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Review Article

Ameliorative effect of Phytochemicals Extracted from Moringa Olifera: A Review

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Abstract

Moringa olifera Lam, popularly known as 'drumstick tree' is a vital source of many phytochemicals having various therapeutic properties. The high phenolic content present in the leaves and flowers of this plant is very effective against liver dysfunction. Almost all plant parts of Moringa contain vitamins, polyphenols, and flavonoids effectively used to care for anaemia, bronchitis, diarrhoea, asthma, cardiac problems, rheumatism, body aches, diabetes, and many more diseases. This article will enrich the researcher's knowledge about the active phytochemicals in the Moringa plant parts and their ethnopharmacological applications against different diseases. The morphological, and taxonomical description of the plant, the presence of nutrient content, and the extraction procedure of the phytochemicals have also been summarized in this article.

Keywords: phytochemicals; therapeutics; extraction; taxonomical; mode of action

Introduction

Due to nutritional deficiencies in vital nutrients, the great majority of people in the world experience malnutrition. The *Moringa oleifera* Lam., (MO) high resistance to arid conditions also called the "drumstick" or "horseradish" tree, is a member of the Moringaceae family (2n = 28) and can completely erase malnutrition and is a cost-effective and accessible source of important critical nutrients including vitamins, minerals, protein, and essential amino acids [1].

MO and the thirteen other *Moringa* species are widely distributed in Arabia, Africa, India, South America, the Caribbean, and the Pacific Island [2]. They are supplied to Sudan, the Philippines, Ethiopia, and Florida [3]. MO can grow in tropical rainfall patterns to semi-dry soil and desert [4]. Almost all parts of the MO like its leaves, flowers, pods, seeds, and bark are used for various medicinal and therapeutic purposes as these are rich in alkaloids, flavonoids, tannic acids, steroids, terpenoids, glycosides, saponins, and essential oils [5-7]. With twice the protein of yogurt, four times the vitamin A of carrots, three times the potassium of bananas, seven times the vitamin C of oranges, and four times the calcium of milk, Moringa leaves are extremely nutrient-dense [8]. MO contains large amounts of flavonoids, including quercetin, apigenin, kaempferol, and isorhamnetin [9].

One well-known hepatoprotective substance found in MO is quercetin [10].

Within the flavone family, quercetin can either stop or postpone the body's oxidative deterioration [11]. MO is thought to have protective effects against hepatopathy as quercetin, a well-known hepatoprotective agent, present in it [12]. MO is effectively used against cancer, infertility, high blood sugar, high blood cholesterol, obesity, asthma, fibrosis, helminthiasis, toothache, bacterial growth, etc., [13-17].

In addition to the plant's physical characteristics, taxonomical details. and distribution, the current review paper identifies the specific phytochemicals found in each plant region, their extraction procedure, and their potential for treating various ailments.

Morphological and Taxonomical description of *Moringa oleifera*:

MO, a deciduous tree genus of the order Brassicales, family Moringaceae is widely cultivated in several countries along with its 17 other species [18] *M. oleifera* thrives on soil with a pH of 4-9, at altitudes up to 2000 meters, and at heights ranging from 3 to 12 meters. MO stems can grow to be 20 to 40 cm in diameter, with whitish-grey bark. Furthermore, it's leaves are green and usually grow at the terminals of the branches [19]. The tree has fragile branches having feathery foliage of tripinnate leaves. The leaves are typically 3-compound pinnate, with 4 to 10 pairs of pinnate leaves, 25-75 cm long, and 3 to 9 opposing smooth whole leaflets; glue seeps out from the base of the leaflet, leaving a white or milky white translucent egg [20]. Abundant whitish flowers and elongated drooping fruits with many seeds are found during flowering and fruiting season. MO flowers are panicle-shaped, bisexual, and symmetrical on both sides, with fragrant white or creamy yellow petals. MO seeds are roughly spherical and brown, with three-sided margins that are covered in membrane white wings. The seeds are also enclosed in long, slender pods [19, 20].

