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A Review on Cultivation, Nutritional, Phytochemical and Ethnopharmacological Characteristics of Moringa Oleifera

Tabinda Fatima*
Department of Pharmaceutical Chemistry, College of Pharmacy, University of Hafr Al Batin, Hafr Al Batin, Saudi Arabia
*Corresponding Author: Dr.Tabinda Fatima, Department of Pharmaceutical Chemistry, College of Pharmacy, University of Hafr Al Batin, Hafr Al Batin, Saudi Arabia

Abstract:
Moringa oleifera Lam. (referred as Moringa) gained a lot of interest in last decade from a seasonal vegetable to ethnopharmacological plant which was traditionally used for nutritional requirement. Scientifically Moringa oleifera belongs to family Moringaceae. Flowers, Leaves, pods and Seeds of Moringa oleifera plant has been used as functional food. Articles were searched by using a key word of moringa oleifera on google scholar and all articles were cited which are published in last 10 years and recently in 2024. Water, temperature, humidity and fertilizers play a significant role in the cultivation of the plant. Phytoconstituents are reported into the categories including proteins and amino acids, carotenoids, alkaloids, phenolic acid, glucosinolate, flavonoids, sterols, terpenes, saponins and tannins, fatty acids, glycosides and polysaccharides. Moringa Oleifera plant for phytoconstituents was widely searched between 2010 and 2023 leading to the exploration of more than 90 phytoconstituents. Pharmacological properties range from antimicrobial to cytoxic activities which increase the significance of this nutritional plant to medicinal plant. Toxicity validation data show that plant has safe at the dose of 2000 mg/kg. An ample amount of experimental based data is collected, it is right time to move forward for clinical trial studies by formulation of most active parts of the plant. Separation of active phytoconstituents for specific disease and dosage formulation of particular phytoconstituents should be target for pharmaceutical industry. Secondly, nutritional homeopathic formulation can be used chronically to treat various diseases related to pain, gastrointestinal tract and metabolic disorders like diabetes which will lessen the health burden on population.

Keywords: Moringa oleifera Lam; Moringaceae, Phytochemical; Cytotoxic; Pharmacological activities.

Introduction

Moringa oleifera Lam. (referred as Moringa) gained a lot of interest in last decade from a seasonal vegetable to ethnopharmacological plant which was traditionally used for nutritional requirement. Taxonomically Moringa oleifera specie belongs to family Moringaceae. Flowers, leaves, Seeds and pods of Moringa oleifera plant has been used in cooking along with some non-vegetarian dishes to fulfil the needs of nutrition and taste along with health. Genus of Moringa contains 13 species [1] but 2 species *Moringa oleifera* and *Moringa stenopetala* [2] are widely used. Moringa has proven its effectiveness by proving 15 time more potent in potassium content than banana, protein content was 9 time greater than yogurt, antioxidant content due to Vitamin C was 7 time greater than orange and Vitamin A content was 10-fold superior than carrot [3]. Moringa is normally known as drumstick tree'' or horseradish tree [4] which is used by many countries of Asia like Pakistan, India, Bangladesh, Sri lanka [5], subtropical part of the world [6], Kenya, Baringo and coast region [7]. All parts of this this tree including leaves, flowers, fruits, bark and roots (Figure 1) are utilized for nutritional and medicinal purposes.

Seeds of the *Moringa oleifera* are useful for community in multiple ways and manners. Oil is extracted from seeds (38 – 40 %) which are used in curry powder and cleaning of wastewater, Ben oil which is used for art and

lubricant in the machines of watches and other deliciated machines[8]. *Moringa oleifera* is used for nutritional purpose by using leaves and fruits by drinking as tea and eat as salad [9]. Medicinal uses of the *Moringa oleifera is one of the unnoticed benefits in past decades.* A survey in 6 departments of Guatemala revealed that Moringa oleifera is known by 18 different names and is used for food, animal fodder, live fence, soap, ornament, insect repellent, mellifluence, fuelwood, construction, shade and, especially, medicine for skin, digestive, respiratory and joint diseases [10].

Figure 1: Different parts of the Moringa oleifera tree a) Moringa oleifera tree; b) branches; c) leaves; d) flowers and e) pods. (the picture was taken from Muzaffar Garh district of Punjab, Pakistan).

