree forms a long unbranched long tap root (up to 6-8 m and more) plus a dense mass of superficial feeder roots. Effective root system of an 18- year old mango tree may observe a 1.2 m depth with lateral spread as far as 7.5m [8]. The leaves are simple alternately arranged, 15-45 cm in length. The petiole varies in length from 1 to 12 cm, always swollen at the base. Leaves are variable in shapes like oval-lanceolate, lanceolate, oblong, linear-oblong, ovate, obovate-lanceolate or roundish-oblong [9]. The upper surface is shining and dark green while the lower is glabrous light green. Hermaphrodite and male flowers are produced in the same panicle, usually with a larger number of the later. The size of both male and hermaphrodite flowers varies from 6 to 8 mm in diameter. They are subsessile, rarely pedicellate, and have a sweet smell. The pollen grains are of variable shapes, with the size varying from 20 to 35 micron [10-11]. The fruit is more or less compressed, fleshy drupe, varies considerably in size, shape, colour, presence of fibre, flavour, taste and several other characters.

Fig 1: Mango buds and flowers.

Fig 2: Mango fruits.

Fig: Mango tree with fruits.

5. Ethnomedicinal uses

Various parts of mango are used for more than thousands of years as wide variety of ethnomedicinal use [12].

- **Roots and Bark:** Used as astringent, acrid, refrigerant, styptic, anti-syphilitic, vulnerary, anti-emetic, anti-inflammatory and constipating. They are useful in vitiated conditions of pitta, metrorrhagia, calonorrhagia, pneumorrhagia, lecorrhoea, syphilis, uteritis, wounds, ulcers and vomiting. The juice of fresh bark has a marked action on mucous membranes, in menorrhoea, leucorrhoca, bleeding piles and diarrhoea.
- **Leaves:** Used as astringent, refrigerant styptic, vulnerary and constipating. They are also useful in vitiated conditions of cough, hiccup, hyperdipsia, burning sensation, hemorrhages, haemoptysis, haemorrhoids, wounds, ulcers, diarrhoea, dysentery, pharyngopathy, scorpion string and stomachopathy. The ash of burnt leaves are useful in burns and scalds. The smoke from burning leaves is inhaled for relief of throat diseases.
- **Flowers:** Used as astringent, refrigerant, styptic, vulnerary, constipating and haematinic. The dried flowers are useful in vitiated conditions of pitta, haemorrhages, haemoptysis, wounds, ulcers, anorexia, dyspepsia, uro-edema gleet, catarrh of bladder, diarrhoea, chronic dysentery and anemia.
- **Fruits:** The unripe fruits are acidic, acrid, antiscorbutic, refrigerant, digestive and carminative. They are useful in dysentery ophthalmia, eruptions, urethrorrhoea and vaginopathy. The ripe fruits are refrigerant, sweet, emollient, laxative, cardiotonic, haemostatic, aphrodisiac, and tonic. They are also used in vitiated conditions vata and pitta, anorexia, dyspepsia, cardiopathy, haemoptysis, haemorrhages from uterus, lungs and intestine, emaciation, and anemia.
- **Stone:** The seed kernel in rich source of protein (8.5%) and gallic acid. It is sweet, acrid, astringent, refrigerant, anthelmintic, constipating, haemostatic, vulnerary and uterine tonic. It is useful in vitiated conditions of pitta and cough, helminthiasis, chronic diarrhea, dysentery, haemorrhages, haemoptysis, haemorrhoids, ulcers, bruises, leucorrhoea, menorrhagia, diabetes, heat burn and vomiting.

6. Nutrient and Phytochemicals

The energy value per 100 g (3.5 oz) is 250 kJ (60 kcal) and that of the apple mango is slightly higher (79 kcal per 100g). Mango contains a variety of phytochemicals [13] and nutrients [14]. Mango peel and pulp contain other compounds, such as pigment carotenoids and polyphenols, and omega-3 and -6 polyunsaturated fatty acids [15]. Mango peel pigments have

biological effects, including carotenoids, such as the provitamin A compound, beta-carotene, lutein and alpha-carotene, [16] polyphenols [17-18] such as quercetin, kaempferol, gallic acid, caffeic acid, catechins, tannins and the unique mango xanthonoid, mangiferin [19] which are under preliminary research for their potential to counteract various disease processes [20-21]. Phytochemical and nutrient content appears to vary across mango cultivars [22]. Up to 25 different carotenoids have been isolated from mango pulp, the densest of which was beta-carotene, which accounts for the yellow-orange pigmentation of most mango cultivars [23].

