Mangifera Indica (Mango)

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ABSTRACT

Mangifera indica, commonly used herb in ayurvedic medicine. Although review articles on this plant are already published, but this review article is presented to compile all the updated information on its phytochemical and pharmacological activities, which were performed widely by different methods. Studies indicate mango possesses antidiabetic, anti-oxidant, anti-viral, cardiotonic, hypotensive, anti-inflammatory properties. Various effects like antibacterial, anti fungal, anthelmintic, anti parasitic, anti tumor, anti HIV, antibone resorption, antispasmodic, antipyretic, antidiarrhoeal, antiallergic, immunomodulation, hypolipidemic, anti microbial, hepatoprotective, gastroprotective have also been studied. These studies are very encouraging and indicate this herb should be studied more extensively to confirm these results and reveal other potential therapeutic effects. Clinical trials using mango for a variety of conditions should also be conducted.

Key words: *Mangifera indica*, mangiferin, pharmacological activities, phytochemistry

INTRODUCTION

Mangifera indica (MI), also known as mango, aam, it has been an important herb in the Ayurvedic and indigenous medical systems for over 4000 years. Mangoes belong to genus *Mangifera* which consists of about 30 species of tropical fruiting trees in the flowering plant family Anacardiaceae. According to ayurveda, varied medicinal properties are attributed to different parts of mango tree.

Mango is one of the most popular of all tropical fruits. Mangiferin, being a polyphenolic antioxidant and a glucosyl xanthone, it has strong antioxidant, anti lipid peroxidation, immunomodulation, cardiotonic, hypotensive, wound healing, antidegenerative and antidiabetic activities.

Various parts of plant are used as a dentrifrice, antiseptic, astringent, diaphoretic, stomachic, vermifuge, tonic, laxative and diuretic and to treat diarrhea, dysentery, anaemia, asthma, bronchitis, cough, hypertension, insomnia, rheumatism, toothache, leucorrhoea, haemorrhage and piles. All parts are used to treat abscesses, broken horn, rabid dog or jackal bite, tumour, snakebite, stings, datura poisoning, heat stroke, miscarriage, anthrax, blisters, wounds in the mouth, tympanitis, colic, diarrhea, glossitis, indigestion, bacillosis, bloody dysentery, liver disorders, excessive urination, tetanus and asthma.

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Ripe mango fruit is considered to be invigorating and freshening. The juice is restorative tonic and used in heat stroke. The seeds are used in asthma and as an astringent. Fumes from the burning leaves are inhaled for relief from hiccups and affections of the throat. The bark is astringent, it is used in diphtheria and rheumatism, and it is believed to possess a tonic action on mucus membrane. The gum is used in dressings for cracked feet and for scabies. It is also considered anti-syphilitic. The kernels are converted into flour after soaking in water and eliminating the astringent principles. Most parts of the tree are used medicinally and the bark also contains tannins, which are used for the purpose of dyeing.

TAXONOMICAL CLASSIFICATION

Kingdom	:	*Plantae*
Class	:	*Mangoliopsida*
Phylum	:	*Mangoliophyta*
Order	:	*Sapindales*
Family	:	*Anacardiaceae*
Genus	:	*Mangifera*
Species	:	*Indica*

Species of mango:

Mangifera altissima	*Mangifera persiciformis*
Mangifera caesia	*Mangifera camptosperma*
Mangifera casturi	*Mangifera decandra*
Mangifera foetida	*Mangifera indica*
Mangifera griffithii	*Mangifera laurina*
Mangifera kemanga	*Mangifera macrocarpa*
Mangifera longipes	*Mangifera odorata*
Mangifera mekongensis	*Mangifera quadrifida*

Mangifera pajang *Mangifera similis*
Mangifera siamensis *Mangifera sylvactia*
Mangifera torquenda *Mangifera zeylanica*
Mangifera applanata *Mangifera swintonioides*

Botanical description

MI is a large evergreen tree in the anacardiaceae family that grows to a height of 10-45 m, dome shaped with dense foliage, typically heavy branched from a stout trunk. The leaves are spirally arranged on branches, linear-oblong, lanceolate – elliptical, pointed at both ends, the leaf blades mostly about 25-cm long and 8-cm wide, sometimes much larger, reddish and thinly flaccid when first formed and release an aromatic odour when crushed. The inflorescence occurs in panicles consisting of about 3000 tiny whitish-red or yellowish – green flowers. The fruit is a well known large drupe, but shows a great variation in shape and size. It contains a thick yellow pulp, single seed and thick yellowish – red skin when ripe. The seed is solitary, ovoid or oblong, encased in a hard, compressed fibrous endocarp.

Habitat

It is native tropical Asia and has been cultivated in the Indian subcontinent for over 4000 years and is now found naturalized in most tropical countries.

Parts used: Roots, bark, leaves, fruits, seeds, flowers and kernels are used.

