International Journal of Pharmaceutical Drug Design
IJPDD, Vol.-1, Issue-6 (May, 2024)
ISSN: 2584-2897
Website: https://ijpdd.org/

Review

Scope And Therapeutic Potential of *Moringa Oleifera*: Comprehensive Review

Ravi Kumar[1], Mohd. Salman[2], Nasiruddin Ahmad Farooqui[3], Praveen Kumar[4], Dr. Samim Ahmad[5]

[1]*Research Scholar, Translam Institute of Pharmaceutical Education & Research, Meerut*
[2]*Associate Professor, Translam Institute of Pharmaceutical Education & Research, Meerut*
[3]*Professor & HOD, Translam Institute of Pharmaceutical Education & Research, Meerut*
[4]*Professor, Translam Institute of Pharmaceutical Education & Research, Meerut*
[5]*Director, Translam Institute of Pharmaceutical Education & Research, Meerut*

Article History

Received: 28/03/2024
Revised : 20/04/2024
Accepted : 12/05/2024

DOI:
10.62896/ijpdd.1.6.6

Abstract:

Moringa oleifera, also known as the "tree of life" or "miracle tree," is classified as an important herbal plant due to its immense medicinal and non-medicinal benefits. Traditionally, the plant is used to cure wounds, pain, ulcers, liver disease, heart disease, cancer, and inflammation. This review aims to compile an analysis of worldwide research, pharmacological activities, phytochemical, toxicological, and ethnomedicinal updates of Moringa oleifera and also provide insight into its commercial and phytopharmaceutical applications with a motive to help further research.

Keywords: *Moringa oleifera, tree of life, miracle tree, phytopharmaceutical applications.*

***Corresponding Author**

Ravi Kumar

Research Scholar, Translam Institute of Pharmaceutical Education & Research, Meerut

Introduction:

Moringa oleifera belongs to the family Asclepidaceae. It is commonly known in Hausa as Zogale, Kilba-Kabbi, and Fulani-Kabije. According to Harwell, (1971) the flowers are used as folk remedies for tumors, the seed for abdominal tumors, leaves applied as poultice to sores, rubbed on the temples of the head for headaches and said to have purgative properties. The leaves have been reported to have hypocholesterolemic effect (Ghasi, 2000); hepatoprotective effect on anti-tubercular drugs induced toxicity (Pari, 2002) and antimicrobial activities (Cacares, 1991). Moringa oleifera (M. oleifera), the "miracle tree", thrives globally in almost all tropical and subtropical regions, but it is believed to be native to Afghanistan, Bangladesh, India,and Pakistan [1].

The Moringa family comprises 13 species (M. oleifera, M. arborea, M. rivae, M. ruspoliana, M. drouhardii, M. hildebrandtii, M. concanensis, M. borziana, M. longituba, M. pygmaea, M. ovalifolia, M. peregrina, M. stenopetala), of which M. oleifera has become well known for its use in nutrition, biogas production, fertilizer, etc., [2,3]. Moringa has the unique property of tolerating drought [3]. Seeds, leaves, oil, sap, bark, roots, and flowers are widely used in traditional medicine. Moringa leaves have been characterized to contain a desirable nutritional balance, containing vitamins, minerals, amino acids, and fatty acids (Moyo et al., 2011; Teixeira et al., 2014; Razis et al., 2014). Additionally, the leaves are reported to contain various types of antioxidant compounds such as ascorbic acid, flavonoids, phenolics, and carotenoids (Alhakmani et al., 2013; Vongsak et al., 2014).According to several commentaries (Anwar et al., 2007; Mbikay, 2012; Razis et al., 2014), various preparations of M. oleifera are used for their anti-inflammatory, antihypertensive, diuretic, antimicrobial, antioxidant, antidiabetic, anti-hyperlipidemic,

antineoplastic, antipyretic, antiulcer, cardio-protectant, and hepato-protectant activities. The therapeutic potential of M. oleifera leaves in treating hyperglycemia and dyslipidemia was reviewed by M bikay (2012). Razis et al. (2014) summarized potential health benefits of M. oleifera, focusing on their nutritional content as well as antioxidant and antimicrobial characteristics.