2. Botanical Description, Growth, and Production

M. oleifera is a tree with variable short to medium height which grows as tall as 10 m , with an open branches while stems of the tree have a rough texture. Leaves are green to pale green with variable shape elliptical to obovate. The flowers are fragrant, white or creamy-white, (2.5 cm in diameter) while some varieties are tinged pink, borne in sprays, with five unequal petals and have yellow stamens. The pods are triangular (30-120 cm long, 1.8 cm wide), containing seeds embedded in the pith. The pod is tapering at both ends, nine ribbed [9] while seeds are darkish brown in color with papery wings [11].

The plant starts bearing pods(fruits) in first year mostly after 6-8 months of planting, but second year is the best time for continuous pod bearing stage. This tree lives in many years in variable seasons of the year while the Moringa Oleifera survives in region of subtropical and tropical climates, while flowering and fruiting grows continuously and freely on a dry sandy soil.. *M. oleifera* can be easily cultivated by sowing the cutting of the plant. Stem cuttings are usually preferred for cultivation due to its ability to root easily. When Moringa Oleifera is grown for its roots, oftenly seeds planted in rows like farmer do for vegetables [11, 12].

3. Factors Influencing the Growth and Quality of *M. oleifera*

M. oleifera is normally cultivated as home plant instead of having a specified crop field with barriers. Many people cultivated this plant to meet their need for nutrition irrespective of thinking about medicinal use. *M. oleifera* was cultivated in all ethnic groups of African without knowledge of plant biology and factors affecting their cultivation [13]. Among all factors of the cultivation, temperature was considered as one of the major factors which impact on the tree performance, production, its physiology and geographic distribution [14]. Therefore, tropical temperature range 30-35^0 C was considered as an ideal temperature for its cultivation whereas low temperature <15 ^{0}C reduces the blooming of fruit set [15].

Studies have reported that *M. oleifera* tends to grow in poor soil with little or no fertilizer [16]. Reducing or withholding fertilizers tends to slow the overall growth of Moringa [17]. Thus, it is advisable to apply fertilizers for improving its growth and yield in areas with low rainfall and extreme temperatures [18]. It is important to reduce the water supply to increase the flower growth initiation but sufficient irrigation to the plant is necessary to initiate pollination, its yield and fruit set [19]. Moisture content and aging of the seeds are among the major factors [20, 21]. Farmers are advised to store their seeds at temperatures below 20 °C in paper bags for up to12 months, given that the seeds' moisture content remains below 8% [21]. Factors influencing the cultivation of the *M. oleifera* plant have been reported [22].

4. Phytochemical Investigation of *M. oleifera*

All parts of the Moringa oleifera plant (leaves, seeds, stem, barks and flowers) are rich in phytoconstituents which are used for various therapeutic activities. Literature of *M. oleifera* plant for phytoconstituents has been searched extensively between 2010 and 2023 which explored more than 90 phytoconstituents. Phytoconstituents are reported into the categories including proteins and amino acids [5], carotenoids [23], alkaloids [24] phenolic acid [25], glucosinolate [26], flavonoids [27], sterols [27] terpenes [28], saponins and tannins [29], fatty acids [30], glycosides [31] and polysaccharides [32]. Different classes of phytoconstituents are reported to be present in leaves of the plant as shown in Table.1. Detail of phytoconstituents is well reported in recently published data [33].

Leaves are reported rich in flavonoid class which contains Rutin [34], Kaempferol [35], quercetin[36], Isorhamnetin [37] and Myricetin [38, 39]. Among phenolic acid, O-coumaric acid [38, 39], Ellagic acid [39, 40], Ferulic acid [39, 41], Caffeic acid [39, 42], Sinapic acid [43], Gallic acid [39, 44] and Syringic acid [39, 45]. Seeds of *M. oleifera* contains Myricetin and procyaniadin as flavonoid [39, 46], Glucomoringin as Glucosinolate [37], beta sitosterol as phytosterol [47], while among fatty acid class arachidonic acid [48] oleic acid [49], myristic acid [50] and palmitic acid [51] are in abundance. The leaves as well as seeds of *M. oleifera* are rich in several essential, semi-essential and non-essential amino acids that includes lysine, histidine, valine, leucine, isoleucine, threonine, methionine, phenylalanine, proline, glycine, arginine, cysteine, tyrosine, glutamic acid, alanine, aspartic acid, serine.

