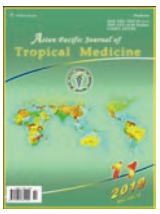

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Phytopharmacological potential of the natural gift *Moringa oleifera* Lam and its therapeutic application: An overview

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ABSTRACT

Traditionally, medicinal plants of family Moringaceae have been well-recognized due to their multipurpose utilization in various fields such as treatment of several diseases for they have a broad range of pharmacological activities, in wastewater treatment as well as food source. Fractionation of this medicinal plants and its bioactivity study discloses the presence of several phytoconstituents and secondary metabolites like terpenes, flavonoids, steroids, phenolic compounds, tannins, carohydrates, flavonoids, vitamins and minerals. The results of bioactivity study results revealed that different extracts such as aqueous, methanolic and ethanolic of *Moringa oleifera* showed notable therapeutic activities. Our present review explore and focus on the phytochemical composition and various pharmacological activities like immunomodulator, antidiabetic, antiulcer, anthelmintic, anti-inflammatory, antipyretic, analgesic, antiepileptic, cardioprotective, lipid lowering, antihypertensive, hepatoprotective, anti-nephrotoxicity and anti-microbial activities to arouse public consciousness about the nutritional and medicinal value of this "miracle tree - *Moringa oleifera*" in favor of humanity.

1. Introduction

For centuries, medicinal plants have been used all over the world to treat many diseases to enhance physical and spiritual wellbeing. Herbal medicines were the only choice available in ancient times, but these are replaced by new synthetic drugs with the development of science. In the last few decades, in global perspective, there has been a shift from synthetic to herbal medicine throughout the developed and developing countries. It can be assumed to say "Return to Nature" with home remedies due to the side effects or long term health hazards of allopathic medicines.

The World Health Organization (WHO) estimated that approximately, 75%-80% of the world's population utilized herbal plant materials as traditional medicines for their primary health care need[1]. Ayurveda and Siddha are the holistic traditional systems of medicine practiced in India and are considered to be safe with fewer side effects and cost effective[2]. Among the various

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medicinal plants, *Moringa (M.) oleifera* which belongs to the family of Moringaceae is one of the plants which have its customary use in most of the disease management. *M. oleifera* is native to the sub-Himalayan tracts of India, Pakistan, Bangladesh and Afghanistan, now it is cultivated all over the world[3,4]. *Moringa* is the taxon name which is originated from muringa or murunggi from Malayalam and Tamil respectively. Thirteen species such as *M. oleifera*, *M. borziana*, *M. rivae, M. peregrine*, *M. concanensis, M. longituba*, *M. hildebrandtii*, *M. arborea*, *M. pygmaea*, *M. ovalifolia*, *M. drouhardii*, *M. stenopetala* and *M. ruspoliana* are reported so far in the genus of Moringa among which *M. oleifera* is most known for its rich nutrient. *Moringa* has been used by ancient kings and queens since 150 B.C. in their diet for healthy skin and mental alertness[5,6]. The plant, *M. oleifera* have high biotechnological potential due to its high content of minerals, vitamins, proteins, lipids, secondary metabolites and other various phytochemicals like sterols, tannins, flavonoids, terpenoids, saponins, alkaloids anthraquinones, carbohydrates and reducing sugar along with anti-cancerous agents. It contains 36 anti-inflammatory compounds, more than 90 recognized nutrients and 46 antioxidants. Scientific report states that *M. oleifera* consists of 539 bio-chemical activities which are much more beneficial to human being[7,8]. Leaves of this plant contain all the essential amino acids which are very much useful to human being. Since 1998, WHO has promoted Moringa as an alternative to imported food supplies to treat malnutrition, and hence so it can be called as "Mother's Best Friend"[7,9-13].

1.1. Botanical description

M. oleifera is a little, agile, quickly developing, deciduous tree with sparse foliage of height 10 m – 12 m (32 ft– 40 ft). Bole is abnormal and frequently forked from the base. Bark is smooth, dull dim in shading and pale yellow. Twigs and shoots are short yet bristly hairy. Crown is wide open typically umbrella shaped and usually a single stem with soft wood and often deep rooted.

Leaves are alternate, large (up to about 90 cm long) and oppositely pinnae dispersed around 5 cm separated up the focal stalk, with leaflets in inverse sets, with a marginally larger terminal leaflet. Leaflets are hunter green above and pale on the under surface. It has variable size and shape, but regularly adjusted elliptic and 2.5 cm long.

Flowers are flourished all throughout the year in free axillary panicles up to 15 cm long. Individual flower stalks are up to 12 mm long and very slender. Each flower has five finely hairy pale green sepals which are 12 mm long and five white uneven petals and little longer than the sepals. There are five stamens with anthers and five without anthers and its style is slender. Flowers are usually very sweet in fragrance.

Fruits are large and distinguishing up to 12 mm broad and 90 cm long, slightly restrained at intervals, gradually tapering to a point with two grooves on each face. It splits along each angle to expose the rows with three papery wings of rounded blackish oily seeds[7,14,15].

1.2. Phytoconstituents

M. oleifera contains rich source of tannins, phenolics, steroids, flavonoids and terpenes. It also contains various nutraceuticals like dietary fiber, carbohydrates, protein, fat, vitamins (riboflavin, thiamine, pantothenic acid, niacin, folate, vitamic C, provitamin A and vitamin K) and minerals (iron, calcium, manganese, magnesium, phosphorus, sodium, potassium and zinc)[9,14]. Apart from these, there are Glycosides-carbamate, isothiocyanate, thiocarbamate, oestrogenic substances, ascorbic acid, β-sitosterol, iron, phosphorus, calcium, copper, vitamin A, B, C, α-tocopherol, riboflavin, nicotinic acid, folic acid, pyridoxine, β-carotene, proteins, essential amino acids – methionine, cystine, tryptophan and lysine novel bioactive nitrile glycosides- niaziridin and niazirin[7-9,16-21]. Phytoconstitutents of the different parts of the *M. oleifera* are given in Table 1, 2 and 3[8,9,12,14,16]. Structures of some phytoconstitutents of *M. oleifera* are shown in Figure 1.

Table 1. Phytoconstituents in different parts of *Moringa oleifera*[8,9,12,14,16].