Fig. 1: Moringa oleifera.

Moringa oleifera is a medium sized tree in the family Moringaceae, consisting of a single genus Moringa. The family has been reported to have parietal placentation, 3-valved fruit and winged seeds. Different species ranging from four to ten has been reported by different people. *Moringa oleifera* leave is distinguished by its tripinnate leaves (Ramachandran *et al*., 1980). The plant is reportedly fast growing and drought resistant (Fuglie, 1999). It is an edible plant reportedly used in African and Asian countries as food and medicine for many centuries (Iqbal *et al*., 2006). The leaves are rich sources of potassium, calcium, phosphorus, iron, vitamins A, C and D, essential amino acids and antioxidants (vitamin C, β-carotene, flavonoids) (Bamishaiye *et al*., 2011).

In spite of the presence of the defence mechanisms in the nervous system, the nervous system still remains susceptible and vulnerable to various dangers and damages, which are up to 600, already identified disorders (Giacoppo *et al*., 2015). With the study of neurodegenerative diseases, there is an increase in the discovery of new natural compounds possessing pharmacological activities. Consequently, a number of studies have shown that plant-derived chemical compounds have potential-health promoting abilities (Giacoppo *et al*., 2015). A wide variety of phytochemicals have been shown to prevent the risk of carcinogenesis and some chronic diseases like neurodegenerative diseases (Calabrese *et al*., 2012; Alrawaiq and Abdullah, 2014; Fuentes *et al*., 2015).

Huntington's disease, multiple sclerosis, amyotrophic lateral sclerosis, traumatic brain injury, spinal cord injury and cerebral ischemia/reperfusion are considered the disorders with the highest incidence in the population worldwide (Giacoppo et al., 2015). The mechanisms triggering neurodegeneration are largely unknown; although it has been suggested that oxidative stress plays a key role in its development (Calabrese et al., 2007). This has resulted in an increased interest in the use of natural compounds as a source of powerful and effective antioxidative agents in the treatment of these pathologies (Giacoppo et al., 2015).

The aim of this article is to review different studies on the effect of Moringa oleifera leave extracts and derivatives on the nervous system, in vivo and in vitro.

General Preparation of the Leave Extract

The *Moringa oleifera* leaves (MOL) are prepared in different ways before being administered to the animal subjects, the most favoured common laboratory rodents (rats and mice). The extracts vary from aqueous form (Ganguly *et al*., 2005; Adedapo *et al*., 2009), alcohol extracted form (Ganguly and Guha, 2008; Kirisattayakul *et al*., 2012; Sutalangka *et al*., 2013), to the air-dried and pulverised form (Nkwukwana *et al*., 2014). The alcohol extracted form seems to be the most widely used form of the extract, with the reported yield varying from 1.34% (Mohan *et al*., 2005), 10% (Ganguly and Guha, 2008), to 17.49% (Kirisattayakul *et al*., 2012; Sutalangka *et al*., 2013). Further analysis or fractionations by some authors (Verma *et al*., 2009; Rajanandh and Kavitha, 2010; Ogbunugafor *et al*., 2012; Vinoth *et al*., 2012; Berkovich *et al*., 2013), recorded the

resence of flavonoids, phenolic compounds, vitamins and some amino acids. Extracts were normally administered per os.

