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A Review of *Moringa oleifera* (Miracle tree) and its Potential Phytochemistry, Traditional, Health Benefits, Pharmacological Applications

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Abstract: *Moringa oleifera L.* (Moringaceae-Family) is one of the species that has a wide range of Folk, traditional, nutritional, industrial, and medicinal values. In folk medicine, this plant is used to treat pain, liver disease, heart disease, ulcers, wound healing, disinfectant, fever, constipation, asthma, and to expel a retained placenta.*M. oleifera* plant parts were tested for various pharmacological activities viz, antioxidant, anti-cancer, antimicrobial, covid sars-2,anti-diabetic, antibiotic, anti-venom, antiobesity, anti-ulcer/gastroprotective, cardiovascular, fertility and anti-fertility, anti-inflammatory, anti-asthmatic, hepatoprotective, oral dental resistant, other medicinal activities. This review explores the health benefits and applications of *Moringa oleifera* traditional, phytochemistry, pharmaceticological activity, commercial, and important medicinal properties.

Keywords: antioxidant; anti-venom; pharmacology; *traditiona*; *Moringa oleifera*.

1. Introduction

Moringa oleifera, the "Miracle tree", thrives in almost all tropical and subtropical regions worldwide but is believed to be native to Afghanistan, Bangladesh, India, and Pakistan [1]. Moringa has drought tolerance [2]. Studies have exhibited that *M. oleifera* is among the cheapest and most reliable substitutes for good nutrition [3]. Almost all parts of the tree are used for their essential nutrients. *M. oleifera* leaves are rich in beta-carotene, minerals, calcium, and potassium [4]. The dried leaves contain 70% oleic acid, making them ideal for making humectants [5]. The powdered leaves are used to prepare several beverages, among which "Zija" is the most popular in India [6]. The bark of the tree is considered very effective in the treatment of various disorders such as ulcers [7], toothache [8], and hypertension [9]. However, the roots have a role in the treatment of toothache [8], helminthiasis [10] and paralysis [11]. Flowers are used to treat ulcers and enlarged spleen and
produce aphrodisiacs [12]. This tree is believed to have incredible properties in treating malnutrition in children and nursing mothers [3]. The present review summarizes updated insights into the pharmacological activities, Universal research analysis, phytochemistry, and ethnomedicinal properties of *M. oleifera*.

2. Traditional/Ethnomedicinal Properties

People worldwide have included *M. oleifera* in their diet since ancient times due to its important therapeutic values. Different medicines prepared from the plant are said to have ethno-medicinal properties to cure diseases and have been used for centuries. Almost every part of this plant (leaf, flower, pod, seed, seed oil, bark, gum, and root) is used to treat some diseases, as presented in Figure 1,2 [13-15].

