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Antioxidant and anti-inflammatory potential of *Moringa oleifera* L

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Abstract
Pharmacological studies revealed the importance of phytoconstituents for therapeutic applications (Prusti, 2008). In India, medicinal plants play a major role in folk medicine. Majority of total world's population depends on phytoconstituents for treatment of various diseases. Almost, 25 to 45% of present-day remedies contain plant-derived molecules as essential sources for medication. Nearly a little less than 50% of the 25 top-selling drugs marketed worldwide are derived directly from natural sources (Ramya *et al.*, 2012).

Keywords: Treatment, diseases, Magnoliopsida

Introduction

Moringa oleifera in traditional medicine

Moringa oleifera L. (MO) is commonly known as drumstick or Miracle tree is a native of Africa and Asia belongs to the family, Moringaceae which is adopted to many countries. MO is popular across the nations due to its multipurpose uses which is cultivated both in humid and dry conditions. Almost all parts of the plant are utilized for medicinal use, vegetable purpose, cosmetic oils and fodder to the cattle.

Scientific classification

- **Kingdom:** Plantae
- **Subkingdom** Tracheobionta
- **Division:** Magnoliophyta
- **Class:** Magnoliopsida
- **Order:** Brassicales
- **Family:** Moringaceae
- **Genus:** *Moringa*
- **Species:** *oleifera*

Other names: Munagachettu (Telugu), Nuggekayee (Kannada), Murungai-kaai (Tamil), and Sahjan (Hindi).

Phytoconstituents of *Moringa oleifera*

Moringa leaves are highly nutritious with double the protein of yogurt, four times more vitamin A than carrots, three times higher in potassium than bananas, seven times more vitamin C content than oranges and four times more calcium than milk (Mathur, 2005) [16]. The leaves of MO contain important phytoconstituents like polyphenols, vitamins, phenolic acids, flavonoids, carotenoids, alkaloids, tannins, and saponins (Leone *et al.*, 2015) [14]. In addition, MO leaves are rich in antioxidant chemicals and other nutrients (Popoola and Omembe, 2013) [21]. Muhammad *et al*. (2016) [18] explained that flavonoids and phenolic acids are collectively referred to as phenolic compounds that were further classified into flavone, flavonol, flavanone, anthocya-nidin, isoflavonoid and chalcones. The high-performance liquid chromatography analysis indicated the presence of phenolic acids (Gallic, chlorogenic ellagic and ferulic acid) and flavonoids: kaempferol, quer-cetin, isoquercetin, astragalin and rutin in *Moringa*. Nouman *et al*. (2016) [20] reported that Quercetin and kaempferol in 3-O-glycoside forms were the predominant flavonoids in MO leaves.

They also reported that the leaves also contain niazirin, niazirinin, 4-[(40-O-acetyl-Lrhamnosyloxy) benzyl] isothiocyanate, niaziminin A and B, quercetin-3-O-(600-malonyl-glucoside), kaempferol-3-O-glucoside and kaempferol-3-O-(600-malonyl glucoside), 3-caffeoylquinic and 5-caffeoylquinic acid. Atawodi *et al*. (2010) [2] confirmed the presence of chlorogenic acid, rutin, quercetin glucoside and rhamnoglucoside in methanol extract of MO leaves which are responsible for various medicinal and therapeutic uses.