Therapeutic potential, Toxicity studies and LD50 of MOL

Before the advent of orthodox medicine, Africans relied on herbs to care for health problems, while also using them as a source of food (Abalaka *et al*., 2009; Awodele *et al*, 2012). Many herbal medicines are believed to have preventive effects on chronic diseases due to their radical scavenging or antioxidative properties (Potterat, 1997). MOL has been shown to have a high level of phenolic contents, which have antioxidative effects. Many phenolic compounds display an antioxidative effect more potent than vitamin E in vitro and also inhibit lipid peroxidation by chain-breaking peroxyl-radical scavenging. They also directly scavenge reactive oxygen species like hydroxyl, superoxide and peroxynitrite radicals (Tsao and Akhtar, 2005); and to scavenge free radicals associated with 2, 2-diphenyl- 1-picrylhydrazyl (DPPH) radical, superoxide, and nitric oxide as well as to inhibit lipid peroxidation (Sreelatha and Padma, 2009). Polyphenols constitute the largest class of phytochemicals and dietary polyphenols have been shown to play important roles in human health (Ogbunugafor *et al*., 2012). So far, only five studies on the use of MOL have been reportedly conducted and published in humans, using powdered whole leaf preparations. These publications demonstrated the anti-hyperglycemic (antidiabetic) and anti-dyslipidemic activities of MOL. No adverse effect was reported in these human studies (Stohs and Hartman, 2015). None of these human studies evaluated the effect on the nervous system.

Several animal studies have been conducted to assess the toxicity of various preparations of MOL and also the ideal dose, all giving varied results and values. Administering the aqueous extract, at doses of 400, 800, 1600 and 2000 mg/kg daily for 21 days (single acute dose at the highest dose) were deemed to be safe in rats, using indices such as blood cell counts and serum enzyme level, although a dose-dependent decline in body weight was observed (Adedapo *et al*., 2009). In 2011, Ambi *et al*., gave rats varying amounts of the powdered MOL incorporated into the feed, for 93 consecutive days. Observable lesions were reported in all organs, including the brain which reportedly showed neuronal degeneration and necrosis of glial cells. Concentrations of MOL used in this study were up to 75% of the feed. The reasons given for some of the pathologies observed were speculated to be probably due to the presence of some trace elements in the leaves, even though observed in the least detectable limits e.g. strontium The authors went further to caution against indiscriminate eating of large quantities of MOL in the area in which the study was carried out. In another study by Asare *et al*., (2012), the aqueous extract of MOL were found to be genotoxic, based on blood analysis at 3000 mg/kg. This dose is higher than what is normally consumed in humans. A further assay by the same authors revealed cytotoxic effects at 20 mg/kg using human peripheral blood mononuclear cells in vitro.

The toxicological effects of the prolonged use of the alcoholic extract of MOL has also been documented by Bakre et al. (2013) and Oyagbemi et al. (2013). According to Bakre et al. (2013), the ethanolic extract of the leaves showed a significant dose-dependent decrease in rearing, grooming, head dips and locomotion; although they also reported an increased anxiogenic effect and enhanced learning[5-8]. The authors concluded that the leaves possessed a CNS depressant and anticonvulsant properties, the action of which was possibly mediated through the enhancement of the central inhibitory mechanism. This probably justifies the use of the leaves to treat epilepsy in traditional medicine. Oyagbemi et al. (2013) demonstrated that the chronic administration of the leaves may predispose the subject to hepatic and kidney damage.

MOL and Neurodegeneration

Derivatives of MOL that have been shown to be effective against neurodegeneration include glucosinolates. Glucosinolates and their breakdown products, isothiocyanates have been reported to be present in little amount in Moringaceae plants. (Galuppo *et al*., 2014; Giacoppo *et al*., 2015). In recent years, glucosinolates have attracted a lot of research interest due to their reported protective effect against neurodegeneration (Giacoppo *et al*., 2015). Some types of glucosinolates (R,S-Sulforaphane – SFN) have been reported to offer protection to mesencephalic dopaminergic neurons from cytotoxicity and oxidative stress by removing intracellular quinone products, prevent reactive oxygen species production, DNA fragmentation and membrane breakdown (Han *et al*., 2007). SFN also protected primary cortical neurons against injuries caused by the oxidized products of dopamine (Spencer *et al*., 2002; Vauzour *et al*., 2007).