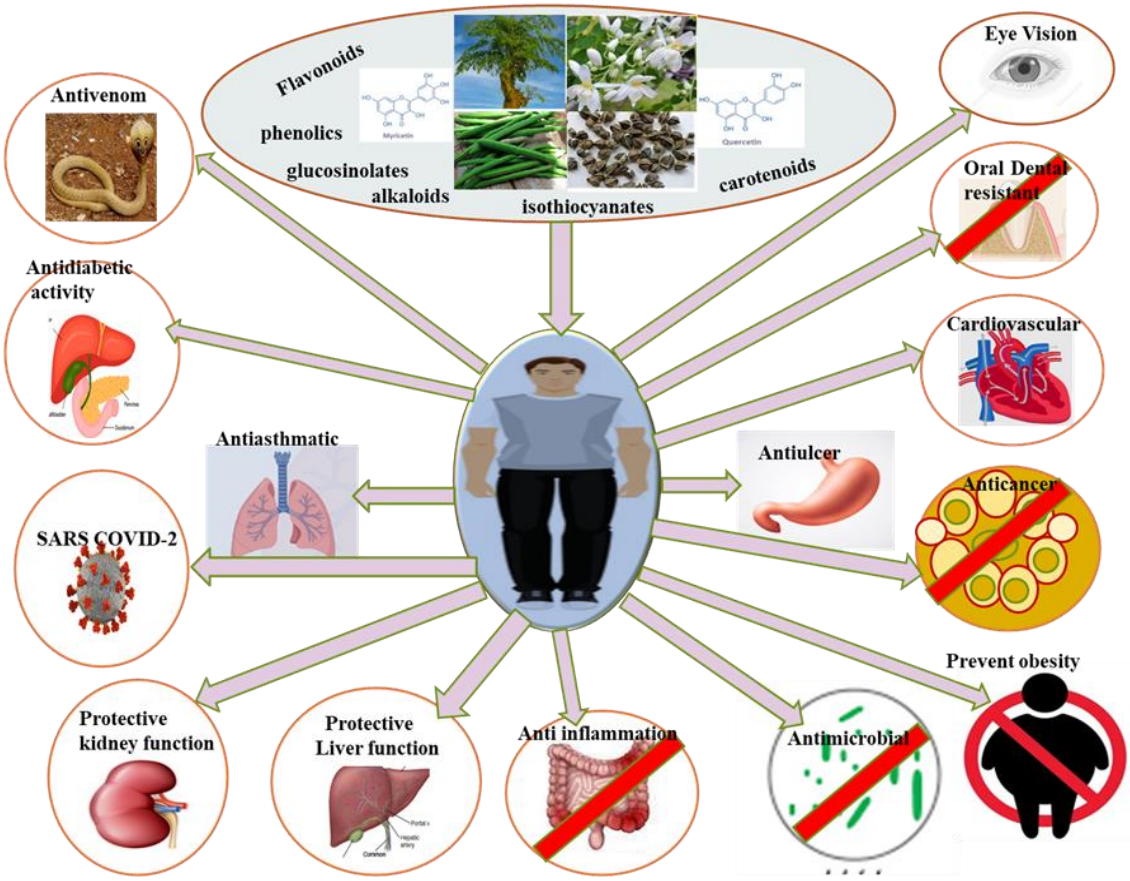

Figure 1. An overview of *Moringa oleifera* health uses and key mods of action.

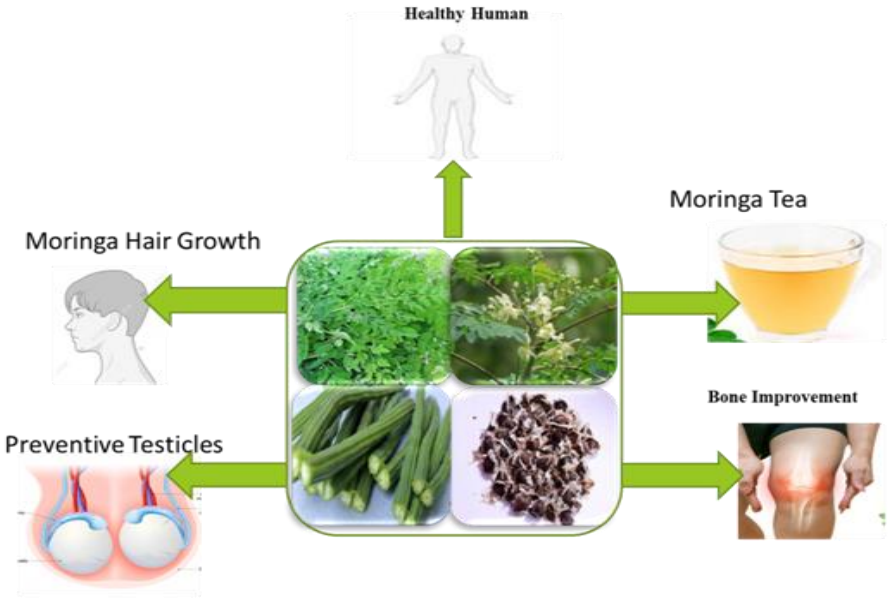

Figure 2. An overview of *Moringa oleifera* health benefits and organ improvements.

Applications of *M. oleifera* are found in pathological changes such as antihypertensive [16], anti-diarrheal [17], and diuretic [18]. Moringa is also used for dysentery [19] and colitis [20]. Poultices prepared from Moringa leaves quickly remedy inflammatory conditions like glandular inflammation, headache, and bronchitis. The pods treat hepatitis and relieve joint pain. The roots are regularly used for kidney stones [21], liver diseases [22], inflammation [23], ulcers [24], and pain associated with ear and teeth [25]. The stem bark treats wounds and skin infections [26]. Indians apply gum extracted from this plant to treat fever, and it is also used to induce abortions [27]. The seeds of the plant act as a laxative and are used in the treatment of tumors and prostate and bladder problems [28]. The seeds show promise for treating arthritis by reversing oxidative stress and reducing inflammation [29]. Products made from plant leaves benefit nursing mothers and malnourished children and improve people's general health. Leaves are useful in treating insomnia [30] and wounds [31]. Moringa is incredibly used in the cosmetic industry nowadays, and in ancient Egyptian history, it was used to make skin ointments [32].

