

International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693
ISSN Online: 2617-4707
IJABR 2023; 7(1): 20-34
www.biochemjournal.com
Received: 15-10-2022
Accepted: 26-11-2022

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Moringa oleifera: Review on herbal healing properties and Nutritional values

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DOI: <https://doi.org/10.33545/26174693.2023.v7.i1a.158>

Abstract

Despite being indigenous to India, Nepal, and the highlands of the Himalayas, *Moringa oleifera* flourishes in all tropical and subtropical regions of the world. Drumsticks or horseradish trees are frequently used for this plant. The *Moringa* plant is affordable, readily available, and extremely nutritious, and it is widely used for its therapeutic properties. The little softwood tree *Moringa oleifera* grows swiftly and adapts well to a dry, sandy environment. *Moringa* plants include substances that are anti-inflammatory, anti-cancer, anti-tumour, cardiovascular, and central nervous system support. The manufacturing of antifungal and antibacterial drugs, the production of biofuels and oils, and the treatment of wastewater are just a few of the many uses for which *Moringa* plants have been one of humanity's most significant suppliers. This review discusses the various medical applications of *Moringa* as well as its morphology, nutritional needs, notable pharmacological qualities, commercial uses, safety studies, and commercial viability.

Keywords: *Moringa oleifera*, antidiabetic, anticancer, antimicrobial, safety studies

Introduction

Since plants fulfil the producers' role in the ecosystem, they are independent of other species in terms of food. There are many different types of plants on our planet. Plants are essential to life for a variety of reasons, including providing oxygen, conserving soil, producing food, and providing lumber. Plants have long been used as a treatment for a range of illnesses. The key benefit of using herbs as medicine and why they are preferred more is that they have fewer side effects, which boosts public trust in plant-based therapies. Various ailments can be treated using plant components such as roots, leaves, bark, and extracts ^[1]. The World Health Organization (WHO) has stated that the finest sources of pharmaceuticals are medicinal herbs and plants. Humans considerably benefit from therapeutic plants, especially those who are frail owing to privilege, poverty, unemployment, illness, and low-income sources. It makes it straightforward to treat them with easily available plant components for little cost and also boosts public confidence in plant-based therapy. Again, WHO has said that herbs and plants with medicinal properties are the finest sources of medications. *Moringa oleifera* is the most common plant throughout various parts of the world, from Asia to Africa. The healing properties of this plant, also known as "Mother's best friend," "the miracle tree," "the horseradish tree," and "the drumstick tree," have made it a blessing to mankind. The *Moringa* plant is widely available, affordable, very nourishing, and well-known for its therapeutic properties ^[2, 3]. *Moringa* leaves include a wide variety of macronutrients and micronutrients that are essential to both people and other living things. It contains many sources of proteins, vitamins, minerals, and carotenoids. *Moringa* is frequently referred to as the "Miracle plant" because of its beneficial and precious therapeutic properties. *Moringa oleifera* is a little softwood tree that may grow quickly and bear fruit in a dry, sandy environment. One of the distinguishing features of the species is its long, drumstick-shaped pods, which contain seeds. In its first year of development, *Moringa* has shown the ability to grow up to 4 meters and bear fruit, both of which are shorter than average. The seeds, flowers, leaves, roots, and pods of the *Moringa* plant are all extremely valuable both commercially and medicinally.