7. Pharmacological uses

7.1. Anticancer: Noratto *et al.*, (2010) compared the anticancer properties of polyphenolic extracts from several mango varieties in cancer lines, including Molt-4 leukemia, A-549 lung, MDA-MB-231 breast, LnCap prostate, SW-480 colon cancer cells and non-cancer colon cell line CCD-18Co [24]. Ali *et al*., (2012) and Timsina *et al*., (2015) determined that ethanol extract had significant cytotoxicity to HeLa cells and the bioactive fraction from the crude extract had antiproliferative effects with an IC_{50} value of<10µg/ml [25-26]. The significant cytotoxic activities of mango are also found against the breast cancer cell lines MCF 7, MDA-MB-435, MDA-N; colon cancer cell line (SW-620); renal cancer cell line (786-0) [27] and K562 leukemia cells [28]. Percival S *et al*., (2010) found whole mango juice and juice extracts has anticancer activity and saw that incubation of HL-60 cells with whole mango juice and mango juice fractions resulted in an inhibition of the cell cycle in the G_0/G_1 phase [20]. Research also indicates that mangiferin may have impaired or interfered with the assembly or functioning of microtubule filaments or cellular matrix components, thus disrupting the cells' adhesion/ attachment ability [28-32]. The other possible mechanisms of mangiferin included inhibition of the telomerase and the gene [30], and the enhancement of the cellular apoptosis [30, 33]. The anti-proliferative activities of mango peels and flesh were also investigated by Kim *et al*., (2012) [34].

7.2. Antidiabetic: Bhowmik *et al*., (2009) found that Single oral administration of a dose of 250 mg/ kg body weight produces a potent and strong hypoglycemic effect in Type-2 diabetes on rats [35]. Similar result was found by Reda MY, (2010) [36]. A significant decrease in mean concentration of plasma glucose two weeks after administration of high (1 g/kg/d) dose of powdered part, aqueous extract and alcoholic extract of leaves of *Mangifera indica* were found [37]. In another study, Wadood *et al*., (2000) found the anti-diabetic effects of alcoholic extract of the leaves of *Mangifera indica* at doses of 50, 100,150 and 200 mg/kg body weight in rabbits [38]. The leaves of *Mangifera indica* (MI) used for antidiabetic properties discovered by scholars [39-42]. Also, Miura T *et al*. (2001) and Mangola EN, (1990) observed that aqueous extract from mango leaves showed a clear hypoglycemic effect in diabetic rats [43-44]. And other scientist found antidiabetic activities of *Mangifera indica* stem bark [45-46]. Oliver-Bever B, (1986) found that the bark and roots extracts of mango significantly lowered the blood sugar level of hyperglycemic rats [47].

7.3. Anti-inflammatory: Dhananjaya BL & Shivalingaiah S, (2016) reported anti-inflammatory activity of standard aqueous stem bark extract of *Mangifera indica* in inhibition of Group IA sPLA2 enzyme activity up to 98% at ~40 µg/ml concentration [48]. Beltrana AE *et al*., (2004) reported that anti-inflammatory action of mangiferin is related with the inhibition of iNOS and cyclooxygenase-2 expression [49]. The possible anti-inflammatory mechanisms of mangiferin include the balance between the overwhelming anti-inflammatory cytokines and proinflammatory mediators, inhibition of inflammatory cellular activations, regulations of inflammatory gene expressions, and enhancements of the cellular resistance against inflammatory injuries [50-52]. The sub-cellular targets of the anti-inflammatory effects located at the thermoregulatory neural centers for their reducing prostaglandin synthesis in fever [53] and the lysosomal membrane for its lowering hydrolase activity in isoprenaline-induced myocardial necrosis [54]. Anti-inflammatory activity of mango are also reported by many other scientists [54-58].