Synonyms

Sanskrit: Ambrah; Madhuulii; Madhuula; Madhuulaka; English: Mango; Hindi: Aam; French: mangot; mangue; manguier; Portuguese: manga; mangueira; Dutch: manja; Tamil: Ambiram; Mambazham; Mambalam; Mangai; Punjabi: Amb; Wawashi; Gujarati: Ambo, Keri; Marvo (unripe); Kashmiri: Amb; Malayalam: Amram; Choothaphalam; Manga; Manpalam; Mavu; Marathi: Amchur; Amba

PHYTOCHEMISTRY

Chemical constituents of MI are always of an interest. The different chemical constituents of the plant, especially the polyphenolics, flavonoids, triterpenoids. Mangiferin a xanthone glycoside major bio-active constituent, isomangiferin, tannins & gallic acid derivatives. The bark is reported to contain protocatechic acid, catechin, mangiferin [Figure 1], alanine, glycine, γ-aminobutyric acid, kinic acid, shikimic acid and the tetracyclic triterpenoids cycloart-24-en-3β,26diol, 3-ketodammar-24 (*E*)-en-20S,26-diol, C-24 epimers of cycloart-25 en 3β,24, 27-triol and cycloartan-3β,24,27-triol.[1]

Indicoside A and B, manghopanal, mangoleanone, friedelin, cycloartan-3β-30-diol and derivatives, mangsterol, manglupenone, mangocoumarin, n-tetacosane, n-heneicosane, n-triacontane and mangiferolic acid methyl ester and others isolated from stem bark of MI.[2] Mangostin, 29-hydroxy mangiferonic acid and

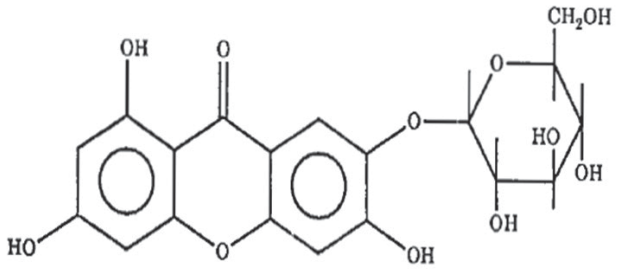

Figure 1: Structure of Mangiferin

mangiferin have been isolated from the stem bark together with common flavonoids.[3] The flower yielded alkyl gallates such as gallic acid, ethyl gallate, methyl gallate, n-propyl gallate, n-pentyl gallate, n-octyl gallate, 4-phenyl gallate, 6-phenyl-n-hexyl gallate and dihydrogallic acid.[4] Root of mango contains the chromones, 3-hydroxy-2-(4'-methylbenzoyl)-chromone and 3-methoxy-2-(4'-methyl benzoyl)-chromone. The leaf and flower yield an essential oil containing humulene, elemene, ocimene, linalool, nerol and many others. The fruit pulp contains vitamins A and C, β-carotene and xanthophylls.[5] An unusual fatty acid, cis-9, cis-15-octadecadienoic acid was isolated from the pulp lipids of mango.[6] Phenolic Antioxidants, Free Sugars and Polyols isolated and analyzed from Mango (MI) Stem Bark. All structures were elucidated by ES-MS and NMR spectroscopic methods. Quantitative analysis of the compounds has been performed by HPLC, and mangiferin was found to be the predominant component.[7]

Polyphenols have been characterized in mango puree concentrate by HPLC with diode array and mass spectrometric detection.[8] A rapid method was developed for quantitative determination of beta-carotene, including cis-isomers, in dried mango.[9] HPLC method was developed to determine carotenoids in Taiwanese mango.[10] 5-Alkyl- and 5-alkenylresorcinols, as well as their hydroxylated derivatives, extracted from mango (MI) peels, purified on polyamide and characterized by high-performance liquid chromatography/atmospheric pressure chemical ionization mass spectrometry (HPLC/APcI-MS) for the first time.[11] Xanthophyll esters, carotenes, and tocopherols has been identified and quantified in the fruit of seven mexican mango cultivars by liquid chromatography-atmospheric pressure chemical ionization-time-of-flight mass spectrometry [LC-(APcI (+))-MS].[12] A simple, precise, and rapid HPTLC method was established for quantitative determination of the bioactive marker compound mangiferin in the stem bark & leaves of MI. The method was validated for selectivity, linearity, precision, accuracy, and robustness.[13] The natural C-glucoside xanthone mangiferin [2-C-β-Dgluco-pyranosyl-1,3,6,7-tetrahydroxyxanthone; $C_{19}H_{18}O_{11}$; Mw, 422.35; melting point, anhydrous 271°C[14] has been reported in various parts of MI leaves,[15] fruits, stem bark, heartwood and roots. The presence of a phenolic compound from leaves of MI which was named as homomangifirin.[16]

Pharmacology

Although a lot of pharmacological investigations have been carried out based on the ingredients present but a lot more can still be explored, exploited and utilized. A summary of the findings of these studies is presented below.