Nutrient content:

Furthermore, dried leaves of MO contain 10 times more vitamin A than carrots, 9 times more protein than yogurt, 25 times more iron than spinach, 17 times more calcium than milk, and 15 times more potassium than bananas [21]. However, the dried leaves contain half as much vitamin C as oranges. [22] Studies have demonstrated that MO contains little antinutrients like saponins, oxalates, phytates, and tannins [23]. MO is popular in many developing nations due to its high nutrient content and lack of antinutrients. Surprisingly, fresh MO leaves have more protein, calcium, and potassium than yogurt, milk, and bananas. Vitamin A levels in MO fresh leaves are four times higher than in carrots, seven times higher in oranges, four times higher in hog meats, and six times higher in rapeseed oil. Furthermore, dried leaves provide more nutrients than fresh MO leaves [21, 22].

Presence of phytochemicals in MO:

Different plant parts of different Moringa species are rich sources of phytonutrients of diverse groups like tannin, steroids, glucosinolate, saponins, flavonoids, etc. which are used to combat various diseases in both traditional and conventional ways. Still, a total of a hundred and ten bioactive compounds have been isolated from this plant [22]. Some common and most useful components have been listed below in tabular form [Table I].

Name of the Phytochemical groups	Nature of phytochemicals	Effects of the phytochemicals	References
Flavonoids	Flavonoids are a diverse group of phytochemicals known for their antioxidant and anti-inflammatory properties. Moringa contains several flavonoids including quercetin, kaempferol, catechins, and rutin.	These compounds contribute to the plant's ability to scavenge free radicals and reduce oxidative stress in the body.	24
Phenolic Acids	Phenolic acids such as chlorogenic acid and caffeic acid, tannins are abundant in Moringa leaves and seeds.	These compounds also possess antioxidant properties and contribute to the plant's overall antioxidant capacity.	25
Isothiocyanates	Moringa is rich in various isothiocyanates, including benzyl isothiocyanate and 4-(α-L-rhamnopyranosyloxy) benzyl isothiocyanate	These compounds have been studied for their antimicrobial, anti-inflammatory, and potential anti-cancer effects	26
Glucosinolates	Glucosinolates are sulfur-containing compounds found in cruciferous vegetables, and Moringa is known to contain them as well	These compounds can be hydrolyzed to form bioactive compounds like isothiocyanates, contributing to Moringa's health benefits.	27
Carotenoids	Moringa leaves are rich in carotenoids, including beta-carotene, lutein, and zeaxanthin.	Carotenoids are important antioxidants that contribute to eye health and overall antioxidant defence	28
Triterpenoids	Moringa leaves contain lutein, Z-lutein, luteoxanthin, E-Zeaxanthin like terpenoids	MO contains various triterpenoids, which have been studied for their anti-inflammatory and hepatoprotective properties.	29
Alkaloids	N, α-L-rhamnopyranosyl vincosamide (VR), Glycosides of pyrrole alkaloid are the most common alkaloid present in Moringa leaves	While less studied compared to other compounds, alkaloids are also present in Moringa and may contribute to its pharmacological properties. It helps protecting cardiovascular diseases	30
Chlorogenic acid		Helps in lowering high cholesterol and blood glucose, prevents obesity and fight against some carcinogenic gene expression	31

Table I: A list of some common phytochemicals present in MO along with their chemical nature and effects

Methods of Extraction of Phytochemicals:

Various methods are used to extract phytochemicals from MO to separate and concentrate these beneficial substances for further research or application in food, pharmaceutical, or other industries. Here are some commonly used extraction methods:

