IJPSR (2012), Vol. 3, Issue 02 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 20 September, 2011; received in revised form 20 January, 2012; accepted 28 January, 2012

PHARMACOLOGICAL POTENTIALS OF *MORINGA OLEIFERA* LAM.: A REVIEW

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Keywords:
Moringa oleifera, Antioxidant, Antidiabetic, Hepatoprotective, Antibacterial

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ABSTRACT

The aim of this literature review was to provide advance research information for the future scientists to discover new drug molecules from the medicinal plant, *Moringa oleifera* Lam. (Moringaceae). The plant provides a rich and rare combination of zeatin, quercetin, beta-sitosterol and kaempferol.

In addition to its high nutritional value, *Moringa oleifera* Lam is very important for its medicinal value. Various parts of this plant such as leaves, roots, seed, bark, fruit, flowers and immature pods act as cardiac and circulatory stimulants, possess antitumor, antipyretic, anti-inflammatory, antiulcer, antispasmodic, diuretic, antihypertensive, cholesterol lowering, antioxidant, antidiabetic, hepatoprotective, antibacterial and antifungal activities, and are being employed for the treatment of different ailments in the indigenous system of medicine. This review gives the scientific information regarding pharmacological potentials of *Moringa oleifera* Lam. (Moringaceae).

INTRODUCTION: *Moringa oleifera* Lam. (Moringaceae) is a highly valued plant, distributed in many countries of the tropics and subtropics. It has an impressive range of medicinal uses with high nutritional value. Different parts of this plant contain a profile of important minerals, and are a good source of protein, vitamins, beta-carotene, amino acids and various phenolics [1].

The leaves and young buds of the plant are used as vegetable and can be rubbed on the temples for relieving headache while root and root bark are regarded as anti scorbutic and can be used externally as counterirritant [2]. The eye diseases are treated with the juice of the leaves with honey [3]. The plant is also known to possess high nutritional value and is used in a folklore medicine to treat various ailments related to pain and inflammation [4].

Dried seeds of *Moringa oleifera* are used in ophthalmic preparation, venereal affection anti-inflammatory, purgative and as tonic.

The alcoholic extract of the leaves of *Moringa oleifera* are reported to have analgesic activity[5] and the aqueous extract of *Moringa oleifera* roots also shows antifertility profile [6]. The plant is reported to possess wide range of pharmacological effects that include antitumor [7], antipyretic [1], antispasmodic, diuretic [8], antiulcer [9], hypotensive [10], hypolipidemic [11], Hepatoprotective [12], antifungal [13] and antibacterial activities [14].

The purpose of this review is to summarize the pharmacological properties of different parts of the plant, *Moringa oleifera*.

Pharmacological properties of *Moringa oleifera*:

Antibacterial and Antifungal Efficacy: A considerable reduction in the growth of test bacteria was observed by distillate of *M. oleifera* suggesting antibacterial effect. Among bacteria tested, more inhibition was observed in case of *E. coli* followed by *S. aureus, K. pneumoniae, P. aeruginosa and B. subtilis.* Inhibition of fungi was also observed as reduced colony diameter in plates poisoned with distillate as compared to control plates. More inhibition of *A. niger* was found followed by *A. oryzae, A. terreus and A. nidulans*. The antimicrobial activity and antifungal activities of steam distillate of *M. oleifera* might be possibly due to the essential oil fraction of the plant material present in the distillate fraction [15].

Anti-Oxidant Effect: The antioxidant property of *Moringa* may be due to the presence of phenolic compounds that was confirmed by phytochemical screening of the hydro-ethanolic extract. In this respect, *Moringa* pods contain important bioactive compounds including glucosinolates, isothiocyanates, thiocarbamates, and flavonoids [16]. These compounds quench ROS, chelate metal ions and regenerate membrane-bound antioxidants [17].

β-carotene, the major component reported from the drumsticks of the plant [16] and vitamin A and C present in *M. oleifera* serve as an explanation for their mode of action in the induction of antioxidant profiles in the present investigation. The biochemical basis of the chemopreventive potency of *M. oleifera* extract may be attributed to the synergistic action of the constituents of the extract and the induction of Phase-II enzymes (GSTs) and antioxidant enzymes, which might be implicated in the anticarcinogenic activity [18].

The aqueous extract of *Moringa oleifera* exhibited strong scavenging effect on 2, 2-diphenyl-2-picryl hydrazyl (DPPH) free radical, superoxide, nitric oxide radical and inhibition of lipid per oxidation. The free radical scavenging effect of *Moringa oleifera* leaf extract was comparable with that of the reference antioxidants. The extracts of *Moringa oleifera* both mature and tender leaves have potent antioxidant activity against free radicals, prevent oxidative damage to major biomolecules and afford significant protection against oxidative damage [19].

