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Review on pharmacological activities of *Mangifera indica* and *Zingiber officinale*

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Abstract
Mango (*Mangifera indica*) which belongs to the family of Anacardiaceae, is a rich source of biologically active compound mangiferin, which is a natural xanthone C-glucoside. Mangiferin has been traditionally used in some parts of world as anti-inflammatory, antibacterial, analgesic, antipyretic, antioxidant, anti-cancer, antiviral, immunomodulatory, anthelminthic, anti-ageing, antidiabetic, lipometabolism regulating, cardioprotective, anti-hyperuricemic, neuroprotective and in obesity treatment. Ginger (*Zingiber officinale*) which belongs to the family of Zingiberaceae, has a long history of use in Chinese and Ayurvedic medicine as an antiemetic, anticoagulant, anti-inflammatory, anti-ageing, gastrointestinal, and antiarthritic activities.

Keywords: *Mangifera indica*, *Zingiber officinale*, Anti-inflammatory, Antidiabetic, Antiemetic, Antiarthritic

Introduction
Mangifera indica (L.) belonging to family Anacardiaceae is one of the most important tropical plants marketed in the world. The genus Mangifera contains several species that bear edible fruit comprising of high nutritional and medicinal value [1]. It is reported that mango was first found in Indo-Burmese region, approximately 4000 years ago, but now it is being commercially grown in more than 87 countries [2]. Mangiferin ($C_{19}H_{18}O_{11}$), a glucoxanthone (1,3,6,7-tetrahydroxyxanthone-C 2-b-D-glucoside), is an active phytochemical that has been reported to be present in various parts of *Mangifera indica* L *viz* leaves [3], fruits [4], stem bark [5], heartwood [6], and roots [7]. Mangiferin is a natural C-glucoside xanthone (2-C-β-D-gluco-pyranosyl- 1,3,6,7-tetrahydroxyxanthone; $C_{19}H_{18}O_{11}$; Molecular weight, 422.35; melting point, anhydrous 271 °C), a polyphenol xanthone has been reported in various angiosperms and ferns [8]. Mangiferin is reported to be stable to acid and enzymatic hydrolysis [9]. Mangiferin (MGF) is a xanthone glycoside found in the leaves, bark, fruit, and roots of *M. indica* and other plants such as *Salacia chinensis*, *Swertia chirata*, and *Hypericum aucheri* [10, 11, 12]. The oral bioavailability of mangiferin was only 1.2%. This may be due to its low lipophilicity properties, poor intestinal membrane permeability and low oral absorption [13].

Image 1: *Mangifera indica* plant and leaves

Zingiber officinale
Zingiber officinale belonging to family Zingiberaceae is an ancient Indian medicine used in several disorders. It has various vernacular names such as Ginger, Srngaveram, Adrak, Sunthi Ginger is a well-known tropical herb whose root is used in both Traditional Chinese Medicine and Western Herbal Medicine [14]. In addition, ginger is also a good source of antioxidants and shows high antioxidant activity following alcohol extraction [15].

Several reports have documented the effect of ginger as an antioxidant on delaying the ageing of several organs [16]. Moreover, ginger extract is also considered an effective anti-inflammatory agent in preventing osteoarthritis and rheumatoid arthritis [17]. On the other hand, ginger extract has shown a protective effect on the development of cardiovascular diseases such as coronary atherosclerosis and hypertension [18]. This study demonstrated that the risk of hypertension and coronary heart disease was significantly decreased to 8% and 13% by consuming 1 gram of ginger per day [19]. As oxidative stress and inflammation contribute to the pathogenesis of ageing and degenerative diseases, ginger (*Z. officinale* Roscoe) has been used as an antiageing agent. Ginger and its active compounds, exhibited antiageing effects in various types of age-related and degenerative diseases through their antioxidant and anti-inflammatory properties [20].

Image 2: *Zingiber officinale*

Pharmacological activities

Mangifera indica

Antimicrobial activity: Mangiferin was isolated by column chromatography from the ethanolic extract of stem bark of *M. indica*. Mangiferin was further converted to 5-(N-phenylamino methyleno) mangiferin, 5-(N-p-chlorophenyl amino methyleno) mangiferin, 5-(N-2-methyl phenylamino methyleno) mangiferin, 5-(N-p-methoxy phenylamino methyleno) mangiferin, 5-(N, N-diphenylamino methyleno) mangiferin, 5-(N-α-napthylamino methyleno) mangiferin and 5-(N-4-methyl phenylamino methyleno) mangiferin. Mangiferin and its analogues were characterized by melting point and R_f value determination and through spectral technique like UV, IR, and NMR spectral analysis. The antimicrobial effect of mangiferin and its derivatives was studied according to the disc diffusion method [21].

Anti-viral activity

Mangiferin was considered as an antiviral agent upon herpes simplex virus [22, 23], HIV and hepatitis B virus [24]. 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 [23]. In *in vitro*, mangiferin was also able to inhibit HSV-1 virus replication within cells [22], and to antagonize the cytopathic effects of HIV [25].

Anti-inflammatory activity

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 [26]. Beltrana AE *et al*., (2004) reported that anti-inflammatory action of mangiferin is related with the inhibition of iNOS and cyclooxygenase-2 expression[27]. 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 [28, 29, 30]. The sub-cellular targets of the anti-inflammatory effects located at the thermoregulatory neural centres for their reducing prostaglandin synthesis in fever [31], and the lysosomal membrane for its lowering hydrolase activity in isoprenaline induced myocardial necrosis [32]. Anti-inflammatory activity of mango is also reported by many other scientists [32, 33, 34, 35, 36].