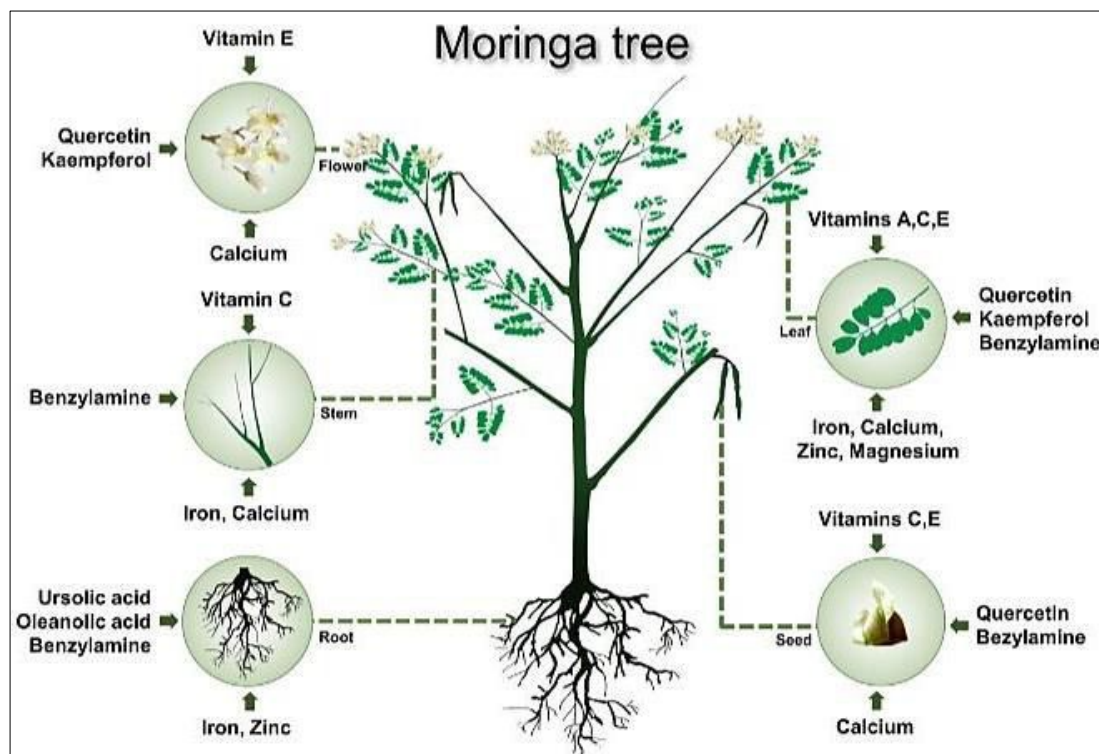


Fig 1: *Moringa oleifera* plant parts and uses [4].

There are a few traditional and medicinal uses for *Moringa*. It has been used as a nutritional supplement for more than 20 years in Ghana and other countries. Hence, it has grown to be well-known throughout society. Regardless of the nutraceutical value, the plant's diverse sections have unique pharmacological effects. Malnutrition is very well treated by the *Moringa* tree, especially in mothers and newborns.

The entire plant, including the leaf, flowers, root, bark, gum, seed, and seed oil, has been used for a variety of purposes in South Asian Traditional medicine, including the treatment of infectious and inflammatory diseases as well as hematological, cardiovascular, gastrointestinal, and hepato-endocrine disorders [5, 6, 7]. The leaves of the *Moringa* plant contain a variety of chemicals, including flavonoids, ascorbic acid, phenolics, and carotenoids, which are good sources of natural antioxidants [8]. The juice from the leaves is used to treat eye infections. The leaf is exceptionally nutrient-dense and contains significant amounts of rough protein (20-29%), vitamins, and minerals [9, 10]. *Moringa* seeds are said to have antibacterial properties. The separated roots and seeds have demonstrated antibacterial activity [11]. The antimicrobial action of the *Moringa* leaves was attributed to their ethanolic extract [12]. The plant is renowned for a variety of medicinal qualities, including the ability to treat tumors, prevent infertility, lower blood pressure, and have antibacterial effects [13, 14]. Urinary stone formation is reduced and prevented by using the aqueous and alcoholic extracts of *Moringa* root wood [15]. The *Moringa* plant has been linked to a sizable number of primary and secondary metabolites as well as pharmacological actions.

Morphology

The slender, freely branching *Moringa* tree can grow incredibly quickly (Figure 1). Although it can grow taller than 10 meters, it is typically classified as a small to medium-sized tree. Green to dim green, fluffy, tripinnate numerous leaves with 2cm long, elliptical leaflets. The

tree's large, finely fragmented blooms are carried on inflorescences 10 to 25 cm long and are typically white to cream in color, though they can occasionally be tinted with pink in some kinds. The tree is frequently mistaken for a legume because of its leaves. The fruit, which has a three-lobed shell, is frequently called a "pod". Light green, and in certain varieties, reddish, are the colors of immature pods. The fast-growing, drought-tolerant tree can withstand poor soil, a wide range of annual rainfall (28-300), and a pH range of 5.3-9.0. Dried seeds have a round or triangular shape when fully grown and a faintly forested capsule with three papery wings surrounds the kernel.