Anti-oxidant

Reactive oxygen species (ROS) possess a strong oxidizing effect and induce damage to biological molecules, including proteins, lipids and DNA, with concomitant changes in their structure and function.[17] The major nutritional antioxidants, vitamin E, vitamin C and β-carotene, may be beneficial to prevent several chronic disorders[18] considerable interest has arisen in the possible reinforcement of antioxidant defenses, both for chemoprevention and treatment purposes.[19] The extract showed a powerful scavenging activity of hydroxy radicals and acted as a chelator of iron. It also showed a significant inhibitory effect on the peroxidation of rat brain phospholipid and prevented DNA damage caused by bleomycin or copper-phenenthroline systems[20] The interaction of Vimang (MI extract) with Fe (III) was studied and the results justify the high efficiency of Vimang as an agent protecting from iron-induced oxidative damage.[21] The work has been carried out to investigate the pulp composition of four mango cultivars (Haden, Tommy Atkins and Ubá) at the ripening stage in relation to three components with antioxidant potential (total phenolics, carotenoids and ascorbic acid). These results corroborated previous information that mangoes are a good source of antioxidants in human diet.[22] *In vitro* antioxidant and free radical scavenging properties of a stem bark aqueous extract of mango tree (MI), whose formulations are used in Cuba as food supplements under the brand name of Vimang, Luminol-enhanced chemiluminescence was used to elucidate the effect of this extract on the generation of reactive oxygen species in PMA- or zymosan-stimulated human polymorphonuclear leukocytes and on superoxide radicals generated in the hypoxanthine–xanthine oxidase reaction. Part of this MI extract antioxidant activity could be ascribed to the presence of mangiferin as its main component.[23] The iron-complexing ability of Vimang as a primary mechanism for protection of rat liver mitochondria against Fe^{2+} -citrate-induced lipoperoxidation was reported. The results are of pharmacological relevance since Vimang could be a potential candidate for antioxidant therapy in diseases related to abnormal intracellular iron distribution or iron overload.[24] The protective abilities of MI stem bark extract (Vimang) 50-250 mgkg(-1), mangiferin 50 mgkg(-1) and selected antioxidants (vitamin C 100 mgkg(-1), vitamin E 100 mgkg(-1)and beta -carotene 50 mgkg(-1)) against the 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced oxidative damage in serum, liver, brain as well as in the hyper-production of reactive oxygen species (ROS) by peritoneal macrophages was compared.[25]

Anti-diabetic

A 50% ethanolic extract of the leaves of MI produced a significant hypoglycemic effect at a dose of 250 mg/kg, both in normal and streptozotocin-induced diabetic animals. The stimulation of β-cells to release insulin was thought to be part of the mechanism of action.[26] The effect of the aqueous extract of the leaves of MI on blood glucose level in normoglycaemic, glucose - induced hyperglycaemic and streptozotocin (STZ)-induced diabetic rats has been assessed. The results indicate that the aqueous extract of the leaves of MI possess hypoglycaemic activity. This action may be due to an intestinal reduction of the absorption of glucose.[27] The leaves of MI used for antidiabetic properties using normoglycaemic, glucose-induced hyperglycaemia and streptozotocin (STZ) induced diabetic mice. The aqueous extract of the leaves of MI possess hypoglycaemic activity.[28] The effect of mango (MI) ingestion on blood glucose levels of normal and diabetic rats has been studied. The results from this research suggest that mango flour can possibly help in the treatment of diabetes.[29] The stem-bark of aqueous extract of MI was used to examine the antiinflammatory, analgesic and antidiabetic properties. The different chemical constituents of the plant, especially the polyphenolics, flavonoids, triterpenoids, mangiferin, and other chemical compounds present in the plant may be involved in the observed antiinflammatory, analgesic, and hypoglycemic effects of the plant's extract. The results of this experimental animal study lend pharmacological credence to the suggested folkloric uses of the plant in the management and control of painful, arthritic and other inflammatory conditions, as well as in the management of adult-onset type 2 diabetes mellitus in some rural African communities.[30] Investigations were carried out to evaluate the effect of MI on glucose absorption using a rat intestinal preparation *in situ*. The ethanol extracts of stem-barks reduced glucose absorption gradually during the whole perfusion period in type 2 rats.[31] In glucose-loaded normal rats, mangiferin induces a significant improvement in oral glucose tolerance but without alteration of basal plasma glucose levels[32] these studies show that mangiferin (10 and 20 mg/kg, i.p.) exhibits potent antidiabetic, antihyperlipidemic, antiatherogenic and antioxidant properties without causing hypoglycaemia; mangiferin would then offer a greater therapeutic benefit for the management of diabetes mellitus and diabetic complications associated with abnormalities in lipid profiles. It has been reported that long standing hyperglycaemia with diabetes mellitus leads to the formation of advanced glycosylated end-products which are involved in the generation of ROS, leading to oxidative damage, particularly to heart and kidney.[33]

Antiviral activity

In vitro the effect of mangiferin was studied against *Herpes simplex* virus type 2; mangiferin does not directly inactivate HSV-2 but inhibits the late event in HSV-2 replication.[34] *In vitro* mangiferin was also able to inhibit HSV-1 virus replication within cells[35] and to antagonize the cytopathic effects of HIV.[36]

