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Research advances on the multiple uses of *Moringa oleifera*: A sustainable alternative for socially neglected population

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ABSTRACT

Moringa oleifera Lam (Moringaceae) is a plant with high nutritional and medicinal value. Native to India, it is now widely distributed throughout tropical and subtropical regions of the world. Its different parts are sources of proteins, vitamins and minerals and present different pharmacological and biotechnological potential. Moreover, *M. oleifera* seeds are widely used in water and effluent treatment, for their coagulation, flocculation and sedimentation properties, their ability of improving water quality, by reducing organic matter and microbial load, with special applicability in intensive animal production systems, such as aquaculture. In addition, due to its high nutritional value and several medicinal properties, this tree may act as a nutritional and medical alternative for socially neglected populations. In this context, this review gathers information on *M. oleifera*, emphasizing its chemical constituents, nutritional, pharmacological and antimicrobial properties, applications in the treatment of water effluents, and ecological and social aspects.

1. Introduction

Medicinal plants have posed as natural resources of compounds with pharmacological and nutritional properties aiding humans to prevent and treat diseases [1]. Among several plants evaluated in bioprospective studies, *Moringa oleifera* (Lam) (*M. oleifera*), popularly known, in Brazil, as “moringa”, “lírio branco” or “quiabo-de-quina”, and, in some parts of the world, as drumstick tree or horseradish tree, has stood out in alternative medical therapies, showing benefits for the control of several diseases [2,3]. Its medicinal potential derives from secondary metabolites, such as alkaloids, tannins, flavonoids, steroids, saponins, coumarins, quinones and resins [3].

M. oleifera is native to Northern India, but currently it is widely distributed in the Americas, Africa, Europe, Oceania and Asia [4–6]. Leaves, flowers, pods and seeds of this tree are considered a food source of high nutritional value in the African continent and other countries, particularly in India, Philippines and Pakistan [1]. Three nongovernmental organizations, Trees for Life, Church World Service, and the Educational Concerns for Hunger Organization, have advocated the motto “*Natural nutrition for the tropics*” to stimulate the use of several plant species as food sources, including *M. oleifera* [2]. Leaves can be consumed cooked or fresh and they can be stored as dried powder unrefrigerated with no nutritional losses, for several months. Undoubtedly, *M. oleifera* adds substantial health benefits to countries where hunger is a problem [3].

In addition to medicinal and nutritional applications, one of the most applied properties of *M. oleifera* is the highly efficient coagulating effect of its seeds, which are used in water

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treatment. These seeds act as coagulants of organic matter suspended in water and are used in water treatment stations for natural cleaning before performing other cleansing processes. Furthermore, seeds have more stable activity in different pH ranges, when compared to aluminum sulfate, the most frequently used coagulating substance in water treatment stations [7]. *M. oleifera* has also been assessed for its potential to treat aquaculture waste water. The results have shown the simultaneous elimination of water turbidity, suspended particles and microorganisms, making it suitable to completely or partly replace the usual coagulating agents, leading to economic, health and environmental gains [8,9].

Based on the above, this review gathers information on *M. oleifera* (Lam.), emphasizing its chemical constituents, nutritional, pharmacological and antimicrobial properties, applications in the treatment of water effluents, and ecological and social aspects.

2. Chemical constituents

The chemical constituents of *M. oleifera* stems, leaves, flowers, pods and seeds have been analyzed for the presence of bioactive compounds, demonstrating the predominance of secondary metabolites, such as phenolic acids, gallic acid, ellagic acid, chlorogenic acid, ferulic acid, glucosinolates, flavonoids, quercetin, vanillin and kaempferol, which have nutritional, pharmaceutical and/or antimicrobial properties [10,11]. However, the amount of these metabolites in *M. oleifera* extracts varies according to geographic location, soil, sun exposure and climatic conditions [12]. Moreover, the method and solvents used for extraction can modify the content of the compounds obtained from the plant, mainly phenols and flavonoids [13].

Many phytoconstituents of *M. oleifera* have been isolated and studied, as shown in Table 1. The main phytochemicals obtained from the plant include: tannins, saponins, alkaloids, flavonoids, phenols and glycosides from leaves [22]; tannins, steroids, flavonoids, alkaloids, glycosides, quercetin and terpenoids from flowers [23]; gallic acid, catechins, epicatechin, ferulic acid, vanillin, caffeic acid, protocatecuic acid, cinnamic acid, phytosterol, quercetin, glycosides and phenols from seeds [24]; procyanidins, aurantiamide acetate, 3-dibenzylurea, quercetin glycoside, rhamnoglucoside quercetin, and chlorogenic acid from roots; and procyanidin, sterols, triterpenoids, glycosides, tannins, alkaloids, β-sitosterol and octacosanoic acid from stem bark [17].

