The Role of Moringa Oleifera

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The Role of *Moringa Oleifera* Leaves Against Oxidative Stress and Chronic Inflammation: A Review

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ABSTRACT

M. oleifera leaves are rich in nutritions, micromineral, macromineral and bioactive compounds such as polyphenols, flavonoids, tannins, alkaloids, and steroids. The contained compounds indicate their role in preventing diseases. A variety of studies have shown the effect of *M. oleifera* leaves as antioxidant and anti-inflammatory agent. *In vivo* studies in laboratory animals also have revealed its role in inhibition of inflammation and oxidation process induced by any exposures, resulting in prevention of oxidative stress and inflammation responses.

Keywords: *Antioxidant, Inflammation, Oxidative stress, Moringa oleifera*

INTRODUCTION

Moringa oleifera is a plant commonly found in tropical areas. Almost its parts could be used. This plant may grow and is distributed among many countries, such as India, Pakistan, Uzbekistan, Sri Lanka, China, Malaysia, Arab, Indonesia and other Asia and Africa countries[(1)]. *M. oleifera* leaves contain beneficial chemical compounds, nutritions, and minerals for body[(2)]. Antioxidant compounds of natural substances could give support in maintaining health or preventing degenerati diseases[(3)]. Compounds in the leaves extract are tannins, steroids and triterpenoids, flavonoids, saponins, anthraquinones, alkaloids[(4)].

Uganda communities consume *M. oleifera* leaves to treat diseases such s hypertension, asthma, fever, allergy and diabetes[(4)]. Both *in vitro* and *in vivo* studies have shown that *M. oleifera* possesses antioxidant[(5)], antiinflammatory and immunomodulatory[(6),(7)], hypolipidemic[(8)], antibacterial, wound healing(7) and anticancer properties[(9)].

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Many factors may contribute to occurring oxidative stress in human such as food, environmental pollution and behavior. Development of disease also involves inflammation response which could influence oxidative ss. This article aims to provide description of the potential of *M. oleifera* as antioxidant and anti-inflammatory agent.

METHO The review focuses on *M. oleifera,* antioxidant and anti-inflammatory properties. All *in vitro* and *in vivo* study publications in animals met the inclusion criteria. We limit the resources included in this review to studies published during 2008-2017.

FINDINGS AND DISCUSSION

M. oleifera as antioxidant agent

Low levels of reactive oxygen species (ROS) can result in cell proliferation and activation of antioxidant defenses, but higher ROS levels trigger DNA damage, p53 activation, cell cycle blockade, and cell death via apoptosis and/or necrosis[(10)]. Varying protection mechanisms are involved in scavenging ROS and protecting cells from ROS effects (cellular antioxidant system)[(11)]. *M. oleifera* leaves extract could protect against acetaminophen-induced hepatotoxicity in Balb/c mice by elevating levels of antioxidant enzymes in liver[(12)]. Methanolic extract acted as antioxidant due to its DPPH, NO dan H_2O_2 scavenging activity, as well as

Fe^{2+} chelating activity[13].

The imbalance between ROS and natural defense by antioxidant leads to oxidative stress. Human body has defense systems including primary antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxide) and secondary antioxidants (glutathione reductase and glucose-6-phosphate dehydrogenase)[14]. The presence of tannins, flavonoids, steroids, terpenoids, alkaloids, and cardiac glycosides in methanolic extract of *M. oleifera* leaves[13]. Previous studies have found phenolic compounds, flavonoids and alkaloid in small quantities[15],[16]. Ascorbic acids, sterols, isoquercetin glucoside, carotenes and kaempferitrin were also present[17]. In *M. oleifera* leaves extract, *total phenolic*, flavonoid and flavonol levels were found to be 120 mg/g of GAE, 40.5 mg/g of QE and 12.12 mg/g of QE, respectively. There are quercetin (89.8 mg/100 g fw), kaempferol (36.3 mg/100 gfw), isorhamnetin (2.9 mg/100 g fw) giving a total flavonoid level of 129 mg/100 gfw in *M. oleifera* leaves[18].

