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REVIEW PAPER

Moringa marvel: navigating therapeutic insights and safety features for future functional foods

Sonu K. Shivanna[1] · N. Laxmana Naik[2] · Basavaprabhu H. Nataraj[2] · Priyanka Singh Rao[2]

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Abstract

Moringa oleifera, commonly known as the drumstick tree or horseradish tree, has long been recognized for its nutritional and therapeutic properties. This article revisits the therapeutic and safety aspects of Moringa while exploring recent trends in its utilization in the formulation of functional foods. A comprehensive analysis of the literature reveals the rich nutritional profile of Moringa, encompassing vitamins, minerals, and bioactive compounds with potential health benefits. The therapeutic properties, including anti-inflammatory, antioxidant, antidiabetic, ACE inhibition, and antimicrobial activities, are discussed in the context of contemporary research findings. Additionally, safety considerations, dosage, and potential adverse effects are addressed, providing a balanced perspective on the consumption of Moringa. The second focus of this article is the emerging trend of incorporating Moringa into functional foods. The recent surge in interest is attributed to its diverse bioactive components, which can enhance the nutritional value and health-promoting qualities of food products. Examples of functional food formulations are explored to illustrate the versatility of integrating Moringa into modern dietary practices. By revisiting the therapeutic and safety aspects of Moringa and exploring its recent applications in functional foods, this article contributes to a nuanced understanding of the multifaceted role of this plant in promoting health and wellness. The synthesis of traditional knowledge with contemporary scientific insights provides a foundation for informed decision-making regarding the utilization of Moringa in functional food formulations.

Keywords *Moringa oleifera* · Malnutrition · Bio-functional properties · Phytoconstituents · Toxicity · Livestock · Feed

Introduction

The surge in functional food consumption within the human diet is driven by an increasing focus on promoting healthy lifestyles, leading to significant expansion and innovation in the global functional food market [1, 2]. Functional foods, characterized by the incorporation or enhancement of nutrients offering health benefits through modulation of physiological functions, immune response augmentation, or disease risk mitigation, have become a key area of healthcare research [2, 3]. Notably, medicinal plant-based functional foods and plant-derived dietary components have re-emerged as prominent subjects of investigation, leveraging their therapeutic advantages and nutritional contributions [4].

Among these medicinal plants, *Moringa oleifera*, a cruciferous plant in the Moringaceae family, stands out with enormous functional value. With a historical usage dating back to 150 B.C., Moringa is recognized for its health benefits and is extensively utilized across more than 80 countries [5]. *M. oleifera*, among the 13 cultivars of Moringa, is the most researched and widely utilized species due to its phytochemical and pharmacological properties related to human health.

It is worth mentioning that, *M. oleifera* is traditionally employed in global traditional medicine to address diverse

✉ Sonu K. Shivanna
sonuksgowda@gmail.com; sonu.ks@icar.gov.in

✉ N. Laxmana Naik
laxmandcnaik@gmail.com; Laxmana.N@icar.gov.in

Basavaprabhu H. Nataraj
basavaprabhu73@gmail.com

Priyanka Singh Rao
priyankasinghrao@gmail.com

[1] Dairy Chemistry Division, ICAR-National Dairy Research Institute, Karnal, Haryana 132001, India

[2] Dairy Chemistry and Bacteriology Section, ICAR-National Dairy Research Institute, Southern Regional Station, Bengaluru, Karnataka 560030, India

health conditions, including scurvy, intestinal worms, bronchitis, infections, abnormal blood pressure, and diabetes. Moringa has transcended its indigenous roots in the Indian subcontinent and is now extensively cultivated in Asia, Africa, and Europe to adapt to various climates and soil conditions [6]. Moringa witnessed a significant rise in popularity in the 1990s, emerging as a highly valuable crop, especially in underdeveloped nations. Moringa has earned it colloquial names like "man's best friend," "the miracle tree," and "medicine chest" due to its notable nutritional and health benefits [7, 8]. It founds extensive applications across various sectors such as food, industry, agriculture, and medicine [9, 10].

Addressing food security concerns, Moringa's leaves, pods, and seeds are rich sources of nutrition, with dried Moringa leaf powder surpassing other food items in nutrient content, containing notably higher levels of iron, calcium, vitamin A, protein, and vitamin C [11].This nutritional richness extends to diverse bioactive components, such as functional peptides, carbohydrates, phenolic acids, flavonoids, carotenoids, tocopherols, fatty acids, and minerals. The myriad phytoconstituents of *M. oleifera* confer antioxidant, anticarcinogenic, antidiabetic, anti-inflammatory, and antimicrobial activities [11].

Moringa oleifera's integration into functional foods worldwide is attributed to its substantial medicinal value coupled with its resilience to harsh climatic conditions [12]. Its edible components prove beneficial for both human immunity and livestock feed [13]. *M. oleifera* food products outshine other items in terms of its macro and micro nutrient [14]. Additionally, Moringa-enriched foods enhance antioxidant capacity, fortify immunity, protect against oxidative stress, and reduce the incidence of diseases threatening human health [15]. With this background, the aim of this review lies in its comprehensive exploration of Moringa's therapeutic insights and safety features specifically tailored for its application in future functional foods. Unlike previous studies which may have focused solely on either the therapeutic or safety aspects of Moringa, this research uniquely integrates both dimensions. It delves into the botanical, taxonomic, and nutritional aspects of Moringa, shedding light on its potential role in addressing malnutrition and promoting health. Additionally, the critical examination of recent applications in functional foods underscores the novelty, as it emphasizes the importance of nutritional enhancement, sensory attributes, and shelf life extension. Furthermore, the consideration of safety features ensures a thorough evaluation for human consumption, highlighting the study's innovative approach towards establishing Moringa as a versatile and promising ingredient in the realm of functional foods.

Botanical and taxonomic aspects of *M. oleifera*

M. oleifera Lamarck, a rapidly growing, evergreen or deciduous tree, belongs to the Moringaceae family within the Moringa genus. Table 1 provides the taxonomic classification. Among the 13 species in the Moringa genera, *M. oleifera* is the most extensively cultivated and studied, standing out from others like *M. arborea*, *M. longituba*, *M. rivae*, *M. stenopetala*, *M. pygmaea*, *M. concanensis*, *M. borziana*, *M. drouhardii*, *M. ruspoliana*, *M. ovalifolia*, *M. hildebrandtii*, and *M. peregrine* [16]. Commonly referred to as the drumstick tree (due to its long, slender, triangular seed pod), horseradish tree (because of the root's horseradish-like taste), ben oil tree, or benzolive tree (for its oil extracted from seeds), *M. oleifera* has various regional names in India, such as *Shigru*, *Sahijjan*, and *Munaga* in Hindi, *Sajina* in Bengali, *Sevaga* in Marathi, *Sobhanjana* in Sanskrit, *Muringa* in Malayalam, *Sehjan* in Urdu, *Munagai* in Tamil, *Nugge mara* in Kannada, *Munaga kaya* in Telugu, *Saragyo* in Gujarati, *Sujuna* in Orissa, *Surjana* in Punjab, and Horseradish tree or drumstick tree in English.

While native to northern India, Moringa is widely utilized in the southern part of India and distributed across other Asian countries such as Pakistan, Bangladesh, Afghanistan, the sub-Himalayan regions, and continental countries including America, Africa, Europe, and Oceania [17]. With historical usage by ancient Romans, Greeks, and Egyptians, Moringa is known for its drought resistance [18], adaptability to a wide soil pH range (pH 5.0–9.0), preference for well-drained sandy or loamy soil with a pH of 6.3–7.0, and ability to thrive in temperatures between 25 and 35 °C, tolerating up to 48 °C in the shade and surviving light frost. Moringa trees require minimal chemical fertilizer, exhibit pest resistance [19], and reach a height ranging from 5 to 10 m [20]. The tree is characterized by feathery and light green leaves (30–60 cm in length), growing mostly at the branch tips.

Table 1 Taxonomy of *Moringa oleifera*

Taxonomy categories	Details
Kingdom	Viridiplantae
Subkingdom	Tracheophyta
Super division	Spermatophyta
Division	Magnoliophyta
Class	Eudicotyledons
Subclass	Rosids
Order	Brassicales
Family	Moringaceae
Genus	Moringa

Source Montesano et al. [151]

The flowering typically commences within the first 6 months after plantation, occurring once a year in seasonally cold regions, twice a year, or throughout the year in regions with constant seasonal temperature and continuous rainfall [21].

The aromatic, bisexual, zygomorphic, and pentamerous flowers (average length 1.0–1.5 cm, breadth 2.0–2.5 cm) with unequal creamy or white petals are a distinct feature [22]. The fruit, a three-valve capsule with a length ranging from 10 to 100 cm, is commonly referred to as "pods" due to their resemblance to drumsticks. The immature pods are green, turning brown upon maturation, and split along each angle to expose the seeds fully. The capsule houses 15–20 rounded seeds, approximately 1 cm in diameter, surrounded by three papery wings up to a length of 2.5 cm. The whitish-grey bark or stem is encased in thick cork. Triangular or round in shape, the seeds are enclosed within pods, with a semipermeable brownish seed hull.

Nutritional value of Moringa

The Moringa plant, encompassing its leaves, pods, seeds, flowers, roots, and bark, offers nutritional benefits for both human and livestock well-being. Serving as a valuable resource to enhance nutritional security and fortify immune systems, Moringa stands out as a rich source of macronutrients, micronutrients, and diverse phytoconstituents, contributing to its exceptional nutraceutical profile. With an impressive array of over 90 nutritional compounds, including proteins, carbohydrates, lipids, and dietary fibers [23], Moringa's versatility extends to various culinary applications. Its leaves, green pods, flowers, and toasted seeds are utilized as vegetables,roots serve as spices; seeds find use in cooking and cosmetics as oil; and Moringa fruits can be consumed whole, either cooked (boiled) or pickled.

Moringa leaves

Abundant in proteins, minerals, vitamins, and beta-carotene, Moringa leaves also house bioactive components such as dietary fiber, phenolic acids, flavonoids, carotenoids, alkaloids, glucosinolates, isothiocyanates, saponins, tannins, phytates, and oxalates [24]. Surpassing other food items in nutritional content, *M. oleifera* provides 9 times more protein than yogurt, 17 times more calcium than milk, 7 times more vitamin C than oranges, 10 times more vitamin A than carrots, 25 times more iron than spinach, and 15 times more potassium than bananas [11]. The leaves, with approximately 31.82% crude protein, 2.57% crude fat, 10.30% crude fiber, 11.50% ash, and 38% carbohydrates, boast significant levels of calcium, total phenolic content (TPC), total flavonoid content (TFC), and tannins. Leaves also contain a significant amount of iron (17.5 mg/100 g DW), and they have superior bioavailability than ferric citrate, making them useful in addressing iron deficiency [25]. Nevertheless leaves are also rich in poly unsaturated fatty acid (PUFA) such as C18:3 (49–59%) and C18:2 (6–13%). Palmitic acid (C16:0) is the major saturated fatty acid (SFA) and contributes to 16–18% of the total fatty acids in leaves.

Moringa pods

The immature pods stand out as the most esteemed and extensively utilized parts of the tree. They boast exceptional nutritional value, encompassing all essential amino acids, numerous vitamins, and various other nutrients. These tender pods can be consumed in their raw state or prepared akin to green peas or green beans. In contrast, mature pods are commonly fried, imparting a flavor reminiscent of peanuts. Notably, immature pods contain approximately 46.78% fiber and about 20.66% protein [26]. Due to their fibrous nature, these pods are valuable for addressing digestive issues and preventing colon cancer [26]. Analysis of the immature pods revealed comparable levels of palmitic, linolenic, linoleic, and oleic acids. Amino acid content is reported as 30% in pods, 44% in leaves, and 31% in flowers. Additionally, the pods yield a non-drying, edible oil, constituting 38 to 40% of the total, known as Ben oil or Behen oil [27]. This oil possesses clarity, sweetness, and an odorless quality, demonstrating high stability against rancidity [28].