Table 1
Phytoconstituents of different parts of *M. oleifera*.

Plant part	Phytoconstituents	Group
Seeds	β-sitosterol [14]	Phytosterol
Leaves, stem and roots	4-α-L-rhamnopyranosyloxy-benzylglucosinolate [15]	Glucosinolate
Leaves, seeds and roots	4-(α-L-rhamnosyloxy-benzyl) isothiocyanate [14,16]	Glucosinolate
Leaves	4-O-glucopyranosyl-caffeoyl quinic acid [15]	Caffeoylquinic acid
Seeds	Glycerol-1-(9-octadecanote) [14]	Glycoside
Seeds, leaves, stem and roots	Kaempferol [15,17,18]	Flavonoid
Leaves and seeds	Niazimicin [14,19]	Glycoside
Leaves and seeds	Niazinin [14,19]	Glycoside
Leaves	((α-L-rhamnosyloxy)benzyl) carbamate [16]	Glucosinolate
Seeds, leaves, stem and roots	Quercetin [16–18]	Flavonoid
Roots and flowers	Pterygospermin [20,21]	Glycoside

3. *M. oleifera* and its applications

3.1. Nutritional potential

M. oleifera contains more than 90 nutritional chemical compounds, including proteins, lipids, carbohydrates and dietary fibers (Table 2). It is used in the tropics as a food source to overcome malnutrition, especially in children and infants [2,5].

Among the several nutrients found in different parts of *M. oleifera*, proteins are the most abundant, accounting for approximately 25% of dry weight [3], and at least 19 amino acids have been identified in this plant (Table 3). Furthermore, *M. oleifera* also contains several minerals and vitamins (Table 4). Lipids are abundant in seeds, mainly stearic acid, saturated palmitic acid and oleic acid, representing about 30% of dry weight [31]. The lipidic compounds linolenic acid and palmitic acid are the main constituents of *M. oleifera* leaves. In addition, the high nutritional content found in dried leaves is an indicator of the usefulness of the plant as a food resource [25].

3.2. Hepato and nephro-protective activity

Scientific evidences suggest a potential role of *M. oleifera* leaves in the reduction of liver and kidney drug-induced damage in animals (Table 5). For instance, studies have reported the hepato and renal-protective properties of *M. oleifera* against several drugs, such as gentamicin, pyrazinamide, rifampicin, isoziazide and acetaminophen, which are mainly attributable to its leaves [40,41,45,58]. The authors also observed a reduction in serum levels of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase [40], urea and creatinine [41] in animals treated with *M. oleifera* leaf extract. These findings were confirmed by histological tests, which showed reduction of drug-induced hepatic and renal damage in animals treated with *M. oleifera* leaves. Additionally, aqueous and alcoholic root and flower extracts of *M. oleifera* have been shown to have hepatoprotective activity against the effects of acetaminophen, reducing serum transaminases (alanine aminotransferase and aspartate aminotransferase), alkaline phosphatase and bilirubin levels [51]. In addition, this activity also enhances the recovery of cadmium-induced hepatotoxicity in rats [40]. However, further studies are still needed to better define the pharmaceutical applicability of *M. oleifera*.

Table 2
Macronutrients of leaves, pods and seeds of *M. oleifera* [25–29].

Nutrients	*M. oleifera* (g/100 g of plant)		
	Leaves	Pods	Seeds
Proteins	25.0–30.3	6.7–43.5	29.4–38.3
Lipids	0.1–10.6	0.1–5.1	30.8–41.2
Carbohydrates	0.1–43.9	0.1–38.2	0.1–21.1
Fibers	0.1–28.5	0.1–27.0	0.1–7.2

Table 3
Amino acids of leaves, pods and seeds of *M. oleifera* [5,22,25–27].

Amino acids	*M. oleifera* (g/100 g)		
	Leaves	Pods	Seeds
Essential			
Arginine	0.4–1.8	0.36	4.5
Histidine	0.1–0.7	0.11	2.3
Leucine	0.4–2.2	0.65	6.7
Lysine	0.3–1.4	0.15	1.5
Methionine	0.1–0.5	0.15	2.4
Phenylalanine	0.3–1.6	0.43	4.0
Threonine	0.1–1.3	0.39	3.1
Tryptophan	0.1–5.2	ND	1.6
Valine	0.4–1.4	0.54	4.3
Non-Essential			
Alanine	1.8–3.0	ND	6.9
Aspartate	1.4–2.2	ND	5.0
Cysteine	0.01–0.10	ND	2.0
Glutamate	2.5–2.5	ND	20.9
Glycine	1.3–1.5	ND	10.9
Proline	1.2–1.4	ND	4.5
Serine	1.0–1.2	ND	4.4
Tyrosine	0.01–2.60	0.08	1.6

ND: Not determined.