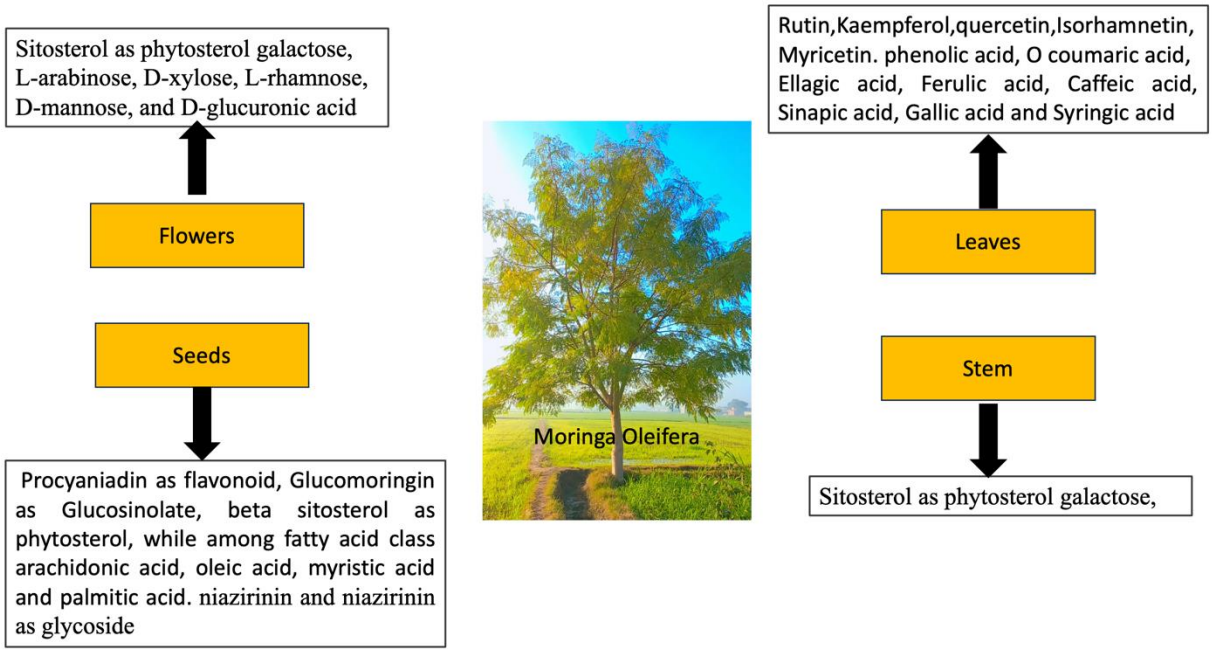

Figure 2: Phytoconstituents present in different parts of Moringa Oleifera plant.

5. Mineral Contents of Dried *Moringa oleifera* Leaves

The leaves of *M. oleifera* are also the source of macrominerals and microminerals [52]. The macrominerals present in higher level includes Potassium (1752 mg/100 g DW) Calcium (1475 mg/100 g DW), sulphur (983 mg/100 g DW) and phosphorous (352 mg/100 g DW) while sodium and magnesium are comparatively less abundant [53]. Several microminerals present in the leaves include iron, zinc, copper, manganese, boron, among this iron (25 mg/100 g DW) is the most abundant one. The appreciable amounts of macro and microminerals in addition to the various useful organic compounds recommends *M. oleifera* to be used as nutraceutical.