Moringa seeds

Seeds serve as a valuable source of fat, sharing a fatty acid profile similar to olive oil with the exception of linoleic acid [29]. On a dry matter basis, seeds can exhibit a fat content ranging from 38.67 to 43.60 g/100 g, crude protein from 9.98 to 51.80 g/100 g, carbohydrates from 3.36 to 18.0 g/100 g, crude fiber from 17.26 to 20.0 g/100 g, and ash content from 3.6 to 5.0 g/100 g [30]. Moringa's lipid content boasts a healthier fatty acid profile, with Moringa seed oil containing approximately 76% PUFA, making it an excellent substitute for olive oil. Beyond PUFA and lower levels of SFA, it also harbors elevated monounsaturated fatty acids (MUFA). The seeds and seed oil showcase significant amounts of C18:1 (oleic acid, 70–80%), C16:1 (palmitoleic acid, 6–10%), C18:0 (Stearic acid, 4–10%), and C20:0 (Arachidic acid, 2–4%), and reduced levels of C18:2 (linoleic) and C18:3 (linolenic acid) (Amaglo et al. 2010). In contrast, immature pods and flowers possess higher MUFA (16–30%) and lower PUFA (34–47%) in comparison to leaves [25]. According to Jain et al. [31], Moringa seeds exhibit a high protein content (around 52%) with all essential amino acids, positioning them as a potential source of functional protein isolate. Moringa seed protein isolate (MPI) presents a promising alternative protein source for human and animal diets due to

its well-balanced amino acid profile. It offers a comprehensive composition of essential and non-essential amino acids, including charged, aromatic, and sulfur-containing ones. Notably, the high concentrations of cysteine and methionine in MPI make it comparable to protein sources like chicken eggs, cow milk, and human milk [32]. Numerous studies have demonstrated that protein and peptide fractions derived from Moringa seeds exhibit a wide array of bioactivities, including antimicrobial effects [33], antioxidant properties [34–36], antiviral activity [37], anti-diabetic effects [38], hepatoprotective benefits [39], anticancer properties [40], and cardio-protective activity [41, 42].

Moringa flowers

Moringa flowers constitute a rich reservoir of various nutrients, encompassing proteins, potassium, phosphorous, iron, calcium, antioxidants (tocopherol), and polyunsaturated fatty acids [43]. As per a proximate analysis, the dry weight of these flowers comprises 18.92% protein, alongside ash (9.68%), lipids (2.91%), dietary fiber (32.45%), and non-structural carbohydrates (36.04%), indicating a parallel nutritional composition to the leaves [44]. A thorough examination of dried Moringa flowers unveiled percentages of crude protein, crude fat, crude fiber, ash, and carbohydrates at 17.1%, 11%, 10.55%, 6.79%, and 57.72%, respectively. Additionally, the flowers exhibit an iron content of 56.37 ± 4.32 mg/100 gdb., calcium of 1016 ± 8 mg/100 gdb., TPC of $10{,}425 \pm 88$ mg GAE/100 g dry extract, TFC of 3320 ± 22 mg QE/100 g dry extract, and tannin content of 2379 ± 25 mg/100 g dry extract [43]. Comprehensive amino acid analysis reveals the presence of all 20 amino acids, with balanced proportions of essential and non-essential amino acids. Notably, Moringa flowers exhibit elevated vitamin C concentrations (77.50–224.67 mg/100 g) compared to other plant parts. Qualitative analyses of various floral extracts indicate the existence of phenols, steroids, terpenoids, alkaloids, flavonoids, and saponins. In a gas chromatography–mass spectrometry (GC–MS) investigation of a methanol extract, 26 compounds were identified, with quinic acid, ethyl oleate, and *cis*-9-hexadecenal as primary constituents, demonstrating antioxidant, anticancer, and anti-inflammatory properties [44]. These flowers serve as a prophylactic measure for various ailments, including pertussis, asthma, infertility, muscular issues, and spleen-related concerns. Furthermore, they possess diuretic, hepatoprotective, and antitussive qualities [43].

Role of Moringa in combating malnutrition

Malnutrition, defined by the World Health Organization [45], encompasses deficiencies, excesses, or imbalances in energy and nutrient intake, including both undernutrition (stunting, wasting, vitamin, and mineral deficiencies) and over nutrition (overweight, obesity). Approximately two billion individuals globally face health challenges due to malnutrition and hunger, with insufficient dietary variety contributing to nutrient deficiencies [46]. Beyond individual health risks, malnutrition impedes socioeconomic progress, perpetuating poverty by diminishing workforce productivity. Addressing this global issue, the integration of Moringa trees presents a locally accessible and cost-effective strategy. In regions like India and Africa, Moringa, termed "vegetarian gold," serves as a vital nutritional resource, especially for children and infants. Research by Wang et al. [47] underscores its significance. In Africa, Moringa leaf powder serves as a dietary staple, while in other countries, it supplements various food items like bread and noodles, aiming to alleviate issues of hunger and malnutrition [46]. This strategic use of Moringa demonstrates promise in combatting malnutrition on both nutritional and economic fronts. It plays a crucial role in addressing malnutrition through various aspects:

i. Nutrient density: Moringa is rich in essential vitamins and minerals, effectively combating micronutrient deficiencies associated with malnutrition [48]. Its leaves, notably high in calcium, protein, potassium, and iron, surpass other foods in nutritional value.
ii. Protein source: Moringa seeds and leaves are recognized for their high protein content and balanced amino acid profile, effectively addressing protein malnutrition. With Moringa seeds containing approximately 52% protein and Moringa leaves boasting nearly double the protein content of milk, they stand out among plant-based foods [31, 49, 50]. This nutritional richness, coupled with Moringa's higher digestibility compared to other sources, has garnered significant attention, establishing it as a sustainable protein source.
iii. Antioxidant properties: Moringa's antioxidants combat oxidative stress and inflammation associated with malnutrition, promoting overall health [51].
iv. Potential for fortification: Moringa leaves and powder can be easily incorporated into various food products, providing a practical means of fortifying diets with essential nutrients [52].
v. Support for growth and development: Micronutrients in Moringa, such as calcium and phosphorus, are crucial for proper growth, particularly in children, addressing stunted growth linked to malnutrition [53].
vi. Economic and agricultural benefits: Moringa's adaptability and economic feasibility make it a sustainable solution in regions with challenging agricultural conditions [54].

In conclusion, Moringa's nutritional richness, protein content, antioxidant properties, and adaptability position it as a promising tool to combat malnutrition. Continued research is essential to explore its potential impact further and integrate it into effective dietary strategies.

Phytoconstituents of Moringa

Phytochemicals, which are secondary metabolites present in plants, play a limited role in plant growth and development but significantly contribute to plant physiology and defense mechanisms. These phytochemicals can be categorized into five main groups based on their chemical structure: polyphenols, carotenoids, alkaloids, terpenoids, and sulfur-containing compounds [55]. The Moringa plant contains various phytochemicals, including polyphenols such as flavonoids, phenolic acids, and tannins. The Folin–Ciocalteau assay is commonly used to quantify the total phenolic content in Moringa, with leaves showing the highest concentration ranging from 2000 to 12,200 mg GAE/100 g [9, 10]. Flowers and seeds also contain polyphenols, although in lower concentrations than leaves [56]. Advanced chromatography techniques, including HPLC, GC–MS, and LC–MS, are increasingly employed for the identification and quantification of polyphenols.

Flavonoids

The predominant flavonoids in various parts of the Moringa tree are quercetin and kaempferol glycosides (glucosides, rutinosides, and malonyl glucosides) [25]. Quercetin and kaempferol concentrations in Moringa leaves range from 0.46–16.64 and 0.16–3.92 mg/g dry weight, respectively [56]. Other flavonols, such as rutin, myricetin, and epicatechin, are also present in lesser quantities. Geographical variations in flavonoid concentrations have been observed among different varieties [57]. Major phenolic acids in Moringa include gallic acid, chlorogenic acid, caffeic acid, coumaric acid, and ellagic acid [9, 10, 58]. Tannins, complex polyphenol molecules with protein-binding properties, vary in concentration among different parts of the Moringa tree, with dried leaves exhibiting the highest concentration at 20.7 mg/g, while seeds contain a lower amount of tannins [56].

Glucosinolates

Glucosinolates are nitrogen and sulfur-containing glycosidic compounds found in various parts of the Moringa plant. Glucomoringin is the most prevalent glucosinolate, with Moringa seeds containing a higher concentration (up to 8620 mg/100 g) than leaves (78 mg/100 g) [59]. Geographical variations have been reported in glucosinolate concentration [57]. Breakdown products of glucosinolates, such as glucose, nitriles, isothiocyanates, and thiocarbamates, are also identified in Moringa [56].

Carotenoids

Carotenoids, responsible for the characteristic colors of fruits and vegetables, are present in Moringa leaves, immature pods, and flowers. Leaves contain the highest total carotenoids on a fresh weight basis, with ß-carotene being a major component (6.6–17.4 mg/100 g). Dried leaves have even higher ß-carotene contents (23.31–39.6 mg/100 g dry weight). Various carotenoids, including all-E-lutein, have been identified in different parts of Moringa cultivars in India [25]. The Bhagya (KDM-1) cultivar shows the highest content of all-E-zeaxanthin, all-E-carotene, and total carotenoids.

Alkaloids

Although uncommon, Moringa contains alkaloids, nitrogen-containing organic compounds derived from amino acid metabolism. The most commonly isolated indol alkaloid in Moringa leaves is N,-L-rhamnopyranosyl vincosamide, and leaves also contain glycosides of a pyrol alkaloid. The actual quantification of these alkaloids in Moringa leaves is yet to be determined.

In summary, Moringa presents a unique combination of zeatin, quercetin, beta-sitosterol, kaempferol, and caffeoylquinic acid, serving as a rich source of antioxidants such as beta-carotene, vitamin C, quercetin, and chlorogenic acid. Notably, chlorogenic acid exhibits properties that lower blood sugar levels. Additionally, Moringa leaves contain additional chemical components such as Niazirin, Niazirinin, three mustard oil glycosides, Niaziminin A, Niaziminin B, a thiocarbamate, quercetin-3-*O*-glucoside, quercetin-3-*O*-(6″-Malonyl-glucoside), Niazimicin, pyrrole alkaloid (pyrrolemarumine 400-*O*-a-L-rhamnopyranoside), and 4-alpha and gamma-tocopherol, enhancing their nutritional and therapeutic significance.

Bio-functional properties of Moringa: an in-depth exploration

The comprehensive exploration of Moringa's bio-functional properties reveals a rich array of bioactive constituents across all plant parts, conferring a myriad of health benefits (Fig. 1). This review delves into the intricate details of these properties, encompassing antioxidant, antidiabetic, antihypertensive, immunomodulatory potentials, and more. Table 2 illustrates the bio-functional properties of Moringa.