Table 4
Micronutrients of leaves, pods and seeds of *M. oleifera* [5,22,25,28,30].

Micronutrients	*M. oleifera* (mg/100 g of the plant)		
	Leaves	Pods	Seeds
Minerals			
Calcium	440–3 650	30.0–237.7	263.5
Magnesium	24–1 050	9.6–83.4	78.4
Sulfur	137–925	137	ND
Sodium	164.0–272.1	210.5	ND
Potassium	259–20 616	259.0–2 097.2	ND
Phosphor	70–300	110.0–194.3	ND
Iron	0.85–126.20	4.4–15.5	44.8
Zinc	0.16–3.30	ND	ND
Copper	0.6–1.1	2.7–3.5	1.3
Vitamins			
A	6.78–18.90	ND	ND
B2	0.05–20.50	ND	ND
B3	0.8–8.2	ND	ND
B7	423	ND	ND
B12	0.06–2.64	ND	ND
C	17.3–220.0	ND	ND
E	77	ND	ND

ND: Not determined.

3.3. Hypocholesterolemic, hypolipidemic and anti-atherosclerotic activity

Ghasi *et al.* observed a hypocholesterolemic activity after the administration of a crude extract of *M. oleifera* leaves to rats fed on a high-fat diet, causing a reduction of up to 14% in serum cholesterol levels [42]. *M. oleifera* fruit consumption is also effective in reducing very-low-density lipoprotein, low-density lipoprotein and high-density lipoprotein serum levels [54]. In addition to these effects, *M. oleifera* leaf extract has also been reported to reduce the formation of atherosclerotic plaques [32].

Although there are only a few studies in humans, some researches have demonstrated the potential benefits of using *M. oleifera* for the treatment of hyperglycemia and dyslipidemia (Table 5). For instance, a study with 46 individuals with type-2 diabetes, daily treated with 8 g of *M. oleifera* leaf powder for 40 d, showed that fasting and postprandial glycemia were reduced by 28% and 26%, respectively, when compared to untreated individuals [43]. In addition, total cholesterol, triglycerides and low-density lipoprotein and very-low-density lipoprotein cholesterol were also lower than those of the control individuals [43]. Another study with 35 type-2 diabetic individuals showed that the consumption of 4.6 g-tablets of *M. oleifera* leaves, for 50 d, was able to increase high-density lipoprotein levels and decrease total cholesterol [38].

Table 5
Pharmacological activity of different parts of *M. oleifera*.

Plant part	Pharmacological activity
Leaves	Antiatherosclerotic [32]
	Anti-inflammatory [33]
	Anticancer [34–36]
	Antimicrobial [37]
	Antioxidant [32,34,38,39]
	Hepatoprotective [40,41]
	Hypocholesterolemic [42]
	Hypoglycaemic [43]
	Hypolipidaemic [32]
	Immunomodulatory [44]
	Nephroprotective [45]
	Neuroprotective [46–48]
Roots	Anti-inflammatory [49]
	Antimicrobial [21,28,50]
	Hepatoprotective [51]
	Nephroprotective [40]
Flowers	Antimicrobial [52]
	Hepatoprotective [41,51]
	Nephroprotective [40]
Pods	Anticancer [35]
	Anti-inflammatory [53]
	Antimicrobial [3]
	Antioxidant [10]
	Hypocholesteromic [54]
Seeds	Anti-inflammatory [49,55]
	Anti-cancer [36]
	Antimicrobial [56,57]
	Antioxidant [10]
	Antitumor [14]
	Immunomodulatory [49]

3.4. Anticancer potential

In general, there are a few *in vitro* studies to evaluate the anticancer potential of *M. oleifera* (Table 5). However, the existing results suggest the potential anticancer properties of *M. oleifera*. One of the first studies on *M. oleifera* antitumor effect was performed with compounds obtained from its ethanol seed extract, showing that the compounds 4-(α-L-rhamnosyloxy)-benzyl isothiocyanate, 3-O-(6′-O-oleoyl-β-D-glucopyranosyl)-β-sitosterol, β-sitosterol-3-O-β-D-glucopyranoside and niazimicin are potent tumor inhibitors [14].

