



The Journal of Anatomical Sciences
Email: journalofanatomicalsciences@gmail.com

J. Anat Sci 17(1) Mar

Submitted: October 27th, 2025

Revised: December 12th, 2025

Accepted: February 6th, 2026

Toxicological Assessment of the Moringa Species: A Minireview

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ABSTRACT

Moringa oleifera, a plant of the moringa species, is known for its nutritional and medicinal properties. It is a major constituent of several polyherbal supplements, particularly consumed in Sub-Saharan Africa. Despite its extensive application in herbal medicines, there are still concerns regarding its safety. The aim of this mini-review is to report recent toxicological findings on the genus *Moringa*. Several studies have reported bioactive phytochemicals in moringa species, including alkaloids, flavonoids, carotenoids, and saponins. These constituents may exert protective, therapeutic, or deleterious effects in humans, depending primarily on concentration/dose and duration of exposure. Toxicodynamic studies revealed that the extract of *Moringa oleifera* inhibited cell proliferation; generated free radicals such as reactive oxygen species (ROS), and induced apoptosis by activating caspase-3 in both liver cancer cells (HEPG2) and normal hepatocytes. Phytochemicals such as glucosinolates and tannins can cause hepatotoxicity, nephrotoxicity, and reproductive toxicity at high doses, due to the formation of nitriles that induce cellular oxidative stress. The toxicity of moringa has been linked to the presence of heavy metals, which can induce oxidative stress, enzyme inhibition, and neurotoxicity at high concentrations. In a case report, it was shown that *Moringa oleifera* caused toxicoderma in a 57-year-old woman. This was reversed by discontinuation of *Moringa oleifera* and the use of antihistamines. Despite these restrictions, it can be argued that the moringa species has low toxicity at lower doses, but it must be used with caution at higher doses. Further research on carcinogenicity and other drug-herb interactions is needed.

Keywords: *Moringa oleifera*, oxidative stress, bioactive, teratogenic, toxicodynamic, phytochemicals, safety evaluation

INTRODUCTION

The moringa species is regarded as one of the world's most valuable trees. They belong to the *Moringaceae* family. The most studied of the species is the *Moringa oleifera*, known as the 'Horseradish or Drumstick Tree'. Due to the folkloric claim that it has the ability to improve lactation in breastfeeding women, it is often termed as *The Mother's Best Friend*¹. Moringa species are widely cultivated in Africa, India, the Middle East, Pakistan, Asia, and South America². Although its use cuts across several continents, its safety profile, teratogenicity, and possible drug-herb interactions still pose a major public health concern, particularly amongst women, lactating mothers, and children. This necessitates the need for consistent novel findings on its safety; therefore, this minireview reports recent toxicological findings on the moringa species.

Ethnobotany of Moringa species

There are 13 known species of moringa found in Africa and Asia, including *Moringa borziana*, *Moringa hildebrandi*, *Moringa oleifera*, *Moringa stenopetala*, *Moringa arborea*, *Moringa ovalifolia*, *Moringa drouhardi*, *Moringa peregrina*, *Moringa rivea*, *Moringa concanensis*, *Moringa longituba*, *Moringa ruspoliana*, and *Moringa pygmaea*³. However, the most commonly cultivated species are *Moringa oleifera*, *Moringa peregrina*, and *Moringa stenopetala*⁴. *Moringa oleifera* flowers are white, and they bloom at night with a fragrant aroma. At the same time, the leaves are small and dark green with a high phytomedicinal content that includes protein, antioxidants, minerals, and vitamins⁵.

