Medicinal and Therapeutic Properties of Moringa

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N. Manavalan, N. Manikanda Boopathi, and M. Raveendran

Abstract

There are many medicinal plants that have been used for thousands of years and due to the recent COVID-19 pandemic, these plants can now be found in several healthcare products because of their therapeutic efficacy. Due to its rich medicinally imperative phytochemicals, *Moringa oleifera* has attracted several health industries. Besides, Moringa has been preferred as an affordable resource to fight malnutrition owing to its abundant nutritional properties. A large array of reports has repeatedly shown that Moringa can be used as anticancer, antidiabetic, anti-inflammatory and antioxidant products. Though such references provided evidence for its potentials as a functional food, yet the basic questions on its mechanisms of action, especially on its medicinal properties remain to be unclear. This chapter summarizes the individual bioactive phytocompounds present in Moringa and their medicinal properties. It also highlights those further studies that need to investigate the likely mechanisms of actions of the Moringa phytochemicals that foster its informative applications in the prevention and management of chronic diseases.

4.1 Moringa: A Treasure Trove for Therapeutic Properties

Ancient Indians, Romans, Greeks and Egyptians have long been using Moringa (*Moringa oleifera*) as one of the medicinally imperative plant products. Evidence for this usage is found in the large arrays of traditional and tribal medicinal knowledge and non-peer-reviewed sources (Fahey 2005).

Likewise, during the past three and half decades, enormous numbers of reports have surfaced in contemporary scientific periodicals that experimentally proven its pharmaceutical, therapeutic and prophylactic properties and its economic and societal importance. Above and beyond, Moringa has also been utilized in water clarification, lubricating and cosmetics industry, timber, wood coal and natural fencing.

Recent rigorous scientific proofs have critically examined the pharmaceutical properties of Moringa leaves, flowers, pods and other parts of the tree and justified that Moringa can be utilized as a "healthy food' or "superfood". Though it cannot be a panacea as promoted by the suppliers of Moringa products, constantly accumulating scientific reports supported the therapeutic and

N. Manavalan
Government Yoga and Naturopathy Medical College, Chennai, India

N. M. Boopathi (✉) · M. Raveendran
Department of Plant Biotechnology, Centre for Plant Molecular Biology and Biotechnology, Tamil Nadu Agricultural University, Coimbatore, India
e-mail: nmboopathi@tnau.ac.in

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prophylactic value of the Moringa products in almost all cases.

Moringa has been advocated for a long time as "natural nutrition for the tropics" and it has been used to combat malnutrition (which is a cause of several life-threatening diseases or disorders) in infants and nursing mothers. Moringa leaves can be consumed as fresh or cooked. They can also be stored as dehydrated powder in an air-tight container for several months. Such storage does not require any refrigeration and it has been reported that there is no loss of its nutritional value during these storing procedures. Furthermore, when other food sources are insufficient during the dry season, Moringa is in its full leaf production potential at the end of the dry season and hence, it has been known as a hopeful food source in the tropics.

Moringa possesses a rich amount of several vitamins and minerals as well as carotenoids (including β-carotene or pro-vitamin A). In addition to that Moringa also has a range of unprecedented unique compounds. For example, Moringaceae is rich in glucosinolates and isothiocyanates which are phytocompounds containing the simple sugar, rhamnose (Bennett et al. 2003). The exclusive compounds that are present in Moringa include 4-(a-L-rhamnopyranosyloxy) benzyl isothiocyanate, 4-(4'-O-acetyl-a-L-rhamnopyranosyloxy) benzyl isothiocyanate, niazimicin, pterygospermin, benzyl isothiocyanate and 4-(a-L-rhamnopyranosyloxy) benzyl glucosinolates and they have been reported to have hypotensive, anticancer, and antibacterial activity (Fahey et al. 2001, 2002; Fahey 2005). The above phytocompounds are only to quote few examples; other unique and valuable compounds are provided in the subsequent sections.