3. Bioactive Components and Pharmacological Applications of *Moringa oleifera*

It is well known that scientists are shifting their focus to finding alternatives to bioactive compounds, especially those found in medicinal plants [33–35], due to the rapidly growing drug resistance. Due to 'Moringa's high resistance to dry conditions and the fact that every part of the tree is valuable, its application varies from medicinal use and functional food production to biodiesel production and water purification [36]. The most important bioactive compounds of *M. oleifera* include phenolic compounds, carotenoids, alkaloids, glucosinolates, folates, tannins, saponins, isothiocyanates, and fatty acids [37].

Flavonoids (apigenin, myricetin, quercetin, luteolin, kaempferol), lignans (secosolariciresinol, isolariciresinol, medioresinol, epiphenoresinol glycosides) and phenolcarboxylic acids and their derivatives phenolics (coumaroylquinic, caffeoylquinic, feruloylquinic acids)compounds found in the Moringa leaves. Hydroxyl groups are responsible for antioxidant activity [37–39].

Carotenoids are natural pigments in plants and foods and are responsible for protecting against cellular damage by acting as antioxidants. In research conducted by Saini (2014), six major carotenoids were found, including 13-Z-lutein, all-E-lutein, all-E-luteoxanthin, all-E-zeaxanthin, all-E-β-carotene and 15-Z-β-carotene [40].

Various secondary metabolites, such as glucosinolates, alkaloids, and isothiocyanates, are found in *Moringa oleifera* leaves. Myrosinase, an enzyme found in the idioblasts of the plant cell, is activated when the plant is damaged, processed, harvested, or chewed and produces β-D-glucose hydrolysis when the pH is neutral, resulting in the formation of isothiocyanates (I.T.C.s), thiocyanates, sulfates, and nitriles. The last-mentioned compounds give plants a strong taste and smell and have biological properties such as antifungal and antibacterial [41,42].

In addition, proteins and peptide fractions with a high nutritional profile have been investigated as attractive molecules in Moringa. These compounds showed several biological activities such as antioxidant, anti-cancer, antibacterial, hepatoprotective, and anti-diabetic. For example, aromatic and hydrophobic amino acids of peptides are responsible for antioxidant activity. Also, in *Moringa oleifera* seeds, researchers reported the presence of 7 essential and 10 nonessential amino acids, glutamic acid being the highest value (22.71g/100g protein), followed by arginine (15.78g/100g protein) [43-45].

3.1.Antioxidant potential of Moringa.

Generally, the human body maintains a balanced ratio between oxidants and antioxidants. Due to external stresses in daily life, the animal body continuously produces reactive oxygen species [46]. Antioxidants are produced by body cells to balance the body against these free radicals. Any imbalance in these systems is called oxidative stress. It can be caused by many diseases or imbalances in the regular physiological system [47]. In the acute phase, oxidative stress leads to cell damage, leading to different chronic diseases [48]. Kattapagari *et al*. [49] reported that antioxidants' positive feedback prevents further damage in chronic conditions. Regarding antioxidants, the Moringa tree can be considered an excellent source as it exhibits higher productivity than conventional plant-derived sources. Extracts from the Moringa tree are capable of producing a variety of compounds. Moringa leaf extract has shown antioxidant activity both in vivo and in vitro owing to its flavonoids and phenolic content [50–57]. Methanol and ethanol extracts of *M. oleifera* leaves of Indian origin have the highest antioxidant activity, with 65.1% and 66.8%, respectively [58].

3.2. Anti-cancer potential of Moringa.

Besides the antimicrobial effect of Moringa leaves, seeds, and roots, Moringa has also been reported for its antiproliferative activity. Various extracts of Moringa induced reactive oxygen species in cancer cells, resulting in apoptosis. Moringa extracts also inhibit caspase 3 and 9 in the apoptotic pathway [59– 61]. Tiloke *et al*. [61] reported the stimulatory effect of crude extract of *Moringa oleifera* on enzymes such as glutathione S transferase, which inhibits the antioxidant system and makes it a potential anti-cancer agent. Besides this production of oxidative stress in a mouse model, Moringa extract was reported to inhibit human hepatocellular carcinoma (HepG2) cells and A549 cells.