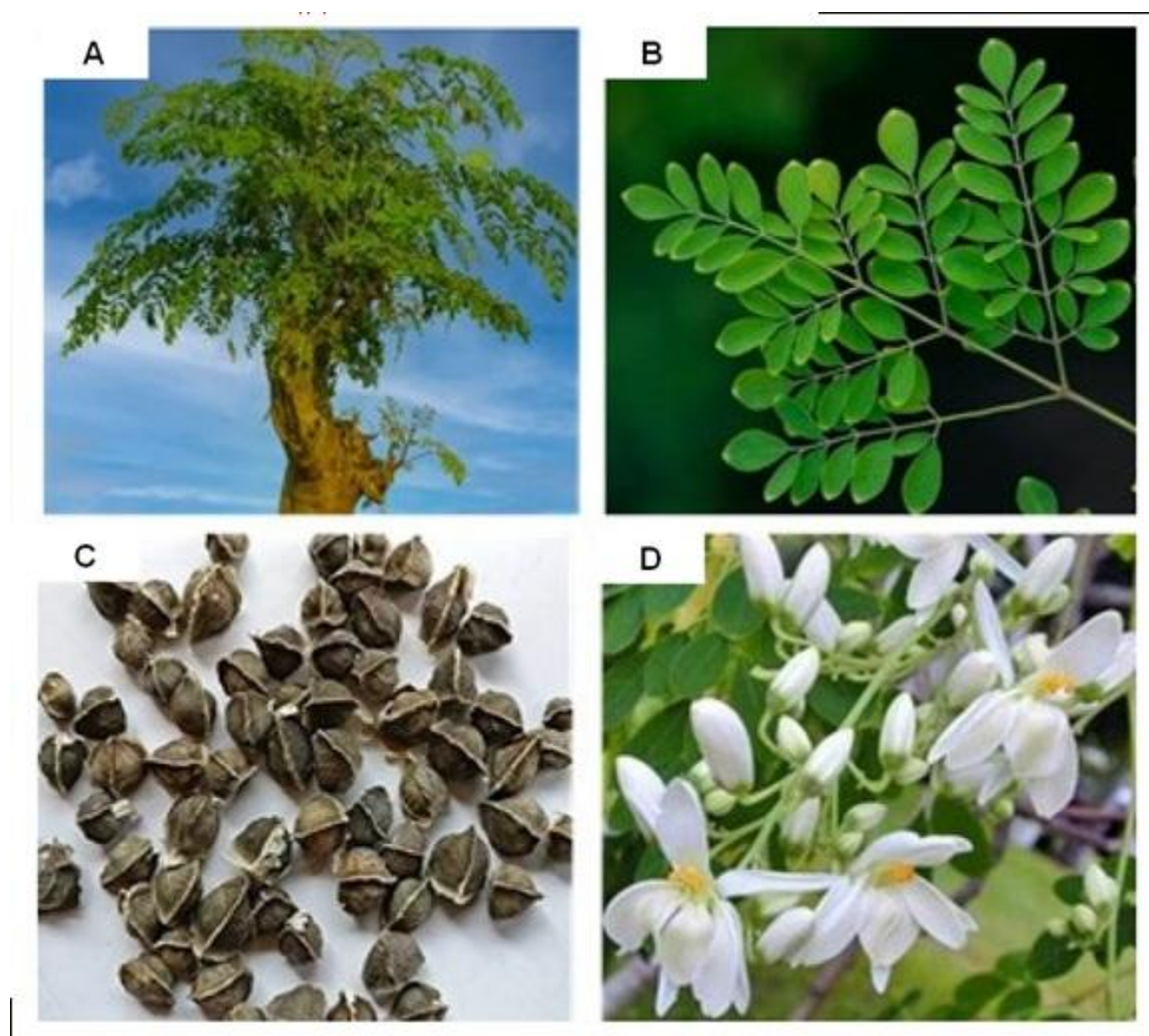


Figure 1. (a) *Moringa oleifera* tree; (b) *M. oleifera* leaves; (c) *M. oleifera* seeds, and (d) *M. oleifera* at its flowering stage. (Adapted from Anzano *et al.*⁶)

Phytochemistry data on Moringa species

Moringa oleifera can be grown in various soil types, except waterlogged soil types; however, moderately alkaline loamy soils provide the best medium for these plants. This is attributed to the good drainage; this soil type provides². *Moringa oleifera* seeds germinate up to 2 cm within 2 weeks of sowing. After 3-6 weeks post-germination in the nurseries, at a height of approximately 30 cm, they are repotted. The seeds are stored and preserved at a humidity of about 5-8% and a temperature of 3°C⁷.

The moringa species are deciduous and perennial in nature, thriving in cold temperatures but can't survive extremely low temperatures. It is optimal at temperatures ranging from about 26 to 37°C⁸.