Anti-cancer activity

Nora to *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 [37]. 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 IC50 value of<10µg/ml [38, 39]. 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) [40] and K562 leukemia cells [41]. 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 G0/G1 phase [42]. 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 [41, 43-46]. The other possible mechanisms of mangiferin included inhibition of the telomerase and the gene [44], and the enhancement of the cellular apoptosis [44, 47]. The anti-proliferative activities of mango peels and flesh were also investigated by Kim *et al*., (2012) [48].

Antidiabetic activity

OT Adedosu *et al*., studied that a significant ($P< 0.05$) increase in the fasting blood glucose concentrations was obtained in the alloxan-induced diabetic rats. When those diabetic rats were treated with the ethanol leaves extract of *M. indica* showed significant ($P< 0.05$) decreases in the fasting blood glucose levels compared with the untreated diabetic rats[49]. CD Luka and A Mohammed studied that aqueous extract of *M. indica* leaf decreased blood sugar level in diabetic rats. It is also confirmed that the extract at a dose of 400mg/kg body weight reduce significantly ($P< 0.05$) the blood glucose level. But the mechanism of action of plant extract was unknown. The extract significantly ($P< 0.05$) decreased the serum cholesterol level in diabetic rats[50]. MS Rajesh and J Rajasekhar studied that he long term (21 days) administration of methanolic and aqueous extract of *Mangifera indica* was effective in decreasing the blood glucose level and normalizing the other biochemical parameters in diabetic rats. Te single dose study of the extract has no hypoglycemic effect on normal rats. Further studies need to be carried out to define the active principle(s) present in the extracts. They also confirmed that oral administration of *Mangifera indica* seed kernel extracts lowered total cholesterol and triglycerides level in diabetic rats when compared to diabetic controls[51]. Amrita Bhowmik *et al*., [52]. Investigated about hypo/antihyperglycemic activity of *M. indica* leaf and stem-bark extracts in no diabetic, type 1 and

type 2 diabetic model rats. The extracts of *M. indica* leaves and stem barks showed significant antihyperglycemic effect in type 2 diabetic model rats when the extracts were fed simultaneously with glucose. Single oral administration of a dose of 250 mg/ kg body weight produces a potent and strong hypoglycemic effect in type 2 rats.10 Ahmad Muhtadi *et al*., [53]. Studied that the leaves extract of *M. indica* L. used for ant diabetic properties using normoglycemic, glucose-induced hyperglycemia, and STZ-induced diabetic mice. The aqueous extract of the leaves of *M. indica* L. possesses hypoglycemic activity [53].

Cardioprotective activity

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 [54].

Zingiber officinale

Antiemetic activity

The mechanism of action of ginger's effect on nausea and vomiting remains uncertain. However, there are several proposed mechanisms. The components in ginger that are responsible for the antiemetic effect are thought to be the gingerols, shogaols, and galanolactone, a diterpenoid of ginger [55, 56, 57]. Recent animal models and *in vitro* studies have demonstrated that ginger extract possesses antiserotoninergic and 5-HT3 receptor antagonism effects, which play an important role in the etiology of post-operative nausea and vomiting [58, 57, 56]. In a randomized, placebo-controlled, crossover trial of 16 healthy volunteers, ginger (1g orally) had no effect on gastric emptying [59]. It appears unlikely that ginger's anti-emetic or anti-nausea effects are mediated through increased gastro duodenal motility or through increased gastric emptying. Using gastro duodenal manometry, Micklefield *et al*. demonstrated that oral ginger increases antral motility during phase III of the migrating motor complex (MMC) and increases motor response to a test meal in the corpus [60]. However, ginger had no significant effect in the antrum or corpus during other phases, except for a significant decrease in the amplitude of antral contractions during phase II of the MMC. Additionally, there was no effect of ginger on duodenal contractions or on the "motility index."

Antioxidant activity

In vitro, ginger has been shown to exhibit antioxidant effects [61]. (6)-gingerol appears to be the antioxidant constituent present in ginger, as it was shown to protect HL-60 cells from oxidative stress [62]. Ginger oil has dominative protective effects on DNA damage induced by H_2O_2. Ginger oil might act as a scavenger of oxygen radical and might be used as an antioxidant [63].

Antiarthritic activity

A study investigated the antiarthritic effects of ginger and its bioactive constituents. A well characterized crude ginger extract was compared with a fraction containing [6]-gingerol and their derivatives to inhibit joint swelling in an animal model of rheumatoid arthritis, streptococcal cell wall-induced arthritis. Both extracts demonstrated anti-inflammatory activity. The crude dichloromethane extract, containing essential oils and more polar compounds, was more efficacious, when normalized to [6]-gingerol content, in preventing, both joint inflammation and destruction. Non-gingerol components enhance the antiarthritic effects of the more widely studied [6]-gingerol [64].

Gastrointestinal activity

There is evidence that ginger rhizome (root) increases stomach acid production. If so, it may interfere with antacids, sucralfate (Carafate), H2 antagonists, or proton pump inhibitors. In contrast, other *in vitro* and animal studies have revealed gastro protective properties [65, 66], in addition, (6) shogaol, generally more potent than (6)-gingerol, has inhibited intestinal motility in intravenous preparations and facilitated gastrointestinal motility in oral preparations. Ginger extract has also been reported to inhibit the growth of Helicobacter pylori *in vitro* [67].

However, Desai *et al*. observed a significant increase in the exfoliation of gastric surface epithelial cells following the consumption of 6g or more of ginger (after examining gastric aspirates in 10 healthy volunteers) [68].

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. 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, radioprotective, recognition of memory and many others. The experimental advances in gingerol and analogues. So far, reveals the empirical use of ginger in several ayurvedic medicinal products.

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