Anthelmintic and anti-allergenic activity

Anthelminthic and antiallergic activities of MI stem bark components Vimang and mangiferin was investigated in mice experimentally infected with nematodes, *Trichinella spiralis*.[37] The study was carried out to find out anti-allergic properties of vimang and mangiferin, a C-glucosylxanthone isolated from extract of MI. The results constitute the anti-allergic properties

of Vimang on allergic models, as well as suggesting that this natural extract could be successfully used in the treatment of allergic disorders. Mangiferin, the major compound of Vimang, contributes to the anti-allergic effects of the extract.[38]

Antiparasitic activity

In a neonatal mouse model, mangiferin at 100 mg/kg has a similar inhibitory activity on *Cryptosporidium parvum* than the same dose (100 mg/kg) of an active drug, paromomycin.[39]

Antibone resorption

Four water extracts of *Kampo* formulae were screened for their inhibitory effect on bone resorption induced by parathyroid hormone in organ culture of neonatal mouse parietal bones. Mangiferin isolated and tested *in vitro* showed a significant inhibitory effect on this model.[40]

Anti-tumor-anti-HIV

The significant cytotoxic activities has been demonstrated by the stem bark extract of mango against the breast cancer cell lines MCF 7, MDA-MB-435 and MDA-N, as well as against a colon cancer cell line (SW-620) and a renal cancer cell line (786-0).[41] The ethanol/water (1:1) extract of dried aerial parts of mango administered intraperitoneally to mice at a dose of 250.0 mg/kg was inactive on Leuk-P388.[42] *In vitro,* mangiferin dose- and time-dependently inhibited the proliferation of K562 leukemia cells and induced apoptosis in K563 cells line, probably through down-regulation of bcr/abl gene expression.[43] These results suggest that mangiferin has a potential as a naturally-occurring chemopreventive agent.[44]

Antispasmodic and antipyretic activity

The stem bark extract of MI was evaluated for antiplasmodial activity against *Plasmodium yoelii nigeriensis*. The extract was also screened for antipyretic activity in mice. The extract exhibited a schizontocidal effect during early infection, and also demonstrated repository activity. A reduction in yeast-induced hyperpyrexia was also produced by the extract.[45] 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.[46]

Immunomodulatory

Immunomodulatory activity of alcoholic extract of stem bark of MI was investigated in mice. It is concluded that test extract is a promising drug with immunostimulant properties. Mangiferin mediates the down-regulation of NF-ϰB, suppresses NF-ϰB activation induced by inflammatory agents, including tumor nuclear factor (TNF), increases the intracellular glutathione (GSH) levels and potentiates chemotherapeutic agent-mediated cell death; this suggests a possible role in combination therapy for cancer.[47] It is likely that these effects are mediated through mangiferin ROS quenching and GSH rising; increased intracellular (GSH) levels are indeed known to inhibit the TNF-induced activation of NF-ϰB.[48]

Anti-diarrhoeal

The potential anti-diarrhoeal activity of methanolic (MMI) and aqueous (AMI) extracts of seeds of MI has been evaluated in experimental diarrhoea, induced by castor oil and magnesium sulphate in mice. The results illustrate that the extracts of MI have significant anti-diarrhoeal activity and part of the activity of MMI may be attributed to its effect on intestinal transit.[49]

Anti-inflammatory

An ethanolic (95%) extract of the seed kernel of MI exhibited significant anti-inflammatory activity in acute, subacute and chronic cases of inflammation. The MI leaf extract exhibited antibacterial activity against Bacillus subtilis, staphylococcus albus and Vibrio cholerae.[50] Analgesic and anti-inflammatory effects of MI extract (Vimang) has studied. The polyphenols found in the extract were found to account for the activity reported[51] *In vivo* and *in vitro* anti-inflammatory activity of MI extracts (VIMANG) was investigated. MI extract, administered topically (0.5-2 mg per ear), reduced ear edema induced by arachidonic acid (AA) and phorbol myristate acetate (PMA, ED50 = 1.1 mg per ear) in mice. The results represent an important contribution to the elucidation of the mechanism involved in the anti-inflammatory and anti-nociceptive effects reported by the standard MI extract VIMANG.[52]

Anti-bacterial and antifungal activity

In an *in vitro* agar diffusion technique, mangiferin showed activity against 7 bacterial species, *Bacillus pumilus*, *B. cereus*, *Staphylococcus aureus*, *S. citreus*, *Escherichia coli*, *Salmonella agona*, *Klebsiella pneumoniae*, 1 yeast (*Saccharomyces cerevisiae*) and 4 fungi (*Thermoascus aurantiacus*, *Trichoderma reesei*, *Aspergillus flavus* and *A. fumigatus*).[53]

Anti-microbial

The antimicrobial activities of methanolic extracts of *P. guajava* and MI have been investigated. The results show that *P. guajava* and MI extracts exhibited antimicrobial activities at a concentration of 20 mg/ml. Overall, *P. guajava* extract show more antimicrobial activity than MI extract against tested organisms.[54]