4.2 Phytochemical Compounds of Moringa

Secondary metabolites that are accumulated in high concentrations in response to both biotic and abiotic environmental stimuli are referred to as phytochemicals and they are also shown to possess several medicinal properties. Since time immemorial, such phytochemicals are used as a therapeutic agent to cure as well as to prevent against various contagious and non-contagious diseases. Owing to the abundant content of biologically active phytochemical and nutritional compounds, Moringa has long been explored as health-promoting plant products and large numbers of studies have and being undertaken to understand its medicinal properties.

Plant-derived phytochemicals are grouped into five classes according to their chemical structures: polyphenols, carotenoids, alkaloids, terpenoids, and sulphur-containing compounds. Interestingly, among the plant species, Moringa has almost all of these phytochemicals and it was strongly thought that the diverse biological activities and disease preventive potential of Moringa are largely because of such phytochemicals (Ma et al. 2020).

For example, Moringa has been shown to contain rich amounts of polyphenols including flavonoids and phenolic acids. Generally, polyphenols are having either one (e.g. phenolic acids) or more than one phenol ring (e.g. flavonoids) in their chemical structure and one of the key components of phytochemicals that have medicinal properties. Among the flavonoids, myrecytin, quercetin and kaempferol are found in Moringa leaves in the concentrations of 5.8, 0.207 and 7.57 mg/g, respectively (Mohammed and Manan 2015).

It should also be noted that the concentrations of each flavonoid varied depending on which part of the Moringa plant was used for the analysis using advanced chromatography techniques such as HPLC, GC–MS and LC–MS. For example, quercetin and kaempferol glycosides (glucosides, rutinosides and malonyl glucosides) were not present in roots and seeds. However, 0.46–16.64 and 0.16–3.92 mg/g dry weight of leaf were quercetin and kaempferol, respectively (Saini et al. 2016). Similarly, a lower amount of myricetin, rutin and epicatechin were also detected in Moringa leaves.

Phenolic acids such as gallic acid, caffeic acid, chlorogenic acid, coumaric acid and ellagic acid were also found in Moringa leaf and pod. These are a sub-group of phenolic compounds that are

mostly originated from hydroxybenzoic acid and hydroxycinnamic acid and shown to possess antioxidant, anti-inflammatory, antimutagenic and anticancer properties.

The antioxidant activity of phenolic compounds (such as neutralizing free radicals, quenching singlet or triplet oxygen, or decomposing peroxides) may be due to the inactivation of lipid-free radicals or owing to their redox properties that help in avoid decomposition of hydroperoxides into free radicals.

The chief phenolic acid present in Moringa is chlorogenic acid (CGA), which is an ester of dihydrocinnamic acid, which impedes glucose-6-phosphate translocase in the liver and thus reduce hepatic gluconeogenesis and glycogenolysis. Therefore, CGA has been shown to have an important role in glucose metabolism regulation.

Total phenolic concentrations in Moringa leaves were in the range of 2000–12,200 mg GAE/100 g as determined by Folin–Ciocalteau assay (Leone et al. 2015). The reason for the great variation in phenolic content is attributed to the fact that it depends on genotype, geographical location and environmental conditions. Though flowers and seeds were found to have polyphenols, they were present in relatively lesser concentrations than the leaves (Alhakmani et al. 2013).

Significant amounts of tannins (which are complex polyphenol molecules and have the ability to bind and precipitate protein, amino acids, alkaloids and other organic molecules in aqueous solutions) were also found in Moringa leaves. The highest concentration of tannins was reported in dried leaves (20.7 mg/g) and small amounts of tannins were also found in seeds (Mohammed and Manan 2015).

Different parts of Moringa plant were found to possess different types of glucosinolates (which are heterogeneous groups of sulphur and nitrogen-containing glycosidic compounds). Moringa contains 4-(α-L-rhamnopyranosiloxy) benzyl glucosinolates and is also called as glucomoringin and it has been reported in Moringa stem, flowers, pods, leaves and seeds. The maximum amount of glucomoringin was found in seeds (8620 mg/100 g) followed by leaves (78 mg/100 g) (Maldini et al. 2014).