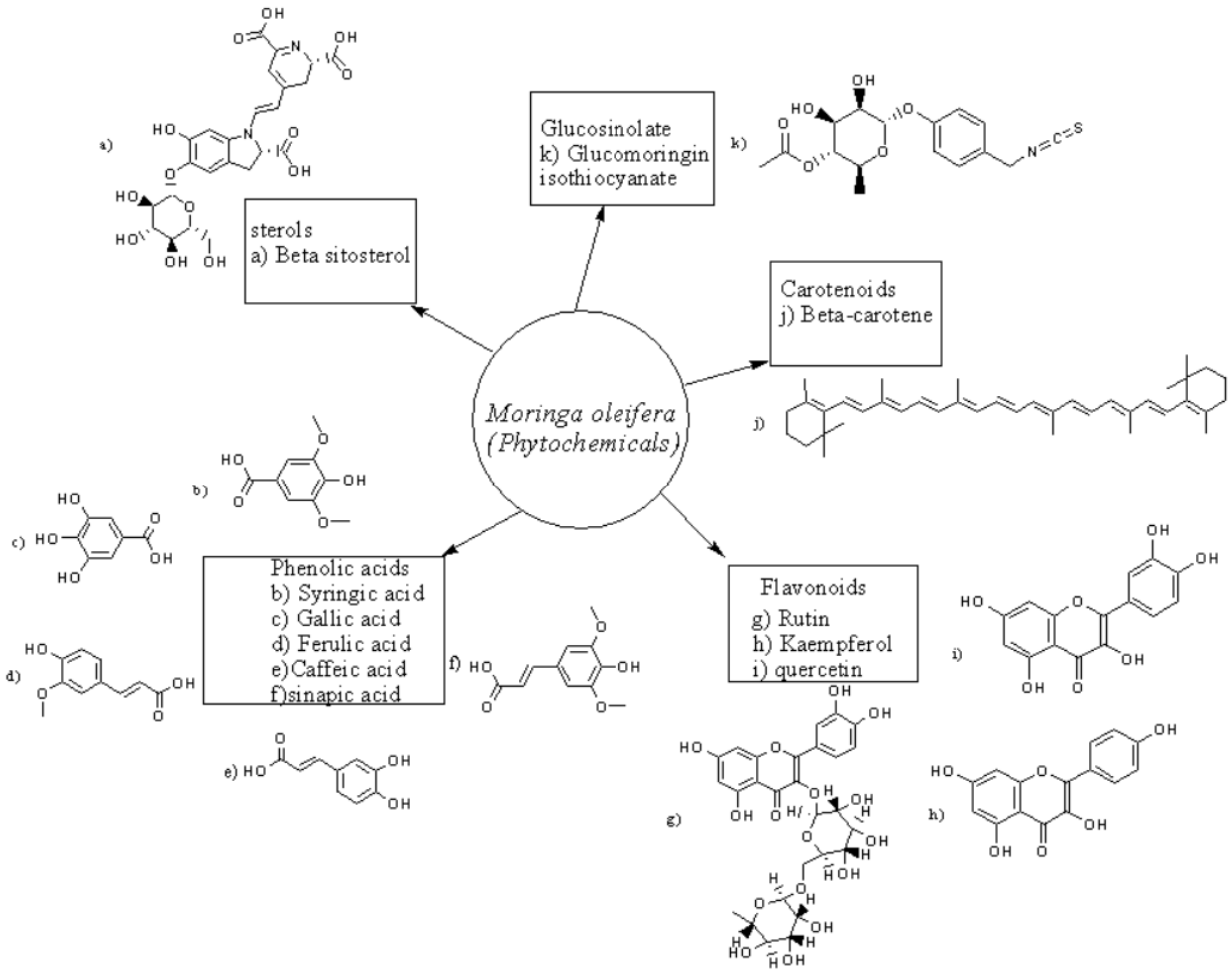

Figure 3: Chemical structures of some representative compounds from different classes of phytochemicals (secondary metabolites) present in Moringa Oleifera plant.

Table 1: Phytoconstituents classes in different fractions of Moringa leaves

Sr. no.	Class of Phytoconstituents	Methanolic Leave	Ethanolic leaves	Aqueous leaves
1	**Flavonoids**	+	+	+
2	**Alkaloids**	+	+	+
3	**Saponins**	+	+	+
4	**Tannins**	+	+	+
5	**Terpenoids**	+	+	+
6	**Glycosides**	+	+	+
7	**Steroids**	+	+	+
8	**Starch**	-	-	-
9	**Coumarins**	+	+	-
10	**Proteins**	-	-	-

Flowers of the *M. oleifera* contains D-mannose as carbohydrate[54] while stem parts contain beta sitosterol as phytosterol [47]**.** Exudate of the gum contains galactose, L-arabinose, D-xylose, L-rhamnose, D-mannose, and -glucuronic acid [32]. Ethanolic extract of *M. oleifera* was reported to contains two glycosides namely niazirinin and niazirinin [31]. Phytoconstituents present in various parts of *M. oleifera* are summarized in Figure 2.