Hepatoprotective

Chemopreventive properties of lupeol and mango pulp extract (MPE) was evaluated against 7, 12-dimethylbenz (a) anthracene (DMBA) induced alteration in liver of Swiss albino mice. Lupeol/MPE was found to be effective in combating oxidative stress induced cellular injury of mouse liver by modulating cell-growth regulators.[55]

Gastroprotective

A novel gastroprotective agent, mangiferin, a naturally occurring glucosylxanthone from MI (Anacardiaceae), was evaluated in mice on gastric injury induced by ethanol and indomethacin. The effects of mangiferin on gastric mucosal damage were assessed by determination of changes in mean gastric lesion area or ulcer score in mice and on gastric secretory volume and total acidity in 4-h pylorus-ligated rats. These findings provide evidence that mangiferin affords gastroprotection against gastric injury

induced by ethanol and indomethacin most possibly through the antisecretory and antioxidant mechanisms of action.[56]

Other activity

Ethanolic extracts of *Punica granatum*, MI, *Boerhaavia diffusa*, *Embelia ribes, Phyllanthus maderaspatensis*, and *Withania somnifera*, has been tested for their effect on α-amylase activity (*in vitro*). *P. granatum* and MI were found to exhibit interesting α-amylase inhibitory activity.[57] The ethanolic extracts of *Lawsonia inermis* leaves, *Holarrhena antidysenterica* bark, Swertia chirata whole plant and MI bark was tested for *in-vitro* α-glucosidase inhibitory activity. MI extract was found to be the most potent, with an IC_{50} value of 314 μg/ml.[58] The effects of the MI (Vimang) extract, and mangiferin (a C-glucosylxanthone of Vimang) on the inducible isoforms of cyclooxygenase (cyclooxygenase-2) and nitric oxide synthase (iNOS) expression and on vasoconstrictor responses in vascular smooth muscle cells and mesenteric resistance arteries, has investigated respectively, from Wistar Kyoto (WKY) and spontaneously hypertensive (SHR) rats. They concluded that, the antiinflammatory action of Vimang would be related with the inhibition of iNOS and cyclooxygenase-2 expression, but not with its effect on vasoconstrictor responses.[59] The activity of the MI leaf extracts against Clostridium tetani, has been investigated which causes many deaths around the world. Ether and ethanolic leaf extracts were obtained by sequential extractions. The chemical tests showed that the ether extract had saponins, steroids and triterpenoids, while the ethanol extract had alkaloids, anthracenosides, coumarins, flavonones, reducing sugars, catechol and gallic tannins, saponins, steroids and triterpenoids. Both the ethereal and ethanolic fractions showed anti-clostridium tetani activity with an MIC of 6.25 and 12.5 mg ml−1, respectively.[60] The cytotoxic effects of Vimang on rat hepatocytes, possible interactions of the extract with drug-metabolizing enzymes and its effects on GSH levels and lipid peroxidation was studied. The effect of the extract (50–400 μg/mL) on several P_{450} isozymes was evaluated. A 36-h pre-treatment of cells with Vimang (25–200 μg/mL) strongly inhibited the decrease of GSH levels and lipid peroxidation induced by t-butyl-hydroperoxide dose- and time-dependently.[61]

CONCLUSION

The extensive survey of literature revealed that MI is an important source of many pharmacologically and medicinally important chemicals such as mangiferin, mangiferonic acid [Figure 2], hydroxymangiferin, polyphenols and carotenes. Many different pharmacological activities, antioxidant, radioprotective, immunomodulatory, anti-allergic, anti-inflammatory, antitumor, antidiabetic, lipolytic, antibone resorption, monoamine oxidase-inhibiting, antimicrobial and antiparasitic, have been reported for mangiferin. All these studies indicate that a wide part of activities acknowledged to preparation based on MI bark could be attributed to this C-glucosyl-xanthone (mangiferin). Based on the knowledge of the many properties of mangiferin, phytomedicines should be adequately standardized regarding this active compound. MI has been used successfully in Ayurvedic medicine for centuries, more clinical trials should be conducted to support its therapeutic use.

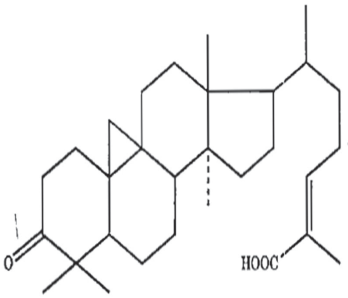

Figure 2: Structure of Mangiferonic acid

SUMMARY

Mangifera indica (MI), also known as mango, aam, it has been an important herb in the Ayurvedic and indigenous medical systems for over 4000 years. Mangoes belong to genus *Mangifera* which consists of about 30 species of tropical fruiting trees in the flowering plant family Anacardiaceae. According to ayurveda, varied medicinal properties are attributed to different parts of mango tree. Mango possesses antidiabetic, anti-oxidant, anti-viral, cardiotonic, hypotensive, anti-inflammatory properties. Various effects like antibacterial, anti fungal, anthelmintic, anti parasitic, anti tumor, anti HIV, antibone resorption, antispasmodic, antipyretic, antidiarrhoeal, antiallergic, immunomodulation, hypolipidemic, anti microbial, hepatoprotective, gastroprotective have also been studied. Pharmacologically and medicinally important chemical such as mangiferin, being a polyphenolic antioxidant and a glucosyl xanthone, it has strong antioxidant, anti lipid peroxidation, immunomodulation, cardiotonic, hypotensive, wound healing, antidegenerative and antidiabetic activities.