Hepatoprotective effect of *Moringa oleifera*

Toppo *et al.* (2015) [30] reported that MO leaf extract @ 500 mg/kg significantly ($p<0.01$) decreased the elevated ALP, AST, ALT, LPO levels with the increase in SOD levels. They revealed that the hepatoprotective action of MO leaf extract was mainly attributed to its antioxidant and free radical scavenging property due to the presence of flavonoids such as quercetin and kaempferol, vitamin A, ascorbic acid. Fattah *et al*. (2020) [31] reported that aqueous extract of MO significantly restored the lead perturbations by its antioxidant potentiality, reduction of oxidative stress–induced DNA damage via amelioration of NF-kB and TNF-α which kept hepatocyte integrity and reduced serum hepatic enzyme activities. Muzumbukilwa *et al*. (2019) [32] reported that methanolic extract of MO significantly restored the damaged hepatocellular architecture and also provided dose dependent protection against hepatic injury which was attributed to its phenolic bioactive compounds. Soliman *et al.* (2020) [33] in a study on methotrexate induced hepato-renal damage revealed that the increased NF-κB activity led to increased inflammation. Pre-treatment with MO inhibited the NF-κB activation and thereby reduced the inflammation in rats.

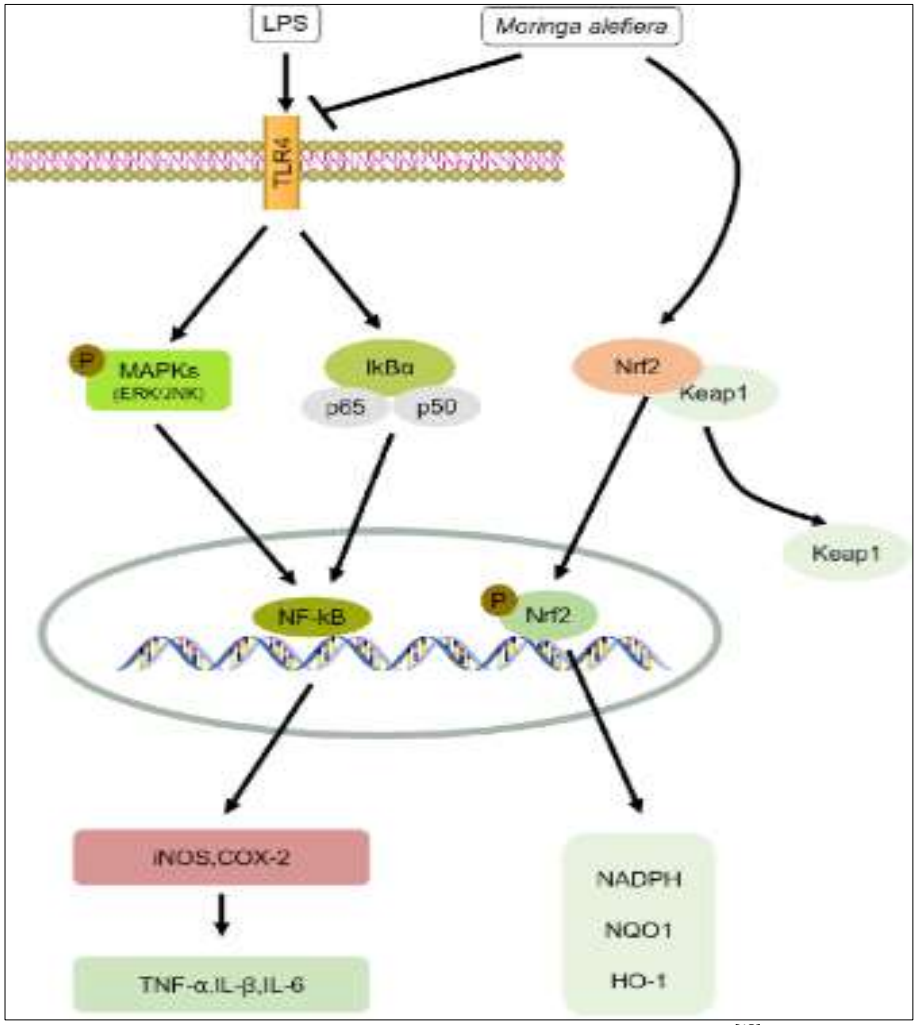
***Moringa oleifera* as a nutraceutical source for attenuating metabolic disorders**