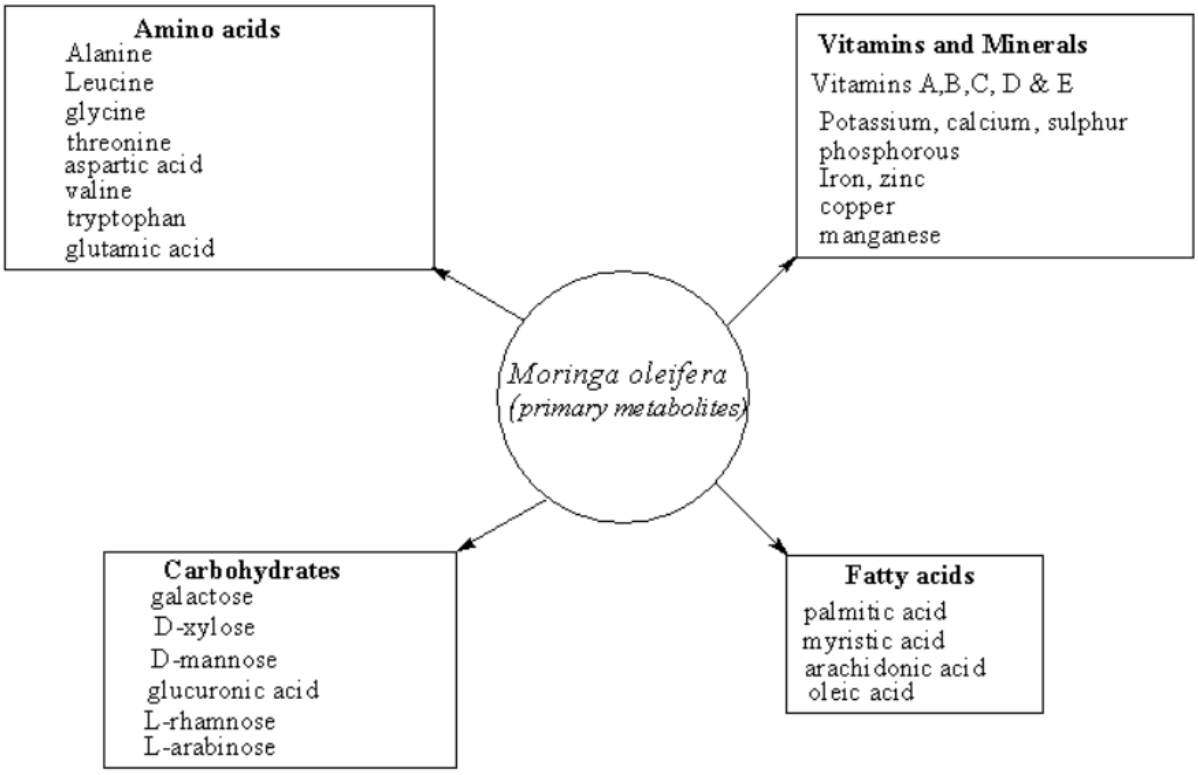

Figure 4: Important nutrients present in Moringa Oleifera plant.

6. Pharmacological Activities of *Moringa Oleifera*

6.1 Antimicrobial and antifungal activity

Ethanolic extract of the *M. oleifera* seeds stem and leaves are reported to have antimicrobial and antifungal activities [55], while methanolic extracts were found effective against gram negative and gram-positive bacteria of urinary tract infection [54]. One of the phytoconstiteuent 4-(alpha-L-rhamanosyloxy) benzyl isothiocyanates known as glucomoringin isothiocyanate (GMG-ITC), present in seeds of the plant is reported to be involved in the antimicrobial activity [56], while the juice of moringa leaves is reported to have a potential against human pathogenic bacteria [57]. Leaves, fruits and seeds of the Moringa plant have been reported to possess anntimicrobial activities against different bacteria and fungi [58-61].