It has been discovered that the composition of *Moringa oleifera*, includes a fatty acid profile, and determined that *Moringa oleifera* oil is high in oleic acid (>80%). *Moringa oleifera* seeds contain between 33 and 41% w/w of vegetable oil. The oil found in the seed, which is shown to be a source of biofuel and to be significant medically, makes up about 40 to 50 percent of the seed.

Different parts of the *Moringa* plant are as follows:

Stem: The stem is naturally lengthy but occasionally has an improper form. The tree is 1.8 to 3 meters tall and has a short, straight trunk [16].

Branch: The branches formed in an irregular pattern, and the covering became the shape of an umbrella.

Leaves: Tripinnate complex leaves are fluffy and have 1-4 cm long, green, curving leaflets. Because of its leaves, the tree is frequently mistaken for a leguminous plant. In general, the branch tips are where the alternating twice or three times pinnate leaves appear (shown in figure 2). They range in length from 20 to 70 cm, with a long petiole with 8 to 10 pairs of pinnae, each bearing two sets of inverted elliptical leaflets and one at the apex that is 1-2 cm long, and are grayish in color when young [17].

Flowers: Inflorescences 15-25 cm long bear prominent, delicately scented flowers that are 2.5 cm in diameter, primarily white to cream in color, and tinged pink in a few variations (shown in figure 2). The 2.5 cm broad, agreeably scented flowers are delivered in abundance on supplementary, 10 to 25 cm long panicles. They have white dots at their bases. The straight lanceolate five-reflexed sepals. The five petals are speculatively thin. Except for the lowest, they consist of the five stamens and five staminodes and are reflexed.

Fruits: Fruits have three lobes and are frequently referred to as pods. Young pods are green and, in some varieties, have

radish-like coloring. Pods are triangular, brown, and split longitudinally into three pieces when dried. They are between 35 and 130 cm long and 12.8 cm wide. The pith contains about 20 sec.

Seeds: The oval, tan, semi-permeable seeds have three papery wings and are arranged in an oval shape (figure 2). The majority of seed arrangements are brown to dark brown, although they can sometimes be white if there are insufficiently viable sections. Within a week, viable seeds begin to grow. The body itself features three white wings that continuously beat at 130 seconds intervals from beginning to end.

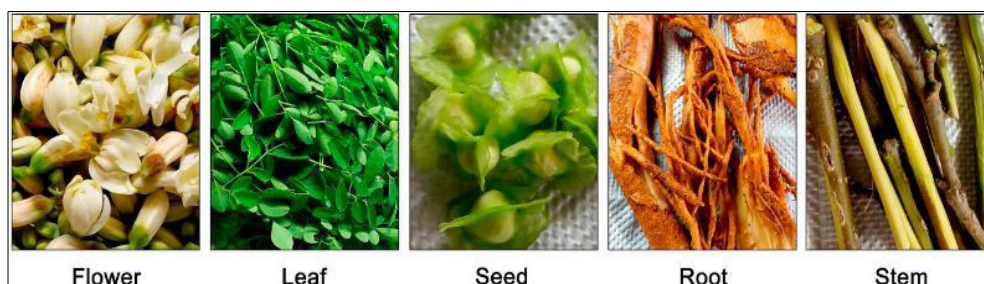


Fig 2: Morphology of various tissues in *M. oleifera* [18].

Nutritional Properties:

Every component of the *Moringa oleifera* plant contains valuable nutrients and antinutrients. Minerals like Calcium, Potassium, Zinc, Magnesium, Iron, and copper are abundant in *Moringa oleifera* leaves [19]. There are vitamins like vitamin A's beta-carotene, vitamin B's pyridoxine, nicotinic acid, and folic acid, as well as vitamins C, D, and E [20]. Anti-cancerous substances such as glucosinolates, isothiocyanates, glycoside compounds, and glycerol-1-9-octadecanoic are present along with phytochemicals like tannins, sterols, terpenoids, flavonoids, saponins, anthraquinones, alkaloids, and reducing sugar [21]. Additionally low in calories, *Moringa* leaves can be included in an obese person's diet. Fibrous pods are useful for treating digestive issues and preventing colon cancer [22, 23]. A study reveals that immature pods have a protein level of about 20.66% and a fiber content of about 46.78%. Amino acid concentration is 30% in pods, 44% in leaves,