Parts of the plant	Phytoconstituents
Leaves	4- [4′-O-acetyl- α -L-rhamnosyloxy) benzyl] isothiocyanate, glycoside niazirin, mustard oil glycosides, niaziminin A and B
Stem	β-sitosterone, vanillin, octacosanic acid, 4-hydroxymellein, β-sitosterol and 4-(α-L-rhamnopyranosyloxy)-benzylglucosinolate
Root	4-(α-L-rhamnopyranosyloxy) benzylglucosinolate and benzylglucosinolate
Gum	D-galactose, D-xylose, D-mannose, D-glucuronic acid, L-arabinose, L-rhamnose and leucoanthocyanin
Mature flower	Protein, D-glucose, ascorbic acid, D-mannose and polysaccharide
Pod	Isothiocyanate,Thiocarbanates, o-ethyl-4-[(α -1-rhamnosyloxy)-benzyl] carbamate, o-[2′-hydroxy-3′-(2′′-heptenyloxy)] propylundecanoate, nitriles, β-sitosterol and methyl-p-hydroxybenzoate
Seed oil	Vitamin A, β-carotene, precursor of Vitamin A and also has crude protein, carbohydrate, crude fat, cysteine, 4-(α-L-rhamnopyranosyloxy)-benzylglucosinolate, methionine, benzylglucosinolate, moringyne, mono-palmitic and di-oleic triglyceride, benzyl isothiocynate

Table 2. Phytoconstitutents/Nutrients value of different parts of *Moringa oleifera*[8,9,12,14,16].

Phytoconstitutent/Nutrients	Leaves	Seed	Pods
Magnesium	0.11 mg/kg	45.00 mg/kg	-
Phosphorous	1.36 mg/kg	-	-
Sodium	2.73 mg/kg	-	-
Potassium	21.70 mg/kg	75.00 mg/kg	-
Calcium	26.40 mg/kg	752.00 mg/kg	-
Iron	175.00 mg/kg	5.20 mg/kg	-
Manganese	51.80 mg/kg	-	-
Zinc	13.70 mg/kg	0.05 mg/kg	-
Copper	7.10 mg/kg	-	-
Carbohydrate	12.50 g/kg	8.67 g/kg	3.7 g/kg
Protein	6.70 g/kg	35.97 g/kg	2.5 g/kg
Fat	1.70 g/kg	38.67 g/kg	0.1 g/kg
Fibre	0.90 g/kg	2.87 g/kg	4.8 g/kg
Vitamin B1	0.06 mg/kg	0.05 mg/kg	0.05 mg/kg
Vitamin B2	0.05 mg/kg	0.06 mg/kg	0.07 mg/kg
Vitamin B3	0.80 mg/kg	0.20 mg/kg	0.20 mg/kg
Vitamin C	220.00 mg/kg	4.50 mg/kg	120.00 mg/kg
Vitamin E	448.00 mg/kg	752.00 mg/kg	–

Table 3. Composition of amino acids in *Moringa oleifera*[14].

Amino acids	(g/kg)
Essential amino acids	
Thr	30.8
Val	43.5
Ile	32.5
Leu	67.5
Lys	15.3
Phe	39.7
Tyr	15.9
Met	23.5
Cys	20.1
Trpe	16.3
His	22.6
Non-essential amino acids	
Asx	50.5
Glx	209.5
Ser	43.6
Gly	108.9
Ala	69.1
Arg	145.3
Pro	45.0

2. *Moringa oleifera* and its pharmacological activities

2.1. Immunomodulator

Recently, phytoconstituents from *M. oleifera* is utilized for immunomodulatory treatment Nfambi *et al.*, investigated the immunomodulatory activity of methanolic leaf extract of *M. oleifera* in Wistar albino rats at 250, 500 and 1 000 mg/kg body weight. *M. oleifera* has shown significant immunostimulatory effect on both the cell-mediated and humoral immune systems in the Wistar albino rats. Wistar albino rats were immunosuppressed by cyclophosphamide at 200 mg/kg body weight. Dose of 1 000 mg/kg body weight showed an increment in lymphocyte, White blood cells and neutrophil counts when compared with the positive control, Levamisole hydrochloride BP 40 mg syrup. Increment in mean hemagglutination antibody titre was observed in sheep red blood cells in a dose-dependent manner. The dose dependent increment in the heamatological parameters may be due to the presence of different micro and macronutrients present in the leaf extract[22]. Gupta *et al.*, studied the immunomodulatory effect of ethanolic (50%) leaf extract of *M. oleifera* in different dose levels such as 125, 250 and 500 mg/kg in mice model using cyclophosphamide at 30 mg/kg as immunosuppressant. Hematological parameters like white blood cell, red blood cell, hemoglobin, percent neutrophils and organ weight were estimated. The result revealed that *M. oleifera* leaf extract significantly reduced the immunosuppression, and increased hematological parameters and organ weight in a dose-dependent manner. The reason for immunomodulatory effect may be the restore of immune cells by alleviating the myelosupression and subsequent leucopenia induced by cyclophosphamide[23]. Immunomodulatory effect of *M. oleifera* leaves of different extract *viz.* petroleum ether, chloroform and methanol were assessed in different dose levels like 100, 200, and 400 mg/kg body weight in Wistar albino rats. Parameters such as humoral antibody titre, delayed type hypersensitivity, T cell population tests and cyclophosphamide-induced myelosuppression were assessed and compared with standard, Levamisole 50 mg/kg body weight. Among the three extracts, methanol extract showed very good immunomodulatory activity by restoring the hematological parameters and humoral antibody of cyclophosphamide-induced immunosuppression through stimulation of both cellular and humoral immunity[24]. Deshmukh *et al.*, examined the immunomodulatory effect of aqueous and ethanolic extracts of *M. oleifera* in albino rats. The results observed have shown that aqueous and ethanolic extracts of *M. oleifera* have immunomodulatory effect by increasing the humoral antibody, delayed type hypersensitivity, and phagocytic index[25]. Sharma *et al.*, investigated the ethanolic extract of *M. oleifera* root for its immunomodulatory effect at 100 and 200 mg/kg body weight in Wistar albino rats. The investigational results concluded that ethanolic root extract of *M. oleifera* possess immunomodulatory effect by increasing the haemagglutination antibody titre, carbon clearance rate, phagocytosis and prevented the myelosuppression which may be due to saponins and flavonoids [26]. Furthermore, research results showed that *M. oleifera* leaf extract have immunomodulatory effects[27-30]. The results suggested that phytoconstituents such as flavonoids, polyphenols, saponins, macronutrients and micronutrients which are widely present in the different parts of this plant have the ability to induce immunomodulatory effect by both cellular and humoral immunity.