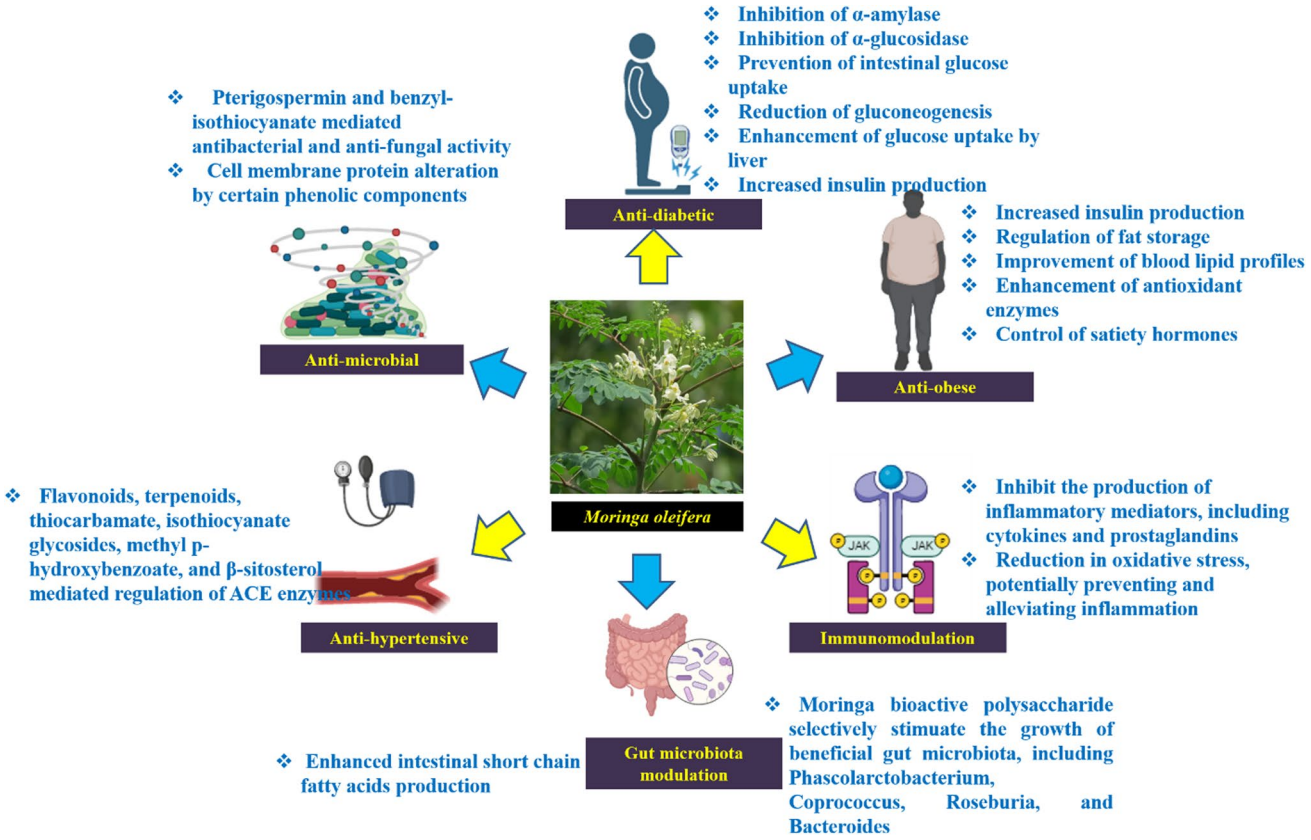

Fig. 1 Schematic representation of bio-functional attributes of *Moringa oleifera*

Antioxidant activity of Moringa

The antioxidant capabilities of *M. oleifera* are prominently evident in its leaf, pod, and seed extracts, as highlighted by Kou et al. [6]. This robust antioxidant activity is attributed to the diverse phytoconstituents present in the plant. The mechanism underlying this antioxidative prowess involves the neutralization of free radicals, modulation of oxidative pathways, and the reduction of oxidative stress and inflammation, as detailed by Yadav et al. [43]. Examining *M. oleifera* leaves, Hamed et al. [60] specifically investigated the antioxidant potential of flavonoids extracted from the leaves. Their study revealed significant scavenging activity against 2, 2-diphenyl-1-picrylhydrazyl (DPPH) free radicals (85.99% at 100 g/mL) and 2, 2-azino-bis-(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) radicals (84.72% at 50 g/mL). Additionally, extracts obtained through subcritical ethanol extraction demonstrated antioxidant activities, as confirmed by ferric ion reducing antioxidant power (FRAP) and DPPH assays [7, 8]. Moving to *M. oleifera* seed extracts, Jahan et al. [61] employed various assays, including DPPH, ABTS, Nitric oxide (NO) free radical scavenging, and reducing power tests. The water extract exhibited significant scavenging activities against DPPH, ABTS, and NO free radicals, surpassing standard antioxidant compounds such as ascorbic acid and butylated hydroxyanisole. Notably, the EC50 values were 36.89 ± 0.154, 13.20 ± 0.049, and 217.95 ± 0.327 g/mL, respectively.

In a comprehensive assessment by Luqman et al. [62], both *M. oleifera* leaf and fruit extracts were examined. The aqueous leaf extract demonstrated a concentration-dependent increase in glutathione levels and a reduction in malondialdehyde levels. The ethanolic fruit extract exhibited superior phenolic content, robust reducing power, and potent free radical scavenging capacity. Interestingly, ethanolic extracts outperformed aqueous extracts in in vitro antioxidant assays, while the latter showed higher potential in vivo. Importantly, safety evaluations indicated the absence of toxicity in extracts up to a dose of 100 mg/kg body weight. This collective evidence underscores the remarkable antioxidant capabilities of *M. oleifera*, providing insights into specific constituents and extraction methods contributing to its therapeutic potential.

Antimicrobial activity of Moringa

The literature extensively documents the antibacterial efficacy of *M. oleifera*, attributing this property to its

Table 2 Studies on the bio-functional properties of *Moringa oleifera*

Part/extract of moringa	Bio-functional activity: study	Findings/mechanism of action	References
Leaves: aqueous	Antidiabetic activity in STZ induced diabetic rats	Extract decreases NF-κB and VCAM-1 overexpression in the retina, showcasing its antidiabetic activity through the inhibition of angiogenic mediators and the regulation of inflammatory markers	[138, 139]
Seed extract and it's isothiocyanate	Anti-inflammatory effects in a mouse ear edema model induced by 12-*O*-tetradecanoylphorbol-13-acetate (TPA)	Demonstrates anti-inflammatory characteristics through the nuclear factor erythroid 2-related factor 2 (Nrf2) and nuclear factor-kappa B (NF-κB) pathways	[152]
Seed powder	Cardioprotective properties in rats with L-NAME-induced hypertension	Resulted in decreased blood pressure, heart acetylcholinesterase (AChE), and monoamine oxidase (MAO) activities in hypertensive rats. The mechanism of action is associated with antioxidant activity and the modulation of AChE and MAO activities	[153]
Root: polysaccharide	In vitro prebiotic activity: human intestinal microflora	Results in a 3- to 5-fold rise in short-chain fatty acid levels and an increase in beneficial microflora like Bacteroidetes, accompanied by a reduction in the abundance of detrimental microflora such as Proteobacteria	[154]
Leaves: hydro-alcoholic (rutin)	Anti-lipidemic and anti-adipogenic activity: 3T3-L1 adipocytes	Rutin effectively reduces lipid levels and adipogenesis while enhancing glucose uptake by modulating the PPAR-γ and AMPK signaling pathways	[155]
Seed and leaves: methanol	Antidiabetic activity in alloxan-induced diabetes in mice	An administration of 500 mg/kg per day of body weight effectively brought fasting blood glucose levels back to normal. Reduction in cholesterol, triglycerides, creatinine, liver enzymes, and oxidative markers, accompanied by an increase in antioxidant biomarkers	[156]
Flowers: ethanol	Antidiabetic effects in dexamethasone induced hyperglycemic albino wistar rats	A dosage of 100 and 200 mmg/kg body weight lowers serum glucose, total cholesterol, triglycerides, and LDL, while elevating HDL	[157]
Leaves: 3-*O*-glucoside of kaempferol	Antiadipogenic and lipolytic activity in 3T3-L1 adipocytes	Reduce TAG and lipid buildup in adipocytes. Concentration of 20 µg/mL, there is a reduction in leptin secretion and an increase in adiponectin secretion	[158]
Flowers and leaves: hydroethanolic extract	Antidiabetic activity in STZ induced diabetic rats	Dose of 200 mg/kg b.w. exhibit significant activity	[76]
Leaves: ethanol extract	In vitro antioxidant (DPPH) antidiabetic activity (α-amylase inhibition assay)	The extract (IC50 55.6 ± 0.18 µg/mL) demonstrated a DPPH scavenging activity that is similar to ascorbic acid (IC50 46.71 ± 0.24 µg/mL). Exhibits α-amylase inhibitory activity with an IC50 value of 27.54 ± 0.07 µg/mL, whereas Acarbose has an IC50 value of 19.45 ± 0.26 µg/mL	[159]

Table 2 (continued)

Part/extract of moringa	Bio-functional activity: study	Findings/mechanism of action	References
Seed: water extract (4-[(α-L-Rhamnosyloxy) benzyl] isothiocyanate)	Anticancer activity on renal cell carcinoma (RCC) cells. In vivo study: Xenograft Model in Nude Mice	Isothiocyanate suppresses the growth and migration of 786-O cells by blocking the PTP1B-mediated activation of the Src/Ras/Raf/ERK signaling pathway. Isothiocyanate significantly hinders the growth of xenograft tumors in mice and substantially increases the Bax/Bcl-2 ratio in tumor tissues	[160]
Leaves: hexane, methylene chloride, methanol and water extract	Therapeutic potent on ethanol-induced fatty liver: mice model	Best result was found for water extract. Demonstrated a hepatoprotective effect by reducing biochemical markers associated with liver damage, inflammation, and lipid droplet accumulation caused by ethanol exposure. Effectively alleviated ethanol-induced oxidative stress by decreasing lipid peroxidation and inhibiting the expression of CYP2E1	[161]
Leaves: hydro alcoholic extract	Antiobesity activity of (Astragalin, (3-*O*-glucoside of kaempferol): cell line study—3T3-L1	Astragalin demonstrated a significant reduction in triglycerides and lipid accumulation in 3T3-L1 adipocytes, along with a dose-dependent increase in glycerol release. At a concentration of 20 mg/mL, astragalin significantly increased the secretion of adiponectin ($p < 0.01$) while decreasing leptin secretion in 3T3-L1 adipocytes	[158]
Leaves: hydro ethanol extract	Impact on metabolic syndrome in Sprague Dawley rats subjected to a high-fructose, high-fat diet for a duration of 60 days	The 30 days moringa treatment markedly contributed to the alleviation of characteristics associated with metabolic syndrome, including hyperinsulinemia, insulin resistance, and notable increases in low-density lipoprotein (LDL), visceral fat, and liver weight ($p < 0.05$)	[162]
Leaves: aqueous extract	Therapeutic effect on constipation mice	Exhibits a gentle and prolonged laxative impact, enhancing both the quantity and moisture of bowel movements	[87, 88]
Leaves: aqueous extract	Anticancer activity: human laryngeal carcinoma, Ehrlich ascites carcinoma, and breast adenocarcinoma mice	Impede the advancement of the tumor without impacting the regular physiological processes and functions of the body	[163]
Leaves: ethanol extract	Antiobesity activity in high fat diet induced Wistar rats	Improved high-fat diet (HFD)-induced obesity, adiposity, and alterations in serum biochemistry and hepatic histopathology were mitigated via anti-obesity, anti-inflammatory, and antioxidant properties of the diverse bioactive compounds	[164]
Leaves: hydro ethanol extract	In vitro antidiabetic activity (α-glucosidase inhibition)	Purified flavonoids (100 µg/mL) inhibits the enzyme activity by 48.44%	[165]
Leaves: ethanol extract (alkaloid)	Antitumor activity in human non-small-cell lung cancer	Extract hinders the growth and movement of A549 cells, promoting apoptosis and halting the cell cycle. This is achieved by disrupting the activation of the JAK2/STAT3 pathway	[166]

Table 2 (continued)