and 31% in flowers. Similar quantities of palmitic, linolenic, linoleic, and oleic acids were found in the immature pods and flowers [24]. Among the several elements found in *Moringa* that are crucial for growth and development, Calcium is regarded as one of the key minerals for human growth. *Moringa* leaves can be consumed for 1000 mg, and *Moringa* powder can be consumed for more than 4000 mg, compared to the 300-400 mg found in 8 ounces of milk. In order to treat anemia, *Moringa* powder can be used in place of iron supplements. While *Moringa* leaf powder contains 28 mg of iron, beef only has 2 mg. According to some reports, *Moringa* has a higher iron content than spinach [25]. Zinc needs to be consumed in adequate amounts for DNA and RNA production as well as for healthy sperm cell development. The zinc content of *Moringa oleifera* leaves ranges from 25.5 to 31.03 mg/kg, which matches the recommended daily intake of zinc [26].

Table 1: The nutrient compositions of leaves, leaf powder, seeds, and pods [30, 31, 32].

Nutrients	Fresh Leaves	Dry Leaves	Leaf Powder	Seeds	Pods
Calories(cal)	92	329	205	-	26
Protein(g)	6.7	29.4	27.1	35.97±0.19	2.5
Fat(g)	1.7	5.2	2.3	38.67±0.03	0.1
Carbohydrate(g)	12.5	41.2	38.2	8.67±0.12	3.7
Fiber(g)	0.9	12.5	19.2	2.87±0.03	4.8
Vitamin B1(mg)	0.06	2.02	2.64	0.05	0.05
Vitamin B2(mg)	0.05	21.3	20.5	0.06	0.07
Vitamin B3(mg)	0.8	7.6	8.2	0.2	0.2
Vitamin C(mg)	220	15.8	17.3	4.5±0.17	120
Vitamin E(mg)	448	10.8	113	751.67±4.41	-
Calcium(mg)	440	2185	2003	45	30
Magnesium(mg)	42	448	368	635±8.66	24
Phosphorus(mg)	70	252	204	75	110
Potassium(mg)	259	1236	1324	-	259
Copper(mg)	0.07	0.49	0.57	5.20±0.15	3.1
Iron(mg)	0.85	25.6	28.2	-	5.3
Sulphur(mg)	-	-	870	0.05	137

Linoleic, linolenic, and oleic acids are PUFAs that have the power to regulate cholesterol. According to research, *Moringa* seed oil has about 76% PUFA, which makes it a great alternative to olive oil [27]. The content of the nutrients varies based on the place; it should be noted. The nutrient composition is affected by the seasons, according to Fuglie [25]. It has been demonstrated that whereas vitamin C and

iron were more prevalent in the cool-dry season, vitamin A was more prevalent in the hot, wet season [28]. The variance in results can be related to the fact that the nutrient content of the tree is greatly influenced by the location, climate, and environmental factors [29]. Tables 1 and 2 provide a comprehensive list of the nutrients found in leaves, pods, and seeds along with their medicinal uses.

Table 2: Nutritional compositions and medicinal uses of different parts of *Moringa* [32].