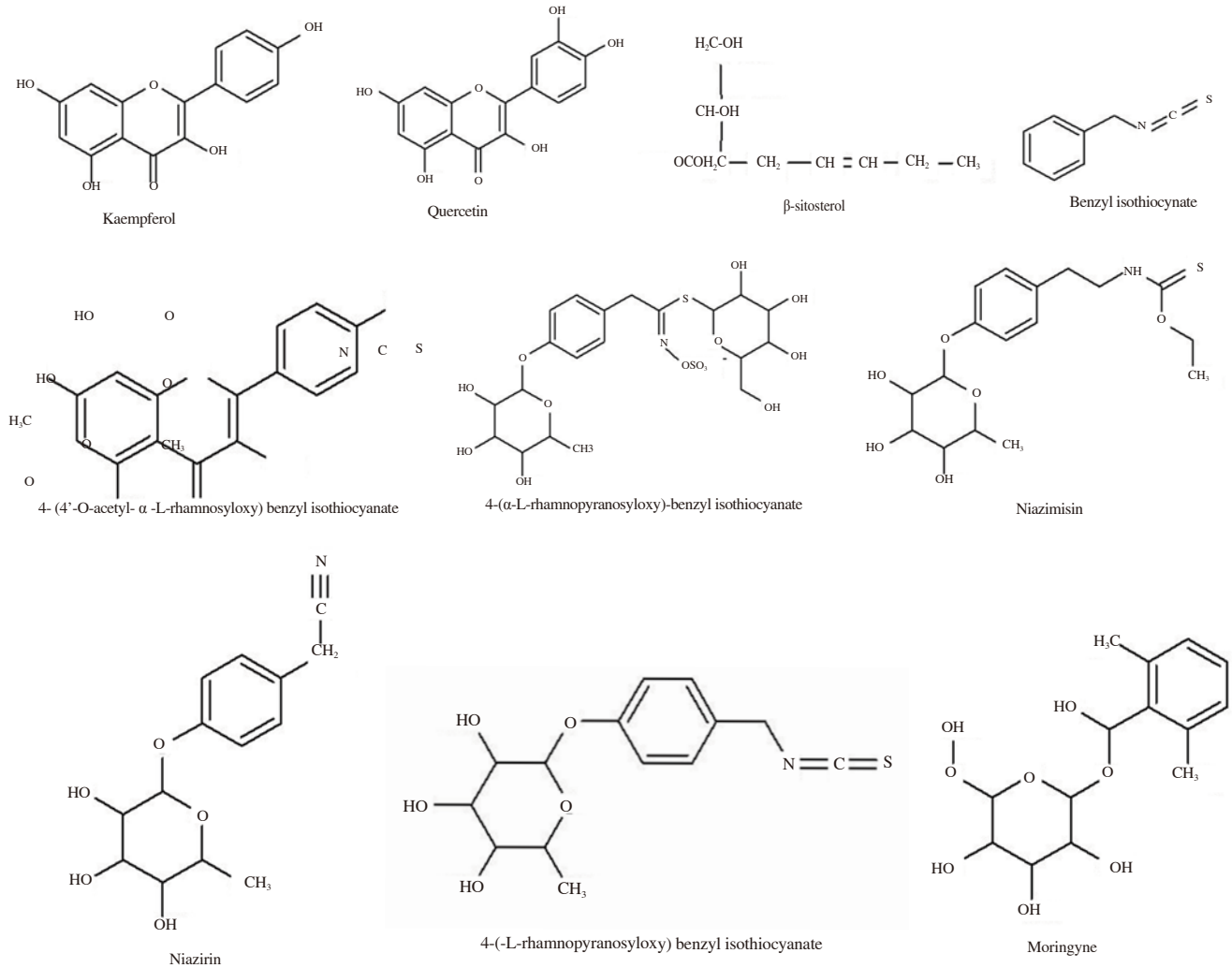

Figure 1. Structures of some phytoconstitutents of *Moringa oleifera.*

2.2. Anti-diabetic

Soliman investigated the anti-diabetic effect of ethanolic extract of *M. oleifera* leaves in streptozotocin-induced diabetic albino rats at a dose of 50 mg/ kg body weight. The study has shown that there was significant (P<0.05) reduction in the blood glucose level in rats treated with *M. oleifera*[31]. Adeeyo *et al.*, demonstrated the antihyperglycemic effect of aqueous extract of *M. oleifera* leaves on Streptozotocin -induced diabetic male rats. Study has shown that the aqueous extract of *M. oleifera* leaves normalized the insulin level to near normal value, decreased the pancreatic malondialdehyde levels and increased the pancreatic superoxide dismutase and glutathione indicating it is useful in the management of diabetic hyperglycemia[32]. Aja *et al.*, investigated the hypoglycemic activity of ethanolic extract of *M. oleifera* leaves by assessing the glucose level in alloxan-induced diabetic rats for 21-days at different doses of 200, 400 and 800 mg/kg body weight. This study has shown that ethanolic extract of *M. oleifera* leaves reduced the glucose level significantly[33]. Une *et al.*, performed a comparative study of metformin and ethanolic extract of *M. oleifera* Lam. pod for its hypoglycemic activity by assessing the oral glucose tolerance, blood glucose, body weight and biochemical parameters like serum glutamic pyruvic transaminase, serum glutamic oxaloacetic transaminase and creatinine at 50, 100 and 200 mg/kg body weight for 21 days. The results indicated the reduction of blood glucose level and improvement in the glucose tolerance after 21 days. Also, the extract significantly reduced the elevated serum glutamic pyruvic transaminase, serum glutamic oxaloacetic transaminase and creatinine, secondary complications and improved the body weight of alloxan treated rats[34]. Another study by Ali *et al.*, on the potential of *M. oleifera* leaf extracts in alloxan-induced diabetes rats demonstrated that phytoconsitutents quercetin, chlorogenic acid and moringinine normalized the elevated serum levels of total cholesterol, triacylglycerol, glycose, malondialdehyde, protein carbonyl content, c-peptide and total antioxidant capacity. The results showed its potent antidiabetic activity against the alloxan-induced diabetes[35]. Ajibola *et al.*,[36] observed the effect of aqueous extract of *M. oleifera* seed on alloxan-induced mild and severe hyperglycemia in rats. The