Part/extract of moringa	Bio-functional activity: study	Findings/mechanism of action	References
Leaves: water and ethanol extract	In vitro *antioxidant* (ABTS, SOD-like activity, & DNA nicking assay) & antidiabetic activity (α-Glucosidase and lipase inhibition)	Ethanol extracts exhibits higher activities than water extracts. The expression of PPARγ, FAS, and ACC was progressively inhibited with increasing concentrations of extracts	[167]
Roots and leaves: acetone, ethanol, and water extract	Antimicrobial activity: Microdilution methods	Acetone extract shows good activity against *E. coli*, *B. Subtilis*, *S. aureus*, and low activity against *C. albicans*	[168]
Roots leaves: water extract	In vitro antidiabetic activity (α-glucosidase inhibition)	Leaves shows significantly higher activity than roots	[168]
Stem: methanol extract	Ameliorative effect on acute kidney injury induced by glycerol in rats	Enhances recovery from glycerol-induced acute kidney injury by suppressing indicators of inflammation, oxidative stress, and renal damage through the modulation of KIM-1 and NF-κB signaling pathways	[169]
Leaves: ethanol extract	In vitro and in vivo study on the proliferation & migration of PC3 human prostate cancer cells	Alkaloids of extract hinders PC3 cell proliferation and migration, promoting apoptosis and cell cycle arrest. At a dosage of 150 mg/kg, MOA markedly impeded the growth of xenograft tumors in mice and significantly decreased protein expression levels of COX-2 and β-catenin in the tumor tissues	[170]
Leaves: ethanol extract	Anti-inflammatory (colon) activity in dextran sulfate sodium-treated mice	The extract alleviates colitis induced by DSS, mitigating various symptoms such as body weight loss, colon shortening, inflammatory cytokine secretion, colon tissue damage, and inflammatory cell infiltration. Mechanism involve is inhibiting the activation of the NF-κB signaling pathway	[171]
Leaves: ethanol	Antiobesity: cell line study—3T3-L1	Extract and iso-quercetin exhibited anti-proliferative effects at a concentration of 280.5 µg/mL and 4.95 µg/mL, respectively. The higher concentrations of extract treatment resulted in the downregulation of adipogenesis-related genes, leading to a reduction in triglyceride content accumulation	[172]
Leaves: ethyl acetate extract	Antidiabetic activity in STZ induced diabetic rat	Dose @ 200 mg/kg b.w reduced blood glucose and glycosylated hemoglobin after 30 days. Exhibits antidiabetic activity via increasing antioxidant levels and inhibition of pro-inflammatory mediators	[173]
Leaves powder	Antidiabetic activity in Alloxan induced diabetic rat	Dose @ 50 mg/day reduced blood glucose significantly after 8 weeks	[174]
Leaves, roots, flowers, bark, and seeds: water, alcohol, and acetone	In vitro *antioxidant* (DPPH, reducing potential, and total antioxidant capacity assays) and antibacterial activity (Disc diffusion assay and MIC)	Leaves exhibit highest antioxidant activity than other parts of the plant Water, methanol, ethanol, ethyl acetate, and acetone extracts shows zone of inhibition against *Erwinia carotovora* and *Pseudomonas aeruginosa*	[175]

Table 2 (continued)

Part/extract of moringa	Bio-functional activity: study	Findings/mechanism of action	References
Moringa: purified compounds	Antidiabetic activity of 4 hydroxyphenylacetonitrite, fluoropyrazine, methyl-4-hydroxybenzoate, vanillin,4-α-L-rhamnopyranosyloxybenzyl isothiocyanate, and 3,4-dihydroxy benzonitrile	Identified compounds contribute to lowering blood glucose levels in diabetic rats by promoting insulin release from pancreatic islets. This process is likely mediated by the PKA-dependent insulin secretory pathway	[82]
Leaves: aqueous ethanolic extract	Antidiabetic activity in diet induced obesity mice model	Dose @ 500 mg/kg b.w reduces blood glucose level significantly. Exhibit antidiabetic activity via inhibiting the secretion of IL-2 and modulates T cell calcium signaling in hypertensive rats	[176]
Leaves: hydro ethanol extract	Antidiabetic activity in STZ induced diabetic rats	95% (v/v) ethanol fraction exhibits significant antihyperglycemic activity	[177]
Leaves: aqueous extract	Antidiabetic activity: in vitro, STZ induced and high fat induced diabetic mice	Inhibited the activity of α-amylase and α-glucosidase and it displayed improved antioxidant capacity, glucose tolerance and rate of glucose uptake in yeast cell. Significantly reduces blood glucose level in high fat induced diabetic mice even after one week of treatment	[78]
Leaves: ethanol	Antidiabetic activity in type 2 diabetic rat	Dose @ 150 mg/kg/day lowers fasting blood glucose from 483 to 312 mg/dL after 5 weeks	[178]
Leaves: methanol	Antidiabetic activity in STZ induced diabetic rats	Dose @ 250 mg/kg b.w lowers blood glucose after 6 weeks	[179]
Leaves: aqueous	Cytotoxic effect on colon cancer cells like HCT116, $CaCo_2$, and HCT116P53 by MTT assay	Reduction in the viability of cancer cells with IC50 value ranges from 0.02 to 0.05%	[180]
Leaves: ethanol	Antidiabetic activity in diabetic rat	Dose of 300 mg//kg b.w lowers blood glucose level after 21 days	[181]
Leave, fruit, and flower: methanol	Antidiabetic activity in STZ induced diabetic + Ovariectomized Wistar rats	The fruit extract showed significant effectiveness in reducing both elevated glucose levels and osteoclastic bone markers compared to the other two components	[182]
Leaves: methanol	Antidiabetic activity in alloxan induced diabetic model	Dose at 300 and 600 mg/kg b.w enhanced glucose tolerance and lowers blood glucose after 6 weeks	[183]
Leaves, bark and seed: ethanol	Anticancer activity: breast and colorectal cancer cell lines (HCT-8 & MDA-MB-231)	Seed and leaves extract exhibit excellent anti-cancer activity due to the presence of compounds eugenol, isopropyl isothiocynate, D-allose, and hexadeconoic acid ethyl ester	[184]
Leaves: methanol	Anti-obesity activity in high fat diet induced rats	Dose of 200 mg/kg b.w reduces body weight, liver and kidney weight, Serum cholesterol and TAG	[185]
Leaves: aqueous	Anticancer activity: H358, H23, COS-7, A431, MCF-7, HT1080, A549 cell lines	Extract @ 400-600 µg/mL inhibit the proliferation of A549 cells (50–80%). Shows antineoplastic activity on cancer cells including lung cancer cells	[101]
Leaves: aqueous	Antidiabetic and antioxidant activity in STZ induced diabetic rats	Decrease in both malondialdehyde and fasting plasma glucose and increase in reduced glutathione	[186]

Table 2 (continued)

Part/extract of moringa	Bio-functional activity: study	Findings/mechanism of action	References
Leaves: hydro alcohol	Cerebroprotective activity in male Wistar rats	The extract (Dose @ 100–400 mg/kg/day) reduced infarction volume in the cortex and sub cortex. Lower and medium doses protected all areas by mitigating oxidative stress, while the high dose extract exhibited a similar protective effect in the striatum and hippocampus	[187]
Pod: methanolic	Antidiabetic and antioxidant activity in STZ induced diabetic albino rats	Dose of 150 and 300 mg/kg b.w decreases serum glucose and increases serum insulin Increased pancreatic tissue antioxidant with decreased thiobarbituric acid-reactive substances	[188]
Pod: water	Anticancer activity in mouse	Exhibits chemoprotective activity against colitis related colon carcinogenesis	[189]
Leaves: methanol	Immunomodulatory activity in mice model	Daily dose of 250 and 750 mg/kg stimulated both humoral and cellular immune responses	[190]

rich phytoconstituent profile. Notably, flavonoids such as quercetin and myricetin play a crucial role in inhibiting nucleic acid synthesis in bacteria. Moreover, various constituents, including alkaloids, phenolics, and terpenoids such as gallic acid, chlorogenic acid, caffeic acid, ferulic acid, quercetin, and kaempferol, exhibit noteworthy antimicrobial activities [63, 64]. The antimicrobial effects of certain phenolic components are attributed to their interactions with proteins and enzymes on microbial cell membranes, leading to structural alterations and functional inhibition, ultimately causing microbial death [65].

Secondary metabolites derived from *M. oleifera* exhibit significant antimicrobial effects against a spectrum of microorganisms, including pathogenic bacterial genera like *Shigella*, *Pseudomonas*, *Salmonella*, and *Bacillus*. Saadabi and Zaid [66] and Rahman et al. [67, 68] highlight the antibacterial properties present in both the leaves and seeds of the Moringa plant. These studies demonstrate the efficacy of Moringa against both Gram-positive and Gram-negative bacteria. The focus of attention lies on Pterigospermin, a substance present in Moringa leaves that has the ability to dissociate into two benzyl-isothiocyanate molecules. This compound has been documented to exhibit robust antibacterial and antifungal properties [69].

The multifaceted antibacterial effectiveness of Moringa seeds involves benzyl-isothiocyanate, a significant contributor found in both seeds and leaves. This substance directly impacts microorganisms by hindering cell membrane synthesis and impeding the production of vital enzymes [70].

Mursyid et al. [71] conducted a comprehensive evaluation of *M. oleifera* leaf extract for antimicrobial activity, employing concentrations of 2% b/v, 4% b/v, and 8% b/v. The extract exhibited antimicrobial efficacy against *Staphylococcus epidermidis*, with zones of inhibition measuring 14 mm, 10.8 mm, and 9.3 mm for concentrations of 8% b/v, 4% b/v, and 2% b/v, respectively. In a separate study, Fouad et al. [72] demonstrated the antimicrobial potential of Moringa leaf extract against pyogenic bacteria, including *Staphylococcus aureus*, *Corynebacterium pseudotuberculosis*, *Corynebacterium ulcerans*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, Micrococcus spp., and Citrobacter spp. Additionally, Dasgupta et al. [73] highlighted the antimicrobial activity of Moringa seed extract against *Bacillus subtilis* and *Escherichia coli*. Collectively, secondary metabolites from *M. oleifera* contribute significantly to its antimicrobial effects, playing a crucial role in the plant's defense mechanisms against various human pathogenic bacteria.

Antidiabetic properties of Moringa

Diabetes mellitus, characterized by inadequate insulin production or tissue resistance to insulin, is a chronic metabolic disorder associated with global health concerns and interconnected comorbidities, particularly cardiovascular diseases. Despite the availability of numerous hypoglycemic medications, increasing attention has been directed towards medicinal plants due to consumer preferences for natural ingredients with minimal side effects. Moringa, a plant with a rich traditional history in diabetes management, exhibits diverse mechanisms targeting key aspects of the disorder.

Various components of the Moringa plant have demonstrated efficacy in reducing blood glucose levels. Proposed mechanisms include the inhibition of crucial diabetes-related enzymes such as α-amylase and α-glucosidase, prevention of intestinal glucose uptake, enhancement of glucose uptake by liver and muscle cells, reduction of gluconeogenesis in the liver, and increased insulin production coupled with heightened insulin sensitivity in muscle cells [74].

Numerous studies, both in vitro and in vivo, have investigated the antidiabetic activity of *M. oleifera*. Extracts derived from *M. oleifera* seeds, roots, and stem bark, including powder, aqueous, ethanol, and methanol extracts, have consistently demonstrated positive outcomes in managing glycemic control in both animal and human diabetic models [75]. Additionally, hydroethanolic extracts from *M. oleifera* flowers and leaves have shown significant antidiabetic effects in streptozotocin-induced diabetic rats [76].

Moringa leaves, recognized as a valuable source of green leafy vegetables, contribute to reducing diabetic complications in affected individuals [77]. Aqueous extracts from *M. oleifera* leaves exhibit inhibitory effects on both α-amylase and α-glucosidase activities, highlighting their potential as a phytopharmaceutical for diabetes management, either as an adjuvant or standalone treatment [78]. Furthermore, research by Magaji et al. [79] explored the inhibitory activities of *M. oleifera* extracts on α-glucosidase, α-amylase, and glucose-induced bovine serum albumin glycation. Hexane and methanol leaf extracts exhibited notable α-amylase inhibitory activity, while hexane root extract demonstrated optimal α-glucosidase inhibition and antiglycation effects, surpassing the activity of the control substances rutin and acarbose, respectively.