1. **Solvent Extraction:** This conventional approach involves combining dried Moringa plant material (e.g., leaves, seeds, or bark) with an appropriate solvent (e.g., ethanol, methanol, water) to dissolve the phytochemicals. The mixture is then filtered to separate the solvent extract with the desired chemicals from the solid residue. The solvent can be evaporated under lower pressure to get a concentrated extract. Carotenoids and chlorogenic acids present in MO are extracted by this method [32].
2. **Steam distillation**: It is commonly used to extract essential oils from Moringa seeds or leaves, which contain volatile phytochemicals like terpenes. Steam passes through the plant material, bringing the volatile compounds with it. The steam is subsequently condensed, and the essential oil separates from the resulting water [33].
3. **Supercritical Fluid Extraction (SFE):** Using carbon dioxide (CO_2) as the solvent, plant material is subjected to supercritical conditions (high pressure and temperature), causing CO_2 to behave as both a gas and liquid [34]. This approach is selective, allowing for the extraction of certain phytochemicals while avoiding heat-sensitive molecules. Using this technique total phenols can be isolated [35, 36].
4. **Microwave-assisted extraction (MAE)**: It employs microwave radiation to heat the solvent and speed up the extraction process. It can be faster than typical solvent extraction and may increase the output of specific phytochemicals [37-39].
5. **Ultrasound-Assisted Extraction (UAE):** Ultrasonic waves agitate the solvent and improve its penetration into plant material, increasing extraction efficiency. UAE is well-known for its efficiency and shorter extraction times when compared to traditional methods. Total flavonoids including polyphenols present in *Moringa* are extracted via this technique [40, 41].
6. **Pressurized Liquid Extraction (PLE):** This process, also known as accelerated solvent extraction (ASE), uses high temperatures and pressures to enhance phytochemical solubility

in the solvent. It can be mechanized and is effective in extracting a wide variety of chemicals [42].

7. **Solid-Phase Extraction (SPE)**: It passes a liquid extract through a solid sorbent material, such as silica gel or activated carbon, to selectively retain and concentrate particular phytochemicals. This procedure is commonly used for purification and concentration following initial extraction [43].

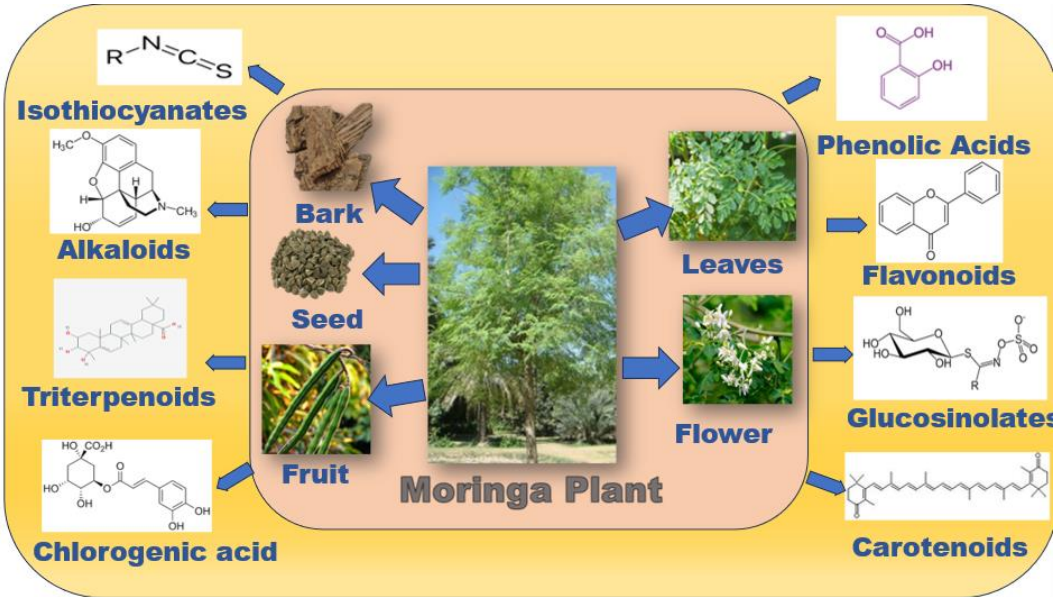

Figure 1: Diagrammetic representation of some phytochemicals extracted from different parts of MO

Therapeutical potency of *M. oliefera*:

MO performed various therapeutic activities against different diseases.

Anticancer Activity

Moringa's fruits, leaves, flowers, and stems have all been found to be effective in the fight against cancer, a terrible disease. Moringa's isolated components thiocarbamate and isothiocyanate suppress tumour cell growth [44, 45]. The dichloromethane fraction was cytotoxic to MCF7 breast cancer cells [46]. Niazimincin has been proposed as a potent chemopreventive agent in chemical carcinogenesis [47]. In the melanoma mouse model, alcoholic and hydro-methanolic extracts of fruits and leaves significantly inhibited tumor growth [48]. Soluble cold distilled Moringa water suppressed tumor cell development and decreased ROS (reactive oxygen species) in cancer cells [49]. A recent study based on computational modeling reveals that MO has rutin with the highest binding affinity to BRAC-1 (Breast Cancer Gene-1) [50].