However, the major glucosinolate found in the roots of the Moringa plant is benzyl glucosinolate (also called as glucotropaeolin) though there were reports on significant variations in its concentration which are due to geographical regions in which the Moringa plants are grown (Bennett et al. 2003). Myrosinase catabolizes glucosinolates into glucose, isothiocyanates, nitriles and thiocarbamates and these compounds were also reported in Moringa (Waterman et al. 2015).

Colours of leaves, fruits and vegetables are mainly due to carotenoids. Both green and dried leaves of Moringa contain different types of carotenoids. For example, green Moringa leaves contain 6.6–17.4 mg/100 g β-carotene (also known as pro-vitamin A) and dried leaves has 23.31–39.6 mg/100 g β-carotene, which are much higher than those found in carrots, pumpkins and apricots (Glover-Amengor et al. 2017).

It was also reported that the Moringa cultivars grown in India contain several other carotenoids too in the foliage, flowers and immature pods (fruits). More than 50% of total carotenoids was All-E-lutein and it was found in foliage and fruits. Besides, other classes of carotenoids such as All-E-luteoxanthin, 13-Z-lutein, all-E-zeaxanthin and 15-Z-b-carotene has also been reported in smaller quantities in Moringa (Saini et al. 2016).

Moreover, Moringa has also been confirmed to possess alkaloids (which are derived from amino acids metabolism) and N, α-L-rhamnopyranosyl vincosamide is the most abundantly reported indol-alkaloid in its leaves. Besides, pyrrolemarumine 4″-O-α-L-rhamnopyranoside (marumosides A) and 4′-hydroxyphenylethanamide (marumosides B) (which are unusual glycosides of a pyrol alkaloid) were also reported but their concentration in Moringa leaves are yet to be quantified (Sahakitpichan et al. 2011).

A plentiful amount of saponins in Moringa freeze-dried leaves (64–81 g/kg of dry weight) was also found. Saponins greatly minimize the absorption of cholesterol by binding bile acids

and boosting fecal excretion and ultimately the lowering plasma cholesterol. Besides, saponins also prevent cancer developments.

4.3 Moringa for Disease Therapy and Deterrence

Though the voluminous folklore history highlighted the benefits of Moringa based products such as extracts, decoctions, poultices, creams, oils, emollients, salves, powders and porridges as a healthy diet or to cure or prevent disease or infection, it has long been insisted to develop a scientific basis for these claims (Talalay and Talalay 2001).

Accumulating scientific evidence have authenticated the majority of the above healthcare claims and large numbers of scientific literature support the role of Moringa products in antibiotic, antitrypanosomal, antiulcer, antibiosis, antispasmodic, anti-inflammatory, hypotensive, hypocholesterolemic, hypoglycemic activities and even reduction of *Schistosome cercariae* titer (Farooq et al. 2012 and references therein).

Fahey (2005) has provided an extensive list of references that were studied evidently the nutritional, therapeutic and prophylactic applications of Moringa. Recent literature survey on the above line has also been witnessed all-inclusive list of studies that support the utility of Moringa as a medicinal plant (Farooq et al. 2012; Mehwish et al. 2020; Meireles et al. 2020; Padayachee and Baijnath 2020). The below subsections provide few representational references that support several therapeutic and prophylactic properties of Moringa.

But it should also be kept in mind that amidst of in vitro (cultured cells) and in vivo (animal) trials that offered systematic support benefits of Moringa-based traditional medicine lore, it has been underlined on several occasions that none of the experiments has clearly shown their efficacy in human beings. Especially there is a dearth of controlled and randomized clinical experiments and experimental findings published in peer-reviewed journals.

4.3.1 Antibiotic (or Anti-hyperglycemic) Activity

Indeed, the majority of the reports have pinpointed the antibiotic ability of Moringa and few studies have shown the Moringa phytochemicals that possess antibiotic behaviour (Gopalakrishnan et al. 2016). For example, antibiotic activity of 4-(α-L-rhamnopyranosyloxy) benzyl glucosinolate and its cognate isothiocyanate against several species of bacteria and fungi have been reported (Eilert et al. 1981).