Moringa is highly adaptable and can grow in various soil types and environmental conditions. The ideal rainfall range for optimal growth and development is 250-3000 mm. This makes its cultivation possible in many parts of the world⁹. Providing great adaptability presents a potential for large-scale agriculture and substantial subsistence and commercial benefits¹⁰.

Research has shown that almost every part of the plant contains various types of chemicals with important biological activities, such as antioxidants that defend the body against oxidative stress and cancer by scavenging free radicals; antifungal, antispasmodic, antibacterial, antiviral, anti-inflammatory, and diuretic properties¹. This species contains phenolic acids (gallic and ferulic acid), proteins (amino acids), flavonoids (myricetin),

vitamins (tocopherol), fatty acids (omega-6, omega-3), and mineral salts (magnesium, calcium, etc.)¹¹.

Due to their flocculant properties, moringa seeds are used for water purification; the protein in the seeds contains active cationic polypeptides that can be used as a natural polypeptide to sediment particles, owing to the negative electrical charge of the colloids¹². *Moringa oleifera* is rich in macronutrients, micronutrient vitamins, phytohormones, alkaloids, and flavonoids, making it helpful in tolerance to abiotic and biotic stress under stressful environmental conditions¹³. Juice from moringa leaves can be used by diabetics to regulate their blood sugar levels and blood pressure, and *Moringa oleifera* leaves are a good option for developing countries looking for high-quality healthcare services that provide accessible and affordable therapy in areas with limited access to Western medicine¹⁴.

Phytochemical composition of Moringa species

Moringa is commonly used in herbal medicine regimens to manage a broad range of pathological conditions, ranging from skin infections, chest congestion, psoriasis, semen deficiency, tuberculosis, scurvy, diabetes, cholera, abnormal blood pressure, fever, sore throat, and glandular swelling¹⁵. When compounded with other oils, Moringa oil enhances the oxidative stability of the final composition, making it safe for deep-frying in commercial settings and household cooking. In addition to their flocculant properties, the biosorbent properties of the seeds help reduce microbial load during water purification¹⁶.

Some of the bioactive phytochemicals of *M. oleifera*, such as quercetin and *caffeoylquinic* acid (CQA), are the major phenols linked with oxidative stress mitigation, cardiovascular and neurodegeneration risk reduction, as well as enhancing *M. oleifera*'s profile as a medicinal food¹⁷. *M. oleifera* exhibits diverse bioactivities such as antiviral, antibacterial, and anthelmintic, and it has the potential to be used as a natural substitute to synthetic insecticides; it can also be used as a fertilizer and biopesticide.¹⁸ Moringa has a rich zinc content, which is necessary for both DNA and RNA biosynthesis. Thus, it provides a means to achieve the human dietary requirement for zinc¹⁹.

Incorporating Moringa leaf as a food condiment has been reported to improve calcium, beta-carotene, and magnesium supplementation, which is ideal for general well-being²⁰. Comparative nutritive data show that fresh leaves of *M. oleifera* contain more protein than eggs; more vitamin C than oranges of the same proportion, and more iron than spinach.²¹ This justifies the reason why moringa leaf is a major part of food condiments in several parts of Africa.

Moringa oleifera stem-bark is useful in the management of hypertension and ulcer; the roots play a role in the treatment of paralysis and kidney stones, the flowers are used as honey and to produce

aphrodisiac substances²². Alkaloid extracts of both *Moringa oleifera* and *Moringa stenopetala* have been seen to mitigate neurotoxicity by reducing oxidative stress markers and enhancing antioxidant defense mechanisms²³.

Adding Moringa leaves to staple foods can enhance their nutritional value by increasing protein, vitamins, and minerals, and may also modify their nutritional content²⁴. In beverages, co-fermenting Moringa with tea leaves significantly increases the levels of vitamin A and C, alkaloids, minerals, lipids, amino and organic acids, and antioxidants in the final tea product²⁵. Moringa leaf powder has proven to potentially extend the shelf life of food products by reducing bacterial yeast and contamination in foods²⁶.