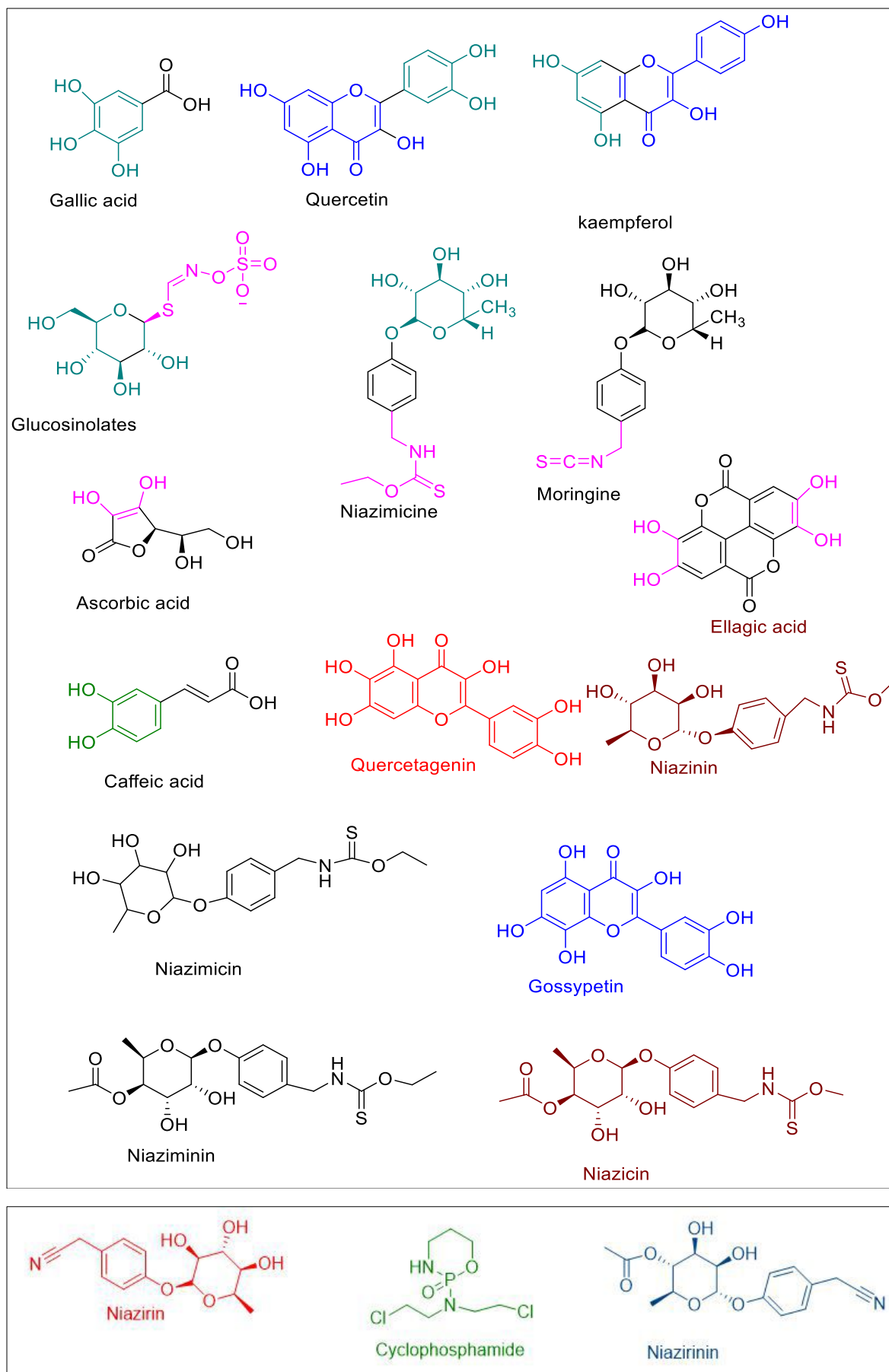
Part of tree	Medicinal Uses	Nutritive Properties	Suggestion
Leaves	<i>Moringa</i> leaves treat asthma, hyperglycemia, Dyslipidemia, flu, heartburn, syphilis, malaria, pneumonia, diarrhea, headaches, scurvy, skin diseases, bronchitis, eye and ear infections. Also reduces, blood pressure and cholesterol and acts as an anticancer, antimicrobial, Antioxidant, antidiabetic and anti-atherosclerotic agents, neuroprotectant.	<i>Moringa</i> leaves contain fiber, fat proteins and minerals like Ca, Mg, P, K, Cu, Fe, and S. Vitamins like Vitamin-A (Beta-carotene), vitamin B-choline, vitamin B1-thiamine, riboflavin, nicotinic acid and Ascorbic acid is present. Various amino acids like Arg, His, Lys, Trp, Phe, Thr, Leu, Met, Ile, and Val are present. Phytochemicals like tannins, sterols, saponins, terpenoids, phenolics, alkaloids and flavonoids like quercetin, isoquercetin, kaemfericetin, isothiocyanates and glycoside compounds are present.	The presence of flavonoids give leaves the antidiabetic and antioxidant properties. The isothiocyanates are anticancer agents. Flavonoids like quercetin and others are known for anti-proliferative, anticancer agent. The presence of minerals and vitamins help in boosting the immune system and cure a myriad of diseases.
Seeds	Seeds of <i>Moringa</i> help in treating hyperthyroidism, Chrohn's disease, anti-herpes simplex virus arthritis, rheumatism, gout, cramp, epilepsy and sexually transmitted diseases can act as antimicrobial and anti-inflammatory agents.	Contains oleic acid (Ben oil), An antibiotic called pterygospermin, and fatty acids like Linoleic acid, linolenic acid, behenic acid, Phytochemicals like tannins, saponin, phenolics, phytate, flavonoids, terpenoids, and lectins. Apart from these, fats, fiber, proteins, minerals, vitamins like A, B, C, and amino acids.	The presence of flavonoids give anti-inflammatory property. The antibiotic pterygospermin is responsible for antimicrobial properties. The other phytochemicals help in treating various diseases.
Root Bark	Root bark acts as a cardiac stimulant, anti-ulcer, and anti-inflammatory agent.	Alkaloids like morphine, moriginine, minerals like Calcium, Magnesium and Sodium.	The alkaloid helps the bark to be antiulcer, a cardiac stimulant and helps to relax the muscles.
Flower	<i>Moringa</i> flowers act as hypocholesterolemia, antiarthritic agents that can cure urinary problems and colds.	It contains calcium and potassium and amino acids. They also contain nectar.	The presence of nectar makes them viable for use by beekeepers.
Pods	<i>Moringa</i> pods treat diarrhea, liver and spleen problems, and joint pain.	Rich in fiber, lipids, non-structural carbohydrates, protein, and ash. Fatty acids like oleic acid, linoleic acid, palmitic acid, and linolenic acid are also present.	The presence of PUFA in the pods can be used in the diet of the Obese.