Dichloromethane and methanolic *M. oleifera* leaf extracts present *in vitro* anticancer activity against human hepatocellular carcinoma, colorectal adenocarcinoma and breast adenocarcinoma, with no toxic effects on human fibroblasts [34]. Other investigators studied the effects of oral administration of hydromethanolic and methanolic *M. oleifera* leaf extracts on a mouse melanoma model. The authors observed that the oral administration of 500 mg/kg, for 15 d, delayed tumor growth and significantly increased mouse lifespan [35]. These anticancer properties may be attributed to the bioactive compounds present in these extracts, such as the hexadecanoic acidethyl ester [36].

3.5. Anti-inflammatory and immunomodulatory activities

The anti-inflammatory activity of *M. oleifera* has been observed after treatment with extracts of roots, stems, leaves, flowers, pods and seeds (Table 5). In a study with rats, *M. oleifera* root extract reduced the development of paw edema, with results similar to those obtained by phenylbutazone, a non-steroidal anti-inflammatory drug with analgesic and antipyretic properties [59]. Furthermore, the butanol extract of *M. oleifera* seeds interrupted the acetylcholine-induced bronchospasms and airway inflammation in guinea pigs, by modifying Th1/Th2 cytokines [49]. In addition, a clinical study with patients with mild to moderate asthma demonstrated that *M. oleifera* dried seed powder significantly improved the forced vital capacity, forced expiratory volume and peak expiratory flow without adverse reactions [55]. Many bioactive compounds may be involved in the anti-inflammatory properties of *M. oleifera*, such as quercetin, which appears to inhibit the activation of NF-κB, essential step to unchain the inflammatory process [58]. However, many other bioactive compounds from *M. oleifera*, such as flavonoids and phenolic acids, may be involved in the anti-inflammatory activity of this plant.

It has also been shown that *M. oleifera* leaf extract and quercetin regulate the expression of iNOS, IFN-γ and C-reactive protein and decrease TNF-α and IL-6 release, in rats [58]. A similar result was found for isothiocyanates obtained from *M. oleifera* leaves, which significantly decreased the production of pro-inflammatory mediators by RAW macrophages, especially IL-1β, iNOS, TNF-α and NO [33].

Regarding the immunomodulatory effects of *M. oleifera*, it has been shown that the ethanolic *M. oleifera* leaf extract reduced cyclophosphamide-induced immunosuppression in rats, with stimulation of cellular and humoral immunity [44].

3.6. Antioxidant activity

The antioxidant activity of *M. oleifera* is particularly strong in leaf, pod and seed extracts (Table 5). The high content of flavonoids and phenols in different parts of the plant, especially leaves, favors the reduction of oxidative damage to the main biomolecules through the inhibition of lipid peroxidation and the action of nitric oxide and induction of deoxyribose degradation, preventing the generation of free radicals [10,39,60].

Studies with normal and diabetic rats showed that treatment with aqueous *M. oleifera* leaf extracts significantly increased the activity of the enzymes superoxide dismutase, catalase and glutathione S-transferase and decreased lipid peroxidation [61]. It has been suggested that the high phenolic and flavonoid content in the extract may protect against oxidative damage in normal and diabetic individuals [61]. Additionally, a research with 60 postmenopausal women showed that supplementation with *M. oleifera* leaf powder for 3 months significantly decreased the serum levels of malondialdehyde, generated by lipid peroxidation, and increased the levels of ascorbic acid, superoxide dismutase and glutathione peroxidase, which are indicators of the antioxidant property of the plant [62].

3.7. Neuroprotective potential

The neuroprotective effects of *M. oleifera* are an emerging area of study (Table 5). It has been shown that aqueous and hydro-alcoholic extracts of *M. oleifera* leaves potentiate the cognitive activity, besides acting as neuroprotector in mice with colinotoxin-induced dementia [46,47]. Reduced levels of brain lipid peroxidation and increased levels of superoxide dismutase and catalase were observed in response to leaf extract administration [46]. In addition, another study has demonstrated the neuroprotective properties of an ethanolic extract of *M. oleifera* leaves, when incubated with a primary culture of hippocampal neurons. The extract promoted neurite outgrowth with significant increase in the number and length of dendrites and axonal branches [48]. These results suggest that *M. oleifera* may provide a neuroprotective benefit by reducing the oxidative stress.