In animal studies, the consumption of *M. oleifera* leaves demonstrated a hypoglycemic effect despite an increase in body weight, emphasizing its potential as a therapeutic agent [80]. The antidiabetic activity of *M. oleifera* seed powder in streptozotocin-induced diabetes in male rats was examined by Al-Malki and El Rabey [81]. The findings revealed a noteworthy decrease in lipid peroxide levels, enhancements in immunoglobulin levels, and a restoration of normal histology in both the kidney and pancreas. Bioactive compounds like 4-hydroxyphenylacetonitrite and fluoropyrazine, isolated from Moringa leaves, exhibited a noteworthy reduction in blood glucose levels in diabetic rats [82]. Notably, in silico studies identified specific phytoconstituents such as 2-phenylchromenylium, anthraquinone, sitogluside, hemlock tannin, and phenolic steroids as responsible for the antidiabetic activity of Moringa [83]. In conclusion, the wealth of evidence presented underscores Moringa's promising role in addressing diabetes through multifaceted mechanisms, positioning it as a valuable natural resource in the management of this prevalent metabolic disorder.

Anti-obesity activity of Moringa

Obesity, defined by an excessive accumulation of fat in adipose tissue and assessed through body mass index, poses a substantial health concern linked to diverse lifestyle disorders. These disorders encompass type II diabetes, cardiovascular disease, hypertension, stroke, and specific cancers. Additionally, obesity exerts adverse effects on psychological well-being, physical capabilities, and social interactions [84]. Despite the availability of pharmacological interventions, there is a growing shift towards natural ingredients with anti-obesity potential due to concerns about the side effects of medications. Moringa, with its rich phytoconstituents, has been extensively documented in the literature for its anti-obesity properties. Redha et al. [85] systematically reviewed 36 articles highlighting the anti-obesity potential of Moringa. In a separate study, the anti-obesity activity of Moringa seed oil extract in male Sprague Dawley rats was explored. The extract demonstrated efficacy in ameliorating metabolic and hematological concerns induced by a high-fat diet, notably reducing resistin and leptin levels [86]. The proposed mechanisms underlying the anti-obesity effects of Moringa [85], includes (i) inhibition of pancreatic lipase, leading to decreased hydrolysis of triglycerides into fatty acids, (ii) improvement of blood lipid profiles by reducing triglycerides, total cholesterol, LDL, VLDL, and increasing HDL, (iii) regulation of fat storage by modulating the expression of proteins associated with fatty acid synthase, peroxisome proliferator-activated receptor γ, and adipose triglyceride lipase, (iv) enhancement of antioxidant enzymes, resulting in decreased lipid peroxidation, protein oxidation, oxidative stress, and inflammation, (v) reduction of gluconeogenesis, improvement of glucose tolerance, and attenuation of glucose uptake, coupled with enhanced insulin signaling and resistance, and (vi) control of satiety hormones by decreasing leptin levels and increasing ghrelin levels. Recent studies have also explored the anti-obesity potential of Moringa polysaccharide in a high-fat diet-induced C57BL/6 J mice model, revealing preventive effects on fat accumulation and weight gain. The supplementation of Moringa polysaccharide maintained a healthy blood lipid profile, ameliorated

insulin resistance, mitigated the production of pro-inflammatory cytokines, modulated gene expression related to bile acid and lipid metabolism, and positively influenced gut microbiota composition [87, 88].

Antihypertensive activity of Moringa

Hypertension, a chronic medical condition characterized by consistently high blood pressure in the arteries, poses a significant risk for serious complications such as heart attacks and strokes. Effective management of hypertension often involves medications that target angiotensin-converting enzyme (ACE) inhibition, as angiotensin-II, produced by ACE, contributes to increased blood pressure by narrowing blood vessels [89]. *M. oleifera* leaves, a traditional component of ayurvedic medicine, have been recognized for their antihypertensive activity [90]. The ACE-inhibitory and angioprotective effects of Moringa have been attributed to flavonoids and terpenoids present in the plant [91].

Thiocarbamate, isothiocyanate glycosides, methyl p-hydroxybenzoate, and β-sitosterol, identified as hypotensive agents in *M. oleifera* pod, further contribute to its antihypertensive properties [92, 93]. Acuram and Hernandez (2019) investigated the antihypertensive activity of Moringa in an *N*-nitro-L-arginine methyl ester or L-NAME-induced hypertensive mouse model. Oral administration of *M. oleifera* crude extracts demonstrated no acute toxicity in mice, while methanolic and ethyl acetate extracts significantly reduced systolic blood pressure in the hypertensive mouse model. Aktar et al. [90] evaluated the in vitro ACE inhibitory activity of methanolic extracts of Moringa leaves, reporting an IC50 of 226.37 g/mL. In comparison, the reference compound captopril, a potent ACE inhibitor, exhibited an IC50 of 0.0289 M. Adefegha et al. [94] conducted a comparative study on the effects of *M. oleifera* leaves and seeds on blood pressure and key enzyme activities associated with hypertension in rats. Rats fed a diet containing 2% and 4% Moringa leaves and seeds exhibited decreased systolic and diastolic blood pressure compared to control groups.

Anticancer activity of Moringa

The escalating global incidence of new cancer cases underscores the imperative for safer therapeutic approaches, given the significant side effects associated with contemporary cancer treatments. In light of this, plant-based solutions are gaining popularity for their ability to selectively target cancer cells without causing adverse effects [95]. Moringa, in particular, demonstrates notable cytotoxicity against various cancer cell lines. Literature reveals that both aqueous and methanolic extracts exhibit cytotoxic effects on diverse cancer types, including human melanoma, colon cancer (HCT116), hepatocellular cancer (Hep3B), breast adenocarcinoma (MCF7), and colorectal cancer ($CaCO_2$) [96–99]. Moringa extracts induce apoptosis, a pivotal process leading to cancer cell death. This apoptotic response is observed through the inhibition of key biomarkers. Mechanistic insights into the apoptotic pathways include the activation of procaspase 3 to caspase 3 in lung carcinoma A549 cells, downregulation of key proteins in the NF-kß signaling pathway in Panc-1 cells of the pancreas, and downregulation of the anti-apoptotic protein Bcl-xL expression with the concomitant activation of caspase 3 by cleavage in hepatocellular cancer HepG2 cells [100–102].

In a recent study by Pappas et al. [103], the antiproliferative activity of crude and hot water extracts from both PKM1 and wild variety Moringa leaves was evaluated on HTC116, MCF-7, and AsPC-1 cells using the MTT test. The results indicated significant inhibition of cell proliferation by the extracts. Notably, the wild variety of Moringa exhibited superior activity compared to the PKM1 variety, as evidenced by the downregulation of p53 expression in the studied cell lines.

Anti-inflammatory activity of Moringa

Moringa has garnered recognition for its potential anti-inflammatory activity, providing a natural approach to alleviating inflammation. Numerous studies have delved into Moringa's anti-inflammatory properties, elucidating its mechanisms and potential applications. Moringa contains diverse bioactive compounds such as flavonoids, isothiocyanates, and polyphenols, demonstrating anti-inflammatory effects by modulating inflammatory pathways and alleviating inflammation-related conditions [104]. Additionally, research suggests that Moringa may inhibit the production of inflammatory mediators, including cytokines and prostaglandins, crucial in the inflammatory response, contributing to its anti-inflammatory effects [105]. The antioxidant capacity of Moringa is also implicated in its anti-inflammatory effects, as it scavenges free radicals and reduces oxidative stress, potentially preventing and alleviating inflammation [106, 107]. In a comprehensive study, the anti-inflammatory activities of ethanol crude extracts from different parts of *M. oleifera*, including leaves, seeds, and roots, were investigated. While all parts exhibited anti-inflammatory properties, the research underscored the leaves of *M. oleifera* as particularly noteworthy. The leaves demonstrated superior anti-inflammatory activity, positioning them as a promising and potent natural source of antioxidants and anti-inflammatory agents. The findings suggest that *M. oleifera* leaves hold significant potential for development into health-promoting dietary supplements, emphasizing their role in fostering overall well-being [108]. In conclusion, the existing literature underscores Moringa's anti-inflammatory properties, attributed to its diverse array of bioactive compounds. While

further research, particularly in clinical trials, is warranted to fully understand the extent of its anti-inflammatory benefits, Moringa stands out as a promising natural agent in combating inflammation.

Prebiotic activity of Moringa

Prebiotic activity, assessing the ability of a substrate to support the growth of organisms compared to non-prebiotic substrates such as glucose, has been explored in *M. oleifera* leaves. Li et al. [109] conducted a study on the prebiotic activities of a bioactive polysaccharide extracted from *M. oleifera* leaves, known as Moringa bioactive polysaccharide (MBP). The study revealed no significant difference in the average molecular weight (MW) of MBP between simulated saliva and stomach digestion. However, during intestinal digestion, a marginal decrease in MW from 155.29 to 145.02 kDa was observed, accompanied by an increase in reducing sugar levels from 0.159 to 0.234 mg/mL, indicating MBP degradation. In the fermentation process with human fecal inoculums, MBP was extensively utilized, resulting in the enhancement of various beneficial gut microbiota, including Phascolarctobacterium, Coprococcus, Roseburia, and Bacteroides. This profound modulation contributed to the restructuring of the microbial community. Furthermore, MBP significantly increased the production of short-chain fatty acids, particularly n-butyric acid, acetic acid, propionic acid, and n-valeric acid, during a 48-h fermentation period. These findings underscore the potential prebiotic activity of Moringa bioactive polysaccharide in supporting the growth of beneficial gut bacteria and fostering a healthy gut microbiota composition.

Application of Moringa in food products

The increasing prevalence of lifestyle disorders and the rise of pandemic diseases have heightened consumer awareness of functional foods. This has led to an exploration of ancient medicinal plants, with a focus on integrating their bioactive components into nutraceutical food formulations. *M. oleifera*, known for its traditional use and nutritional benefits, has gained prominence as a key ingredient in functional, nutraceutical, and designer foods. For instance, Moringa seeds, comprising 52% protein with all essential amino acids, emerge as a promising source of functional protein isolates. This isolate finds applications in the food and biomedical industries, functioning as a thickener, food additive, and milk coagulant. Additionally, *M. oleifera* exhibits potential as a food additive and preservative due to its ability to inhibit lipid oxidation and other deleterious chemical processes [5]. Nevertheless, Moringa leaves have diverse applications in the food industry, serving as additives in products such as yogurt, cheese, biscuits, bread, and animal feed. They enhance the nutritional value, sensory properties, shelf life, and functional attributes of staple foods like weaning food, amala, biscuits, cake, bread, cereal porridge, and yogurt [11, 14, 30, 110–113]. Table 3 presents research findings discussing the utilization of Moringa in diverse food products.

In the dairy industry, research has delved into integrating Moringa extracts or powder into various milk products, demonstrating its potential to enrich these items with essential nutrients, including vitamins and minerals. To address the distinctive green color and herbal aroma associated with Moringa-infused dairy products like cheese and yogurt, strategic formulations are employed. Introducing Moringa extract into milk before fermentation has yielded advantages such as a faster fermentation process, reduced yogurt pH, improved rheological properties, and heightened total phenols content and antioxidant capacity [114]. Additionally, incorporating Moringa leaf powder into yogurt has resulted in elevated sensory scores for flavor and taste, coupled with enhanced nutritional content [115].