Phytochemical Properties

Simple sugar, rhamnose, also known as glucosinolates, and isothiocyanates are among the substances found in *Moringa oleifera* [34, 35]. Two alkaloids, Moringinine and Moringine, are present in the bark and stem of the *Moringa* plant [36]. Galactose, glucuronic acid, L-arabinose and L-rhamnose, xylose, mannose, and degraded-gum polysaccharide consisting of Glucuronic acid, L-mannose, and L-galactose have all been identified in purified gum exudate from *M. oleifera*. This information was obtained by mildly hydrolyzing the whole gum with acid [37]. From the stem of *M. oleifera*, isolating substances such as sitosterol, -sitostenone, vanillin, 4-hydroxymellin, and octacosanoic acid has been done [38]. Nine amino acids, D-glucose, sucrose, quercetin, wax, traces of alkaloids, and kaempferol are all found in the *Moringa* flower; the ash is abundant in Calcium and Potassium [39]. In addition, they included alkaloids, kaempferitrin, kaempferol, rhamnetin, isoquercetin, and other flavonoid pigments. It has been discovered that the acetate phase of the ethanol extract of *Moringa oleifera* pods contains isothiocyanate and thiocarbamate glycosides [40]. The fruit has been reported to contain cytokinins [41]. Recently, research into extracting growth hormones and promoters from *M. oleifera* leaves has gained attention. Even if the nature of the active ingredient is unclear, it has been demonstrated that the application of an aqueous-ethanol extract of *Moringa* leaves increases

black gram nodulation [42]. Because of the presence of numerous types of antioxidant components, including flavonoids, phenolics, ascorbic acid, and carotenoids, *Moringa* leaves serve as a respectable source of natural antioxidants [43, 44]. The leaves and pods of the *Moringa* plant have high concentrations of Calcium, Iron, Phosphorus, Copper, Vitamins A, B, and C, -tocopherol, folic acid, riboflavin, nicotinic acid, pyridoxine, beta-carotene, protein, ascorbic acid, oestrogenic substances, -sitosterol, and some specific essential amino acids like tryptophan, methionine while stigmaterol, -sitosterol, campesterol, Claro sterol, and 5-avenasterol make up the majority of the sterols in *Moringa* seed oil, there are also trace levels of stigmaterol, 7-campesterol, 28-isoavenasterol, and 24-methlenecholesterol [45, 46]. Major *Moringa* seed oil fractions' sterol composition differs significantly from that of traditional edible oils [47]. According to its fatty acid profile, *M. oleifera* seed oil decreases in the category of high-oleic oils (C18:1, 67.90%-76.00%). Essential components are the fatty acids C16:0 (6.04%-7.80%), C18:0 (4.14%-7.60%), and C20:0 (2.76%-4.00%). The concentration of certain tocopherols (alpha-, gamma-, and delta-) in *Moringa oleifera* is found to range from 96.72 to 124.45, 29.90 to 95.70, and 46.00 to 73.26 mg/kg, respectively.