REFERENCES

1. Scartezzini P, Speroni E. Review on some plants of Indian traditional medicine with antioxidant activity. J Ethnopharmacol 2000;71:23-43.
2. Khan MN, Nizami SS, Khan MA, Ahmed Z. New saponins from *Mangifera Indica*. J Nat Prod 1993;56:767-70.
3. Shankarnarayanan D, Gopalakrishman C, Kameswaran L, Arumugum S. The effect of mangostin, mangostin-3, 6-di-O-glucoside and Mangiferin in carbon tetrachloride liver injury. Mediscope 1979;22:65.
4. Khan MA, Khan MN. Alkyl gallates of flowers of *Mangifera Indica*. Fitoterapia 1989;60:284.
5. Ross IA. Medicinal plants of the world. Vol. 1, New Jersey Totowa: Human Press: 1999. p. 199-200.
6. Shibahara A, Yamamoto K, Shinkai K, Nakayama T, Kajimoto G. Cis-9, cis-15-octadecadienoic acid:a novel fatty acid found in higher plants. Biochimi Biophy Acta 1993;1170:245-52.

7. Nunez Selles AJ, Vélez Castro HT, Agüero-Agüero J, Gonzalez-Gonzalez J, Naddeo F, De Simone F. *et al.* Isolation and quantitative analysis of phenolic antioxidants, free sugars, and polyols from Mango (*Mangifera Indica* L.) stem bark aqueous decoction used in cuba as a nutritional supplement. J Agric Food Chem 2002;50:762-6.
8. Andreas S, Wieland U, Reinhold C. Characterization of polyphenols in mango puree concentrate by HPLC with diode array and mass spectrometric detection. Int J Food Sci Nutr 2000;1:161- 6.
9. Pott I, Marx M, Neidhart S, Mühlbauer W, Carle R. Quantitative determination of beta-carotene stereoisomers in fresh, dried, and solar-dried mangoes (*Mangifera Indica* L.). J Agric Food Chem 2003;51:4527-31.
10. Chen JP, Tai CY, Chen BH. Improved liquid chromatographic method for determination of carotenoids in Taiwanese mango (*Mangifera Indica* L.) J Chromatogr A 2004;1054:261-8.
11. Knödler M, Berardini N, Kammerer DR, Carle R, Schieber A. Characterization of major and minor alk(en)ylresorcinols from mango (*Mangifera Indica* L.) peels by high-performance liquid chromatography/atmospheric pressure chemical ionization mass spectrometry. Rapid Commun Mass Spectrom 2007;21:945-51.
12. Ornelas-Paz Jde J, Yahia EM, Gardea-Bejar A. Identification and quantification of xanthophyll esters, carotenes, and tocopherols in the fruit of seven Mexican mango cultivars by liquid chromatography-atmospheric pressure chemical ionization-time-of-flight mass spectrometry [LC-(APcI(+))-MS]. J Agric Food Chem 2007;55:6628-35.
13. Subha R, Pandey MM, Singh AK. A new, convenient method for determination of mangiferin: An anti-diabetic compound, in *Mangifera Indica* L. J Planar Chromatogr 2007;20 :317-320.
14. Muruganandan S, Gupta S, Kataria M, Lal J, Gupta PK. Mangiferin protects the streptozotocin-induced oxidative damage to cardiac and renal tissues in rats. Toxicology 2002;176:165-73.
15. Desai PD, Ganguly AK, Govindachari TR, Joshi BS, Kamat VN, Manmade AH, *et al*. Chemical investigation of some Indian plants: Part II. Indian J Chem 1966;4:457-549.
16. Subbarayan C, Cama HR. Isolation & characterization of a carotenoid-protein complex from *Mangifera indica*(mango). Indian J Biochem 1966;3:225-7.
17. Seifried HE, Anderson DE, Fisher EI, Milner JA. A review of the interaction among dietary antioxidants and reactive oxygen species. J Nutr Biochem 2007;18:567-79.
18. Diplock AT, Charleux JL, Crozier-Willi G, Kok FJ, Rice-Evans C, Roberfroid M, *et al.* Functional food science and defense against reactive oxidative species. Br J Nutr 1998;80:S77-112.
19. Maxwell SR. Anti oxidant therapy: Does it have a role in the treatment of human disease? Expert Opin Investig Drug 1997;6:211-36.
20. Martinez G, Delgado R, Perez G, Garrido G, Nunez Selles AJ, Leon OS. Evaluation of the *in-vitro* antioxidant activity of *Mangifera indica* L: Extract (Vimang). Phytother Res 2000;14:424-7.
21. Pardo-Andreu GL, Sanchez-Baldoquín C, Avila-González R, Yamamoto ET, Revilla A, Uyemura SA, *et al*. Interaction of Vimang *(Mangifera indica* L. extract) with Fe(III) improves its antioxidant and cytoprotecting activity**.** Pharmacol Res 2006;54:389-95.