In the meat industry, Moringa plays a role as a natural antioxidant, effectively retarding oxidation processes and extending shelf life. Research indicates its positive impact on reducing lipid oxidation, regulating pH, and exerting antimicrobial effects when integrated into animal diets or directly incorporated into meat and meat products [69, 116]. The aqueous extract from Moringa leaves has showcased proteolytic activity, contributing to the tenderness and juiciness of buffalo minced meat [117]. In a recent study, the antioxidant potential of Moringa and olive leaf powder, as well as crude extracts, was assessed in chicken burgers to prevent fat oxidation during a 20-day refrigerated storage period. The inclusion of Moringa and olive (in leaf and crude extract forms) impacted the pH, total volatile nitrogen, and sensory properties of the chicken burgers. Particularly noteworthy was the reduction in lipid oxidation and peroxide value (PV) after 10 days of storage, attributed to the phenols' crucial role in mitigating fat oxidation, inhibiting protein degradation, and enhancing fat stability. Collectively, treatments incorporating Moringa and olive leaf demonstrated the ability to slow the degradation of meat, suggesting their potential use as preservatives to extend the shelf life of chicken burgers [118].

Furthermore, in the context of expanding Moringa applications in the bakery industry, multiple studies have investigated its potential. Seed flour and dried Moringa leaf powder find primary application in fortifying bread dough, which can be prepared using wheat flour alone or in combination with other flours. This substitution offers a viable alternative for crafting gluten-free bread, specifically beneficial for individuals with celiac disease, ensuring adequate levels of minerals, proteins, phenols, and other nutrients. The concentrations utilized for fortification typically range from 1

Table 3 Studies on the application of *Moringa oleifera* in food products

Plant part with concentration	Food/formulation	Findings	References
Leaves (25%)	Fuzhuan Brick Tea	Improved sensory scores, enhanced gut health, and normalization of lipid metabolism and insulin resistance were observed, along with improvements in the expression of genes related to lipid metabolism	[191]
Ethanol leaves extract (10 and 20%) and leaves powder (29%)	Yoghurt	The extract demonstrated better stability against whey separation but lower stability TPC compared to the powder. Enhanced antioxidant properties in fortified sample than control	[144]
Aqueous ethanolic extract (0.5%)	Chicken pate	Added extract act as both colourant and antioxidant	[192]
Aqueous leaves extract (0.5%, 1% and 2%)	Ground beef	No negative impact on overall acceptability and other sensory attributes. Slight enhancement in tenderness and juiciness compared to the control	[193]
Root powder (0.1%)	Soy-milk yoghurt	Fortification increases the fiber, fat, protein, copper, iron, and manganese content in the samples ($p < 0.05$)	[194]
Seed sprout powder (9–26%)	Snack bar	The optimal formulation included 8% Moringa, resulting in heightened levels of protein, unsaturated fat, and micronutrients in the product. Moringa significantly increased the concentrations of GABA, phenolics, and glucosinolates in the bars. Consumers demonstrated a positive inclination towards purchasing optimized product	[195]
Seed cake	Goat milk cheese	Goat soft cheeses coagulated with Moringa MCE displayed higher water-soluble nitrogen content and overall sensorial scores than control cheese	[196]
Leaves and flower powder Ratio (11:4, 11.75:3.25, 12.5:2.5, 13.25:1.75, and 14:1)	Herbal biscuit	Increased calcium content (115.73 mg/100 g) in biscuits having higher leaf. Less tannins in biscuit having higher flower	[43]
Seed residue (1%, 3%, 5%, 7% and 9%)	Muffin formulations	Significantly ($p < 0.0001$) increased protein and Fe content for the 7% and 9% formulations	[64]
Leaves powder (0.5%, 1%, 1.5% and 2%)	Mango flavoured yoghurt	The product containing 1% moringa consistently received the highest scores in the majority of sensory attributes, including body and texture, flavor, taste, and overall acceptability, throughout the 15-day storage period at 5 ± 1 °C	[112]
Leaves powder (0–15%)	Pasta	Increased phenol content, minerals and antioxidant activity Decreased swelling index, cooking time and firmness with increased adhesiveness and cooking loss	[197]
Leaves powder (0–5%)	Snack (wheat and maize based)	Snacks containing 1% Moringa were almost as palatable as the control. Increase in crude protein, calcium, magnesium, potassium, phosphorus, zinc, manganese, and iron	[198]
Leaves powder (5, 10 and 15%)	Fresh pasta	Increase in phenolic content, slowly digestible starch, and decrease in the rapidly digestible starch	[199]

Table 3 (continued)

Plant part with concentration	Food/formulation	Findings	References
Leaves powder (1%, 2.5%, 5% and 10%)	Cupcake	Protein levels and antioxidant capacity exhibited a direct rise with increasing moringa content. Cupcakes enriched with moringa were perceived as excessively dark in appearance	[200]
Leaves powder (5 and 10%)	White and Brown Breads	Brown bread samples were notably more acceptable compared to their white bread counterparts ($p < 0.05$) Bread with 5% moringa could be a significant contributor in addressing protein deficiency associated with malnutrition	[201]
Flower powder (1 and 2%)	Goat meat nuggets	The sensory characteristics of the control and moringa added nuggets were statistically similar, except for a notably lower flavor score observed in the 2% moringa ($p = 0.002$). Significantly enhances the dietary fiber and antioxidant content	[202]
Seed flour (0.1 and 0.2%)	Buffalo yoghurt	Yoghurt containing 0.2% moringa showed superior TPC and antioxidant activity over 14 days, with heightened antibacterial effectiveness against *E. coli*, *S. aureus*, *L. monocytogenes*, and *Salmonella* spp. It also had increased calcium, phosphorus, potassium, and iron levels, along with lower magnesium and zinc levels	[203]
Seed powder (0–20%)	Bread	Increased micro and macro nutrients. Sensory acceptability @ 5% Moringa	[204]
Flower extract (1 and 2%)	Chicken nuggets	Increase in dietary fiber content. Increase in shelf life via improved lipid stability	[205]
Leaves extract (0–0.2%)	Yoghurt	Speeds up fermentation, reduced whey separation by 21%, and improved water-holding capacity by 17%. Increases product viscosity and antioxidant property	[14]
Seed flour (1%, 3%, and 5%)	Chicken mortadella	The addition of 3% seed flour to chicken mortadella proved to be optimal, reducing lipid content, improving lipid stability, and maintaining consistent color throughout the 90-day storage period	[206]
Leaves powder (0–10%)	Gluten-free bread	As moringa increased, the lightness of crumb and crust decreased. The addition of MLP increased total phenolic content (TPC) and antioxidant activity. Sensory acceptance was achieved with bread at 2.5% moringa	[111]
Seed extracts (1.5%)	Yoghurt	Reduction in syneresis, increase in protein content, and thickening of product	[207]
Leaves powder (10%)	Complementary food	Significant increase in nutritional profile	[208]
Leaves (1.0%)	Snacks containing maize flour, cassava root	Increase in protein and ash content	[80]
Leaves powder aqueous extract (0.9%)	Yoghurt	Increased total phenolic content and antioxidant activity	[209]

Table 3 (continued)

Plant part with concentration	Food/formulation	Findings	References
Leaves powder (2%, 3% and 5%)	Ofam, Waakye, Porrodge, Jollof rice, Groundnut soup, Nkontomire sauce, Apapransa, Beans and Gari	Significant increase in micronutrients and all the dishes were highly acceptable study group i.e., school children	[210]
Leaves powder (8%, 10% and 12%	Muffin	The muffin with a 12% moringa was most preferred. Product exhibited a significant increase ($p < 0.05$) in various components, including moisture, ash, protein, fat, iron, calcium, potassium, beta-carotene, and vitamin C than control muffin	[211]
Leaves powder (5–20%)	Pan bread	Increased nutritional profile with negative impact on extensograph, farinograph values, and decrease in the value of gumminess, chewiness, resilience, and springiness	[212]
Moringa oil (10, 20 and 30% as milk fat replacement)	Ice cream	No significant changes in total solids, protein, fat, minerals, and pH compared to control. No change in melting point and viscosity	[213]
Leaves powder (0%, 1%, 3%, 5%, and 7%)	Muffins	Muffins enriched with moringa up to a 3% concentration achieve a harmonious blend, meeting both sensory expectations and functional requirements for consumers	[214]
Leaves powder (0–2.5%)	Fortified to amala prepared using plantain flour	Increase in the protein from 3.52 to 10.36%, fat from 1.82 to 2.37% and ash from 1.71 to 2.93% along with enhanced mineral profile	[215]
Leaves extract and oil (600, 800, and 1000 ppm)	Sour cream	Fortified product has higher sensory score with increased shelf life at 5 ± 1 °C	[113]
Leaves powder (15%)	White maize gruel/ogi	Increase in protein content by 94%. Swelling power reduction by 23%	[216]
Leaves powder (Upto 10%)	Complementary food (maize, peanut, soyabean)	Increased protein content along with higher NPR and PER in the experimental rats	[217]
Leaves powder (0.25%, 0.5%, 0.75% and 1%)	chicken sausages	Sausages with 0.5%, 0.75%, and 1% moringa exhibited significantly lower TBARS Sausages with 0.5%, 0.75%, and 1% moringa displayed consistently lower pH values from the 2nd to the 5th week of storage No sensory difference between control and 0.25% and 0.5% moringa added sausage	[69]
Flower powder (20%)	Weaning food (fermented maize and millet blend)	Enhanced nutritional value with higher sensory score	[218]
Flower powder (0–25%)	Fermented yellow maize and millet blend (weaning food)	Increase in crude protein, ash, crude fiber and fat content with increased Moringa concentration decrease in carbohydrate and moisture. 20% Moringa in the blend was highly accepted	[218]
Leaves powder (0–30%)	Cookies	Overall acceptability was higher @ 20% Moringa	[219]
Leaves extract (600 and 800 ppm)	Butter	Increase in storage stability by inhibiting oxidation and decreasing FFA formation	[220]

Table 3 (continued)

Plant part with concentration	Food/formulation	Findings	References
Leaves powder (0–10%)	Fortified to amala prepared using yam flour	Increased protein, calcium, potassium, magnesium, iron and sodium content Usage @ > 2.5% leads to poor sensory acceptance	[221]
Leaves powder (15%)	Yellow maize gruel	Increase in protein content by 44%. Swelling power reduction by 8%	[222]
Leaf powder (5%)	Bread	Increase in both protein and crude fiber by 54% and 56% respectively	[119]
Debittered seed flour (0–15% and 0–30%)	Bread and Cookies	Bread with 10% flour and cookies with 20% flour was acceptable and had more protein, iron and calcium. Increased flour level from 0 to 15% decreased the farinograph water absorption, amylograph peak viscosity, dough stability, and overall quality of bread	[223]
Leaves powder (0–15%)	Cookies	Increased nutritional profile with enhanced farinograph water absorption and decreased peak viscosity, dough stability and amylograph pasting temperature	[224]

to 15% for dry leaf powder and 1–5% for seed flour. Notably, the use of seed flour is highlighted for its comparable protein richness to the leaf. Numerous authors emphasize the enhancement of protein and fiber content in Moringa-enriched bread, sometimes accompanied by reduced moisture, leading to extended shelf life [119, 120]. Overall, the integration of Moringa into bread formulations proves to be a promising strategy for nutritional improvement and product preservation.

In another study, crispy noodles were enhanced with Moringa leaf puree. The concentration of *M. oleifera* leaf puree significantly impacted the aroma and taste of the crispy noodles ($p < 0.05$), while texture and color remained unaffected. Furthermore, these noodles, enriched with *M. oleifera* leaf puree, provided substantial nutrients such as protein, vitamin A and C, calcium, and zinc. Additionally, they contained polyphenols and flavonoids, offering various health benefits. In conclusion, the incorporation of *M. oleifera* leaf puree into crispy noodles presents a promising and nutritious snack option, particularly beneficial for children in food-insecure areas [121].

Overall, the versatile applications of Moringa in various food products highlight its potential as a functional and nutritive ingredient, contributing to enhanced nutritional profiles, quality, and shelf life across different sectors of the food industry.