The rich bioactive profile of moringa includes alkaloids, phenols, and flavonoids, which confer its antimicrobial activity, thereby inhibiting the growth of pathogenic microorganisms²⁷. Extracts from *Moringa Oleifera* seeds and leaves have anti-inflammatory, antibacterial, antioxidant, and antifungal properties, providing supportive therapies in heart functions, diabetic wound healing, fertility management, and overall liver functions²⁸.

Ethnomedicinal uses of the Moringa species

The identified bioactive compounds in moringa species include proteins, carotenoids, flavonoids, phenolic acids, alkaloids, glucosinolates, sterols, tannins and saponins, fatty acids, glycosides, polysaccharides, and terpenes⁸. The hydroxyl groups in flavonoids, lignans, phenol-carboxylic acids, and their derivatives are the major phenolic components of moringa leaves, and are responsible for their radical scavenging prowess²⁹.

Myrosinase, a peptide present in moringa leaves, causes β -D-glucose hydrolysis upon activation. This results in the formation of isothiocyanates, thiocyanates, sulfates, and nitriles. These compounds, formed as a result of the hydrolysis, possess marked biological activities, including antibacterial and antifungal properties²⁹.

Phytomedicinal profile of the Moringa species

Moringa species contain numerous bioactive constituents providing therapeutic and prophylactic management of many diseases. This is attributable to their medicinal properties, including hepatoprotective, antifungal, antibacterial, antidepressant, wound-healing, antioxidant, anticancer, neuroprotective, anti-inflammatory, and anti-diabetic³⁰. *Moringa oleifera* leaves contain components beneficial in managing inflammation, diabetes, hypercholesterolemia, non-alcoholic liver cancer, high blood pressure, and insulin resistance³¹.

Table 1: Summary of the specific phytochemicals present in *Moringa oleifera* ²⁸.

Bioactive Compounds	Parts of Plants
Phenols and Phenolic Acids (benzoic acid, epicatechin, ellagic acid, caffeoylquinic acid, gallic acid, and ferulic acid)	Seeds, leaves, root bark, stems.
Flavonoids (kaempferol, apigenin, genistein, luteolin, myricetin, quercetin, vitexin, catechin)	Leaves, seeds, flowers
Glucosinolates (niazirin, niazirin, moringin, glucobarbarin, glucomoringin, glucomoringin)	Seeds, leaves
Carbamates (niazinin A and B; niaziminin A and B, niazimicin, niazidin, and niazicin A)	Leaves, pods, seeds
Isothiocyanates	Pods, seeds, leaves, and root barks
Sterols	Flowers, seeds, stems, pods, roots.
Fatty Acids	Leaves, seeds, flowers
Esters	Flowers, leaves, seeds, pods
Alkaloids	Stems, roots, seeds, leaves
Carotenoids (β -Carotene, lutein)	Leaves
Vitamins (A, B1, B2, B3, C, E)	Pods, leaves, flowers, seeds
Amino Acids	Leaves, pods, seeds
Minerals (Magnesium, potassium, calcium, zinc, iron, sulfur, sodium, copper, phosphorus, manganese, selenium)	Roots, barks, leaves, seeds, pods

The anti-inflammatory, antibacterial, and antioxidant potential is linked to the rich content of carotenoids, flavonoids, tannins, phenolic acids, saponins, vitamins A, C, and E, triterpenoids, alkaloids, and isothiocyanates ³², which help to mop up free radicals such as reactive oxygen species (ROS), and inhibit lipid peroxidation. These eventually improve the body's antioxidant mechanisms.

Compounds found in *M. oleifera*, such as kaempferol and quercetin, affect the inflammatory pathway, with particular specificity for the cyclooxygenase (COX)

and lipoxygenase (LOX) enzymes. Moringa extracts regulate inflammatory cytokines, inhibit NF- κ B, and enhance antioxidant enzyme activity, which are critical for mitigating degenerative and inflammatory diseases ³⁴. The extracts of *M. oleifera* enhance glucose uptake, stimulate insulin secretion, and improve lipid metabolism, thereby preventing cardiac and metabolic pathologies (35). They also lower inflammatory markers, improve immune function, and prevent spikes in glycated hemoglobin levels and fasting blood glucose (FBG) ³⁶.