results showed 42.8% and 48.6% decrease in the blood glucose level of the mild hyperglycemic rats after treatment with intraperitoneal and oral *M. oleifera* seed extracts, respectively, whereas 89.6% and 69.7% decrease in the blood glucose level of the severely affected hyperglycemic rats. The results proved that aqueous extract of *M. oleifera* seed exhibited potent hypoglycemic activity against mild and severe hyperglycemia[36]. Al-Malki and El Rabey investigated the antidiabetic effect of low doses of *M. oleifera* Lam. seeds on streptozotocin-induced diabetes and diabetic nephropathy in male rats. Different biochemical parameters like lipid peroxide, IL-6, antioxidant enzyme, immunoglobulins (IgA, IgG), fasting blood sugar and glycosylated hemoglobin were assessed during the study. The results indicated the treatment with low doses of *M. oleifera* Lam. seeds ameliorated the levels of all biochemical parameters and restored the normal histology of both kidney and pancreas in diabetic rats[37]. In another study, streptozotocin-induced diabetes rats were treated with aqueous extract of *M. oleifera* leaves antihyperglycemic effect in both insulin deficient and insulin resistant rat models were observed[38]. Gupta and his team investigated the antidiabetic effects of methanol extracts of *M. oleifera* pods in streptozotocin-induced diabetic albino rats by measuring the biochemical parameters in the serum at 150 or 300 mg/kg bodyweight for 21 days. Significant reduction in nitric oxide and serum glucose whereas associated increase in protein and serum insulin were noticed for both dose levels[39]. Arise *et al.*, tested antidiabetic effect of ethanolic extract of *M.oleifera* flower on tretozotocin-induced diabetic rats at 100, 200, and 300 mg/kg body weight and noticed the improvement in lipid metabolism and its potential in lowering glucose level[40]. Luangpiom *et al.*, studied the anti-hyperglycemic properties of aqueous extract *M. oleifera* Lam. leaves in normal and mildly diabetic mice by the Oral Glucose Tolerance Test. Results revealed the improvement in mildly diabetic mice for its glucose tolerance impairment[41]. Different parts of *M. oleifera* have been studied extensively for its antidiabetic activity. The scientific study concluded that the leaf extract showed potent antidiabetic effect in Wistar rats and adult rats[42-47]. The results indicated that phytoconstituents such as flavonoids like quercetin, phenols, chlorogenic acid, moringinine, vitamin C and E have good antioxidant property and scavenging effect on the free radicals. Presence of these phytoconstituents in *M. oleifera* produce its antidiabetic effect by lowering the reactive free radicals released from mitochondria and enhancing the cellular antioxidant defenses by protecting β-cells against ROS-mediated damage in hyperglycemic patients[31,37,39,40].

2.3. Anti-ulcer

M. oleifera seed extracts was studied for its antiulcer activity in the dose level of 150 and 200 mg/kg orally in pylorus ligation and compared with standard drug, omeprazole (20 mg/kg). The results have shown a significant ($P< 0.05$) reduction in the ulcer index such as reduction in gastric volume and decrease in free and total acidity which was comparable with the standard [48]. Das *et al.*, investigated the protective effects of *M. oleifera* (200 mg/kg and 400 mg/kg body weight) on pyloric ligation gastric ulcers induced experimentally by ibuprofen in rats, famotidine (3.6 mg/kg) was used as a standard drug. Results revealed that *M. oleifera* extract show significant ($P<0.001$) reduction of the free and total acidity of gastric juice[49]. Further Verma *et al.*, performed the antioxidant activity and anti-ulcer of *M. oleifera* leaves against ethanol and aspirin-induced gastric ulcer in rats which demonstrated that the alcoholic leaf extract of *M. oleifera* Lam. have shown a dose dependent protective effect against cold restraint stress, ethanol, pylorus-ligation and aspirin-induced gastric ulcer in rats[50]. Extracts of root-bark, stem bark and seed showed antiulcer activity against the ethanol-induced gastric ulcer in rats[48,51,52]. Several investigations suggested that the secondary metabolites such as flavonoids (quercetin) and tannins has antiulcer activity, steroids such as β-carotene and β-sitosterol reduces the gastric ulcer development, alkaloids such as moringine and moringinine in the root-bark treats ulcer. The antiulcer activity of *M. oleifera* is based on the stimulation of mucous membrane protective factors and antioxidant defense mechanism probably by metabolizing lipid peroxides and scavenging endogenous H_2O_2[48,50,51,53].

2.4. Anthelmintic

Nilani *et al.*, investigated the anthelmintic activity of *M. oleifera* seed oil in Indian adult earthworms (*Pheretima posthuma*) and equated with the standard drug piperazine citrate (10 mg/mL). The results showed the paralysis of the worms leads to loss of its motility followed by fading away of their body color and death[54]. Similar study was performed by Srinivasa *et al.*, on the chloroform and methanolic extracts of *M. oleifera* leaves for its anthelmintic activity and noticed that the chloroform extract has more potent anthelmintic activity in Indian adult earthworms (*Pheretima posthuma*) than the methanolic extract[55]. Ethanol and aqueous extracts of leaves have been investigated for its anthelmintic activity against embryonated eggs, fresh eggs, L1 and L2 larvae of *Haemonchus contortus*. Five different concentrations (0.625, 1.25, 2.5, 3.75 and 5 mg/mL) of dry extracts with serial dilution of distilled water were exposed for 6 and 24 h for embryonated eggs and larvae respectively using distilled water and 1.5% DMSO as negative control. The results concluded that ethanolic leaf extract of *M. oleifera* was most efficient on eggs by inhibiting (60.3 ± 8.2)% and (92.0 ± 6.2)% eggs embryonation at 3.75 and 5 mg/mL respectively; (98.8 ± 2.5)% and (100.0 ± 0.0)% mortality of L1 and L2 larvae at 5 mg/mL respectively[56]. Many investigations have been conducted for its anthelmintic

activity with different parts of the plant *M. oleifera*, results with scientific support suggested that *M. oleifera* has anthelmintic activity against Indian earthworm *Pheritima postuma*, *Dracunculiasis* (guinea worm), schistosomes and trypanosomes[57,58]. Presence of the phytoconstituents such as oleic acid, saponins, steroids, carbohydrates, flavonoids, tannins and alkaloids in the extract could be responsible for its anthelmintic activity[54,56].

2.5. Anti-inflammatory

Chandrashekar *et al.*, investigated the anti-inflammatory activity of aqueous and ethanolic extracts of the stem bark of *M. oleifera* in carrageenan-induced rat paw edema method and compared with diclofenac sodium 25 mg/kg body weight as standard drug. The results revealed that both ethanolic and aqueous extracts of the stem bark of *M. oleifera* showed significant drop in the edema volume at a dose of 300 mg/kg body weight and the results were equivalent with the standard[59]. Bhattacharya *et al.*,[60] performed a relative study of anti-inflammatory activity between *M. oleifera* leaves extract at different dose levels such as 50, 100, 200, 400 mg/kg body weight and aspirin (200 mg/kg) as standard drug by carrageenan-induced rat paw edema in Wistar albino rats. The study experiment revealed *M. oleifera* ethanolic leaf extract showed significant ($P < 0.01$) reduction of paw edema at 100, 200, 400 mg/kg by inhibiting the release of prostaglandin like substance. It also suggested that phytoconstituents like flavonoids, β-sitosterol, 4-hydroxymellein and vanillin are attributed to its anti-inflammatory activity [60]. Minaiyan *et al.*, investigated the comparative study of anti-inflammatory effect between *M. oleifera* Lam. seeds extract and prednisolone (4 mg/kg) as standard in acetic acid-induced acute colitis in rats. This study revealed *M. oleifera* Lam. seeds extract was effective to treat experimental colitis[61]. Quite a lot of investigation in leaf and seed extract has been carried out proving its anti-inflammatory effects in rats[62-65]. The anti-inflammatory activity of the *M. oleifera* may be attributed to the presence of phytoconstituents like flavonoids, tocopherols, vitamin C, biophenols, 4-Hydroxymellein, β-sitosterol and vanillin. The mechanism for its anti-inflammatory activity may be by decreasing oxidative stress in inflammation condition, inhibition of enzyme cyclooxygenase which leads to inhibition of prostaglandin synthesis mediated through prostaglandin pathway, obstructive production of several cytokines including IL-4, IL-6 and TNF-α by these phytoconstituents[60,62,63].