22. Rocha Ribeiro SM, Queiroz JH, Lopes Ribeiro ME, Campos FM, Pinheiro Santana HM. Antioxidant in mango *(Mangifera indica* L.) pulp. Plant Foods Hum Nutr 2007;62:13-7.
23. Gabino G, Deyarina G, Cheyla R, Nunez-Selles AJ, Rene D. Scavenger effect of a mango (*Mangifera indica* L.) food supplement's active ingredient on free radicals produced by human polymorphonuclear cells and hypoxanthine–xanthine oxidase chemiluminescence systems**.** Food Chem 2008;107:1008–14.
24. Pardo Andreu G, Delgado R, Velho J, Inada NM, Curti C, Vercesi AE. *Mangifera Indica* L. extract (Vimang) inhibits Fe^{2+}-citrate-induced lipoperoxidation in isolated rat liver mitochondria. Pharmacol Res 2005;51:427-35.
25. Sanchez GM, Re L, Giuliani A, Nuñez-Selles AJ, Davison GP, Leon-Fernandez OS. Protective effects of *Mangifera indica* L. extract, mangiferin and selected antioxydants against TPA-induced biomolecules oxidation and peritoneal macrophage activation in mice. Pharmacol Res 2000;42:565-73.
26. Sharma SR, Dwivedi SK, Swarup D. Hypoglycemic potential of *Mangifera indica* leaves in rats. Int J Pharmaco 1997;35:130.
27. Aderibigbe AO, Emudianughe TS, Lawal BA. Antihyperglycaemic effect of *Mangifera indica* in rat. Phytother Res 1999;13:504-7.
28. Aderibigbe AO, Emudianughe TS, Lawal BA. Evaluation of the antidiabetic action of *Mangifera indica* in mice. Phytother Res 2001;15:456-8.
29. Perpétuo GF, Salgado JM. Effect of mango (*Mangifera indica*, L.) ingestion on blood glucose levels of normal and diabetic rats. J Plant Foods Hum Nutr 2003;58:1-12.
30. Ojewole JA. Antiinflammatory, analgesic and hypoglycemic effects of *Mangifera indica* Linn. (Anacardiaceae) stem-bark aqueous extract. Methods Find Exp Clin Pharmacol 2005;27:547-54.
31. Amrita B, Liakot A, Masfida A, Begum R. Studies on the antidiabetic effects of *Mangifera indica* stem-barks and leaves on nondiabetic, type 1 and type 2 diabetic model rats. Bangladesh J Pharmacol 2009;4:110-4.
32. Muruganandan S, Scrinivasan K, Gupta S, Gupta PK, Lal J. Effect of mangiferin on hyperglycemia and atherogenicity in streptozotocin diabetic rats. J Ethnopharmacol 2005;97:497-501.
33. Rolo AP, Palmeira CM. Diabetes and mitochondrial function: Role of hyperglycemia and oxidative stress. Toxicol Appl Pharmacol 2006;212:167-78.
34. Zhu XM, Song JX, Huang ZZ, Whu YM, Yu MJ. Antiviral activity of mangiferin against herpes simplex virus type 2 in vitro. Zhongguo Yao Li Xue Bao 1993;14:452-4.
35. Zheng MS, Lu ZY. Antiviral effect of mangiferin and isomangiferin on herpes simplex virus. Chin Med J 1990;103:160-5.
36. Guha S, Ghosal S, Chattopadyay U. Antitumor, immunomodulatory and anti-HIV effect of mangiferin: A naturally occurring glucosylxanthone. Chemotherapy 1996;42:443-51.
37. Garcia D, Escalante M, Delgado R, Ubeira FM, Leiro J. Anthelminthic and antiallergic activities of *Mangifera indica* L. stem bark components Vimang and mangiferin. Phytother Res 2003;17:1203-8.
38. Rivera DG, Balmaseda IH, Leon AA, Hernandez BC, Montiel LM, Garrido GG, *et al*. Anti-allergic properties of *Mangifera indica* L. extract (Vimang) and contribution of its glucosylxanthone mangiferin. J Pharm Pharmacol 2006;58:385-92.
39. Perrucci S, Fichi G, Buggiani C, Rossi G, Flamini G. Efficacy of mangiferin against Cryptosporidium parvum in a neonatal mouse model. Parasitol Res 2006;99:184-8.
40. Li H, Miyahara T, Tezuka Y, Namba T, Nemoto N, Tonami S, *et al*. The effect of kampo formulae on bone resorption in vitro and in vivo, I: Active constituents of Tsu-Kan-gan. Biol Pharm Bull 1998;21:1322-6.
41. Muanza DN, Euler KL, Williams L, Newman DJ. Screening for antitumor and anti-HIV activities of nine medicinal plants from Zaire. Int J Pharmacol 1995;33:98.
42. Aswal BS, Bhakuni DS, Goel AK, Kar K, Mehrota BN, Mukhrjee KC. Screening of Indian plants for biological activity: Part X.