6.2 Anti-Inflammatory activity

A significant anti-inflammatory activity was reported by the 80% hydroethanolic flower extract of *M.oleifera* which was considered due to the phenolic compounds (quercetin and kaemferol), the study suggested the inhibition of inflammation by the hydroethanolic extract of flower through NF-kB signaling pathway [62]. Glucomoringin isothiocyanate (GMG-ITC) has also been reported to have anti-inflammatory property [63] while best results were obtained at 500–1000 μg/mL [64]**.** The polyphenols and glucosinolates present in *M. oleifera* have been reported to inhibit inflammation. Other phytoconstituents aurnatiamide acetate and 1,3-dibenzylurea which is reported to be present in roots result in TNF-alpha production [65].

6.3 Oxidative stress

Methotrexate induced oxidative stress effect was reduced by 12 days of pretreatment with *M. oleifera* [66]. At the same time, methanolic extract of *M. oleifera* stem showed antioxidant effects by epidermal oxidative stress injury [67]. The antioxidant activity was observed when *M. oleifera* plant extract was tested against diclofenac induced liver toxicity [68].

6.4 Antioxidant activity

Phytoconstituent like glycosylate [69], thiocarbamate [70] flavonoids [71] and isothiocyanates [37] present in the plant were tested for antioxidant activities in many studies. Some of the previous data reported kaempferol which is present in the leaves of the plant has antioxidant potential [57], while the aqueous extract showed free

radical scavenger activities for reactive oxygen species [72]. Some of the study reported that antioxidant potential was synergistic with piperine and curcumin in Wistar Kyoto rats where oxidative stress was induced by beryllium [73], while in the isolated eye goat lenses it has antioxidant potential by glutathione levels [74]. In vitro studies data showed that phytoconstituents like astragalin, isoquercetin, and crypto-chlorogenic acid lowers the reactive oxygen species (ROS) in HEK-293 cells [75]. *M. oleifera* was found to reduce the malanodialdehyde levels and increase of GSH at the dose of 100 mg/kg without showing any toxic effects [76].

6.5 Anti-Cancer activity

M. oleifera showed a range of activities from nutritional values to pharmacological agent like anticancer which is deadly disease. All parts of the plant were tested, and it was observed that phytoconstituents like isothiocyanate and thiocarbamate are inhibitors of tumors cells [77]. Niazimicin is known to be chemopreventive in chemical carcinogenesis [55], while dichloromethane fraction was reported to be cytotoxic against breast cancer cell lines [78]. Different extracts of leaves and fruits of Moringa showed growth inhibition of cancer cells in the mouse model of melanoma [65]. A recently published data which based on computational modelling proposed that rutin which is present as phytoconstituent in *M. oleifera* has the highest affinity for binding with Breast Cancer Gene-1[79].

6.6 Positive and negative impact on fertility

Moringa has been known to have dual action on the fertility and anti-fertility abilities of female which is dose dependent. A dose range of 200 and 400 mg/kg dose is expected to be an abortifacient which is a negative impact on fertility [55]. Hot and cold extracts of the Moringa leaves causes the fetal maldevelopment due to rigorous uterine contraction [80]. It would be better to avoid use of *M. oleifera* plant in any situation of the pregnancy as it may affects both fetus and uterus.

6.7 Hepatoprotective activity

Flavonoids like quercetin, kaempferol, isoquercetin, rhamnetin which are present in Moringa oleifera plant while quercetin present in flower parts of the plant is considered to play a protective role in the liver [55]. Acetaminophen induced liver toxicity in animals was restored by the hydroethaolic extracts of Moringa flowers and leaves thereby lowering AST, ALT and ALP which was equivalent to standard hepatoprotective drug silymarin [81]. Seeds of Moringa were used to reduce carbon tetrachloride induced liver fibrosis, AST and globulin levels [82]. Treatment with the Moringa extract for 21 days as diet showed hepatoprotective response which is considered due to the presence of flavonoids kaempferol, quercetin and ascorbic acid [65].