The *Moringa oleifera* hydro- alcoholic leaf extracts (1000 mg/kg) and *Moringa oleifera* aqueous pod (fruit) extract (750 mg/kg) contain high amount of tannin, phenolic compounds and flavonoids. The poly phenolic constituents of this plant could be contributory to their ethano-medical use. Thus, it can be concluded that extracts of *Moringa oleifera* produce significant antioxidant activity [20] and the presence of kaempferol in leaves of *Moringa oleifera* showed the antioxidant activity which was also reported by [21].

Gastric Ulcer Protective Activity: Das *et al*., studied the possible antiulcer effects of water extracts of *M. oleifera* in two animal models of ulcers. The water extract of leaves was tested for antiulcer activity at the dose level of 200 mg and 400 mg/kg p.o. in pyloric ligation and ibuprofen induced gastric ulcer models. The severity of gastric ulceration in both the models was assessed based on the means of ulcer index.

Both the models produced moderate to severe ulcers in control group of animals; in that the maximum was by pylorus ligation method. Both famotidine and the extract of *M. oleifera* significantly ($p<0.001$) reduced the ulcer index as compared to control group in both ulcer models. The antiulcer effect of *M. oleifera* was comparable with that of the standard drugs in pylorus ligation and ibuprofen induced ulcer methods. Famotidine and *M. oleifera* extract significantly ($p<0.05$) reduced the free acidity and total acidity of gastric juice. It is equally potent when compared to famotidine [22].

It was also found that the aqueous extract of *M. oleifera* leaf was shown to protect rats from developing gastric ulcer induced by indomethacin in a dose dependent manner. Tannins with its protein precipitating and vasoconstriction effect could be advantageous in preventing ulcer development [23]. Tannins being an astringent may have precipitated microproteins on the site of the ulcer thereby forming an impervious protective pellicle over the lining to prevent toxic substance and resist the attack of proteolytic enzyme [24]. Presence of flavonoids has also been reported to offer some protection in ulcer development by increasing capillary resistance, and improve microcirculation which renders the cells less injurious to precipitating factors [25].

The leaf extract of the plant was found to protect the gastric mucosa against indomethacin effect in a dose dependent manner. Phytochemical constituent of the leaf extract of *M. oleifera* (tannins and flavonoids) that reduced initiation and perpetuation of ulceration may be responsible for the observed effects. The leaf extract thus has the potential of an antiulcerogenic agent, which suggest it's used in traditional medicine [26].

Analgesic Activity and Local Anaesthetic Activity: The analgesic activity of alcoholic extract of *M. oleifera* and its various fractions as Petroleum ether, Ethyl acetate, Diethyl ether, n-Butanol were carried out by using Hotplate and Tail immersion method. Amongst alcoholic extract and its various fractions of seeds of *M. oleifera* alcoholic extract showed potent analgesic activity which is comparable to that of aspirin at the dose of 25 mg/kg of body weight. From this study, it can be concluded that the seeds of *M. oleifera* Lam. possess marked analgesic activity and is equipotent to standard drug (Aspirin) which establishes the use of *M. oleifera* seeds as regular analgesic [5]. The local anaesthetic activity of the methanol extract of *M. oleifera* was tested in frog and guinea pig models and it was seen that in both animals, the plant (root bark) has produced significant local anaesthetic activity [27].

Anti-Inflammatory and Antinociceptive Activity: The anti-inflammatory action of an aqueous extract of root in rats with weight between 120 and 160 g was investigated by Ndiaye *et al* [28]. At a dose of 750 mg/kg the *M. oleifera* treatment significantly inhibited the development of oedema at 1, 3 and 5 hours (reduction by 53.5, 44.6 and 51.1% respectively). Increasing the dose of *M. oleifera* to 1000 mg/kg did not increase the inhibitory effect on oedema development at 1 and 3 hours, whereas this dose potentiated the oedema at 5 hours.