3.8. Antimicrobial potential

Many *in vitro* studies have demonstrated the inhibitory activity of *M. oleifera* root, stem, leaf, flower, pod and seed extracts on Gram-positive (*Enterococcus faecalis*, methicillin-resistant *Staphylococcus aureus* and *Staphylococcus epidermidis*) and Gram-negative bacteria (*Salmonella enterica*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli*) isolated from clinical samples [50,56,59,63–67]. The antimicrobial effect of the crude extracts on *E. coli* and *K. pneumoniae* strains has been compared to that of the antibiotic streptomycin [64,66]. The *in vitro* antibacterial potential of *M. oleifera* has been demonstrated against other bacterial species, as shown in Table 6. This potential is associated with the biocompound benzyl-isothiocyanate which inhibits bacterial growth by disrupting the mechanisms of membrane and enzyme synthesis [73]. In addition, the antibacterial activity of *M. oleifera* extracts is also attributed to gallic acid and tannins, which inhibit *Vibrio* spp. [74], and saponins, tannins, isothiocyanates and phenolic compounds, such as alkaloids and flavonoids, which have inhibitory activity [63,75,76].

Several studies have demonstrated the antifungal activity of *M. oleifera* seed extracts against *Mucor* spp. and *Rhizopus* sp.; pod extracts against *Alternaria* sp., *Colletotrichum* sp., *Candida albicans* and *Fusarium* sp.; and root extracts against *C. albicans* and *Aspergillus flavus* [50,56,65–67]. Other fungal species are also susceptible to *M. oleifera* seed and leaf extracts, such as the dermatophytes *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum* and *Microsporum canis* isolated from clinical samples [8,75], as well as *Candida* species, such as *C. famata*, *C. guilliermondii*, *C. parapsilosis sensu lato*, *C. tropicalis* and *C. ciferri* isolated from prawn farming [57]. *M. canis* isolated from cases of feline dermatophytosis, as well as *C. albicans* from the oral microbiota of dogs were also susceptible to flower and seed extracts [52,57]. The *in vitro* antifungal effects of *M. oleifera* have also been demonstrated on other fungal species, as shown in Table 7. In addition to these extracts, seed essential oil has an inhibitory effect on *Penicillium* spp. and *Aspergillus niger*. The antifungal activity of this essential oil was attributed to polyphenols, hydrocarbons, hexacosane, pentacosane, heptacosane, phytol and thymol [80]. Moreover, flavonoids and the compounds pyterigospermin and isothiocyanates obtained from seeds and leaves also have antimicrobial activity [2,75,76].

Table 6

Antibacterial activity of *M. oleifera* extracts expressed in inhibition diameter and minimum inhibitory concentration (MIC).

Microorganism	Extract	Disc-diffusion		MIC (mg/mL)	References
		Concentration (mg/mL)	Inhibition diameter (mm)		
Acinetobacter baumannii	aqueous (leaves)	30	12	7.5	[68]
Bacillus spp.	ethanolic (leaves)	2	16	0.91	[69]
	chloroformic (bark)	2	11	1.5	[70]
Escherichia coli	aqueous (leaves)	30	15	20	[68]
	ethyl acetate (bark)	2	18	0.75	[70]
	ethanolic (leaves)	2	20.23	0.45	[69]
Proteus vulgaris	aqueous (leaves)	30	15	30	[68]
Pseudomonas aeruginosa	chloroformic (bark)	2	14	1.5	[70]
	methanolic (leaves)	30	13	3.75	[68]
Salmonella typhi	ethyl acetate (bark)	2	14	1.5	[70]
Shigella spp.	ethanolic (leaves)	2	17.5–21.5	0.45–0.91	[70]
	ethyl acetate (bark)	2	21	1.5	[70]
Staphylococcus aureus	chloroformic (bark)	2	16	2	[70]
	ethyl acetate (bark)	2	17	0.75	[70]
Streptococcus pneumoniae	aqueous (leaves)	10	8	0.25	[71]
Vibrio spp.	chloroformic (flowers)	–	–	0.625–1.250	[72]
	ethanolic (stem)	–	–	1.25–2.50	
	ethanolic (leaves)	–	–	0.078–5.000	
	ethanolic (seeds)	–	–	2.5–5.0	
	ethanolic (pods)	–	–	0.312 5–5.000	
Yersinia enterocolitica	aqueous (leaves)	30	15	30	[68]

Table 7

Antifungal activity of *M. oleifera* extracts expressed in inhibition diameter and minimum inhibitory concentration (MIC).