Toma *et al*. (2014) [34] reported the antihyperglycemic and antihyperlipidemic activity of MO by inhibition of α-glucosidase and pancreatic α-amylase. They also demonstrated that inhibition of lipase and cholesterol esterase enzymes aids in the antihyperlipidemic activity of MO. Swamy and Meriga (2020) [29] demonstrated that MO has potent antioxidant activity and significantly inhibited pancreatic lipase, α-amylase and α-glucosidase, the key metabolic enzymes associated with obesity. Hamed *et al.* (2020) [10] elaborated that Caffeoylquinic acid (CQA) was a term given to phenolic compounds and explained that CQAs and flavonoid glycosides represent most of the phenolic substances in the MO which will efficiently reduce the levels of pancreatic lipase, α-amylase and α-glucosidase. Sangkitikomol *et al.* (2014) [26] revealed that MO has the ability to inhibit the expression of several lipid metabolism genes including HMG-CoAR, PPARα1 and PPARγ in Hep G2 cells so as to reduce the cholesterol, lipid complexes and to maintain the lipid homeostasis. The compounds, quercetin and kaempferol monoglycoside-based flavonoid glycosides in MO were the main bioactive components for hypoglycemic and hypolipidemic effects (Chen *et al.*, 2020) [5]. They recognized MO as a neutraceutical source for attenuating metabolic disorders.

Anti-inflammatory potential of *Moringa oleifera*

Alhakmani *et al*. (2013) [1] demonstrated the utility of medicinal plants as anti-inflammatory agents as a viable and logical alternative due to their safety and effectiveness. They reported that 36 anti-inflammatory compounds were present in MO. The active ingredients in MO that were contributing to anti-inflammatory property were tannins, phenols, alkaloids, flavonoids, carotenoids, β-sitosterol, vanillin, hydroxymellein, moringine, moringinine, β-sitostenone and 9-octadecenoic acid (Rao *et al*., 1999) [25].

Ndiaye *et al*. (2002) [19] reported the anti-inflammatory activity of aqueous extracts of MO (750 mg/kg) by inhibiting carrageenan-induced edema in rats in a similar fashion as the potent anti-inflammatory drug, indomethacin. Anti-inflammatory activity of leaf extract was reported in a carrageenan-induced paw edema model (Rakesh and Singh, 2011; Singh *et al*. 2012 and Bhattacharya *et al.* 2014) [23, 27, 4]. Kinase (2014) [11] demonstrated the role of MO in governing the anti-inflammatory activity which was attributed to the regulation of neutrophils and c-Jun N-terminal kinase pathway. Muangnoi *et al.* (2012) [17] reported the anti-inflammatory activity of ethanolic extract of *Moringa oleifera* against the proinflammatory mediators secreted by LPS-induced murine macrophage cells and concluded MO extract exhibited anti-inflammatory activity by the inhibition of mRNA expression of IL-6, TNF-α, iNOS and COX-2 in a dose dependent manner. They also reported that the anti-inflammatory action was mediated by inhibiting phosphorylation of inhibitor kappa B protein and mitogen activated protein kinases (MAPKs). Kooltheat *et al*. (2014) [12] reported that the ethyl acetate extract of *Moringa* leaves inhibited macrophage cytokine production (TNF-α, IL-6 and IL-8) induced by smoking. *Moringa* leaf concentrate and isothiocyanates decreased the gene expression and production of inflammatory markers *viz*., iNOS and IL-1β, IL-6, production of NO and TNF-α in a study on RAW macrophage cell system (Chimedza *et al*., 2017) [7]. Das *et al.* (2013) [8] confirmed that the active component, quercetin present in MO was responsible for the anti-inflammatory effect in mice and reported that quercetin inhibited the release of TNF-α, IL-6 and expressions of nuclear factor kappa B, iNOS, interferon gamma and C-reactive protein. Liao *et al*. (2018) [15] identified β-Sisosterol (A phytosterol from plants) as an anti-inflammatory agent from *Moringa oleifera* which has the ability to supress the production of inflammatory factors such as TNF-α, IL-1β, IL-6, IL-8, NFκB and ROS separately. In addition, it also reduced the expression of NLRP3, a key component of NLRP3 inflammasomes and inhibited the activation of caspase-1which ultimately reduced the inflammation in rats. Kou *et al*. (2018) [13] reported a wide range of medicinal and therapeutic properties in MO by its potent anti-inflammatory activity through inhibition of NF-κB and PI3K/Akt pathways; mitigating oxidative stress by scavenging free radicals.