Use of MOL and derivatives in *in vivo* studies

The hippocampus plays a vital role in the spatial memory (Parron *et al*., 2006), while the dorsal hippocampus provides animals with a spatial map of their environment. This it does by making use of reference and working memory (Liu and Bilkey, 2001). Lesions in this region cause problems relating to goal-directed navigation and also impair the ability to remember precise location (Herbert and Das, 2004). Mohan *et al*. (2005) reported the nootropic activity of MOL and so, the ability to improve memory in male and female rats. The leaves displayed a facilitatory effect on retention and acquired learning, using the passive shock avoidance test and elevated plus maze. The extract administered at 100 mg/kg significantly reduced the number of mistakes and latency time to reach the shock free zone. With the elevated plus maze, the extract at 50 mg/kg significantly reduced the transfer latency on the second day of testing, while also antagonising the effect of scopolamine [9]. In a previous study by Sutalangka *et al*. (2013), experimental rats were administered AF64A (a cholinotoxin) via the intracerebroventricular route, to induce dementia, administration of the alcoholic extract of MOL showed a significant reduction in the escape latency time when subjected to Morris water maze. Also, a corresponding increase in neuronal density of the CA1, CA2, CA3 and the dentate gyrus regions were also observed in groups administered the extract as a treatment to AF64A. The extract also significantly attenuated the decreased activities of superoxide dismutase and catalase induced by AF64A, and decreased malondialdehyde level.

Some compounds isolated from MOL have been shown to have protective effects on the components of the CNS. Protease inhibitors (proline and alanine) isolated from MOL was successfully used to alleviate the extent of axonal damage treat degenerating axons in rats induced with spinal cord injury resulting in paraplegia in the experimental rats[10].

The protease inhibitors were administered intraperitoneally for the first three post-operative days. Recovery of some level of hind limb function was reported to be better in the drug-treated rats after 7 days post-operation. Quantitative analyses of secondary axonal degeneration at sites remote from the direct mechanical insult was reported to have provided solid evidence for the beneficial effects of protease inhibitors. In the rats treated with proline, the amount of degenerating axons was 13% less than that in untreated controls ($P < 0.001$), and a similar effect was observed in the rats treated with alanine at a dose of 500 mg/kg of body weight, the amount being 12% less than in untreated controls. These protease inhibitors however were said to not cross the blood brain barrier (Singh *et al*., 2012).

Kirisattayakul *et al*. (2012; 2013) demonstrated the potential benefit of the hydroalcohol MOL extract in decreasing brain infarct volume, and also its neuroprotective effect against focal cerebral ischemia. Ischemic stroke was induced by occlusion of the middle cerebral artery, and the animals were fed extract of MOL. Results showed cerebroprotective effect and enhanced superoxide dismutase activity in the hippocampus, and decreased malondialdehyde levels in cerebral cortex, hippocampus and the striatum.

Use in neuronal cell culture

MOL has been used in ayurvedic medicine to treat a number of central nervous system (CNS) ailments, ranging from paralysis, nervous debility to nerve disorders (Hannan *et al*., 2014). There has been evidence for nootropic and neuroprotective disorders in cell cultures of neural cells and in animal models (Hannan *et al*., 2014). Using hippocampal neurons, Hannan *et al*., (2014) reported that the addition of MOL ethanolic extract significantly increased the number and length of neurites and their branching, in a dose-dependent manner, with the optimal concentration achieved at 30 μg/ml. In the same experiment, neuronal viability was increased, cellular injury was decreased and the rate of neuronal differentiation was also accelerated [11-13]. No cytotoxicity was observed. Neurons also exhibited more extended and multiple branching, an increase in the number and length of primary dendrites and also the appearance of more secondary and even tertiary dendrites. MOL was also observed to modulate axonal development and promote synaptogenesis[14-15]. The reasons for this multiple branching and differentiation observed could be due to the presence of β-carotene, which is abundant in MOL. β-carotene has been reported to be an inducer of neuronal cell differentiation (Lee *et al*., 2013).

CONCLUSION

The mechanism of action of *Moringa oleifera* leaves is probably due to the high level of polyphenols and other antioxidative compounds it possesses, which confer neuroprotection by scavenging free radicals or activating cellular antioxidant system (Luqman *et al*., 2012). There is an abundance of data on the use of MOL to treat

conditions relating to diabetes, hyperlipidemia, hypertension, hypoglycaemia and some other related conditions, but currently very little information on pure compounds derived from MOL which have been successfully used to treat neurodegeneration, neurological or related conditions.