Some of the important bioactive Phytocompounds from *Moringa oleifera*:



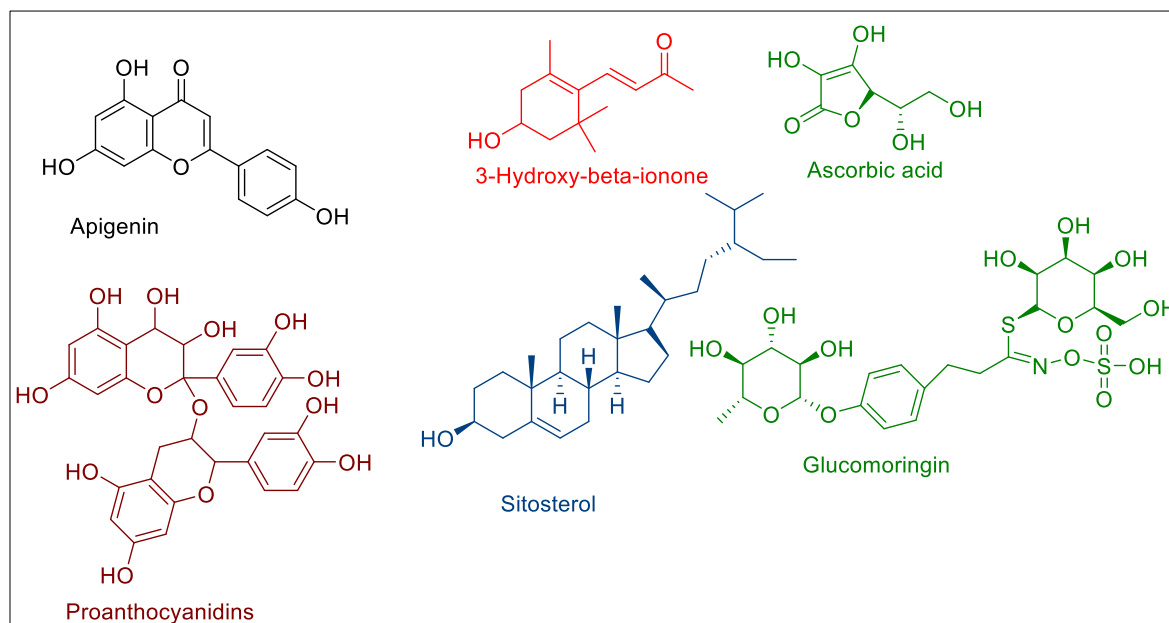


Fig 3: Bioactive compounds are present in *Moringa oleifera* [48].

Medicinal Properties

More than 300 ailments can be cured by *Moringa oleifera*, which is frequently regarded as a panacea. Local populations in Asian nations have traditionally used *Moringa* as an herbal remedy. It works well as a medicinal agent because of the phytochemicals contained. The following list of its significant health advantages is provided.

Anti-Diabetic Properties

Type 1 and Type 2 diabetes have both been found to be cured by *Moringa*. Patients with type 1 diabetes do not produce insulin, a hormone that is necessary to keep blood glucose levels at the desired normal range. Insulin resistance is one that is connected to type 2 diabetes. Beta cell malfunction, which fails to detect glucose levels and lowers insulin signaling, as a result, may also contribute to type 2 diabetes and result in elevated blood sugar levels [49]. Numerous research has demonstrated the anti-diabetic properties of *Moringa*. According to a study, *Moringa oleifera*'s aqueous extracts can treat rats with both insulin-resistant Type 2 diabetes and Type 1 diabetes caused by streptozotocin [50]. In a different study, the researchers observed a decrease in fasting blood glucose levels after feeding *Moringa* seed powder to STZ-induced diabetes mice [51]. Additionally, the serum levels of antioxidant enzymes rose when the rats were given 500 mg of *Moringa* seed powder per kg of body weight. This demonstrates that the antioxidants in *Moringa* can reduce the ROS that STZ induction causes in the Beta-cells. In Beta cells, STZ induces ATP dephosphorylation processes that aid xanthine oxidase in producing superoxide and reactive oxygen species (ROS) [52]. Patients with hyperglycemia experience beta cell destruction. As a result, when there is excessive glucose inside the mitochondria, reactive oxygen species are released. Beta cells undergo apoptosis because they have a low level of antioxidants [53, 54]. As a result, there will be less insulin secreted, which will cause hyperglycemia and eventually Type-2 diabetes. It has been suggested that flavonoids like quercetin and phenolics act as antioxidants by scavenging ROS. The flavonoids in *Moringa* are thought to scavenge the ROS generated from mitochondria, preserving the beta cells and, in turn, preventing