Application of moringa in livestock feed

The nutritional richness and diverse bioactive components found in Moringa offer a significant opportunity for its application as livestock feed, aiming to enhance the health, growth performance, milk production, and meat quality of animals [122]. In poultry production, the inclusion of Moringa leaf meal in diets has shown enhancements in egg production and quality [123–125]. The potential mechanisms behind the observed enhancements in egg production and quality could be attributed to the rich nutritional profile of Moringa, which includes vitamins, minerals, and bioactive compounds. These components may positively influence the overall health and reproductive performance of poultry, leading to improved egg-related parameters. In a study, researchers assess the influence of Moringa on broiler growth performance, meat quality, and intestinal health. The results indicated that both Moringa and fermented Moringa positively influenced broiler flesh color and breast muscle tenderness, with statistical significance ($p < 0.05$) [126]. In a separate investigation, broiler chickens fed with Moringa demonstrated elevated levels of haemoglobin, red blood cells (RBC), and white blood cells (WBC), along with improved intestinal health characterized by increased lactobacillus growth and decreased *Escherichia coli* population [127].

On the other side, the impact of *M. oleifera* polysaccharide (MOP) on various parameters, including growth performance, serum biochemical indicators, immune organ indicators, colonic morphology, colonic microbiomics, and colonic transcriptomics, was assessed in newborn calves. Notably, the supplementation of MOP led to a significant increase in the body weight of newborn calves, a reduction in the incidence of calf diarrhea, and an overall promotion of calf growth. The linear decrease in fecal scores observed with MOP supplementation further supported its positive effects. MOP exhibited a regulatory effect on the abundance of Firmicutes and Bacteroidetes in the intestinal tract, contributing to a decrease in diarrhea occurrence. Moreover, at the molecular level, MOP demonstrated the ability to modulate genes associated with inflammatory signaling pathways such as the mitogen-activated protein kinase (MAPK) signaling pathway, transforming growth factor-beta (TGF-ß) signaling pathway, phosphatidylinositol 3-kinase and protein kinase B (PI3K-Akt) signaling pathway, and tumor necrosis factor (TNF) signaling pathway in the calves' intestine, thereby mitigating the occurrence of intestinal inflammation [128]. The inclusion of Moringa in livestock feed has shown positive effects on milk yield and quality in sheep, goats, and cows [129–131]. Substituting 25% of alfalfa hay feed with Moringa leaf powder in the diets of goats and ewes resulted in increased milk yield with higher fat, lactose, and solid non-fat (SNF) content compared to diets containing 40% alfalfa hay. Additionally, vitamin C levels and the oxidative stability of milk improved [130]. Cohen-Zinder et al. [131] reported an increase in milk yield with high fat content in cows fed with a diet formulated using Moringa leaf compared to a diet formulated with wheat hay. Furthermore, the addition of Moringa leaves to the diets of goats, pigs, and grill chickens enhanced characteristics such as color, odor, lipid profile, and chemical composition without negatively impacting carcass features [132]. In a study, Feeding lactating ewes with Moringa leaf extracts did not adversely affect the chemical composition of their yogurt during a 14-day storage period at 4 °C. Instead, the dietary supplementation positively influenced the physicochemical composition of both milk and yogurt [133]. In another research, Friesian cows were fed with Moringa dry leaves at concentrations of 40 g and 60 g per day, and milk obtained after 30 days was used for cheese production. The results showed that cheese yield, fat content, total nitrogen (TN), and water-soluble nitrogen (WSN) significantly increased ($p < 0.05$). Cheese from the group with 60 g/day Moringa had higher phosphorus and calcium, and recorded the highest value of α-Linolenic (omega-3, n-3) unsaturated fatty acids. Organoleptic properties of this cheese were significantly higher and more preferred, indicating that adding Moringa to dairy cattle ration enhances the nutritional value of the resulting cheese [134].

Non-food application of Moringa

Beyond its applications in food, Moringa exhibits versatility in non-food sectors. Moringa seed powder serves as a natural coagulant for water treatment, effectively removing suspended particles from rivers and murky streams. Figure 2 illustrates the versatile applications of Moringa across various sectors. The presence of cationic polyelectrolyte in both seeds and pods facilitates the purification of water for human consumption by causing the clumping of colloidal particles, subsequently removed through filtration or decantation. The antimicrobial properties of Moringa seeds make them effective in removing hardness, biological contaminants, and unwanted chemicals from water. In a research endeavor, the utilization of Moringa seed powder in conjunction with a bucket filter was investigated to establish a hybrid system aiming to match the effectiveness of the BioSand filter (CBSF) but with reduced expenses and weight. The bucket filter, incorporating a high dose (125 mg/l) of Moringa, exhibited an E. coli removal efficiency ranging from 81 to 98%, comparable to the CBSF. Additionally, the filtered water adhered to WHO guidelines concerning turbidity, organic matter, and pH, although there was a marginal decrease in pH compared to the original water [135]. Other research group by Rifi et al. [136] illustrated the efficacy of Moringa as an organic coagulant for mitigating pollution in olive oil mill wastewater.

Moreover, the bark of Moringa yields fiber that, when processed, produces high α-cellulose pulp for use in textiles and cellophanes. The oil derived from the seeds serves multiple purposes, including its utilization as a fertilizer in plantations to stimulate the growth of various species. Additionally, it finds application in cosmetics like soaps and perfumes, as well as in the production of biodiesel. Extracts from Moringa have the capability to generate zeatin, which is known for its effectiveness in enhancing plant development and subsequently boosting crop yields [137]. Furthermore, due to its easy absorption into the skin, the oil is highly sought after in the cosmetic industry for aromatherapy and massage purposes [138, 139]. In addition, Moringa leaves extract (MLE) has been utilized in agriculture to enhance the growth and yield of various crops. This effectiveness of MLE is credited to its rich composition of essential nutrients including minerals, proteins, vitamins, sugars, fiber, phenolics, and free proline. Moreover, MLE contains notable quantities of plant hormones such as auxins, cytokinins, and gibberellins. Additionally, MLE serves as a beneficial product that stimulates seed germination, boosts plant growth and root development, prolongs fruit freshness, and enhances crop yield and quality, even in challenging environmental

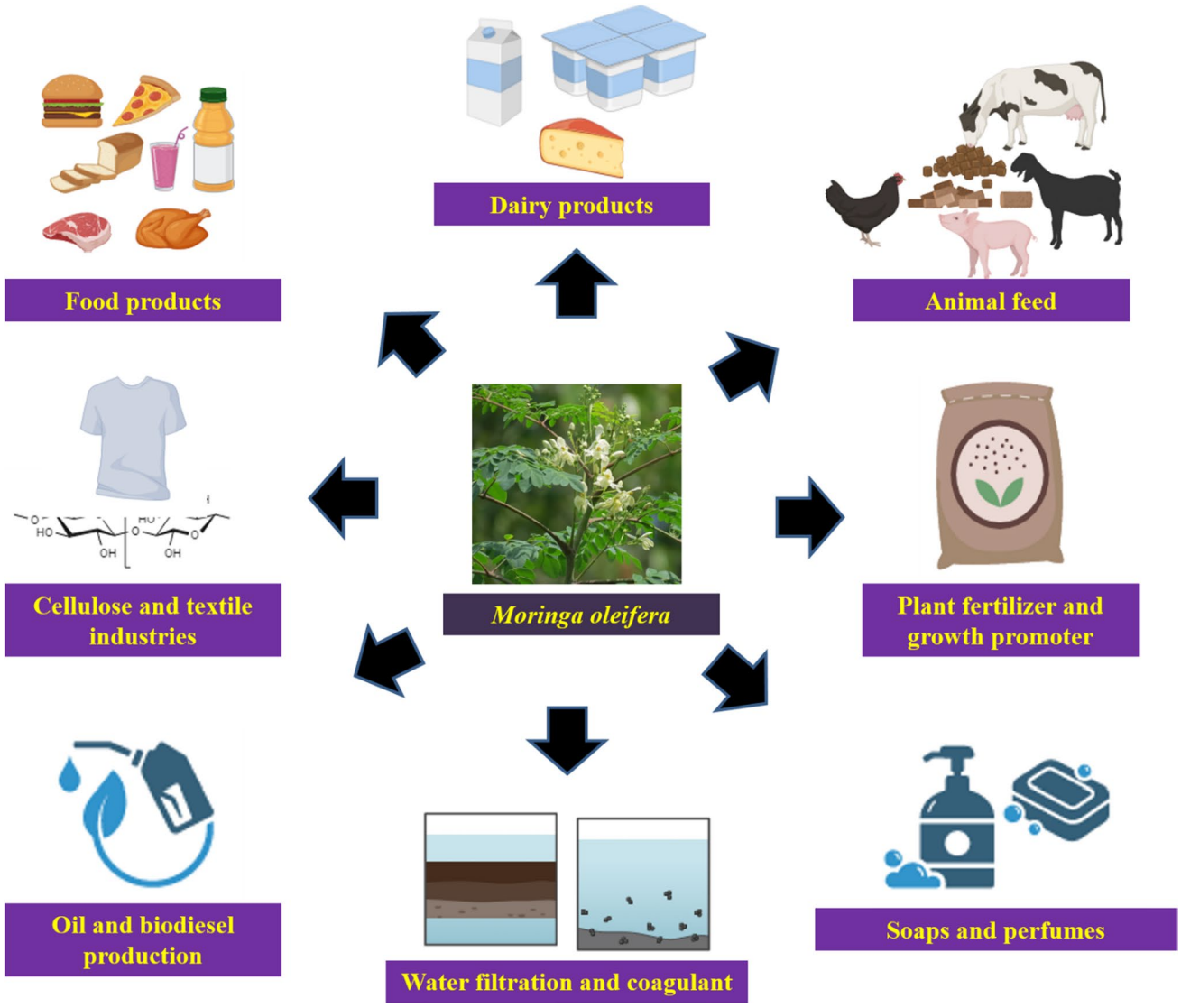

Fig. 2 Schematic view of the application of *Moringa oleifera*

conditions [140]. In summary, the multifaceted applications of Moringa extend beyond the realm of food, demonstrating its potential as a sustainable resource in its diverse applications.

Safety and toxicology of *M. oleifera*: research insights

Although various parts of *M. oleifera* are being used in traditional medicine and production of food products for human nutrition, it is essential to decipher the safety and toxicity profile of *M. oleifera* before it is being marketed as therapeutic or neutraceuticals product. Since there are no standard regulatory guidelines underscoring the safer upper limit for extracts of various parts of this plants, researchers undertook in vitro and in vivo safety (oral toxicity studies) in cell culture and animal models, respectively, to determine a safe dose for neutraceuticals applications. The safety outcomes of different parts of *M. oleifera* have been complied and presented in Table 4. The in vitro safety or toxicity tests are conducted to screen a safer dose from a larger number of doses for in vivo safety studies. Also, these tests are often used to estimate the potential of a new food additive, or other chemical product to be hazardous to humans. The in vitro toxicity testing is provides insights on the toxic effects of test substances on cultured bacteria or mammalian cells. Under in vitro milieu, various tests viz. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) dye reduction, neutral red uptake, Lactate dehydrogenase (LDH) release, and trypan blue exclusion assays are conducted on the eukaryotic/mammalian cell lines

Table 4 Studies on safety and toxicity assessment of different parts of *Moringa oleifera*