The current economic recession being experienced world-wide, especially in African countries, is likely to make people seek out the use of herbal medicine more, thereby necessitating the need for further research on this plant. Further investigation still needs to be carried out to isolate and determine a compound that is ideal for combating generalization.

References:

1. Fuglie, L.J. Producing Food without Pesticides: Local Solutions to Crop Pest Control in West Africa, 1st ed.; Church World Service: Dakar, Senegal, 1998; pp. 1–158.
2. Gandji, K.; Chadare, F.J.; Idohou, R.; Salako, V.K.; Assogbadjo, A.E.; Glèlè, R.L.K. Status and utilisation of Moringa oleifera Lam: A review. Afr. Crop Sci. J. 2018, 26, 137–156.
3. Alrawaiq N.S. and Abdullah A. (2014). An evaluation of sulforaphane as a potential agent fordisease prevention.Res. J. Pharm. Biol. Chem. Sci., 5: 1335–1349.
4. Araújo LCC, Aguiar JS, Napoleão TH, et al. 2013. Evaluation of cytotoxic and anti-inflammatory activities of extracts and lectins from Moringa oleifera seeds. PLoS One 8: e81973.
5. Asare GA, Gyan B, Bugyei K, et al. 2012. Toxicity potentials of the nutraceutical Moringa oleifera at supra-supplementation levels. J Ethnopharmacol 139: 265–272.
6. Asiedu-Gyekye IJ, Frimpong-Manso S, Awortwe C, et al. 2014. Micro- and macroelemental composition and safety evaluation of the nutraceutical Moringa oleifera leaves. J Toxicol. DOI:10.1155/2014/786979.
7. Hannan A., Kang J., Mohibbullah M.,Hong Y., Lee H., Choi J., Choi I.and Moon S. (2014).Moringa oleifera with promising neuronal survival and neurite out growth promoting potentials. Journal of Ethnopharmacology, 152:142–150.
8. Ijeomah A. U., Ugwuona F. U. and Abdullahi H. (2012). Phytochemical composition and antioxidant properties of Hibiscus sabdariffa and Moringa oleifera. Nigerian Journal of Agriculture, Food and Environment, 8(1): 10–16.
9. Kirisattayakul W., Wattanathorn J., Tong-Un T., Muchimapura S., Wannanon P., and Jittiwat J.(2013). Cerebroprotective Effect of Moringa oleifera against Focal Ischemic Stroke Induced by Middle Cerebral Artery Occlusion. Oxidative Medicine and Cellular Longevity, Volume 2013, Article ID 951415, 10 pages.
10. John, T.A. and Onabanjo, A. O. (1990). Gastroprotective effect of an aqueous extract of *Entandro phragmautile* bark in experimental ethanol-induced peptic ulceration in mice and rats. J. Ethnopharmacol. **29:** 87 – 93.
11. Jaiswal D, Kumar RP, Kumar A, et al. 2009. Effect of Moringa oleifera Lam leaves aqueous extract therapy on hyperglycemic rats. J Ethnopharmacol 123: 392–396.
12. Lee H.A., Park S., and Kim Y.(2013).Effect of β-carotene on cancer cell stemness and differentiation in SK-N-BE(2)C neuroblastoma cells. *Oncol.Rep*,.30:1869–1877.
13. Liu P. and Bilkey D.K. (2001). The effect of excitotoxic lesions centeredon the hippocampus or perirhinal cortex in object recognitionand spatial memory tasks.*Behavioral Neuroscience*, 115(1): 94–111.
14. Stohs S.J. and Hartman M.J. (2015). Review of the Safety and Efficacy of *Moringa oleifera*. *Phytotherapy Research*, 29: 796–804.
15. Sofowora, E.A. (1994). Medical Plant and Traditional Medicine in Africa. University of Ife Press, Nigeria: pp. 1 – 23

*****