Fertility and Antifertility Activity:

Moringa's many portions also have fertilization and abortion-inducing characteristics, which adds to its list of benefits. The aqueous extract at doses of 200 and 400 mg/kg has been shown to have higher abortifacient and anti-fertility effects. Recent research on hot and cold extracts of MO leaves suggests that consuming Moringa before, after, or during pregnancy may harm fetal development by promoting severe constriction of the uterine wall [51].

Cardiovascular activity:

The freeze-dried aqueous and alcoholic extracts of MO showed cardioprotective action in mice induced with myocardial infarction by isoproterenol [52]. Chronic therapy with MO enhanced isoproterenol-induced hemodynamics and enzyme levels such as SOD, catalase, lactase dehydrogenase, glutathione peroxidase, and creatine kinase. Butanolic extract is an excellent source of antioxidants in rats with isoproterenol-induced cardiac necrosis. The chemical N-α-rhamnopyranosyl vincosamide has greatly reduced inflammation and cardiac necrosis [52]. Moringa leaves drastically reduce cholesterol levels by protecting hypertensive rats. The active elements responsible for this activity were identified as niazirmin A, niazirimin B, and niazimincin [53].

Oxidative Stress

MO produced effects in mice that had been stimulated with methotrexate. The study aims to investigate the potential palliative effect of MO extract on mice. The mice were given the extract one week before receiving a methotrexate injection, and the treatment was continued for 12 days. The study found that pretreatment with an MO extract on mice poisoned with methotrexate could protect them from oxidative stress [54]. The antioxidant activity of ethanolic extract M. oleifera stems protected keratinocytes from epidermal oxidative stress injury caused by H_2O_2. The results demonstrated that the stems have antioxidant capacity, making them a good and preventative source in animal epidermal oxidative stress injury [55].

Anti-ulcer/gastroprotective Activity:

Moringa leaves contain bisphenols and flavonoids, which lower ulcer index, duodenal ulcer, and stress ulcer in an ibuprofen-induced stomach ulcer model [56]. Moringa extract has been found to decrease free radicals, neutralize acidic gastric juice, and prevent stomach ulcers [57]. Flavonoids found in plants can protect against ulcer formation by enhancing capillary resistance and boosting microcirculation, leading to less cell harm [58].

Anti-obesity activity:

A study demonstrated that oral therapy with MO leaf powder for 49 days effectively reduced body mass index (BMI) in rats suffering from Hypercholesterolemia [59]. In rats, down regulation of mRNA expression of resistin and leptin led to increased regulation of adiponectin. A recent study found that MO has an anti-obesity impact through a specific mechanism. The plant helped reduce body weight and enhance lipid profile. It controlled genes related to adipogenesis, improved glucose tolerance, and lowered hormone levels such as vaspin, leptin, and resistin [60].

Antimicrobial and Antifungal effects:

The water-soluble seed lectin and phenolic extract of MO seed flour are highly sensitive to *Escherichia coli* and *Staphylococcus* aureus [61, 62]. Arora and Onsare in 2014 experimentally proved that the flavonoids and diterpenoids of MO pod husks have antibacterial and antifungal properties against both Gram-positive and Gram-negative bacteria and yeast [63]. One year later they also showed that the flavonoid extract of seeds is effective against the growth of *Pseudomonas aeruginosa*, *Staphylococcus*

aureus, and *Candida albicans* [64]. In vitro, ethanol extracts show antifungal properties against dermatophytes, including *Microsporum canis*, *Epidermophyton floccosum*, *Trichophyton rubrum*, and *Trichophyton mentagrophytes* [65].

Mechanism of actions of MO extract:

Numerous studies on MO have uncovered the functions and activities of several phytochemicals that have been isolated from various MO sections. Different possible ways of action of the phytochemicals have been thoroughly investigated by molecular-level investigations. Some of these effects with supporting data have been included below.