Part of the plant	Dose	Cell line/animal model	Type of test	Observation	References
Aqueous and methanol extract of leaf	0.05 to 5 mg/l	Primary human skin fibroblasts	Ex-vivo	Aqueous extract was non-toxic	[225]
Methanol extract of leaf	5%	Fibroblast cells	In vitro	Moderately toxic	[226]
Aqueous extract of seed	100 µg/mL	Human peripheral blood mononuclear cells (PBMCs)	In vitro	Non-toxic	[227]
Aqueous, chloroform, and ethanolic extract of leaf	1500–11.71 µg/mL	Vero cell line	In vitro	Concentration below 300 71 µg/mL was non-toxic	[228]
Methanol extract of leaf	10, 50, 100 µg/mL	3T3L1 mouse fibroblast cells	In vitro	Non-toxic	[229]
Methanol extract of leaf	25, 50, 100, 200, 400 µg/mL	HepG2 cells	In vitro	Non-toxic	[230]
Methanol extract of leaf	31.25, 62.5, 125, 250 and 500 µg/mL)	Macrophages RAW 264.7	In vitro	Non-toxic	[231]
Methanol extract of leaf	1000 µg/mL	HaCaT cells	In vitro	Non-toxic	[232]
Aqueous extract of leaf	0.125, 0.075, 0.050 and 0.025 mg/mL	Caco-2 cells	In vitro	Non-toxic	[146]
Aqueous extract of leaf	5,000 mg/kg for acute toxicity and 40 mg/kg to 1000 mg/kg for subacute toxicity study	Sprague–Dawley Rats	In vivo (Acute and subacute oral toxicity)	No observed adverse reactions	[148]
Leaves powder	2000 and 5000 mg/kg for acute toxicity and 50, 500 and 1000 mg/kg	Mice model	In vivo (Acute and subacute oral toxicity)	Although there was no toxic signs observed in acute toxicity test, the moringa powder at 500 and 1000 mg/kg promoted liver and kidney damages	[233]
Aqueous extract of leaf	2000 mg/kg	Wistar albino rats	In vivo (Acute oral toxicity)	LD50 of the leaf extract was found to be > 2000 mg/kg in female wistar albino rats	[234]
Aqueous extract of leaf	2000 mg/kg	Wistar rats	In vivo (Acute and subacute oral toxicity)	Non toxic	[235]
M. oleifera leaf powder	2000 mg/kg	Sprague Dawley rats	In vivo (Acute oral toxicity)	LD50 of the leaf extract was found to be > 2000 mg/kg	[236]
M. oleifera leaf methanol extract	Acute toxicity: 2000 mg/kg Subchronic toxicity 150, 300, and 600 mg/kg	Wistar albino rats	In vivo (Acute and subacute oral toxicity)	Acute toxicity study revealed no mortality at 2,000 mg/kg dose	[106, 107]
M. oleifera leaf ethanol extract	450 mg/ mL	Albino rats and rabbits	In vivo (Acute toxicity)	Non toxic	[237]
M. oleifera stem bark extract	2000 mg/ kg	Swiss albino mice	In vivo (Acute and subacute oral toxicity)	Non toxic	[238]
Ethanolic extract from the seeds of *Moringa oleifera*	100, 500 and 1000 mg/kg	Rats	In vivo (Subchronic toxicity)	Toxicity was found to be variable as there was significant decrease in RBC and eosinophil cells at 1000 and 500 mg/kg dose	[239]

Table 4 (continued)

Part of the plant	Dose	Cell line/animal model	Type of test	Observation	References
Isothiocyanate-1 (MIC-1)-enriched hydro-alcoholic moringa seeds extract	8 (low), 257 (mid-low), 772 (mid-high), or 2571 (high) mg/kg	Sprague–Dawley CD® IGS rats	In vivo (Acute oral toxicity)	No observed adverse effect level (NOAEL) was 257 mg/kg b.w/d	[240]
Methanol extract of leaves and seeds of *M. oleifera*	100, 200, 400 and 1000 mg/kg	Wistar rats	In vivo (Subacute oral toxicity)	Physical changes like agitation, confusion and disorientation in various tissues were observed at the highest dose tested (1000 mg/kg) of the seed extract	[241]
Aqueous and ethanol extracts of *Moringa oleifera* leaves	16.1, 8.05, 4.02, 2.01 g/kg of aqueous extract and 39.8, 19.9, 9.95, 4.97 g/kg of ethanol extracts	Swiss albino rats	In vivo (Subacute oral toxicity)	Non toxic	[242]
Methanol extract of leaves and seeds of *M. oleifera*	3000–5000 mg/kg	Rats	In vivo (acute and subacute oral toxicity)	The median lethal dose of the extract in rat was 3,873 mg/kg	[243]
Water extract of *M. oleifera* leaves	10, 100 and 1000 mg/kg	Wistar rats	In vivo (Chronic toxicity for 6 months)	Serious chronic toxicity in experimental animals	[149]
Moringa oleifera leaf extract	2000 mg/kg, 3000 mg/kg, 5000 mg/kg and 7000 mg/kg	Wistar rats	In vivo (acute oral toxicity)	Toxic effect at higher dose (> 3000 mg/kg)	[244]
Moringa oleifera seed extract	100 and 200 mg/kg	Rats	In vivo (acute and subacute oral toxicity	Non toxic	[245]
Leaf extract	1000 mg/kg	Albino mice	Acute toxicity	Non toxic	[246]
M. oleifera leaf extract	2000 mg/kg	Rats	In vivo (Acute oral toxicity)	Non toxic	[247]
M. oleifera leaf extract	5000 mg/kg	Swiss albino mice	In vivo (Acute oral toxicity)	Non toxic	[248]

(HeLa, HCT-116, HepG2, MCF-7, Caco-2, and L929) [141, 142]. However, care should be taken while selecting the cell lines for toxicity evaluation as most of the cytotoxicity studies were carried out on carcinogenic cells and thereby the results obtained from such studies do not truly indicate the safety on normal cells [143]. Numerous in vitro and in vivo studies have investigated the toxicity of *M. oleifera* leaf powder and extracts. Findings from experiments with normal human cell lines indicate the overall safety of leaf extracts, with some observed cytotoxicity dependent on the dose. The in vivo studies with rats revealed the safety of *M. oleifera* leaf powder and extracts, presenting acute toxicity only at extremely high dosages (3000 mg/kg). Human studies using *M. oleifera* leaf powder reported no adverse effects, although there is a lack of research on human toxicity related to leaf extracts. It is essential to conduct further toxicity studies to ensure the safe use of supplements derived from *M. oleifera* leaves for human health [144]. In a study, a research team investigated the toxic effects of *M. oleifera* leaf extract on Madin-Darby Canine Kidney (MDCK) cell line and found that methanolic extracts of *M. oleifera* inhibit 50% of cellular viability at a concentration 70 µg/mL. Furthermore, none of the extracts produced any adverse effects on the viability on the MDCK cell lines at low concentrations. In another study, the cytotoxic effects of alcoholic and aqueous extracts of *M. oleifera* was studied on Hela cell line using MTT reduction and trypan blue exclusion assays, and results indicated that as increase in the concentration from 10 to 100 µg/mL, the per cent inhibition increased from 8 to 60%. Also, the IC50 value was found to be 70 µg/mL [145]. In a similar study, direct treatment with 0.125 mg/mL microencapsulated Moringa extract on Caco-2 cells showed a slight anti-proliferative effect with a cell viability of about 87% (non-cytotoxic), supporting the safety of the proposed formulation and potential use within the food field. On the contrary, the aqueous extract of *M. oleifera* leaf showed a marked cytotoxic effect on SAF-1 (at doses above 0.01 mg/mL) and PLHC-1 (at doses above 0.25 mg/mL) cell lines [146]. The ethanolic extract improved the viability of SAF-1 cells and decreased the viability of PLHC-1 cells when used at higher concentrations [147]. These studies indicate that safety of *M. oleifera* is dose and cell line specific, and therefore requires in vivo oral toxicity trials for determining a safer/ No observed effect level (NOEL) dose.

Safety studies using laboratory animals is generally carried out via repeated dose oral toxicity tests such as acute, sub-acute, and sub-chronic toxicity trials in accordance with the Organization for Economic Co-operation and Development (OECD) guidelines [148]. Acute toxicity study (14 days) provides insights into the effect of single exposure to test compound at a high dose on toxicological behavior of test animals. Whereas the sub-acute toxicity is conducted to gather information obtain on hazardous information likely to arise from the repeated single dose exposure to test compound for 28 days, preferably in the rodent/rat model. On the contrary, the subchronic toxicity is conducted to determine the NOEL dose of the test compound after experimenting on animals. This test is generally carried out for 90 days for at least three different dose that are selected based on the experimental insights obtained from acute and subacute toxicity study. These tests generally measure effect of test compound on feed and water intake, and detailed observations on ophtalmological parameters haematology, clinical biochemistry and urinalysis as well as gross necropsy and histopathology. Additionally, a year-long chronic toxicity trial is conducted to evaluate the effect of repeated exposure to test compounds on behavioral, physiological and other hematological parameters of experimental animals. Alternatively, six months long chronic toxicity studies of various parts of *M. oleifera* have also been conducted in animal model [149]. In a study by Asare et al. [150] assessed the acute oral toxicity of *M. oleifera* aqueous leaf extract in Sprague–Dawley (S–D) rats. Accordingly, *the extract* was found to be cytotoxic at 20 mg/mL with genotoxic potential at supra-supplementation levels of 3000 mg/kg but not at ≤ 1000 mg/kg. These results suggest that lower doses of extract are found to be non-toxic. In another study, the acute and sub-acute toxicity of methanolic extract of *M. oleifera* was studied in rat model. Although signs of acute toxicity were observed at a dose of 4000 mg/kg in the acute toxicity test, and mortality was recorded at 5000 mg/kg. Further, no adverse effect was observed at concentrations lower than 3000 mg/kg. The median lethal dose of the extract in rat was 3873 mg/kg. Sub-acute administration of the seed extract caused significant increase in the levels of alanine and aspartate transferases (ALT and AST), and significant decrease in weight of experimental rats, at 1600 mg/kg. These results conclusively indicate that the extracts of various parts of *M. oleifera* is safe at relatively lower doses, and therefore lower doses may exhibit safe therapeutic potential.

Future perspectives

Firstly, the potential for botanical innovation in Moringa should be explored, contemplating advancements in cultivation practices, breeding techniques, and genetic studies aimed at amplifying its therapeutic properties. Additionally, the discussion must extend to the formulation of novel functional foods incorporating Moringa, considering strides in food technology and the tailoring of products to address specific health concerns. Exploring biotechnological applications, such as genetic modification and the establishment of Moringa-based biofactories for sustainable production, is paramount. The section should underscore the ongoing and future research endeavors focusing on ensuring the safety

of Moringa-enriched products. This involves refining dosage recommendations, conducting toxicological studies, and contemplating regulatory considerations for widespread commercial use. Moreover, the global impact of Moringa in mitigating nutritional challenges, including collaborative initiatives for cultivation, processing, and integration into global diets, should be thoroughly discussed. The promotion of interdisciplinary research, involving collaboration among botanists, food scientists, pharmacologists, and related fields, is crucial to unlocking Moringa's full potential. Furthermore, the importance of sustainability in Moringa cultivation and processing, addressing environmental impact and ethical sourcing, should be emphasized. Lastly, acknowledging the imperative of heightened consumer awareness regarding Moringa's health benefits, the section should advocate for education campaigns and marketing strategies to solidify its acceptance as a pivotal ingredient in future functional foods. By encompassing these future perspectives, the review is poised to offer a forward-looking vision that shapes the trajectory of Moringa in the realms of therapeutic and functional foods, providing valuable insights that steer future research and applications.

Conclusion

This review delves into the manifold dimensions of Moringa, shedding light on its multifaceted potential as a functional food source and beyond. The examination encompasses botanical and taxonomic elements, accompanied by a thorough exploration of its nutritional value and its role in addressing malnutrition, thereby emphasizing its relevance in tackling global health challenges. The elucidation of phytoconstituents and bio-functional properties unveils the extensive array of compounds inherent in Moringa, showcasing its attributes as an antioxidant, antimicrobial, antidiabetic, anti-obesity, antihypertensive, and anticancer agent. The diverse applications of Moringa in food products, livestock feed, and non-food sectors underscore its versatility and adaptability across multiple industries. Furthermore, the review critically assesses the safety and toxicology aspects associated with Moringa, consolidating research findings to present a balanced perspective on its consumption and utilization. In conclusion, this comprehensive review underscores the substantial potential of Moringa as a nutritional powerhouse, a functional food ingredient, and a resource with versatile applications. It significantly contributes to the comprehension and exploration of this plant's therapeutic attributes and safety considerations.

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