M. oleifera leaves with different cultivars had varying quantities of flavonoid molecules[19]. Characterization (µg/g dry matter) of polyphenolic compounds contained in 80% methanolic extract of *M. oleifera* leaves collected from San Pedro: gallic acid (49.074.53), chlorogenic acid (286.13), luteolin (44.562.03), rutin (603.3513.48), quercetin (46.180.6), kaempferol (46.432.14), apigenin (24.412.16). In Lombardia contained polyphenolic compounds (µg/dry matter): gallic acid (43.28, chlorogenic acid (479.53, luteolin (94.277.6), rutin (845.2518.83), quercetin (49.896.98), kaempferol (67.367.86) dan apigenin (8.740.95)[2].

Total flavonoid level (CE g/100 g DW) *M. oleifera* leaves extracted with absolute ethanol using shaker and reflux extracting techniques were 5.33 and 4.19, respectively. Total flavonoid level of *M. oleifera* leaves extracted with 80% ethanol using shaker and reflux extracting techniques were 6.21 and 5.31, respectively. Extraction with 80% ethanol and 80% methanol showed higher antioxidant activity than absolute ethanol and absolute methanol[20]. The results of subcritical ethanol extraction using 70% ethanol at 126.6 °C for 2.05 hours yielded the highest result of flavonoids. FRAP and DPPH assay showed that the extract had strong antioxidant and free radical scavenging activities[21]. Stage of maturity of leaves may affect the contained compounds. A study in India found total phenolic levels of 45.81 mg/g and total flavonoid levels of 27 mg/g for mature leaves extract. Total phenolic levels of 36.02 mg/g and total flavonoid levels of 15 mg/g were found in tender leaves extract[22].

M. oleifera leaves were also found to reduce levels of malondyaldehide (MDA) induced by gamma irradiation[23]. Flavonoid compounds contained in the leaves were quercetin and kaempferol[18]. Quercetin had pneumoprotective effect, increased antioxidant status and reduced inflammatory cytokines production[24]. Antioxidant action can include suppression of ROS either by inhibition of enzymes or chelating trace elements involved in free radical generation, scavenging ROS, and upregulation or protection of antioxidant defenses[25]. Administration of extract of *M. oleifera* leaves had a protective effect against α-irradiation-induced oxidative damage in rats[26]. Dose 100 mg/kg BW to Wistar rats for 10 days before treated with cadmium could improve liver function and prevent cadmium-induced liver damage[27]. *In vitro,* ethanol and aqueous as solvents at concentrations of 10, 50, 100, 250, 500, 1000 µg/mL, and *in vivo* experiment in mice at doses of 0.01, 0.1, 1, 10, 100 mg/kg showed antioxidant potential. Administration of extracts up to a dose of 100 mg/kg BW could still be tolerated due to showing no toxicity[28]. Antioxidant activity from both *in vivo* as well as *in vitro* studies suggested that the regular intake of its leaves through diet could protect diabetic patients against oxidative damage. The extracts could scavenge free radicals and exert a protective effect against oxidants, cause of cellular damage. *In vitro* study showed that the leaves extract could also protect against oxidative injury induced by diabetes and enhance the activities of hepatic enzymes implicated in combating ROS[29]. Administration of ethanol extract (95%) at dose of 400 mg/kg BW in Wistar rats exposed to cement dust showed its antioxidant activity [30].

M. oleifera as anti-inflammatory agent

M. oleifera could reduce the expression of proinflammatory cytokines in BALB/c mice model of atopic dermatitis[31]. Both polar and non-polar extracts could inhibit inflammatory responses in experimental models[32]. *M. oleifera* contains polyphenols, phenolic acids, flavonoids, glucocinolates, tannins, saponins, oxalates and phytates[6]. At the early stage (10th week) has the highest carbohydrate level (55.14%), and mid stage (15th week) recorded the highest moisture (6.3%), the late stage (20th week) has highest protein level

(28.08%). In both aqueous and methanolic extracts of each of the different stage of leaves maturation were the same except for tannin which was present in aqueous extract but was not detected in methanolic extracts. The presence of saponins and flavonoids explained its potential in treating diseases[33].