2.6. Antipyretic

Bhattacharya *et al.*, investigated the antipyretic activity in ethanolic extracts of *M. oleifera* leaves at 50, 100, 200, 400 mg/kg body weight and compared with paracetamol (100 mg/kg) as standard pyrexia model in Wistar albino rats. In rats, pyrexia was induced by subsctaneous injection of Brewer's yeast in normal saline in the dose of 10 mL/kg body weight. Significant antipyretic activity was observed in the dose level of 100, 200 and 400 mg/kg body weight when compared with standard[60]. Ahmed *et al.*, performed a comparative antipyretic activity study between hydro alocholic extract of *M. oleifera* bark at the dose level of 25 mg, 50 mg and 100 mg/kg, paracetamol 50 mg/kg body weight was used as standard drug in rabbits against *E.coli*-induced pyrexia. The extracts of *M. oleifera* bark at the dose level of 100 mg/kg significantly reduced the body temperature[66]. Sutar *et al.*, made an evaluation between ethanolic extract of *M. oleifera* seed at the dose of 100 mg, 200 mg and 300 mg/kg and paracetamol 150 mg/kg body weight as standard against yeast-induced pyrexia in albino rats. Results showed a significant dose dependent reduction of temperature at doses of 100, 200 and 300 mg/kg body weight. The antipyretic effect of the ethanolic extract *M. oleifera* seed was comparable with the standard paracetamol[67]. Hukkeri *et al.*, examined the antipyretic effect of ethanolic and ethyl acetate extracts of *M. oleifera* seed at 300 mg/kg. The study demonstrated that *M. oleifera* seed extract have antipyretic effect which was comparable with paracetamol 200 mg/kg body weight in Wistar male rats. They also identified phytoconstitutents such as phytosterols, phenolic compounds, glycosides, carbohydrates and amino acids are present in the seed extract of *M. oleifera*[68]. The phytoconstituents like moringinine, flavonoids, tannin, saponins, phenolics, terpenoids and alkaloids are widely distributed in the various part and recognized those phytoconstitutents for its antipyretic effect of *M. oleifera*[60,66,67].

2.7. Analgesic

Bhattacharya *et al.*, investigated the analgesic activity of *M. oleifera* leaf extracts at doses of 400, 200 and 100 mg/kg body weight by acetic acid-induced writhing and eddy's hot plate method. The results demonstrated that ethanolic extract of *M. oleifera* leaf extract reduced writhes in a dose dependent manner and percentage inhibition of writhes in the range of 81%, 51% and 26%, respectively. The inhibition of writhes at 400 mg/kg body weight was similar with the standard whereas in Eddy's hot plate method, it produced a significant increase in the reaction time. Presence of phytoconstituents like flavonoids, tannin, saponins and terpenoids are anticipated for its analgesic effect[60].

2.8. Anti-epileptic

Jou *et al.*, investigated the anti-epileptic activity of *M. oleifera* leaf extracts in Swiss albino mice, by maximal electro shock seizure,

pentylenetetrazole method and pilocarpine induced seizure method. The observed results showed that the extracts prevented the hind limb extension induced by maximal electro shock, decreased the convulsion duration produced by pentylenetetrazole and eradicated the epilepticus status induced seizures by pilocarpine[69]. Jay *et al.*, performed a comparative study between *M. oleifera* root extract and oxcarbazepine for its protective effect against seizures induced in male Wistar albino mice by maximal electro shock method and quantified the biogenic amine before and after treatment. The root extract showed a dose dependent significant reduction in various phases of epileptic seizure on comparison with the standard oxcarbazepine 20 mg/kg. The levels of biogenic amines such as serotonin, dopamine and nor-adrenaline in the forebrain region were restored in significant level in the extract treated animals and a significant decrease in the time taken for recovery was observed in the experimental animals[70]. Different parts of extract like root, leaf and fruits of *M. oleifera* were investigated[71-73] and the results suggested that the mechanism of *M. oleifera* for its anti-epileptic activity could be by blockage of sodium, chlorine, T type calcium channel, imitative gamma aminobutyric acid glutaminergic mechanism, inhibition of monoamine oxidase enzyme property and prostaglandin synthesis[69,73].