3.3. Antimicrobial potential of Moringa.

Antibiotic resistance is a vital problem of the present era. Due to the indiscriminate use of antibiotics, most infectious agents are resistant to available antibiotics, which is responsible for permanent resistance to chemotherapeutic agents and antibiotics. There is a need to find new antimicrobial agents with multiple activities. Moringa leaves contain various bioactive compounds, and many of their extracts have been well-documented for their antibacterial, antifungal, antiviral, and antiparasitic properties [62–66]. However, few reports suggest that Moringa leaves contain chemical metabolites. Pterygospermin, moringine, and benzyl isothiocyanate were responsible for the antimicrobial activities, with significant reports available in the crude leaf extract. Apigenin is considered a future green chemical to fight against the problem of antibiotic resistance because the enhanced activity of some apigenin derivatives is very effective against both Gram-positive and Gram-negative bacteria such as *Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa* [67].

3.4. Moringa against Covid SARS-2 infections.

Surprisingly, in light of the global and striking circumstances surrounding the coronavirus, scientists advised removing the heat with a large amount of bitter and cold herbs to detoxify the infection in its early stages, as well as to cool the blood and quickly remove blood stasis in the middle and late stages [68]. *Moringa oleifera* leaf has a sweet and bitter taste and is a cooling, venting, and dehumidifying stimulant with successor impact. Because of this,

it is an excellent choice for treating general immune abnormalities deep in disease. When integrated with traditional medicine, it is possible to hypothesize adequate and supportive treatment of coronavirus infection. Kaempferol, pterygospermin, morphine, quercetin and apigenin play an important role in moringa components. Apigenin has high anti-SARS activity against MPro-Cov-2 [69]. In a molecular docking simulation investigation, three flavonoids, kaempferol, isorhamnetin, and apigenin, demonstrated excellent binding of empathy stable protein-ligand complexes with high binding energy against the recognized SARS-CoV-2 Mpro inhibitor baicalein [70]. Moringa flavonoids, rutin, and isorhamnetin-3-O-rutinoside are potent inhibitors of SARS-CoV-2 selective target major protease (Mpro), as reported in a dynamic simulation study, which was confirmed by in vivo and in vitro studies [71].

3.5. Anti-diabetic potential of Moringa.

Aqueous extracts exhibit anti-diabetic effects in rats by controlling blood glucose levels, proteins, sugar, and hemoglobin [72–75]. The leaves of the plant were found to lower glucose levels within three hours of ingestion, but not more than the standard drug glibenclamide. When administered orally, Moringa seeds contain insulin-like proteins with insulin-like antigenic epitopes and exhibit antihyperglycemic activity [76]. Plant leaf extracts have anti-diabetic activity as they increased CAT and MDA levels, reduced FPG levels, hemoglobin levels, LDL-C, and VLDL-C in type 2 diabetic patients, and, most importantly, increased insulin levels in healthy subjects [77]. The seed extract of the plant reduced the LPO level and amplified the antioxidant effect induced by streptozotocin in rats. The seed extract was also able to reduce IgG, IgA, and IL-6 parameters and pancreatic β-cell activity, and the biochemical compound responsible for this effect was suggested to be quercetin, glucomoringin, chlorogenic acid, kaempferol, and isothiocyanates [78].

3.6. Antibiotic potential of Moringa.

The preponderance of evidence–classical science and extensive anecdotal evidence – is overwhelming. Scientific evidence has been available for over 50 years, even though much of it is completely unknown to Western scientists. In the late 1940s and early 1950s, a team from the Department of Biochemistry at the University of Bombay (BR Das), the University of Travancore (PA Kurup), and the Indian Institute of Science, Bangalore (PLN Rao) identified a compound called pterygospermin [79], which they reported readily splits the mosilyan compound into two molecules [80-83]. Benzyl isothiocyanate was earlier understood to have antimicrobial properties. This group identified pterygospermin and performed a detailed and elegant characterization of its antimicrobial mechanism in the mid-1950s. Although others have shown that pterygospermin and its isolated Moringa plant extracts are antibacterial against various microorganisms, identifying pterygospermin as an artifact of isolation or structure determination has been challenged [84].

3.7. Anti-venom potential of Moringa.

The leaves of the plant extract are effective against *Naja nigricolis* (a species of snake) venom in mice. This snake's venom contains potent neurotoxins that cause the degradation of phospholipids in the plasma membrane, impair the normal neurotransmission process, and cause hemolysis and hemorrhage. The results showed that Moringa extract effectively treated

severe anemia, and a significant increase in micronucleated polychromatic erythrocytes was observed in mice treated with *M. oleifera* [85].