7.4. Hepatoprotective: Hepatoprotective activities in mango seed kernels studied by Nithitanakool *et al.*, (2009). Chemopreventive properties of mango pulp extract (MPE) was evaluated in alteration in liver of Swiss albino mice. MPE was found to be effective in combating oxidative stress induced cellular injury of mouse liver by modulating cell-growth regulators [59].

7.5. Anti-hemorrhagic: Anti-hemorrhagic and anti-dermonecrotic activities of mango extract against snake venoms was evaluated by Leanpolchareanchai *et al.*, (2009) and Pithayanukul *et al.*, (2009) [60-61].

7.6. Anti-tetanus: Godfrey SB *et al*., (2007) reported activity of the MI leaf extracts against *Clostridium tetani*, which causes many deaths around the world. Ether and ethanolic leaf extracts were showed anti-clostridium tetani activity with an MIC of 6.25 and 12.5 mg/ml, respectively [62].

7.7. Analgesic and Antipyretic: The stem bark extract of MI was evaluated for antipyretic activity in mice. A reduction in yeast-induced hyperpyrexia was also produced by the extract [63].

7.8. Kidney damage: Amien AI *et al*., (2015) revealed significant prophylactic effect against kidney injury by enhancement of the kidney function via decreasing serum creatinine, urea and uric acid. Treatment of rats with 500 and 1000mg/kg MPS extract significantly increased the level of reduced glutathione (GSH) and superoxide dismutase (SOD) activity while decreased the level of total malondialdehyde (MDA) and glutathione-S-transferase (GST) [64].

7.9. Anti-ulcer: The antiulcer potential of the petroleum ether and ethanol extracts of leaves of mango was evaluated by Neelima N *et al*., (2012) against in vivo aspirin-induced gastric ulcer. The petroleum ether (250mg/kg) and ethanol extracts (250mg/kg) of leaves of mango tree significantly reduced the ulcer index [65]. Another findings provide evidence that mangiferin affords gastro protection against gastric injury through the antisecretory and antioxidant mechanisms of action [66].

7.10. Lipid profile: Treatment with aqueous extract of *Mangifera indica* leaves significantly decreased total serum cholesterol, triglycerides, low density lipoprotein, very low density lipoprotein and increased in high density lipoproteins in rats. Whereas treatment with aqueous extract of mango leaves (200 mg/kg body weight) showed significant decrease

in elevated total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL-C) and very low density lipoprotein (VLDL), with significant increase in high density lipoprotein (HDL-C) [67].

7.11. Antibone resorption: Mangiferin has been shown to inhibit parathyroid-hormone stimulated bone resorption in mice [68].

7.12. Anti-diarrheal: The potential anti-diarrheal activity of methanolic and aqueous extracts of seeds of *M. indica* was studied by Sairam K *et al*., 2003 [69]. Anti-diarrheal activity of mango kernel aqueous extract at 0.25 to 0.50 mg/ml dose are studied by Alkizim *et al*., (2012) [70].

7.13. Antibacterial: The aqueous and ethanol extract of leaves and stems of mango at 50 and 25 mg/mL has been found sufficient activity against bacteria; *Staphylococcus aureus*, *Streptococcus pyogenes, Streptococcus pneumoniae, Pseudomonas aeruginosa, Candida albicans, Enterococcus faecalis* [71]. The antibacterial ability of extract also found against *Salmonella enterica*, *Listeria monocytogenes*, *Escherichia coli* [72]. Sahrawat A *et al.*, (2013) determines antibacterial activities of *Mangifera indica* leaf on methanol, ethanol and benzene extract were studied against bacteria some as *Proteus vulgaris, Pseudomonas fluorescens*, *Shigella flexneri*, *Klebsiella pneumonia* and *Salmonella typhi* at 100µl/ml concentration [73]. Antibacterial activity of mango extracts upon gram-positive, gram-negative bacteria and yeast *Candida albicans* was also demonstrated [74-75] and it is thought that the antibacterial activity of mango extract is due to the presence of gallotannin and mangiferin [76].

7.14. Antifungal: The antifungal potential of methanol, ethanol and aqueous extracts was found against *Alternaria alternata* at 6.25 mg/mL concentration [72].