2.9. Cardioprotective

Chumark *et al.*, investigated the aqueous extract of *M. oleifera* leaves for its antiatherosclerotic activities in male New Zealand white rabbits fed with high cholesterol diet and compared with simvastatin as standard. Parameters such as conjugated diene, cholesterol levels, thiobarbituric acid reactive substances (TBARS) and plaque formations were measured after treatment. The aqueous extract of *M. oleifera* leaf significantly inhibited the TBARS formation and prolonged the lag time of conjugated diene in a dose dependent manner in both *in vitro* and *ex vivo* experiments. Also the extract reduced the formation of atherosclerotic plaque and cholesterol levels by 50% and 86% respectively at 12 weeks of treatment. The study result noticed that aqueous extract of *M. oleifera* leaf had both hypolipidemic and antiatherosclerotic activities and it could be used for cardiovascular disease prevention[74]. Panda investigated the polyphenolic fraction of *M. oleifera* leaf extract for its preventive effect on cardiac damage at the dose of 50, 100 and 150 mg/kg/day for a period of 28 days; cardiotoxicity was induced in male Wistar rats by isoproterenol. Parameters such as creatine kinase, serum troponin-I, lactate dehydrogenase and heart tissue malondialdehyde contents were measured during the study. Also Electro paramagnetic resonance was measured as scavenging potential of the fraction. Isoproterenol induction increased the levels of creatine kinase, serum troponin-I, lactate dehydrogenase and heart tissue malondialdehyde content. The results demonstrated that polypenolic fraction of *M. oleifera* leaf extract restored the increased levels of creatine kinase, serum troponin-I, lactate dehydrogenase and heart tissue malondialdehyde content to normal levels also reduced the oxidative stress. In conclusion, at the dose of 100 mg/kg/day, *M. oleifera* leaf extract reduced the myocardial damage and the oxidative stress[75]. Nandave *et al.*, investigated the cardioprotective effect of *M. oleifera* hydroalcoholic extract in the isoproterenol (ISP)-induced myocardial infarction in Wistar albino male rats at 200 mg/kg for a period of 31 days. At the end of the treatment, various hemodynamic parameters such as heart rate, left ventricular peak positive and negative pressures and left ventricular end-diastolic pressure were measured. In addition, level of biochemical enzymes such as catalase, glutathione peroxidase, superoxide dismutase, creatine kinase-MB and lactate dehydrogenase were measured; also histopathological and ultrastructural studies in hearts were performed. Chronic *M. oleifera* treatment results demonstrated that mitigating effects were observed for hemodynamic parameters such as mean heart rate, left ventricular peak positive and negative pressures and left ventricular end-diastolic pressure. Also significant effects on biochemical enzymes such as catalase, glutathione peroxidase, superoxide dismutase, creatine kinase-MB and lactate dehydrogenase were observed and the histopathological and ultrastructural perturbations caused by ISP deleterious were prevented. The results established that antioxidant, antiperoxidative and myocardial preservative properties may be the attributing factors for significant cardioprotective effect of *M. oleifera* leaf extract[76]. Randriamboavonjy *et al.*, investigated the cardioprotective effect of *M. oleifera* seeds for ameliorate cardiac dysfunction and spontaneous hypertensive rats at a dose level of 750 mg/d for 8 weeks. Parameters such as arterial pressure and heart rate were measured using a telemetric transmitter. Also left ventricle geometry including anterior and interseptal wall thickness was measured before and after treatment. The study results showed reduction of heart rate but the treatment didn't show any significant modification in blood pressure whereas reduction of left ventricular anterior and interseptal wall thickness was observed. In conclusion, the study report supports *M. oleifera* seeds as a traditional Malagasy medicine against cardiac diseases[77]. Oluwagbamila *et al.*, examined the role of *M. oleifera* leaves on electrolyte levels and cardiovascular function in human at a dose of 5.0 g for the duration of 7 days. The study has shown the significant reduction of chloride and sodium ions and non-significant reduction of potassium ions. This significant reduction of electrolyte levels has beneficial effects on cardiovascular function[78]. Sierra-Campos *et al.*, observed the effect of methanolic extract of *M. oleifera* leaves on nitric oxide synthases and paraoxonase 1 in diabetic rat heart at the dose of 200 mg/kg body weight per day for 21 days. The study results noticed

significant reduction of nitric oxide synthase and paraoxonase 1 activities in heart. The study explored *M. oleifera* leaves has cardioprotective effects on the diabetic condition[79]. Other studies done by Farooq *et al.*,[80], Varmani and Garg[81], Jimenez *et al.*,[82], Koul and Chase[83] and Rada[84] reviewed the potential effects of *M. oleifera* Lam phytoconstituents for its cardioprotective effect. The review report concluded that moringinine alkaloid from root bark of Moringa stimulates cardiac function, β-sitosterol from the leaves of Moringa has cholesterol reducing effect and Flavonoids-Quercetin has hypolipidemic activity. It is predicted that mechanism of cardioprotective effect of *M. oleifera* is probably by inflection of glutathione, superoxide dismutase, catalase, creatine kinase-MB, lactate dehydrogenase and peroxidase enzymatic parameters[79,85].

2.10. Anti-hyperlipidemic

Chatterjee *et al.*, investigated the *M. oleifera* leaf extract for its hypolipidemic activity in cadmium, exposed adult Wistar rats. On exposure to cadmium, both hyperlipidaemia and hypercholesterolemia were observed. Treatment with *M. oleifera* leaf extract showed a significant decrease in the levels of triglyceride, total cholesterol, high density lipoprotein, low density lipoprotein and very low density lipoprotein. The investigation suggest that the elimination of lipids from the body could be the mechanism for its hypolipidemic activity[86]. Ogbuehi *et al.*, evaluated the comparative study of hypolipidemic activity between aqueous leaves extract of *M. oleifera* at the dose level of 100, 200 and 300 mg/kg and atorvastatin (4 mg/kg) as standard drug in albino Wistar rats with high fat diet for 4 weeks. High fat diet significantly raised the levels of triacylglyceride, serum cholesterol, low density lipoprotein, very low density lipoprotin and decreased the level of high density lipoprotein. The observed result showed after the treatment the aqueous leaves extract of *M. oleifera* reduced serum triglyceride, all the serum lipoproteins but increased high density lipoprotein level. The study noticed that *M. oleifera* can be used in the management of hyperlipidemia and associated health conditions[87]. Ghasi *et al.*, investigated the hypocholesterolemic effect of crude leaves extract of *M. oleifera* Lam. in obese patients with high-fat diet. High fat diet increased the serum, liver, and kidney cholesterol levels. On treatment with *M. oleifera* Lam. leaves extract showed statistically significant reduction of serum, liver, and kidney cholesterol levels, and also increased the serum albumin level significantly[88]. Ara *et al.*, made a comparative evaluation of anti-hyperlipidemic effect between the ethanolic leaf extract of *M. oleifera* at the dose of 200 mg/kg body weight and atenolol (standard) at the dose of 50 mg/70 kg body weight in adrenaline-induced rats. Parameters such as serum triglyceride level, serum cholesterol level, blood glucose level, heart and body weight were measured before and after the treatment. In addition to serum triglyceride, other parameters were observed in higher amount in adrenaline-induced rats. On treatment, ethanolic leaf extract of *M. oleifera* significantly reduced all the elevated parameters. In conclusion, the results demonstrated that *M. oleifera* leaves extract possessed very good hypolipidemic activity[89]. Rajanandh *et al.*,[90] evaluated the hydroalcoholic extract of *M. oleifera* leaves for its hyperlipidemic activity in rats for a period of 28 days at two different dose levels such as 100 and 200 mg/kg body weight. Treatment with hydroalcoholic extract of *M. oleifera* leaves shows noteworthy reduction in elevated levels of triglycerides, total cholesterol, body weight, low density lipoprotein, very low density lipoprotein and increases high density lipoprotein level. The study concluded that *M. oleifera* can be given as an adjunct for coronary artery disease. Mehta *et al.*, investigated the *M. oleifera* fruit for the effect on the lipid profile of normal and hypercholesterolaemia rabbits at a dose of 200 mg/kg/day and compared with lovastatin 6 mg/kg/day as standard for 120 days. The result divulged that *M. oleifera* decreased the triglyceride, phospholipid, serum chloesterol, low density lipoprotein, very low density lipoprotein, cholesterol to phospholipid ratio and atherogenic index and increases high density lipoprotein ratio (HDL/HDL-total cholesterol). The study noticed that increased excretion of faecal cholesterol was observed and concluded that *M. oleifera* possesses a hypolipidaemic effect[91]. Sparman investigated a herbal formulation consisting of *M. oleifera*, *Bryophyllum pinnatum* and Vitamin C on blood pressure, cholesterol levels and blood glucose for six months. On treatment with herbal formulation a significant reduction of Low Density Lipoprotein cholesterol and significant increase of High Density Lipoprotein was observed in all the participants. The study demonstrated that this herbal formulation can be used for the management of risk factors for cardiovascular disease[92]. Anti-hyperlipidemic effect of *M. oleifera* is attributed to the presence of β-sitosterol as a main phytoconstituent in the extracts and increased excretion of faecal cholesterol may be attributed for its antihyperlipidemic effect[91,93].