Isothiocyanates in *M. oleifera* control inflammation signaling pathways, reducing TNF- α and IL-1 β levels

³⁷. This compound further reduces pro-inflammatory markers, including TNF- α , IL-1, IL-6, and COX-2, thereby suppressing macrophage-mediated inflammation ³⁸. *Moringa peregrina* extracts lower serum cholesterol, triglycerides, and LDL (low-density lipoprotein) while increasing HDL (high-density lipoprotein). It also increases antioxidant enzyme activity, improves liver function, and reduces hepatic fat accumulation ³⁹.

Moringa extracts demonstrate antibacterial efficacy against pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*; enhance cell migration and proliferation; support essential processes for wound closure and healing, particularly in diabetic conditions ⁴⁰; accelerate tissue regeneration; promote collagen synthesis; and reduce healing time in chronic wounds ⁴¹. *M. oleifera* contains bioactive compounds such as niazimin-A, niaziminin-B, and niazicin-A, which serve as inhibitors of the angiotensin-converting enzyme (ACE), a major control enzyme for blood pressure. They exhibit potent ACE-binding affinity, signifying their potential as a natural ACE inhibitor ⁴².

Moringa exhibits immunomodulatory and immunosuppressive activities that help in controlling immunologic stimuli in various autoimmune conditions, such as ulcerative colitis and asthma ⁴³. *M. oleifera* methanol leaf extract (MMLE) contains glycoside cyanide and isothiocyanates, which enhance immune functions via mobilizing of immune mediators ⁴⁴. The phenolic constituents of *M. oleifera* methanol extract, including isothiocyanates and flavonoids, provide neuroprotective effects against neurodegenerative disorders and oxidative stress by inhibiting inflammatory pathways and reducing DNA damage ³¹.

Moringa extract (MITC-12) has been said to exhibit anticancer properties in various cell lines including A375 (human malignant melanoma), HCT116 (colon cancer in humans), U251 (human glioblastoma astrocytoma), A431 (human squamous carcinoma) and HeLa (human cervix epithelioid carcinoma) by preventing cancer cell proliferation, activation of c-Jun N-terminal kinase (JNK) signaling and induction of apoptosis ⁴⁵. *M. oleifera* methanol leaf extract (MMLE) caused a reduction in cervical cancer cell proliferation, increased p27 expression (a cell cycle-dependent kinase inhibitor), and induced the arrest of the cell cycle at the G0/G1 phase ⁴⁶. The leaf fractions suppressed telomerase activity, induced G2/M checkpoint cell cycle arrest, inhibited colony formation in the HeLa cervical cancer cells, and induced apoptosis via the intrinsic apoptotic pathway ⁴⁷.

Cytotoxic mechanisms of different *Moringa* species against cancer cells and normal cells

Reduction in Cell Viability: Studies indicate that increased leaf extract concentration of *M. oleifera*, *M. peregrina*, and *M. stenopetala* on liver cancer cells

(HepG2) adversely decreased the cell viability ^{48, 49}. However, this was also observed in normal hepatocytes but at higher concentrations (above 100 $\mu\text{g/mL}$) ⁵⁰. Another study conducted on the human cervix carcinoma cell line (HeLa) with the *Moringa oleifera* leaf extracted in ethanol-water (70-30%), establishes that the HeLa cell viability is considerably reduced, and the number of surviving cells decreases with increasing concentration ²⁹.

Generation of Reactive Oxygen Species (ROS) and induction of apoptosis by activation of caspase-3: Another study using *M. oleifera* fruit extract on human liver cancer (HepG2) cells at 25, 50, 75, 100, and 200 $\mu\text{g/ml}$ highlighted that the extract decreased the viability of the liver cells via induction of apoptosis (caspase 3- activity) and intracellular stimulation of ROS production ⁵¹. An in-vitro study confirms that *M. oleifera* leaf extract exhibited cytotoxic effects against inactivated fibroblasts at a concentration above 700 $\mu\text{g/ml}$, which indicates potential concentration-dependent toxicity ⁵².

Toxicological profile of *Moringa* species in animal models

Acute toxicity: Several animal models, primarily rodents, have been utilized to determine *Moringa oleifera*'s acute toxicity profile.