Microorganism	Extract	Disc-diffusion		MIC (mg/mL)	References
		Concentration (mg/mL)	Inhibition diameter (mm)		
Aspergillus spp.	aqueous (seeds)	10	2	38	[77]
	chloroformic (roots)	0.1	17	2	[70]
	ethanolic (roots)	0.1	21	1.5	[70]
Candida spp.	chloroformic (roots)	0.1	17	0.75	[70]
	ethanolic (roots)	0.1	21	0.5	[70]
	chloroformic (flowers)	10	14	0.625	[52]
Fusarium solani	aqueous (seeds)	10	37	26	[77]
Hortaea werneckii	ethanolic (seeds)	–	–	0.312	[57]
Microsporum canis	chloroformic (flowers)	10	30	0.039	[52]
Mucor spp.	chloroformic (seeds)	–	–	1	[56]
Penicillium sp.	aqueous (roots)	15 000	13	–	[78]
Rhizopus sp.	aqueous (seeds)	10	9	1 073	[77]
Trichoderma sp.	chloroformic (roots)	50	8	–	[50]
	methanolic (leaves)	2	25	–	[79]
Trichophyton spp.	ethanolic (leaves)	30	22	–	[68]

In addition to the inhibitory effects on planktonic bacteria and fungi, *M. oleifera* seeds also have antimicrobial activity against biofilms of microorganisms of clinical interest, such as *S. aureus* and *P. aeruginosa* and the yeast *C. albicans* [81]. The biocompounds possibly involved in this activity are saponins, tannins, isothiocyanates and phenolic compounds, such as alkaloids, and, especially, flavonoids, which are present at high concentrations in seeds [63,75,76].

The antiviral potential of ethanol extract of *M. oleifera* seeds was reported against human herpesvirus-4, called the Epstein–Barr virus [14], and herpes simplex virus type 1 [82]. In addition, hydroalcoholic leaf extracts inhibit hepatitis B virus replication [83], and silver nanoparticles synthesized using *M. oleifera* seed extract as reducing and stabilizing agent have inhibitory activity against dengue virus type 2 [84]. The major biocompounds associated with antiviral activity are isocyanate and niaziminin [14]. Despite these reports, there are still few studies on the antiviral potential of *M. oleifera*.

3.9. Insect control

M. oleifera seeds, leaves and flowers present insecticidal, larvicidal and ovicidal activity against the vectors of the species *Anopheles stephensi* and *Aedes aegypti* [85,86]. The larvicidal activity of proteins, such as the water-soluble *M. oleifera* lectin obtained from seeds, has been demonstrated against organophosphate-resistant stage four *A. aegypti* larvae [86]. However, the environmental use of *M. oleifera* products against insects is still questioned, due to toxicity to the green alga *Scenedesmus obliquus* and the crustacean *Daphnia magna*, which are commonly used to evaluate the toxicity of pollutants [87,88]. In addition, according to Prabhu *et al.* [85], the bioefficiency of leaf and seed extracts of this plant can be demonstrated by spraying these extracts in breeding foci of *A. stephensi*, with larvicidal effect on different stages of development, as well as toxicity to the adult stage. Moreover, the aqueous extract of *M. oleifera* seeds is active against

A. aegypti larvae and the methanol root extract is effective for controlling the mosquitoes *Culex quinquefasciatus* and *Aedes albopictus*, vectors of nematodes and viruses of public health importance, respectively [85].

4. Use of *M. oleifera* in water and effluent treatment

Frequently, the water used for human consumption is subjected to physical and chemical procedures to make it drinkable. In a treatment station, water passes through coagulation and flocculation processes which use chemical coagulants, such as aluminum sulfate and ferric chloride. However, *M. oleifera* seeds can be used as natural coagulants to treat water effluents in urban and rural areas for clarification, reduction of microbial load and control of helminths, such as *Schistosoma mansoni* [89,90]. Moreover, seeds are also used to regulate the pH and control the microbial load in the treatment of water for human consumption [3]. *M. oleifera* seeds have been found to promote 90% reduction in turbidity and color of contaminated water, and 90%–99% reduction in the bacterial load [89,91].

The coagulant activity of *M. oleifera* seeds is associated with their water-soluble lectin, which is responsible for their flocculating and sedimenting properties. Seeds reduce turbidity, microparticle content and microbial load, ergo, they are suitable coagulant agents that can replace other commonly used coagulants, such as aluminum sulfate and other organo-synthetic polymers [89], which may be harmful to human, animal and environmental health. In a comparative study, *M. oleifera* seeds were cheaper and more effective than aluminum sulfate in reducing the turbidity of contaminated water, causing up to 95% decrease in turbidity, while aluminum sulfate caused an 80% reduction [91]. In 2001, Okuda *et al.* demonstrated that aluminum sulfate is an efficient coagulant only within a certain pH range, while *M. oleifera* seeds act independently of pH, constituting an additional advantage in poorer regions where controlling the pH of drinking water before the coagulation process is seldom possible [7].