3.8. Antiobesity potential of Moringa.

In one study, oral treatment with leaf powder of *M. oleifera* for nearly 49 days notably reduced body mass index (BMI) in rats suffering from hypercholesterolemia [86]. The mechanistic approach behind this is the downregulation of the mRNA expression of the hormones resistin and leptin and the simultaneous regulation of the adiponectin gene in rats[87]. A present study revealed a mechanistic approach to the antiobesity effect of *M. oleifera*. The plant notably improved lipid profile by decreasing body weight. It also up-regulated genes related to adipogenesis, increased glucose tolerance, and decreased levels of hormones such as vaspin, leptin, and resistin[88].

3.9. Immunomodulatory potential of Moringa.

The methanolic extract of the plant contains active components such as isothiocyanate and glycoside cyanide, which exhibit immunostimulatory activity and effectively improve immunity. A recent review article suggests that different biochemical compounds are used to treat different immune-related disorders such as cancer, hypertension, and diabetes, thereby enhancing host immunity [89].

3.10. Hematological potential of Moringa.

M. oleifera has demonstrated its notable benefits in hematological activities. A randomized, double-blind study suggests that aqueous leaf extract improves women's low hemoglobin levels (8–12g/dL) [90]. Another study found that *M. oleifera* leaves, when taken by healthy volunteers for 14 days, significantly improved platelet counts [87].

3.11. Anti-ulcer/gastroprotective potential of Moringa.

Bisphenols and flavonoids found in Moringa leaves showed decreased ulcer index, duodenal ulcer, and stress ulcer in an ibuprofen-induced gastric ulcer model [87]. Moringa extract was shown to notably reduce free radicals, neutralize the acidity of gastric juice, and have a protective effect on the development of gastric ulcers [91]. The presence of flavonoids in the plant has been shown to protect against ulcer formation by increasing capillary resistance and improving microcirculation, resulting in reduced cell injury [92].

3.12. Cardiovascular potential of Moringa.

A freeze-dried aqueous and alcoholic extract of *M. oleifera* showed cardioprotective activity in animals stimulated with myocardial infarction by isoproterenol [93]. Chronic treatment of *M. oleifera* was effective in isoproterenol-induced hemodynamics and improved the levels of enzymes such as SOD, catalase, lactase dehydrogenase, glutathione peroxidase, and creatine kinase [93]. Butanol extract proved a wealthy antioxidant source in rats with isoproterenol-induced cardiac necrosis. Also, it was found to significantly reduce inflammation levels and myocardial necrosis owing to the compound N-α-rhamnopyranosyl vincosamide [94]. Moringa leaves significantly reduced cholesterol levels by showing a protective effect on

hypertensive rats. The active components responsible for this activity were niazirmin A, niazirimin B, and niazimincin[87].

3.13. Fertility and anti-fertility potential of Moringa.

Among the list of beneficial effects of Moringa, various parts of the plant have fertility and abortion-stimulating properties. Aqueous extract at doses of 200 and 400mg/kg has been found to have high abortifacient and anti-fertility effects [95]. Recent studies on hot and cold extracts of *M. oleifera* leaves propose that consumption of Moringa before, after, and during pregnancy may adversely affect fetal development by causing severe contraction of the uterine wall [96].

3.14. Anti-inflammatory potential of Moringa.

A significant anti-inflammatory effect was observed in various parts of *M. oleifera* (leaf, pods, flowers, and roots). A compound isolated from Moringa (4-[2-o-Acetyl-alpha -l-rahamnoslyloxy) benzyl] thiocynate was observed to have nitric oxide inhibitory activity and was subsequently found to be effective in Raw264.7 cell lines [97]. A compound obtained from *M. oleifera* roots, known as aurnatimide acetate and 1,3-dibenzylurea, inhibits TNF-α production [98]. Active compounds such as alkaloids, flavonoids, tannins, phenols, vanillin, carotenoids β-sitosterol, and moringin have anti-inflammatory properties [87].

3.15. Anti-asthmatic potential of Moringa.

M. oleifera seed kernel improved the treatment of bronchial asthma patients and their concurrent respiratory functions without showing any adverse effects [99].