4.3.2 Anticancer Activity

Numerous recent reviews have provided a list of studies that have reported the anticancer activities of Moringa based products and they were proved to prevent the development of human cancer cells (Ma et al. 2020; Szlachetka et al. 2020; Sodvadiya et al. 2020; Gupta et al. 2020 and references therein). It has been evidently shown that extracts of Moringa leaves, bark and seed have arrested the development of breast (MDA-MB-231) and colorectal (HCT-8) cancer cell lines of humans by reducing cell motility and colony formation and resulted in low cell survival, high apoptosis and enrichment of G2/M.

Similarly, increased apoptosis, DNA fragmentation and oxidative stress were reported when aqueous extract of Moringa leaves was used to treat human cancerous lung cells (A549) and other types of cancer cells and thereby prevent cancer proliferation and invasion.

Dose-dependent inhibition (having both antiproliferative and apoptosis properties) of cell proliferation of human tumor KB cells was also noticed for the Moringa leaf extract by stimulating apoptosis, morphological changes and DNA fragmentation. Likewise, the growth of human cancer pancreatic cells such as Panc-1, p34, and COLO 357 was curtailed by 0.75 mg/ml aqueous extract of Moringa leaves by inhibiting nuclear factor kappa B signaling pathway proteins and improved the cisplatin chemotherapy efficiency. In addition, cytotoxic

effect on human peripheral blood mononuclear cells and nil effect on the hemolytic activity of erythrocytes has also been reported when aqueous extract of Moringa seeds was administrated.

Thus, it can be concluded that extracts from Moringa can be used as a therapeutic as well as preventive agent to significantly limit the progression and invasion of human cancer cells (such as myeloma, cervix, colon, breast, leukemia, lung, liver, neuroblastoma, pancreas, colorectal, epidermoid, oral, ovarian, muscular, prostate, skin).

4.3.3 Antioxidant Activity

Antioxidant properties of extracts obtained from Moringa leaves, seeds and pods have also been established in several studies (reviewed in Ma et al. 2020). For example, hydroethanolic extract of Moringa leaves was investigated in an in vitro study and found that there was a strong antioxidant activity: use of nitric oxide (NO) scavenging assay recorded IC50 of 120 μg/ml and deoxyribose degradation assay recorded IC50 of 178 μg/ml. Further, it was established that the presence of total phenolic and flavonoid content, carotenoids, lycopene, ascorbic acid and anthocyanins in the Moringa leaves might be responsible for the antioxidant property (Vats and Gupta 2017).

Applicability of antioxidant activity of Moringa in the biological system was further confirmed by nourishing carbon tetrachloride (CCl_4)-intoxicated rats with Moringa leaves (50–100 mg/day) for 15 days significantly reduced the lipid peroxides and improved glutathione levels besides reducing the enzyme kinetics of superoxide dismutase and catalase in the liver and kidney, when compared with control. Similar kind of trends was also observed when correlating the antioxidant efficiency of Moringa leaves (100 mg/dl per day) and showed a comparable effect to a group treated with a standard treatment of vitamin E at 50 mg/dL per day (Verma et al. 2009). In the same lines, feeding goats regularly with Moringa leaf powder increased antioxidant enzymes and decreased peroxidation in the liver of goats (Moyo et al. 2012). Correspondingly, daily uptake of 7 g of Moringa leaf powder by postmenopausal women continuously for 3 months have shown to increase antioxidant enzymes, ascorbic acid, serum levels of retinol but reduced serum malondiadehyde (Kushwaha et al. 2014a).

The aforesaid studies clearly indicate that Moringa has robust antioxidant activities and can be effectively used to cure oxidative stress-induced diseases or maladies.