Treatment with indomethacin significantly inhibited the development of oedema 1, 3 and 5 hours (49.1, 82.1 and 46.9% respectively). These findings indicate that an aqueous root extract of *M. oleifera* at 750 mg/kg reduces the carrageenan induced oedema to similar extent as the potent anti-inflammatory drug indomethacin. Moreover, these results provide further evidence that the roots of *M. oleifera* contain anti-inflammatory principle that may be useful in the treatment of the acute inflammatory conditions. Bioassay-guided isolation and purification of the ethyl acetate extract of *M. oleifera* fruits yielded three new phenolic glycosides; 4- [(2'- O- acetyl- alpha- l-rhamnosyloxy) benzyl] isothiocyanate (1), 4-[(3'-O-acetyl-alpha-l-rhamnosyloxy)benzyl] isothiocyanate (2), and S-methyl-N-{4-[(alpha-l-rhamnosyloxy) benzyl]} thiocarbamate (3), together with five known phenolic glycosides (4-8).

The anti-inflammatory activity of isolated compounds was investigated with the lipopolysaccharide (LPS)-induced murine macrophage RAW 264.7 cell line. It was found that 4-[(2'-O-acetyl-alpha-l-rhamnosyloxy)benzyl]isothiocyanate (1) possessed potent NO-inhibitory activity with an IC(50) value of 1.67 microM, followed by 2 (IC(50)=2.66 microM), 4 (IC(50)=2.71 microM), and 5 (IC(50)=14.4 microM), respectively. These isolated compounds 1, 2, 4 and 5 are responsible for the reported NO-inhibitory effect of *M. oleifera* fruits [29] (Cheenpracha *et al*., 2010). *M. oleifera* may also possess some beneficial properties that act against chemically stimulated immune-mediated inflammatory responses that are characteristic of asthma in the rat [30].

Sulaiman et al. evaluated the antinociceptive and anti-inflammatory effects of the aqueous extract of the leaves of *M. oleifera* in laboratory animals, using the writhing, hot-plate and formalin tests as the antinociceptive assays, and carrageenan-induced paw oedema test as the anti-inflammatory assay. The extract (10, 30 and 100 mg/kg) exhibited significant ($P < 0.05$) antinociceptive activity, which occurred in a dose-dependent manner, in all tests used. The extract also exhibited significant ($P < 0.05$) anti-inflammatory activity in a dose dependent manner. In conclusion, *M. oleifera* leaves possess peripherally non-opioid mediated and centrally opioid mediated anti-nociceptive and anti-inflammatory activities. This study also confirms the traditional uses of *M. oleifera* in the treatment of ailments, particularly those related to pain and inflammation [4].

Cardioprotective Activity: Nandave *et al*., evaluated cardioprotective effect of lyophilized hydroalcoholic extract of *M. oleifera* in the isoproterenol (ISP)-induced model of myocardial infarction. Chronic treatment

with *M. oleifera* demonstrated mitigating effects on ISP-induced hemodynamic [HR, (+) LV dP/dt, (-) LV dP/dt, and LVEDP] perturbations. Chronic *M. oleifera* treatment resulted in significant favorable modulation of the biochemical enzymes (superoxide dismutase, catalase, glutathione peroxidase, lactate dehydrogenase, and creatine kinase-MB) but failed to demonstrate any significant effect on reduced glutathione compared to the ISP control group. *Moringa* treatment significantly prevented the rise in lipid peroxidation in myocardial tissue.

Furthermore, *M. oleifera* also prevented the deleterious histopathological and ultrastructural perturbations caused by ISP. Based on the results of the present study, it can be concluded that *M. oleifera* extract possesses significant cardioprotective effect, which may be attributed to its antioxidant, antiperoxidative, and myocardial preservative properties [31].

Wound Healing Activity: The aqueous extract of leaves of *M. oleifera* was investigated for its wound healing activity. The extract was studied at dose level of 300 mg/kg body weight using resutured incision, excision, and dead space wound models in rats. The prohealing actions seem to be due to increased collagen deposition as well as better alignment and maturation. From the study results obtained, it may be concluded that the aqueous extract of *M. oleifera* has significant wound healing property [3].

Hypotensive and Spasmolytic Activities: Bioassay directed fractionation of an ethanolic extract of *M. oleifera* leaves showing hypotensive activity led to the isolation of two nitrile glycosides, niazirin [1] and niazirinin [2], and three mustard oil glycosides, 4-[(4'-O-acetyl-alpha-L-rhamnosyloxy) benzyl] isothiocyanate [4], niaziminin A, and niaziminin B.

Isothiocyanate 4 and the thiocarbamate glycosides niaziminin A and B showed hypotensive activity while nitrile glycosides 1 and 2 were found to be inactive in this regard [32]. Moreover, spasmolytic activity exhibited by the constituents of the plant provides a scientific basis for the traditional uses of the plant in gastrointestinal motility disorders [33].