3.16. Hepatoprotective potential of Moringa.

The characteristics of protection against liver damage are reported in Moringa leaf extracts [100], and they also help in reducing liver fibrosis [101]. Among the numerous flavonoids in Moringa (quercetin, kaempferol, isoquercetin, rhamnetin, etc.), quercetin in moringa flowers is thought to be responsible for the hepatoprotective effect [102]. Methanolic extract at low dose showed significant changes in the hepato-renal and hematological profile of serum aminotransferase concentration, plasma cholesterol level, alkaline phosphate, bilirubin, and serum LPO levels. However, a higher extract dose altered total bilirubin, blood urea nitrogen, and non-protein nitrogen levels and decreased clotting time [103]. The seeds were also fruitful against carbon tetrachloride-induced liver fibrosis, as evidenced by decreased serum aminotransferase activity and globulin levels [104]. Continuous treatment with the extract of this plant for about 21 days significantly reduced dietary liver damage, and this effect was attributed to the alkaloid, quercetin, kaempferol, flavonoids, ascorbic acid, and benzyl glucosinolates present in this plant [105].

3.17. Oral dental resistant potential of Moringa.

A study reported the efficacy of *M. oleifera* crude extract in protecting tooth extraction sockets in Cavia copaea when administered by injection [106]. Another 2 studies reported the potency of *M. oleifera* on surface enamel and dentin remineralization during in vitro testing of extracted teeth [107,108]. *M. oleifera* leaf extracts were antimicrobials in the form of toothpaste

and mouthwash when tested against microorganisms[109]. My analysis included in vivo experiments on humans and animals (mice and guinea pigs) and in vitro studies on oral pathogens and dental extracts. The results of this analysis suggested that *M. oleifera* leaf extract effectively controlled oral conditions. Its leaves were often used for their high concentration of bioactive compounds compared to other parts of the plant, although their contents varied widely depending on climatic factors [109,110]. Vitamins, polyphenols, phenolic acids, phytates, glucosinolates, tannins, flavonoids, alkaloids, carotenoids, oxalates, saponins, and glucosinolates all occur in the leaves of the plant [111–116]. The leaves are readily available and accessible, making them an excellent choice for medicinal use.

According to the results of this study, statistical analysis of clinical trials, i.e., invivo studies, showed significant effects of *M. oleifera* extract in study subjects suffering from different oral diseases such as inflammation, periodontitis, gingivitis, oral cancer, and root canal remineralization during administered intravenously by injection or through toothpaste and mouthwash. An overall reduction in the incidence of oral diseases was observed. Due to its anti-bacterial, antifungal, anti-cancer, anti-inflammatory, and antioxidant properties, *M. oleifera* has been proven useful in oral hygiene[117]. The therapeutic efficacy of *M. oleifera* is attributed to its phytochemical constituents, such as alkaloids, sterols, saponins, flavonoids, and tannins [118]. Compounds such as glycosides, glucosinolates,chyserol-1-9-octadecanoate, and isothiocyanates have anti-cancer activities [119–121]. Anti-inflammatory, antimicrobial, and antioxidant activities are mostly controlled by phenolic compounds [122–125]. The presence of more than 90 various chemical compounds makes this plant a powerful herbal medicine [126].

3.18. Other medicinal uses of Moringa.

M. oleifera pod constituents contain bioactive compounds with anti-inflammatory activity that may contribute to ameliorating the pathogenesis of inflammation-related chronic diseases [127–129]. Ovalbumin-induced airway inflammation in guinea pigs with *M. oleifera* seeds treated with n-butanol extract showed a positive effect as an anti-inflammatory agent [130]. Moringa has been found to ameliorate and benefit the condition against viral infections. Leaf extracts showed selective and potent inhibition of early stages of HIV-1 infection [131].On the contrary, it can help decrease eye problems in children. *M. oleifera,* the hydroalcoholic extract of fruits, showed antihepatitis B virus (HBV) activity [132]. Moringa is a potential source of vitamin A [133], which has great potential to control dietary deficiency of vitamin A source food.

4. Conclusions

Moringa oleifera is a prominent source of nutrients and antioxidants. Still, there is a knowledge gap regarding the potential uses of Moringa as a food supplement and fortification. Moringa has enormous potential uses but is much less explored. It can be utilized to make foods that could be a step towards curbing malnutrition. The published literature gives the total scenario of the chemical constituents, nutritional content, potential uses, and pharmacological activities of the plant. The identification, isolation, and standardization of plant extracts may be considered for detailed studies, which can be useful for further developing promising food products with health benefits and nutrients to cure different lifestyle-related diseases as well as malnutrition.

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Conflicts of Interest

The authors declare no conflict of interest.

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