The analysis of the chemical constitution of *M. oleifera* seeds reveals that the pulp contains low molecular weight proteins and the process of dissolving the pulp in aqueous solutions constitutes an active network that favors colloid aggregation and the adsorption of metal ions [3,92,93]. In a recent study, the effectiveness of coagulation/flocculation using *M. oleifera* seeds was demonstrated by the reduction of turbidity and chemical concentration of biocompounds [93]. In another research, the activity of the seeds in the biodegradation of benzene, toluene, ethylbenzene, p-xylene and o-xylene was identified, with the additional benefit of preserving medium pH and optimizing contact time, when compared to commercial activated charcoal, which is commonly used in cleaning systems of industrial effluent water [94].

Coagulant proteins from *M. oleifera* seeds are also able to reduce bacterial load. In this context, an isolated cationic protein is used for water treatment in some developing countries, hence, its use in antimicrobial therapeutic applications has been proposed. According to Shebek *et al.*, this *M. oleifera* cationic protein fuses the inner and outer membranes of *E. coli* cells [95].

In addition to seeds, biomass obtained from barks has also been suggested as a promising low-cost compound for water effluent treatment, as it has been shown to adsorb heavy metals from farm solid waste [96].

5. Applications of *M. oleifera* in aquaculture

Aquaculture in many countries is under strong political and social pressure to reduce environmental damage caused by intensive production systems, as a result of the use of chemicals and antibiotics for water treatment and disease prevention and control. The use of antimicrobial drugs poses a risk to human and animal health, as an intensive selective pressure for microbial communities, and favors environmental contamination by chemical residues [97]. In this context, *M. oleifera* potentially represents an alternative for aquaculture, since this plant is a source of coagulant, antioxidant, and antimicrobial agents [2,3,97,98]. Suspensions obtained from *M. oleifera* crushed seeds reduce organic matter and turbidity, due to the activity of the protein of the seed extract, which eliminates humic acids from water, improving water quality. In addition, as previously described, these seeds promote sedimentation or suspension and reduce bacterial load in contaminated water [99].

Some studies have reported the potential use of crude, ethanol and aqueous extracts of *M. oleifera* for water treatment and reduction of microbial load in fish and shrimp farming [3,99,100]. Antimicrobial effects of *M. oleifera* seed extracts have been demonstrated against *S. aureus*, *E. coli* and *V. cholerae* isolated from tilapia (*Oreochromis niloticus*) and the shrimp *Litopenaeus vannamei* farming [100]. Moreover, ethanol extract of leaves, pods and seeds, and chloroform extract of flowers have shown antimicrobial activity against microorganisms recovered from *Macrobrachium amazonicum* prawn farming, such as *V. cholerae* serogroups non-O1, non-O139, *V. mimicus* and *V. vulnificus*, as well as *Candida* spp. (*C. ciferri*, *C. famata*, *C. guilliermondii*, *C. parapsilosis* and *C. tropicalis*), and the dematiaceous filamentous fungus *H. werneckii* [58,101].

The antimicrobial potential of *M. oleifera* against bacteria and fungi recovered from aquatic animal farming deserves attention because these micro-organisms are potentially zoonotic opportunistic pathogens that may cause economic losses in aquaculture, as well as public health problems [72]. Most of these pathogens are not necessarily associated with the farmed animals, once they are also commonly found in the water where the animals are kept. Thus, it is important to emphasize that water acts as an important vehicle for the spread of these microorganisms, demonstrating the importance of properly treating water effluents from aquaculture [72].

Considering the potential applications of *M. oleifera* products in aquaculture, the toxicity of *M. oleifera* extracts to cultivated shrimp was investigated [102], showing that flower, leaf and stem extracts are not toxic to *M. amazonicum* prawns at concentrations of up to 200 mg/mL [102]. Therefore, the use of *M. oleifera* is advocated for aquaculture water treatment and microbial control, with reduced risks of harming human, animal and environmental health [99].

Moreover, besides the inhibitory effects of *M. oleifera* on different microorganisms, it has also been reported that crude extracts of *M. oleifera* leaves and seeds also inhibit microbial protease activity, which is responsible for muscular degradation of fish and shrimp during storage [103]. Thus, the potential use of these extracts as seafood preservatives to control their proteolysis and deterioration, during low temperature storage, has been suggested [103].

In this context, the perspective of using *M. oleifera* products in wastewater treatment and microbial control in aquaculture, as well as in seafood conservation, represents an environmental friendly approach to reduce the impacts of aquaculture on the environment and public health.

6. Ecological aspects of *M. oleifera*

M. oleifera is considered ecologically viable for its several applications as an alternative to chemically developed products, reducing the risks associated with the accumulation of non-biodegradable chemical compounds that are harmful to human, animal and environmental health. Among the potential applications of the plant, the coagulating, flocculating and adsorbing properties are remarkable for their ability to clean contaminated water, reducing its turbidity, toxicity and microbial load [7,9,89,91].