Faizi *et al*., also investigated the hypotensive activity of the ethanolic and aqueous extracts of *M. oleifera* whole pods and their parts, namely, coat, pulp, and seed. The activity of the ethanolic extract of both the pods and the seeds was equivalent at the dose of 30 mg/kg. It was found that the ethyl acetate phase of the ethanolic extract of pods was found to be the most potent fraction at the same dose. Its bioassay-directed fractionation led to the isolation of thiocarbamate and isothiocyanate glycosides which were also the hypotensive principles of the pods as observed in case of *Moringa* leaves. Two new compounds, O-[2'-hydroxy-3'-(2"-heptenyloxy)]-propyl undecanoate (1) and O-ethyl-4-[(alpha-L-rhamnosyloxy)-benzyl] carbamate (2) along with the known substances methyl p-hydroxybenzoate (3) and beta-sitosterol have also been isolated in the present studies. The latter two compounds and p-hydroxybenzaldehyde showed promising hypotensive activity [10].

Anti-helmentic, Hypolipidaemic and Antiatherosclerotic Activities: It was observed that the plant showed potent anthelmentic activity and caused paralysis within 6-15 min while death is comparable with that of piperazine citrate as death of worms was observed at 64 min [34]. Chumark *et al*., investigated the hypolipidaemic and antiatherosclerotic activities of *M. oleifera* leaf extract. They found that in hypercholesterol-fed rabbits, at 12 weeks of treatment, the water extract of the plant significantly ($P<0.05$) lowered the cholesterol levels and reduced the atherosclerotic plaque formation to about 50% and 86%, respectively and these effects were at degrees comparable to those of simvastatin [35].

The methanolic extract of *M. oleifera* (150, 300 and 600 mg/kg, p.o.) and simvastatin (4 mg/kg, p.o.) along with hyperlipidemic diet were administered to Albino Wistar rats for 30 days in order to observe hypolipidaemic effect. It was found that the serum cholesterol, triacylglyceride, VLDL, LDL, and atherogenic index were reduced by *M. oleifera* and simvastatin but HDL level was increased as compared to the corresponding high fed cholesterol diet group (control). *M. oleifera* was also found to increase the excretion of fecal cholesterol. Thus, it can be concluded that *M. oleifera* possesses a hypolipidemic effect [36].

Antiurolithiatic Activity: The effect of oral administration of aqueous and alcoholic extract of *M. oleifera* root-wood on calcium oxalate urolithiasis has been studied in male Wistar albino rats. Ethylene glycol feeding resulted in hyperoxaluria as well as increased renal excretion of calcium and phosphate. Supplementation with aqueous and alcoholic extract of *M. oleifera* root-wood significantly reduced the elevated urinary oxalate, showing a regulatory action on endogenous oxalate synthesis. The increased deposition of stone forming constituents in the kidneys of calculogenic rats was also significantly lowered by curative and preventive treatment using aqueous and alcoholic extracts. Thus the results indicate that the root-wood of *M. oleifera* is endowed with antiurolithiatic activity [37].

Other Activities: The *Moringa* powder was also exploited as anti-AIDS agent. Anti-HIV activity could be due to its immunostimulatory effect. It is also known that polysaccharide isolated from the hot aqueous extract of mature pods of *M. oleifera* showed significant macrophage activity through the release of nitric oxide on mouse monocyte cell line. Hence, it speculated that the immunostimulatory activity is due to presence of its constituent in methanolic extract of *Moringa oleifera*. It was also found that both low dose (25 mg/kg, p.o.) as well as high dose (750 mg/kg, p.o.) of *M. oleifera* stimulates immune system by acting through cellular and humoral immunity in experimental models of immunity in animals. However, low dose was found to be most effective than the high dose. This could be due to the presence of toxicant such as isothiocyanate and glycoside cyanides that may pose stress at high concentration and hence reducing the antioxidant potential of *Moringa oleifera* [38].

CONCLUSION: *Moringa oleifera* Lam., an important medicinal plant, is one of the most widely cultivated species of the family Moringaceae. Leaves, barks, roots, stems, buds, flowers etc. have been used for different human ailments. Pharmacologically reported effects include anti-bacterial, antifungal, anti-inflammatory and analgesic, antioxidant, hypotensive, anti-ulcer, anaesthetic cardioprotective, antiurolithiatic activity and wound healing activity etc. This review summarizes only some pharmacological activities of *Moringa oleifera* which can be investigated further to isolate active compounds for novel herbal medicine.

ACKNOWLEDGEMENT: All of the authors are very grateful to Professor Dr. Saroj Kanti Singh Hazari, Vice Chancellor, BGC Trust University Bangladesh, for providing literature survey facility to complete this research work.

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