4.3.4 Anti-inflammatory Activity

Pro-inflammatory mediators secreted by lipopolysaccharide (LPS)-induced murine macrophage cells were used to examine the anti-inflammatory property of ethanolic extract of Moringa pods. Increased concentrations of Moringa extract have shown an increased degree of inhibition on mRNA expression as well as the levels of interleukine-6 (IL-6), tumor necrosis factor-alpha (TNF-α), inducible nitric oxide synthase (iNOS) and cyclooxygenease-2 which may be partly mediated by preventing phosphorylation of inhibitor kappa B protein and mitogen-activated protein kinases (Muangnoi et al. 2012).

Similarly, using the RAW macrophage cell system, the negative impact of Moringa leaf concentrate and isothiocyanates on the gene expression and production of inflammatory markers (viz., iNOS, IL-1β, nitric oxide (NO) and TNF-α) has been demonstrated (Waterman et al. 2015).

In a recent study, Yan et al. (2020) have employed a lipopolysaccharide (LPS)-induced RAW 264.7 cell model to evaluate the Moringa leaf acetone extract for its anti-inflammatory effect and found that it significantly inhibited NO production and inducible NO synthase (iNOS) mRNA levels. Increased dose of Moringa extract has increased inhibitory activity and such activity was attributed to its phenolic compounds (including quercetin derivatives, kaempferol, chlorogenic acid, isothiocyanates, and kaempferol derivatives).

4.3.5 Hepatoprotective Activity

By reducing tissue histopathology, aspartate aminotransferase, alkaline phosphatase, alanine aminotransferase and lipid peroxidation and increasing glutathione, Moringa leaf extracts have been proven to protect the liver from the oxidative damage (Das et al. 2012). Liver damage induced by antitubercular drugs (such as isoniazid, rifampicin, and pyrazinamide) in rats has also been safeguarded by ethanolic extract of Moringa leaves through hepatoprotective activity by diminishing the serum levels of aspartate aminotransferase, alkaline phosphatase, alanine aminotransferase and bilirubin and by inhibiting lipid peroxidation in the liver (Pari and Kumar 2002).

In another study, Artesunate-amodiaquine (an antimalarial drug) induced liver injury in Wistar rats was studied and hepatoprotective activity of Moringa leaf extract was reported as it reduced serum AST values and hepatocyte degeneration in Artesunate-amodiaquine intoxicated rats (Okumu et al. 2017).

4.3.6 Antidiabetic Activity

Elevated concentration of blood glucose leads to a metabolic disorder, diabetes and uncontrollable glucose concentration beyond the recommended ranges will lead to health complications. As recently indicated by International Diabetes Federation (IDF) globally more than 366 million people are under diabetes mellitus and by 2030, this figure may shoots-up to 552 million or even more.

There are two kinds of diabetes mellitus and type II is characterized by abnormal glucose tolerance due to insufficient insulin secretion. Hyperglycemia is metabolic disturbance due to deficient insulin and it is a universal health concern as it causes microvascular complications (retinopathy, nephropathy and neuropathy) and macro-vascular complications, i.e. cardiovascular comorbidities leading to insulin resistance disorder.

Ma et al. (2020 and references therein) have listed out experiments that support the antidiabetic properties of Moringa. *M. oleifera* leaves were reported to have an extreme inhibitory action on α- amylase and α-glucosidase activities (Jaiswal et al. 2009) and anti-hyperglycemic activity (William et al. 1993). The key phytocompounds that attributed to this significant reduction in blood glucose level are glycosides, anthocyanins, anthraquinone, hemlock tannin and A-phenolic steroids. *M. oleifera* leaves were repeatedly shown to contain these compounds in significant amounts.

Recently, an *in silico* analysis of Anthraquinone, Sitogluside (glycoside), Hemlock Tannin, A-Phenolic Steroid, 2-Phenylchromenylium (Anthocyanins) has indicated that they were extremely selective and efficiently intermingled with mutated protein of diabetes (Zainab et al. 2020).

In supporting the antidiabetic property of Moringa, a study conducted by Kushwaha et al. (2014b) has concluded that routine consumption of Moringa leaf powder (7 g per day) by the post-menopausal women for 3 months has considerably lowered the fasting blood glucose to 13.5% and it has also been shown that such glucose-lowering effect of Moringa is due to blocking intestinal glucose, better insulin secretion and reduction in insulin resistance (Muhammad et al. 2016).