The treatment of water effluents with *M. oleifera* seeds has been proposed as a cheaper and more effective alternative to the use of aluminum sulfate, especially in rural areas, where the economical status and the accessibility to these products are key elements for maintaining the standards of fresh water treatment. Additionally, the use of *M. oleifera* seeds avoids the residual accumulation of chemical agents and maintains the optimum water pH values, after removing water turbidity, without requiring sophisticated equipments for pH dosing, nor special facilities for the treatment of drinking water [91,104]. After treating effluent water with *M. oleifera* seeds, the sludge obtained after sedimentation, along with the seeds, can be used as biofertilizers, representing an additional benefit in rural areas [89].

Other studies have also shown the biosorbent properties of the biomass of seed husks, seeds and pods of *M. oleifera* in water contaminated with lead, a heavy metal that is toxic to humans and animals and harmful to the environment [105]. Moreover, the use of *M. oleifera* seeds in the treatment of effluents from coffee fermentation has been proposed as an ecologically viable alternative, once coffee production generates residual water rich in organic nutrients that are harmful for aquatic ecosystems [106]. Based on its ability of treating water effluents, *M. oleifera* has become an alternative for the improvement of public health in socially neglected communities.

M. oleifera is considered an eco-friendly plant for its important applications in socio-environmental issues. This plant is resistant to drought and can be cultivated in low-quality soils, causing little alterations in the nutritional components of its different parts [2,3]. In this context, *M. oleifera* is a promising tree for several applications, such as battling malnourishment and hunger and providing accessibility to therapeutical resources of social relevance. Besides social and medical applications, *M. oleifera* oil can be used to sustainably produce a high quality biodiesel [107]. Therefore, *M. oleifera* is a sustainable resource for biotechnology, animal farming, medical sciences, and food industry, as it has mainly been cultivated as human and animal food source.

7. Leading-role of *M. oleifera* for strengthening traditional medicine in rural communities

Traditional medicine has been practiced by 80% of the world population, especially in developing countries [108], and its practice is responsible for 90% of the pharmacological discoveries in the world [108,109]. This practice relates knowledge and beliefs to plants with medicinal properties, based on regional traditions for the alternative treatment of diseases, providing population with greater accessibility to treatment and well-being, especially for those that are devoid of proper public health conditions. Some studies have shown that publicizing and appropriating the practices of traditional medicine by multidisciplinary health teams may reduce the social losses associated with the lack of public policies to promote health, especially for the socially neglected population [110,111].

In this perspective, *M. oleifera* reinforces the option of using alternative medicine in disease control, as the plant adapts to the most inhospitable climatic conditions of the poor regions of the world [108]. In the semiarid regions of Brazil, for instance, *M. oleifera* is well adapted and can be part of the alternative vegetable groups cultivated for the improvement of health in communities where poverty persists, with limited access to drinking water and unavailable public health resources. Moreover, *M. oleifera* is a relevant food source for the natural nutrition of the tropics that provides health benefits, as source of proteins, essential minerals and antioxidants [2,3,10,13,22,25,112], hence, it becomes a powerful strategy to battle global malnourishment, especially among children and lactating mothers [1,3,5,25,80,111]. Recent studies reveal that the consumption of *M. oleifera* leaves with acidulated fruit sauces improves the bioavailability of iron and zinc, representing a cheap solution for the deficiency of these ions in the diet of socially neglected population [5,113]. Therefore, considering the multiple uses of *M. oleifera*, it is known as the miraculous tree [5,14].

Concerning the ability of *M. oleifera* to improve water quality and promote the cure of several diseases, including the neglected diseases of the tropics, the great social contribution of this tree is evident, as it promotes the improvement of life quality of the socially neglected population that does not have access to public health, by finding solutions for treating and/or preventing their diseases with traditional medicine. In this context, the encouragement for the cultivation of *M. oleifera* trees in rural communities may bring benefits to local health and reduce the expenditure with the treatment of neglected diseases, or, as they are popularly known, diseases of poverty.

8. Final considerations

This review summarized the recent research advances for the use and applications of *M. oleifera* extracts in different areas of biosciences, demonstrating the versatility of this plant. Based on the scientific reports, *M. oleifera* is an inexpensive, eco-friendly and socially beneficial alternative, especially for the socially neglected population, suffering from poverty and malnutrition and for those who have limited access to technological resources.

Conflict of interest statement

We declare that we have no conflict of interest.

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