2.11. Anti-hypertensive

Sana *et al.*, investigated the hypertensive activity of *M. oleifera* root extracts in Normotensive Sprague Dawley rats. Dichloromethane and petroleum ether extracts of *M. oleifera* roots showed a reduction in mean arterial blood pressure which was comparable with control group[94]. The study also demonstrated that the anti-hypertensive effect of *M. oleifera* root extracts may be due to the presence of phytoconstituents such as hydrocarbons, thioureides, steroids, fatty

acid esters and isothiocyanates. It was proven that phytoconstituents such as isothiocyanates and thiocarbamate glycoside were accredited for its anti-hypertensive effect[95-96].

2.12. Hepatoprotective

Dondee *et al.*, investigated the hepatoprotective activity of *M. oleifera* leaf extract at the dose level of 100, 500 and 1 000 mg/kg in mice infected with *Plasmodium (P.) berghei* ANKA). *P. berghei* infection significantly increased the level of alanine aminotransferase, aspartate aminotransferase but decreased the level of albumin in untreated mice. Aqueous leaf extracts of *M. oleifera* showed a dose dependent hepatoprotective activity in liver injury induced by *P. berghei* infection and significantly decrease the elevated level of aspartate aminotransferase and alanine aminotransferase in addition to significant increase of the albumin level[97]. The results also demonstrated that phytoconstituents such as flavonoids, alkaloids, saponins, polyphenol, terpenoids, kaempferol and quercetin are present in the extract. It is speculated that flavonoids and polyphenol contribute for its hepatoprotective activity. Singh *et al.*, evaluated the hepatoprotective activity of *M. oleifera* leaf extract in (CCl_4) intoxicated rats at the dose of 100, 200 and 400 mg/kg body weight/day, for 60 days and compared with silymarin as standard drug. Treatment with *M. oleifera* leaf extract showed significant modification of all serum enzymes in a dose dependent manner. Results noticed that hepatoprotective activity is due to its free radical scavenging activity of phenolics and flavonoids[98]. Saalu *et al.*, investigated the hepato-protective effect of *M. oleifera* leaf extract in alcohol-induced hepatotoxic rats when subjected to 300 mg/kg body weight/day for 56 days. Parameters such as liver histology, liver oxidative stress (superoxide dismutase, catalase, glutathione peroxidase, glutathione and malondialdehyde), and liver biomarker enzymes (serum alanine transaminase, aspartate transaminase, alkaline phosphatase and Gamma-Glutamyl transpeptidase) were evaluated before and after treatment. Alcohol-induced hepatotoxicity showed marked distortion of the liver cyto-architecture, significant reduction of superoxide dismutase, catalase, glutathione peroxidase, glutathione and significant increase in malondialdehyde, serum alanine transaminase, aspartate transaminase, alkaline phosphatase and Gamma-Glutamyl transpeptidase were observed. Treatment with *M. oleifera* showed remarkable preservation in their histological profiles, restoring the liver oxidative stress and liver biomarker enzymes to the normal level. The study revealed that hepatoprotective effect could be due to its free radicals scavenging capability of *M. oleifera* leaf extract[99]. Nanjappaiah and Hugar, studied the effect of 70% ethanolic extract of *M. oleifera* Lam. pods in CCl_4 damaged rat liver at the dose level of 100, 250 and 500 mg/kg in rats. Biochemical marker enzymes such as serum glutamic pyruvic transaminase, serum glutamic oxaloacetic transaminase, alanine aminotransferase, acidic phosphatase, bilirubin, glutathione, malondialdehyde and liver histophology were evaluated. On treatment with 70% ethanolic extract of *M. oleifera* Lam. pods, a significant reduction of biochemical marker enzymes, glutathione, significant increase of malondialdehyde and incredible preservation of liver histological profiles were observed [100]. In other studies, the researchers treated CCl_4-induced liver damage in rats with *M. oleifera* leaf extract and noticed that liver histopathological profile and liver enzymes were restored to its normal level indicating its hepatoprotective effect[101,102]. Several studies have been performed with different parts of *M. oleifera* for its hepatoprotective activity against the acetaminophen, diclofenac, antitubercular drug (isoniazid, rifampicin and pyrazinamide) and cadmium-induced liver damage in rats. The study results showed that *M. oleifera* enhanced the recovery from hepatic damage and it can act as hepatoprotective agent[103-106]. The mechanism for its hepatoprotective activity of *M. oleifera* may be due to its free radicals scavenging ability and enhanced distinctive antioxidant effect[99,102].

2.13. Anti-nephrotoxicity

Paliwal and his research team investigated the *M. oleifera* pods extract for its antinephrotoxicity in 7,12-Dimethylbenz[a]anthracene (DMBA)-induced renal carcinogenesis of Swiss albino mice for 14 days, and assessed the altered renal oxidative stress parameters like superoxide dismutase, lipid peroxidation, and catalase in the kidney of mice. Altered renal oxidative stress parameters results were restored near to the normal values, after extract treatment[107]. The mechanism for its anti-nephrotoxicity is induction of antioxidant profile by the phytoconstituents such as β-carotene, vitamin A and C, also the oxidative free radical scavenging activities by the other phytoconstituents like phenolic, flavonoid and alkaloids. Mansour *et al.*, evaluated the antihepatotoxicity and antinephrotoxicity activity of aqueous extract of *M. oleifera* leaves in rat. Hepatotoxicity and nephrotoxicity were induced by γ-radiation. Induction by γ-radiation showed significant modification in different biochemical parameters such as malondialdehyde, total nitrate/nitrite levels, superoxide dismutase, catalase, glutathione content, aminotransferase, alanine, aspartate aminotransferase, level of creatinine and urea nitrogen in serum. The treatment restored the modified biochemical parameters. The above study results demonstrated that free radical scavenging activity might be attributed for its nephroprotective effect[108].