Source: The anti-inflammatory mechanisms of *M. oleifera* (Kou *et al*., 2018) [13].

Signalling pathways involved in the inhibitory effect of *M. oleifera* on proteins associated with LPS-induced inflammation. Toll-like receptor 4, TLR4; Nicotinamide adenine dinucleotide phosphate, NADPH; Inhibitor of kappa B, IκB; Kelch-like erythroid cell-derived protein with cap'n'collar (CNC) homology (ECH)-associated protein 1, KEAP1. Lipopolysaccharide, LPS; mitogen-activated protein kinases, MAPKs; c-Jun N-terminal kinase, p-JNK; extracellular signal-related kinase, ERK; nuclear factor (erythroid-derived 2)-like 2, Nrf2; nuclear factor-kappa B, NF-κB; inducible NO synthase: iNOS; cyclooxygenase-2, COX-2; tumor necrosis factor alpha, TNF-α; interleukin-1 beta, IL-β; interleukin-6, IL-6; quinone oxidoreductase 1, NQO1; heme oxygenase 1, HO-1 (Kou *et al*., 2018) [18].

Antioxidant potential of *Moringa oleifera*

Sinha *et al*. (2012) [28] noticed the restoration of glutathione (GSH) levels and prevention of lipid peroxidation in liver of irradiated *Swiss albino* mouse which was attributed to the presence of a variety of phytochemicals such as ascorbic acid and phenols (Catechin, epicatechin, ferulic acid, ellagic acid and myricetin) in MO. The protective action was mainly due to the scavenging of radiation-induced free radicals.

Cheng *et al*. (2019) [6] reported that *Moringa* isothiocyanate (MIC-1) is the main active isothiocyanate found in *Moringa oleifera* which activates Nrf2-ARE signalling, increases Nrf2 target genes expression and thus suppresses the inflammation. MIC-1 prevents inflammation and oxidative stress, the two key processes involved in the ethology of many chronic diseases.

Bharali *et al*. (2003) [3] reported the chemopreventive potency or the antitumorigenic activity of MO and further explained that the protective action was due to the synergistic action of the constituents and the induction of Phase-II enzymes and the antioxidant enzymes. Yang *et al*. (2018) revealed that MO was rich in many anti-oxidants like phenolic compounds, ascorbic acid oxidase, vitamin A, C, E, polyphenol oxidase and catalase.

Fayazuddin *et al*. (2013) [9] confirmed that the phytochemicals in *Moringa* include unique glycosidic glucosinolates, Isothiocyanates (ITCs), carbomates, nitriles, and thiocarbomates. *Moringa* ITCs have strong antioxidant and anti-inflammatory effects by the activation of Nrf-2 and inhibition of NFκB.

Conclusion

Looking at preceding text with reference to the animal and *in vitro* studies and being known as a Miracle tree for its medicinal value in the traditional folk medicine and with special reference to the leaves and each and every part of the plant *Moringa oleifera* contain numerous beneficial phytoconstituents which have wide and varied pharmacological activities which can act as promising agents in relieving chronic metabolic syndromes *viz*., Diabetes mellitus, and can also act as an anti-inflammatory and antioxidant agent by activating various pathways in the body such as showing positive correlation with NRF2 activation pathway and simultaneously inactivating the NFκB pathway.

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