Though such studies provided evidence for the Moringa's potential in lowering the blood glucose potential, almost all of these studies were conducted in animals, and only a few studies have focused on humans. Therefore, thorough and long-term randomized controlled investigations on the antidiabetic effect of Moringa leaves, seed and pods in humans are warranted.

4.3.7 Anticardiac Arrest Activity

Investigations on the hypolipidemic effect of feeding Moringa leaves (100 mg/kg of body weight (bw)) to rabbits significantly lowered cholesterol levels by 50% and 86.52% reduction

in atherosclerotic plaque formation in internal carotid and it has been observed that such hypolipidemic effects were on par with simvastatin (reference drug) treated group (Chumark et al. 2008).

In another study, lowering of serum cholesterol by 14.35% was noticed due to continuous consumption of aqueous extract of Moringa leaves (1 g/kg bw) for 30 days by rats and also lowered the concentrations of cholesterol by 6.40% and 11.09% in the liver and kidney, respectively (Ghasi et al. 2000).

Similarly, decreased levels of serum lipids in a dose-dependent manner were noticed in the rats that were fed with methanolic extracts of Moringa leaves at different doses (150, 300, or 600 mg/kg bw) for 30 days and the Moringa diet was shown to significantly reduce the triglyceride, cholesterol, low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), atherogenic index and increase the high-density lipoprotein (HDL) (Jain et al. 2010).

Few reports have also highlighted the antihypertensive property of Moringa in the rat (daily feeding @ 30 mg/kg of bw) and it was shown to be the presence of thiorcarbamate, isothiocyanate glucosides and hydroxybenzoate in the Moringa leaf extracts (Faizi et al. 1998).

Despite the above proofs, it is generally believed that more and critically acclaimed clinical experiments, with animal as well as human, are required to validate the role of Moringa in curing cardiovascular diseases and its antihypertensive activity.

4.3.8 Anti-ocular Disorder Activity

As both leaves and pods of Moringa are shown to be rich in Vitamin A, it can also be used to avert night blindness and eye problems. Deficiency in Vitamin A generally leads to blindness, which ranges from impaired dark adaptation to night blindness. It has been evidently shown that consuming Moringa leaves supplemented with oils (including ben oil, extracted from Moringa seeds) significantly improved the Vitamin A nutrition to the human and hindered the onset of night blindness and/or cataracts (Yan et al. 2020).

4.3.9 Immunomodulatory Activity

Sudha et al. (2010) investigated cellular immunity and humoral immunity in animals by exploring immunomodulatory action of methanolic extract of *Moringa oleifera* (MEMO). It was found that there was a significant increase in serum immunoglobulins and a decrease in mortality due to bovine *Pasteurella multocida* in mice. It has also been shown that MEMO induced substantial rise in adhesion of neutrophils, reduction of cyclophosphamide induced neutropenia but an increase in phagocytic index. Thus, it has been established that Moringa stimulates both cellular and humoral immunity with a low dose of MEMO (Sudha et al. 2010). Several other studies have also been recognized the immunoregulatory activity of Moringa (Mehwish et al. 2020 and references therein).

4.4 Concluding Remarks

Though the mechanism of actions was unknown, Moringa has shown to exhibit several medicinal, therapeutic and prophylactic properties due to their rich nutritional and curative compounds. Further clinical and advanced biochemical studies are required to unravel the mechanism of actions of these phytochemicals and more convincing investigations are needed to declare Moringa as a functional food to prevent and/or manage chronic diseases.

Considering the medicinal and therapeutic potentials of Moringa, Government of Tamil Nadu, India, is supplying Moringa leaf powder to the patients through Yoga and Naturopathy doctors serving in Government Medical College Hospitals and Hospitals located at Headquarters of each District and Taluk, Primary Health Centers, Yoga and Naturopathy Maternity Clinics, and Wellness Centers. An initial survey has shown that the Moringa products are well

received by the patients and positive feedback on the health benefits of Moringa has been obtained so far.

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