Indian J Exp Biol 1984;22:312-32.

43. Peng ZG, Luo J, Xia LH, Chen Y, Song S. CML cell line K562 cell apoptosis induced by mangiferin. Zhongguo Shiyan Xue Ye Xue Za Zhi 2004;12:590- 4.
44. Yoshimi N, Matsunaga K, Katayama M, Yamada Y, Kuno T, Qiao Z, *et al*. The inhibitory effects of mangiferin: A naturally occuring glucosylxanthone, in bowel carcinogenesis of male F344 rats. Cancer Lett 2001;163:163-70.
45. Awe SO, Olajide OA, Oladiran OO, Makinde JM. Antiplasmodial and antipyretic screening of *Mangifera indica* extract. Phytother Res 1998;12:437-8.
46. Bidla G, Titanji VP, Jako B, Bolad A, Berzins K. Antiplamodial activity of seven plants used in African folk medicine. Indian J Pharmacol 2004;36:245- 6.
47. Sarkar A, Sreenivasan Y, Ramesh GT, Manna SK. beta-D-glucoside suppresses tumor necrosis factor-induced activation of nuclear transcription factor κappaB but potentiates apoptosis. J Biol Chem 2004;279:33768-81.
48. Manna SK, Kuo MT, Aggarwal BB. Overexpression of gamma-glutamylcysteine synthetase suppresses tumor necrosis factor-induced apoptosis and activation of nuclear transcription factor-kappaB and activator protein-1. Oncogene 1999;18:4371-82.
49. Sairam K, Hemalatha S, Kumar A, Srinivasan T, Ganesh J, Sarkar M, *et al*. Evaluation of anti-diarrhoeal activity in seed extracts of *Mangifera indica*. J Ethnopharmacol 2003;84:11-5.
50. Das PC, Das A, Mandal S. Anti inflammatory and antimicrobial activities of the seed kernel of *Mangifera indica*. Fitoterapia 1989;60:235-40.
51. Garrido G, Gonzalez D, Delporte C. Analgesic and anti-inflammatory effects of *Mangifera indica* extract (Vimang). Phytother Res 2001;15:18-21.
52. Garrido G, Gonzalez D, Lemus Y, Garcia D, Lodeiro L, Quintero G, *et al*. *In vivo* and *in vitro* anti-inflammatory activities of *Mangifera indica* L. extract (VIMANG). Pharmacol Res 2004;50:143-9.
53. Stoilova I, Gargova S, Stoyanova A, Ho L. Antimicrobial and antioxidant activity of the polyphenol mangiferin. Herb Polonica 2005;51:37-44.
54. Akinpelu DA, Onakoya TM. Antimicrobial activities of medicinal plants used in folklore remedies in south-western. Afr J Biotechnol 2006;5:1078-208.
55. Prasad S, Kalra N, Shukla Y. Hepatoprotective effects of lupeol and mango pulp extract of carcinogen induced alteration in Swiss albino mice. Mol Nutr Food Res 2007;51:352-9.
56. Carvalho AC, Guedes MM, De Souza AL, Trevisan MT, Lima AF, Santos FA, *et al*. Gastroprotective effect of mangiferin: A xanthonoid from *Mangifera indica*, against gastric injury induced by ethanol and indomethacin in rodents. Planta Med 2007;73:1372- 6.
57. Prashanth D, Padmaja R, Samiulla DS. Effect of certain plant extracts on αlpha-amylase activity. Fitoterapia 2001;72:179- 81.
58. Prashanth D, Amit A, Samiulla DS, Asha MK, Padmaja R. αlpha-Glucosidase inhibitory activity of *Mangifera indica* bark. Fitoterapia 2001;72:686- 8.
59. Beltran AE, Alvarez Y, Xavier FE, Hernanz R, Rodriguez J, Nunez AJ, *et al*. Vascular effects of *Mangifera indica* L. extract (Vimang). Eur J Pharmacol 2004;499:297-305.
60. Godfrey SB, Aloysius L, Nathan M, David B, Kyegombe, Paul W, *et al*. The activity of *Mangifera indica* leaf extracts against the tetanus causing bacterium, Clostridium tetani. Afr J Ecol 2007;45:54- 8.
61. Rodeiro I, Donato MT, Jimnenez N, Garrido G, Delgado R, Gomez-Lechon MJ. Effects of *Mangifera indica* L. aqueous extract (Vimang) on primary culture of rat hepatocytes. Food Chem Toxicol 2007;45:2506-12.

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