Root: In a study to assess the acute toxicity of *M. oleifera* aqueous leaf extract in albino Wistar rats, it was observed that at 1000 mg/kg, there was no record of acute toxicity or mortality, but at 1600-5000 mg/kg, there was a record of mortality with the LD50 calculated to be 1264.91 mg/kg ⁵³.

Root Bark: The *Moringa oleifera* ethanol extract of the root bark is rich in nutritious phytochemicals with diverse medicinal applications. Notably, oral administration of this extract showed no signs of acute toxicity, with a median lethal dose (LD50) exceeding 5000 mg/kg, indicating a high level of safety ⁵⁴.

Bark: The experiment conducted for acute toxicity showed that the stem bark extract was safe at doses up to 2000 mg/kg, with no acute signs of toxicity or mortality. Another study indicated that at 5000 mg/kg, there were no observed signs of toxicity or mortality ⁸.

Leaves: Using the Swiss female albino mice model, an oral acute toxicity study was carried out on moringa leaves at doses of 250, 500, 1000, and 2000 mg/kg. Their findings revealed no alteration in weight gain, food and water consumption, biochemical, hematological, and histological parameters ⁵⁵. Another acute toxicity study of the methanolic extract of the moringa leaves in rats found that at 2000 mg/kg oral administration, there were no signs of toxicity or mortality, and this indicates the non-toxicity of the methanolic extract at 2000 mg/kg of body weight ⁵⁶. The hydroethanolic extract of moringa leaves administered to mice at 2000 mg/kg showed no behavioral changes, mortality, or changes in body

weight⁵⁷. The ethanol extraction of the leaf of *Moringa oleifera* showed that an LD50 of 3900 mg/kg produced death in mice. Indicating that it is safe to consume MO to promote health in the right doses,⁵⁸

Seeds: A study concluded that at doses considered for nutritional and medicinal purposes, the *Moringa oleifera* seed oil extracts were relatively safe⁵⁹. Another study found that at high doses (supra-therapeutic doses), *Moringa stenopetala* seed extract was toxic to rat embryos and fetuses, causing delayed development, increased miscarriage, and fetal death. This suggests that excessive consumption of *Moringa stenopetala* seeds may be unsafe⁶⁰. Acute toxicity of the methanolic extract of *M. oleifera* seeds was observed at 4000 mg/kg, and mortality was observed at a dose of 5000 mg/kg⁸.

Flowers: The methanolic flower extract at 2900 mg/kg was safe, whereas administration at 5000 mg/kg resulted in rat mortality. This indicates that the LD50 is below 5000 mg/kg⁶¹.

Subacute toxicity studies

Twenty-eight days of oral administration of *M. Oleifera* extract at 500 and 1000mg/kg promoted liver and kidney damage in Swiss female albino mice, as observed through biochemical and histopathology parameters⁵⁶. Repeated oral administration of the hydroethanolic extract of the *Moringa oleifera* leaf (MOHE) at 1000mg/kg in mice for 28 days resulted in increased serum levels, liver injury, increased creatinine levels, and kidney injury; MOHE is considered toxic and unsafe at high doses (1000mg/kg) for repeated use as a food supplement or complementary medicine. However, reduced doses for short-term use may be safe and beneficial⁵⁸.

A report on the use of *Moringa oleifera* bark extract at doses of 250, 500, and 1500mg/kg was accessed, and the results showed an LD50 of 1585mg/kg without statistically significant changes in hematological and biochemical parameters when compared to the control group⁸. Toxicological research to evaluate the effects of the ethanolic extract of *M. stenopetala* leaves at doses of 250, 500, and 1,000 mg/kg revealed that the highest dose led to a significant reduction in maternal food intake and weight gain, increased fetal resorptions, placental weights, and histopathological changes in the placenta. These findings indicate potential developmental toxicity at high consumption levels during pregnancy⁶².

Subchronic toxicity studies

Some research findings suggest considerable specificity with respect to *Moringa* species. This connotes that those specific parts of the plant must be considered for their toxic and safe doses⁸. A 13-week exposure of *M. Oleifera* leaf extract in albino Wistar mice was safe up to 1000 mg/kg, where there was a significant increase in the liver function enzymes. This suggests a potential deleterious effect on the liver⁶³. While the leaf extract appears to be relatively safe,

high doses of seed and root extracts have been associated with potential liver and kidney damage in animal models. However, a blend of *Moringa stenopetala* and *M. spicata* leaves in herbal tea form is relatively safe, with low toxicity, in subchronic exposure studies on rats, indicating potential safety for moderate use⁶⁴.