6.8 Cardiovascular activity

Aqueous and alcoholic extract of Moringa showed cardioprotective effect against isoproterenol induced myocardial infarction [83]. Chronic treatment with M. oleifera lyophilized hydroalcoholic extract has significantly improved hemodynamics and also improved the levels of antioxidant enzymes like catalases, glutathione, SOD and creatinine kinases [83]. Furthermore, presence of N-α-rhamnopyranosyl vincosamide in Moringa plant reduced the inflammation and cardiac necrosis [84]. The leaves extracts has shown cholesterol lowering effects in hypertensive rats which is considered is due to the phytoconstituents niazimicin and niazinin [65].

6.9 Anti-Ulcer and gastroprotective activities

M. oleifera is a nutritional vegetable, its consumption has been reported to heal the ulcer of duodenum and stress ulcer induced by Ibuprofen model of gastric ulcer in animals [65] and this healing contributions were given to Bisphenols and flavonoids. This flavonoid induced relief in gastric ulcer was attributed due to resistance of capillaries and increasing microcirculation which lessen the cell injuries [85, 86].

6.10 Analgesic and antipyretic activities

Moringa Oleifera extracts of all parts of the plant showed analgesic activities in central and peripheral model of analgesia in animals [65]. All fractions of alcoholic extracts of Moringa showed analgesic activities in animals when compared to standard drug Aspirin [87]. In formalin induced paw edema model of analgesia, leaves extract showed better results at dosage of 30-300 mg/kg when it compared to root and seed extracts [87] which was evident when acetate and ether fractions were utilized in hyperpyrexia model [88].

6.11 Neuropharmacological and neuropathic pain activities

Methanolic extract of Moringa Oleifera were found to be nootropic agent [88], while in electric shock induced convulsion model albino mice, leaf extract showed anticonvulsant activity [89]. Similarly aqueous extract also

showed anticonvulsant activities in epileptic seizure model induced by Penicillin [90]. Studies showed that leaves extract of *M. oleifera* helps to reestablish the monoamine levels in the brain and beneficial for the treatment of Alzheimer disease [89, 90]. Ethanolic leaves extract of *M. oleifera* showed anxiolytic activities which were screened in actophotometer and rotarod device model of anxiety in animals [65].

It was believed that drop in oxidative stress can be an underlying and unexplored mechanism for the management of neuropathic pain [91]. A bioactivity guided model study by using diabetese induced neuropathic pain model reported that Moringa oleifera provide better glycemic control with potential neuropathic pain management with good safety margin [92]. Moringa Oleifera has been reported to have neuroprotective effects and has a potential for developing complimentary neurotherapy [93].

6.12 Wound healing effect

Wound healing property was observed at 300 mg/kg dose of ethyl acetate and water extract of Moringa Oleifera when excision and incision was executed [57]. Preclinical trials have shown that seeds, leaves and pulp of Moringa Oleifera plant resulted in augmentation of wound healing and reduction in skin rupture strength in the wound area [94, 95] . Phytoconstituents present in aqueous extract of Moringa Oleifera showed significant impact on diabetic foot ulcers by suppressing the inflammatory markers [96]. Wound healing *in vitro* analysis have shown that maximum migration properties and cell proliferation was observed with aqueous extract when compared to different extracts [97].

6.13 Immunomodulatory activity

Some of the phytocomponent of this plant like glycoside cyanide and isothiocyanate reported to have immunomodulator activity. Recently published review article [98] summarized that some phytoconstituents of the Moringa plant have been used to treat various diseases like diabetes, cancer and hypertension by increasing the host immunity. It has been reported Moringa leaves improve the immune system in a teaching module to increase the knowledge of HIV/AIDS sufferers about the benefits of Moringa oleifera [99].

6.14 Hematological activity

Moringa Oleifera is reported to play a role in the hematological disorders. It has been reported that aqueous leaves extract of the plant in randomized, double-blind study has increased the low hemoglobin levels of the women (8-12 mg/dl) [100]. Similarly, when leaves of the *M. oleifera* plant were taken by healthy volunteers for 14 days resulted in an improve in the platelet count [65].

6.15 Anti-Obesity activity

Study conducted on rats suffering from hypercholesteremia were treated with leaves powder of Moringa Oleifera for 49 days has significantly reduced the body mass index (BMI) [101]. The idea mechanistic approach was the suppression of resistin and leptin mRNA expression and the concomitant expression of adiponectin in rats [65]. One of the reasons for reducing lipid profile could be due to the reduction in body weight. In addition to this, Moringa oleifera modulates genes related with adipogenesis, reduce the levels of hormones like leptin, resistin and vaspin [102].