7.15. Antiviral: Mangiferin was considered as an antiviral agent upon herpes simplex virus [77-78], HIV and hepatitis B virus [79]. Zhu XM *et al*., (1993) studied *in vitro* effect of mangiferin against *Herpes simplex* virus (HSV) type 2; mangiferin does not directly inactivate HSV-2 but inhibits the late event in HSV-2 replication [78]. In *in vitro*, mangiferin was also able to inhibit HSV-1 virus replication within cells [77] and to antagonize the cytopathic effects of HIV [80].

7.16. Anti-amoebic: Anti-amoebic activities of mango extract was also evaluated by Tona L *et al*., (2000) [81].

7.17. Anthelmintic: Anthelminthic activities of MI stem bark component, mangiferin was investigated in mice experimentally infected with nematodes, *Trichinella spiralis* [82].

7.18. Antimalarial: The stem bark extract of MI was evaluated for antiplasmodial activity against *Plasmodium yoeliinigeriensis*. The extract exhibited a schizontocidal effect during early infection, and also demonstrated repository activity [63]. The *in vitro* antimalarial activity of chloroform: methanol (1:1) extract of MI was evaluated. The extract showed a good activity on *P. falciparum in vitro* with a growth inhibition of 50.4% at 20 µg/mL [83].

7.19. Radio protective: The radio protective actions of mangiferin have been confirmed on radiation-induced immunocytes without changing the susceptibility of malignant cells at 2mg/kg concentration [84-85].

7.20. Immunoregulation: Mangiferin has been considered as a candidate for immunoregulators. As an immuno- stimulant, it rescued the cyclophosphamide-induced immune depression, such as the lymphoid organ atrophy, less cellular response, low antigen-specific IgM, more lipid peroxidation, and decreased superoxide dismutase activities. It also increased remarkably the levels of serum hemolysis IgG and IgM in mice [86]. Its immune modulatory mechanisms might be related to the inhibition on activation-induced T-cell death and the cellular skeleton of the stimulated macrophage resulted in the cytoplasmic spread, long extensions and intercellular contacts [87].

7.21. Cardio protective: Devi *et al*., (2006) investigated the effect of mangiferin on the isoproterenol- induced myocardial infarction in rats. Mangiferin was found to ameliorate the effect of isoproterenol-induced pathological changes, reduced the lipid peroxide formation and retained the myocardial marker enzyme activities at near normal level. The above results indicate the cardio protective effect of mangiferin [88].

7.22. Osteoporosis prevention: Importantly, mango not only improved bone mineral density but also the quality of the bone as shown by improvement in the microarchitecture and strength [89].

7.23. Recognition of memory: Mangiferin stimulated cell proliferation and induced a significant increase in the supernatant levels of nerve growth factor (NGF) and tumor necrosis factor (TNF)-α in vitro in human U138-MG glioblastoma cells. The results indicate that mangiferin enhances recognition memory through a mechanism that might involve an increase in neurotrophin and cytokine levels [90].

7.24. Bronchodilatory: Gbeassor *et al*., (2005) studied the effect of *M. indica* stem bark aqueous extract (mangiferin) on rat trachea contracted by acetylcholine and histamine. These experiments suggested that the aqueous extract of *M. indica* (mangiferin) could block both the histaminic and muscarinic receptors on rat trachea and thus suggesting its potential use in the treatment of asthma [91].

7.25. Laxative: Mangiferin significantly accelerated gastro intestinal tract (GIT) movement at oral doses of 30 mg/kg and 100 mg/kg by 89% and 93%, respectively [92].

8. Conclusion

Plants are one of the most important sources of medicines. The role of medicinal plants in promoting the ability of human health to cope with the unpleasant and difficult situations is well documented from ancient times till date all over the world. One of the cardinal goals of millennium development goals (MDGs) is the quest to combat the incidence of diseases such as malaria, HIV/AIDS and chronic diseases such as age-related degenerative diseases, cancer and cardiovascular diseases. Medicinal plants are rich in secondary metabolites which are potential sources of drugs and of therapeutic importance. There is increasing interest in the use of plant extracts as therapeutic agents. Mango 'king of fruit' belongs to use pharmacological potential as panacea. From the literature survey it is found that mango is a potential source of anticancer, anti-diabetic, anti-inflammatory, antimicrobial

drugs as well as it also used as cardio protective, radio protective, recognition of memory and many others.

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