Failure of guanylyl cyclase activation does not initiate any biological repercussions. This fact causes a rise in the production of cyclic guanosine monophosphate (cGMP), which in turn triggers the activation of certain proteins, leading to various effects such as endothelial permeability, relaxation of smooth muscles, cardiac defence, and neural plasticity [66]. Extracts from M. oleifera reduced phosphodiesterase 5 (PDE-5) enzyme activity which in turn can stop cGMP activity [67]. The ability of medicinal plant extracts, particularly those with high flavonoid concentrations, to suppress PDE-5 activity was demonstrated in earlier studies [64]. Therefore, the essential flavonoid concentration of MO extract may be linked to its capacity to inhibit PDE-5 activity [69].

Furthermore, another study demonstrated the anti-atherosclerotic and hypolipidemic properties of MO leaves [70]. Serum malondialdehyde (MDA) levels are directly linked to atherosclerosis, a chronic inflammatory disease. An increase in oxygen radical levels is indicated by a rise in serum MDA. Therefore, endothelial cell damage is a crucial first step in the pathophysiology of atherosclerosis. The pathophysiology of atherosclerosis starts with "fatty streak" lesions, which are caused by a buildup of high levels of cholesterol and cholesteryl esters in macrophage "foam" cells found in the artery's intima [71].

Another study revealed that the extract from MO leaves dramatically inhibited the growth and formation of atherosclerotic plaque. It's interesting to note that the extract's ability to stop atherosclerotic plaque from forming was very similar to that of simvastatin, an oral antilipemic drug that is a member of the statin class of drugs and is primarily used to control abnormal lipid levels by preventing the liver's inherent generation of cholesterol [72].

Oxidative stress markers like MDA, Hydrogen peroxide, and protein carbonyl were markedly decreased in the heart, liver, and kidney after treatment with the MO extract. A study with diabetic people who received MO extract treatment showed an increased rate of antioxidants than those without treatment [73]. The histologies of the liver and pancreas showed necrotic spots, congestion, and varying degrees of inflammatory cell infiltration. In those treated with Moringa, these tissue damages were minor. Additionally, MO extract increased the expression of glucose transporter 4 (GLUT 4), which is important for correcting insulin resistance like that of the common antidiabetic drug pioglitazone [73].

By expanding colons, reducing colon weight/length ratios, and attenuating disease activity index (DAI) scores, MO seed extract reduced the severity of colitis [74]. Additionally, in cases of acute UC, the extract decreased intestinal damage and histological scores. In both acute and chronic colitis, it reduced the colon's production of pro-inflammatory cytokines, including myeloperoxidase (MPO), nitric oxide (NO), and TNF-α [75]. It has been demonstrated that M. oleifera seed extract treatment lowers fecal lipocalin-2, downregulates the gene expression of pro-inflammatory interleukin (IL)-1, IL-6, TNF-α, and inducible iNOS, and increases the expression of claudin-1 and ZO-1 in both acute and chronic colitis. It also has been shown to increase the expression of GSTP1, a Nrf2 key mediator of phase II detoxifying enzyme, in chronic UC [75].

Quercetin, an important phytochemical present in MO can reduce the gnes associated with lipogenesis and by reducing fatty acid oxidation it can decrease steatosis [76]. It has experimentally proved that both chlorogenic acid and quercetin present in MO extract can modify gene expression and regulation of hepatic triglyceride and cholesterol synthesis and accumulation [77, 78].

Concluding remarks:

This review article concludes that due to rich phytonutrient concentration, the MO plant is a natural integrator for treating different therapeutic issues and malnutrition. According to phytochemical analyses, various plant parts of MO are a rich source of primary and secondary metabolites. Pharmacological research validated the usage of the plant's nutraceutical qualities and ability to treat a variety of illnesses, demonstrating bioactivities such as antioxidant activity, antibacterial and anticancer qualities, antifertility, antidiabetic properties, reducing blood cholesterol, and antihypertensive effects, etc. Further exploitation of phytochemicals from this magic plant will explore new roles in therapeutics and the latest discoveries at the biochemical and molecular level will introduce a new era in scientific convergence soon.

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