Chronic toxicity studies

A study on *Moringa oleifera* aqueous leaf extract in mice revealed that at 250 and 500mg/kg, there were no physiological and hematological alterations, indicating safety and tolerability. However, at 1000mg/kg, there were increased levels of liver function enzymes such as alanine transaminase and aspartate transaminase (ALT and AST), suggesting some level of hepatic damage⁶³. Further to this, a study showed that the ethanolic extract of the moringa leaves at 1000 mg/kg is associated with hepatic and renal toxicity in mice⁵⁸. A study investigated an herbal tea blend of *M. stenopetala* leaves in Wistar rats, in which 559.36, 1,118.72, and 2,237.44 mg/kg were the doses administered daily. The findings showed no significant alteration to food intake, organosomatic indices, biochemical, and hematological parameters. However, there was a significant increase in serum AST, creatine kinase (CK), and lactate dehydrogenase (LDH) levels at the highest dose, suggesting potential liver stress. In the liver, kidney, and pancreas, minor histological lesions were noted, which indicates the relative safety of the formulation, high doses may pose some risks⁶⁴.

Organ toxicity of *Moringa* species

An in vivo study in a murine model revealed that *M. oleifera* seed extract was hepatotoxic and nephrotoxic, and showed blood toxicity as well. At 46mg/kg, the extract significantly altered serum aminotransferase and plasma cholesterol levels, while at 70 mg/kg, there was an alteration of total bilirubin, non-protein nitrogen, blood urea, and plasma protein levels⁶⁵.

When it comes to using *Moringa oleifera*, it's essential to consider both the part of the plant and the dosage. The leaves seem to be relatively safe, but high doses of seeds, leaves, and root extracts have been linked to potential liver and kidney damage in animal studies. This suggests that while *Moringa oleifera* can be beneficial, it's crucial to use it responsibly and with caution⁶⁶.

Toxicology data in Humans

A case of moringa-induced toxicoderma, an adverse effect rarely described in the literature. A woman aged 57 years, with a history of dyslipidemia, fibromyalgia, and hypertension, was referred to the emergency clinic with a 3-day history of generalized pruritic skin rash, tongue edema, and mild respiratory distress. Physical examination revealed a morbilliform rash affecting the face, trunk, and upper limbs. During a verbal interaction with the patient, she denied taking any new

medications or foods. Still, she admitted to taking moringa powder for two weeks, which she added to salads in an unspecified amount, and daily infusions to lose weight. With the suspected diagnosis of moringa toxicoderma, it was decided to discontinue the treatment. Antihistamines and topical corticosteroids were prescribed for symptomatic management of the reaction, which resolved within less than two weeks⁶⁷.

A clinical study on *M. oleifera* found that oral consumption of aqueous leaves up to leaves showed no toxic effect.⁸ A study reported a man who developed symptoms after taking a nutraceutical containing powdered moringa leaves. Stevens-Johnson syndrome has also been reported in a 53-year-old man after consumption of extracts from *M. oleifera* leaves⁶⁸.

Moringa consumption at different physiological states

Pregnancy: Moringa leaves are possibly safe to use in pregnancy during the second or third trimester because they are rich in nutrients and have been shown to increase hemoglobin levels, reduce anemia, and potentially improve breast milk supply. Studies suggest they are safe for pregnant women and can offer nutritional benefits, including reducing the risk of malnutrition, low birth weight, and anemia⁶⁹. However, researchers suggest that the roots, bark, and flowers of the moringa tree are potentially unsafe during pregnancy as they may cause uterine contractions and have been traditionally used to induce miscarriages⁷⁰.

Breastfeeding: Polyphenols and flavonoids present in *Moringa oleifera* contribute to the increased milk production and lactation by enhancing both oxytocin and prolactin hormones. A research study on infants suggests that moringa supplements reduce infant (above 3-month-old) morbidity better than iron supplements⁷¹.