Flavonoids are the most abundant polyphenol component and most commonly found in vegetables, fruits, leaves, roots, stems, etc.[14]. Flavonoids include group of flavonols, flavones, flavonones, flavonols (catechins), isoflavones, anthocyanins[34]. Some studies have shown that its effects are related to anti-inflammatory activity[35],[36]. Flavonoids were efficient inhibitor of TNF-α release. Quercetin also significantly inhibited IκB-α phosphorylation. Similarly to apigenin, kaempferol, rhamnetin, quercetin and luteolin. Luteolin and quercetin may be the most flavonoid candidates to provide anti-inflammatory relief *in vivo* because of their inhibitory effects on TNF-α and iNOS expression[37].

M. oleifera could protect against hepatotoxicity by suppressing inflammatory cytokines, and exhibited a fairly preserved liver tissue by reducing inflammatory cytokines (IL-6, TNF-α) in Balb mice treated with high dose of acetaminophen[12]. Ethanol extract of *M. oleifera* leaves could protect against alcohol-induced liver damage in Wistar rats[38]. The methanolic extract showed anti-inflammatory activity in albino rats with formalin-induced paw edema, with maximum inhibition at 1st hour[39]. They also had antiinfammatory activity in rats with formalin-induced edema[40]. *M. oleifera* had immunoprotective and anti-inflammatory properties on respiratory tract through a mechanism involving neutrophil regulation[41]. The main effect of flavonoid in pulmonary diseases could be related to its antioxidant and anti-inflammatory effects[35]. A study of administration of oral quercetin flavonoid over a period of twenty days showed an important protective role of quercetin in preventing Bleomycin-induced lung fibrosis in Wistar rats. Quercetin reduced plasma TNF-α level and neutrophils count, increased SOD level and decreased lipid peroxidation, decreased collagen deposition, hence, quercetin appeared to have a pneumoprotective effect through enhancement of antioxidant status, decrease in the level of inflammatory cytokines[24]. Ethyl acetate fraction caused decreased production of TNF, IL-6, IL-8 and mRNA in human macrophage induced by cigarette. This fraction could depress expression of *RelA*, a gene important in NF-κB signaling inflammatory reaction. It highlights the ability of *M. oleifera* to inhibit IL-8 which promote infiltration of neutrophils into the lungs and TNF and IL-6 which mediate tissue disease and damage[42].

The important mechanism for anti-inflammatory is inhibition of prostanoid biosynthesis, histamine release, phosphodiesterase, protein kinases and transcriptase activation. The most active flavonoid inhibitors of the TNF-α were 3,5,6,7,8,38,48-heptamethoxy flavone (HMF), 5-desmethylnobiletin, sinensetin, nobiletin and 5-hydroxy-3,6,7,8,38,48-hexamethoxyflavone. Inhibition of TNF-α occurred at the level of transcription. A number of hydroxylated flavones such as apigenin, kaempferol, rhamnetin, quercetin, and tamaraxetin also moderately inhibited TNF-α[35]. Clinicopathological examination of rats' organ treated with oral *M. oleifera* at doses of 400, 800, and 1600 mg/kg showed no significant lesions, hence, concluded that the plant is relatively safe both for nutritional and medicinal uses[43]. A study in Wistar mice model showed that *M. oleifera* is relatively safe when administered orally[44]. However, study in human is expected to use standardized extract[45].

CONCLUSION

M. oleifera leaves may be considered as beneficial food materials to prevent many diseases, particularly those involving oxidative stress and inflammation.

Conflict of Interest: No

Funding Source: Authors.

Ethical Clearance: No (because not involve human).

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