2.14. Anti-microbial

Ratshilivha *et al.*, investigated the antimicrobial activity of acetone extract of *M. oleifera* leaves by utilizing different bacteria such as *Staphylococcus (S.) aureus*, *Enterococcus faecalis, Escherichia (E.) coli* and *Pseudomonas aeruginosa* and different fungi such as *Aspergillus fumigatus*, *Candida albicans* and *Cryptococcus neoformans*. They concluded that acetone extract of *M. oleifera* leaves has antimicrobial activity[109]. Arora and Onsare evaluated the *M. oleifera* pod husks for antimicrobial activity by agar dilution method against Gram negative, Gram positive bacteria and yeast pathogens and the results at the concentration of 0.4–4 mg mL/L were compared with Ciprofloxacin 6.7 mg/L and Amphotericin B 750 mg/L as standard. The minimum inhibitory concentration for the Gram positive bacteria were found to be 400 mg/L; whereas for Gram negative bacteria and *Candida tropicalis* were killed instantly at minimum inhibitory concentration with concentrations ranging from 800 mg/L to 8 000 mg/L. The study concluded that the *M. oleifera* pod husks had antimicrobial activity against Gram negative, Gram positive bacteria and yeast pathogens; also highlighted phytoconstituents such as flavonoids and diterpenes were recognized for its antimicrobial activity[110]. Antimicrobial study of *M. oleifera* leaves was performed by Jayawardana *et al.*, in chicken sausages at various concentration like 0.25%, 0.50%, 0.75% and 1.00%. Parameters such as TBARS value, pH and microbial analysis were assessed. A significant (P<0.05) value was observed for TBARS, pH and microbial analysis at the concentration of 0.50%, 0.75% and 1.00%. They concluded that *M. oleifera* leaves could be used to extend the shelf-life of consumable food materials[111]. Rahman *et al.*, evaluated the antibacterial property of *M. oleifera* leaves extract using disc diffusion and minimimum inhibitory concentration method against some human pathogenic bacteria and compared with tetracycline as standard. The study disclosed ethanol extract of *M. oleifera* leaves at 1 175 μg/disc exhibited antibacterial activity against both Gram negative *Bacillus cereus*, *Bacillus subtilis*, *Sarcina lutea* and *Bacillus megaterium* and Gram positive bacteria *Shigella shinga*, *Pseudomonas aeruginosa*, *Shigella sonnei* and *Pseudomonas* spp, and the potential antibacterial activity of the extract was similar extremely with the standard[112]. Peixoto *et al.*, evaluated the antimicrobial effect of aqueous and ethanolic extract of *M. oleifera* leaf by disc diffusion method at the concentration of 100, 200, 300 and 400 μL of extract at 20 g/180 mL and 10 g/190 mL against *E. coli*, *S.aureus*, *Vibrio parahaemolyticus*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Salmonella enteritidis* and *Aeromonas caviae*. The study results revealed that the discs with 400 μL extract have shown the antimicrobial activity against *S. aureus*, *Vibrio parahaemolyticus*, *Enterococcus faecalis* and *Aeromonas caviae*[113]. Moyo *et al.*, examined the antibacterial activity of acetone extract of *M. oleifera* leaves at a concentration of 5 mg/mL against *E. coli, Enterobacter cloace*, *Proteus vulgaris*, *S.aureus* and *Micrococcus kristinae*. The study result revealed that the acetone extract have both bactericidal activity against *E. coli* and *M. kristinae*; bacteriostatic activity against *S. aureus*, *E. cloace* and *P. vulgaris*[114]. A study performed by Thilza *et al.*, observed the antimicrobial activity of water extract of *M. oleifera* leaf stalk by disc diffusion method against *S.albus*, *Pseudomonas aerogenosa*, *E.coli*, *S.aureus*, *Enterobacter aerogenes* and *Staphylococcus pyogenus* at the dilution of 1 000 mg/mL, 700 mg/mL, 400 mg/mL and 200 mg/mL. The study results determined that water extract of *M.oleifera* leaf stalk showed antimicrobial activity against *E.coli* at 1 000 mg/mL[115]. Saadabi and Zaid investigated the antimicrobial activity of aqueous extract of *M.oleifera* L. seed against different bacterias such as *S. aureus*, *Bacillus subtilis*, *E. coli* and *Pseudomonas aeruginosa* and fungi such as *Aspergillus niger* and *Candida albicans* at 5%, 10%, 20% and 40% extract concentration. The study result concluded that aqueous extract of *M. oleifera* L. seed had antibacterial activity against all bacterial strains whereas for fungi less or no activity was observed[116]. Nikkon *et al.*, isolated an aglycon of Deoxy-Niazimicine (N-benzyl, S-ethyl thioformate) from *M. oleifera* Lam root bark and investigated the same for its antimicrobial activity against fourteen pathogenic bacteria and six pathogenic fungi and compared with the chloroform crude extract of *M. oleifera* Lam root bark. The results revealed that isolated compound had more antibacterial and antifungal activity when compared to the crude extract[117]. Vieira *et al.*, examined the aqueous and ethanolic extract of *M. oleifera* seeds against *S. aureus, Vibrio cholerae*, *E. coli* and *Salmonella enteritidis* at the concentration of 50, 100, 150 and 200 μL/dish. Aqueous and ethanolic extracts of *M. oleifera* seeds showed antibacterial activity against *S. aureus*, *Vibrio cholerae* and *E. coli* [118].

3. Conclusions

M. oleifera served as an effective solution for the harmful effects posed by the synthetic resources and also other disputes prevailing in the modern era. Our present review summarized the high nutritional values and biomedical activities of *M. oleifera* such as immunomodulatory, antidiabetic, anti-ulcer, anthelmintic, anti-inflammatory, antipyretic, analgesic, cardioprotective, anti-hyperlipidemic, anti-hypertensive, hepatoprotective, anti-nephrotoxicity and antimicrobial activity.

The chemical constituents of *M. oleifera* are very well investigated and documented yet it is not clear as to what extent the various constituents present in *M. oleifera* preparations interrelate through additive, synergistic, and /or inhibitory effects. Thus authors suggest

further studies should emphasize on the mechanism of action of the isolates and constituents of the moringa plant. The advances in biotechnological techniques and rich phytochemical profile can lead to generation of new opportunities aimed towards development of overall commercial value of the tree.

The authors conclude that in order to establish and exploit complete uses of the miracle tree, market development strategies, strong policies and research are required. *Moringa* should be promoted for further consumption to develop nutrition and therapeutic functions as well.

Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

AU and SLP conceived the presented idea. AP encouraged SLP to investigate the pharmacological activities of the plant. All the three authors discussed the construction of manuscript. SLP took the lead in drafting the manuscript with support from AU. SLP and AU worked out almost all the technical details, done the critical revision of the article with the support of AP. AU devised the main conceptual ideas and proof outline of the manuscript. All the authors SLP, AU and AP discussed the results and contributed towards the comments on the manuscript.

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