Infants: *M. oleifera* contains multivitamins that are beneficial for malnourished children, improving their nutritional status and reducing morbidity and mortality. Also, extracts from moringa leaves can be used as a nutritional enhancement to infant diets⁷².

Toxicity based on geographic variation, cultivation, and genetics

Environmental factors (such as soil type, climate, and altitude), genetic variability, and cultivation practices (like fertilization and irrigation) may influence the phytochemical composition of Moringa species. A study assessed *M. oleifera* growth across different Ecuadorian climatic regions and found that soil nutrient toxicity and deficiency affected the plant's

mineral content and bioactive compound synthesis, potentially impacting its efficacy and safety⁷³.

The phytochemical content of moringa species, particularly *M. oleifera*, depends on several factors, such as: harvesting season; genetics of the plant; leaf maturity; environmental factors; and methods of drying and extraction². A study carried out in Ekiti, South-western region of Nigeria, found that *M. oleifera* leaves from Ikere, Ekiti had higher concentrations of alkaloids (0.18 mg/g), saponins (0.16 mg/g), phenols (38.70 mg GAE/g) and tannins (14.91 mg Tae/g) compared to other locations within the state, which can implicate both the efficacy and toxicity of the plant's extract⁷⁴.

A study analyzed 57 accessions of *M. oleifera* from various agroecological zones. RAPD-PCR (Random Application of Polymorphic DNA-Polymerase Chain Reaction) and HPLC (High Profile Liquid Chromatography) techniques were used. The technique identified significant diversity in phenolic and flavonoid content across these agroecological zones. For instance, the concentration of polyphenolic compounds varied across samples, ranging from 0.06 to 210.5 mg/kg. This can influence the plant's safety profile and therapeutic properties⁷⁵.

Risk assessment and safety recommendations

Contamination of moringa extract by different bacteria can occur during growing, harvesting, washing, drying, grinding, preparation, and storage of the extract. It can also be contaminated by foodborne pathogens and irrigation water⁷⁶. Another risk factor is the integrity of the raw material used. Pest and disease invasions have resulted in poor-quality materials, retardation in growth patterns, and overall low yields.⁷⁷ Accumulation of heavy metals in moringa also brings about detrimental results to human health when consumed excessively⁷⁸.

Though moringa is rich in minerals and medicinally important, toxic heavy metals found in moringa plants pose serious risks to human health when consumed without regulation⁷⁹. Ensuring adequate care of the moringa plants, and appropriate awareness among farmers to make them understand the importance of maintaining optimal conditions for cultivation⁷⁷. The use of *Moringa oleifera* for nutritional and medicinal purposes requires proper background information about the environment where the tree was grown. This is because the leaves, stem bark, and seeds of the tree can absorb heavy metals from their surroundings, and the accumulation of these metals is detrimental to health. While moringa is used in the treatment and prevention of several diseases, there is a need for caution when it is consumed over long periods⁷⁸.

CONCLUSION

While *Moringa* offers significant health benefits, especially from its leaves and seeds, its use must be approached with caution. Risk increases with high doses, long-term intake, and consumption of roots or bark as they contain more toxic substances. Although acute toxicity studies show a high safety margin, excessive consumption may lead to various adverse effects, such as liver or kidney dysfunction. Pregnant women, individuals on chronic medications, and those with liver or kidney conditions should avoid unsupervised use. Determining the appropriate dosages of chemical constituents prior to use is important and provides a basis for further clinical toxicology research. Future studies that focus on the toxicity of different extracts from *Moringa* species in humans and the mechanisms of toxicity should be carried out. Even as *Moringa* has been said to be a valuable plant with diverse nutritional and medicinal attributes, its usage should be properly guided by adequate dosing, preparation, and awareness of the toxic parts of the plant. Comprehensive human toxicology data, further research, standardization, and regulatory guidelines are urgently needed to ensure effective therapeutic applications and safety.

Conflict of interest: The authors have no conflict of interest to declare.

Author's contribution: SOA and AAN designed the concept of the mini-review. SOA, HAA, OKW, OSA, SMO, and FRB contributed to the writing, proofreading, and final editing of the review article.

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