6.16 Anti-Allergic activity

The ethanolic extract of *M. oleifera* decrease the release of histamine and anti-immunoglobulin G induced anaphylaxis. It may be due to the mast cells stabilizing properties in albumin induced sensitization model [65].

6.17 Anti-Diabetic activity

Moringa Oleifera leaves not only reduced blood glucose levels but also reduce glucose tolerance. Aqueous extract of *M. oleifera* showed antidiabetic activities by reducing the blood glucose level, sugar, protein and hemoglobin [72]. These leaves reduce blood glucose after 3 hours of intake, but this reduction was less than the standard drug glibenclamide [72]. Oral administration of seeds of Moringa oleifera exhibit glucose lowering activity[103]. Similarly leaf extracts of the Moringa Oleifera also possess antidiabetic activity which increase the insulin levels in healthy individuals [104]. The seed extract of the Moringa oleifera plant augmented antioxidant and pancreatic β-cell activity effects in streptozotocin induced diabetic mice [105].

6.18 Diuretic activity

Different extracts of Moringa Oleifera like aqueous and alcoholic reduced the urolithiasis by promoting the excretion of oxalate crystal in male rats and this was observed due to decreased retention of oxalate crystal, blood urea nitrogen, creatinine, phosphates and calcium [106].

6.19 Angiotensin Converting Enzyme (ACE) inhibition activity

Angiotensin converting enzyme play a contribution in the pathogenesis of hypertension by converting angiotensin I to angiotensin II. Some phytoconstituents like niazimin-A, niazimin-B and niazicin-A are reported to be present in *M. oleifera* plant. These compounds have been reported to block the ACE enzyme because of their high affinity with ACE protein when compared to captopril and enalapril as observed in docking study [107]. Phytocompound Beta sitosterol present in *M. oleifera* was reported to have ACE inhibitor activity which was reported to be 72 % when compared to standard drugs captopril and enalapril [108].

6.20 Miscellaneous effects

Leaves of the Moringa oleifera showed a positive effect by increasing gut motility and improving constipation in rats [109]. In this study, laxative activity was attributed to signals from 5-HT and acetyl choline in the gut which increased the gut motility and fluid secretion. *M. oleifera* also reported to alleviate the constipation in mice [110] which is supported by another study on the mice which claim that alleviation of constipation by changing the gut microbiota [111]. *M. oleifera* have been found to play beneficial effects in dental health [112].

6.21 Cytotoxicity effect

Research have shown that flavonoids and alkaloids present in the Moringa Oleifera plant have structure similarities with the vincristine and vinblastine so it is assumed that this plant can be recommended for the herbal treatment of Myeloma patients [77]. In support to this study, researcher shown that ethanolic extract of this plant can lessen the testicular toxicity induced by cyclophosphamide by promoting enlargement of DNA in spermatogonia [113].

7. Toxicity

Toxicity study on this medicinal plant showed that administration of 2000 mg/kg dose of the methanolic extract of *M. oleifera* was found safe so its toxic dose is higher than 2000 mg/kg [38, 114]. Methanolic extracts of Moringa Oleifera showed acute signs of toxicities at the dose of 4000 mg/kg and mortality was observed at 5000 mg/kg which indicates the safety of Moringa oleifera at the dose less than 3000 mg/kg [115]. The result of subacute toxicity test at different doses of 250, 500, and 1500 mg/kg for 60 days showed that lethal dose was observed as 1585 mg/kg without significant changes in sperm quality parameters, biochemical changes, and hematological parameters when compared to the control group [100].

8. Conclusion and Prospects

An ample amount of experimental based data is collected, it is right time to move forward for clinical trial studies by formulation of most active parts of the plant. Separation of active phytoconstituents for specific disease and dosage formulation of particular phytoconstituents should be target for pharmaceutical industry. Secondly, nutritional homeopathic formulation can be used chronically to treat various diseases related to pain, gastrointestinal tract and metabolic disorders like diabetes which will lessen the health burden on population.

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