hyperglycemia [55, 51]. Diabetes can cause retinopathy, nephropathy, atherosclerosis, and other problems. Such illnesses can be prevented with *Moringa*. Blood glucose combines with proteins in hyperglycemia to produce advanced glycated end products (AGEs). RAGE, which is expressed on the surface of immune cells, is bound by these AGEs. Interleukin-6 and interferon transcription are both elevated as a result of this relationship. The surface endothelium of arteries expresses cell adhesion molecules concurrently [56]. This promotes trans-endothelial migration, which results in artery irritation and atherosclerosis. Atherosclerotic agents are treated with *Moringa* [57]. The antioxidant qualities of *Moringa* can be used to explain its antiatherogenic tendency.

Anticancer Properties

MO has the potential as an anticancer agent against several cancers [58]. MO leaf extract inhibited the cell viability of hepatocellular carcinoma, acute lymphoblastic, and myeloid leukemia [59]. The bioactive compounds responsible for the inhibition were attributed to niazimicin, β -sitosterol-3-O- β -D-glucopyranoside, and 4-(α -L-rhamnosyloxy) benzyl isothiocyanate. Berkovich *et al.*, 2013 showed that MO leaves inhibited pancreatic cancer cell growth [60]. It targeted the cell cycle resulting in cell accumulation at the sub-G1 phase. In addition, MO leaves downregulated the NF κ B pathway by decreasing the expression of I κ B α , p-I κ B α , and p65 proteins. It synergistically induced cytotoxicity with cisplatin in pancreatic cancer cells. It is also effective against breast cancer cells [58]. In rats, diethyl nitrosamine was used to develop liver cancer, and Sandek *et.al.* research demonstrated that MO leaves had the ability to prevent cancer [61]. The hot water MO leaf extract was studied by Madi *et al.* because it had antiproliferative effects on A549 lung cancer cells [62]. The extract induced p53, caspases, and PARP-1 cleavage through increasing reactive oxygen species. The cancer cell line underwent apoptosis as a result of this. Additionally, we demonstrated that both A549 lung cancer cells and SNO esophageal cancer cells were resistant to the proliferative effects of the hot water crude aqueous extract [127]. The extract caused DNA fragmentation and controlled oxidative stress. Additionally, the extract increased apoptotic signals, which caused cancer cells to

die. In human melanoma A2058 cells, MO fruit extract boosted ROS generation, caspase 9, -3/7 activity, and MAPK activation to cause apoptosis via the mitochondria [64]. The MO's glucosinolate content prevents cancer [65]. It is able to trigger apoptosis. Anticancer medications are needed to target the cancer cells' high rate of proliferation. It's interesting to note that MO has been demonstrated to have a wide range of activity and can target a number of proteins and molecules to impede the growth of cancer cells [65]. As depicted in Figure 4, MO has the potential to be used in the creation of a brand new complementary and alternative therapeutic agent for the treatment of cancer.

Effective anticancer compounds can be found in the leaves and bark [66]. It displayed antiproliferative effects in HCT-8 and MDA-MB-231 cancer cell lines. However, the seed extract was not effective. Apoptosis occurred with G2/M phase cell cycle arrest. The anticancer effect was attributed to bioactive compounds such as D-allose, hexadecanoic acid ethyl ester, eugenol and isopropyl isothiocyanate. This is particularly important as the bioactive compounds identified possessed a sugar moiety, aromatic rings and long chain hydrocarbons. Therefore, it can be seen that MO's potential in novel drug development.

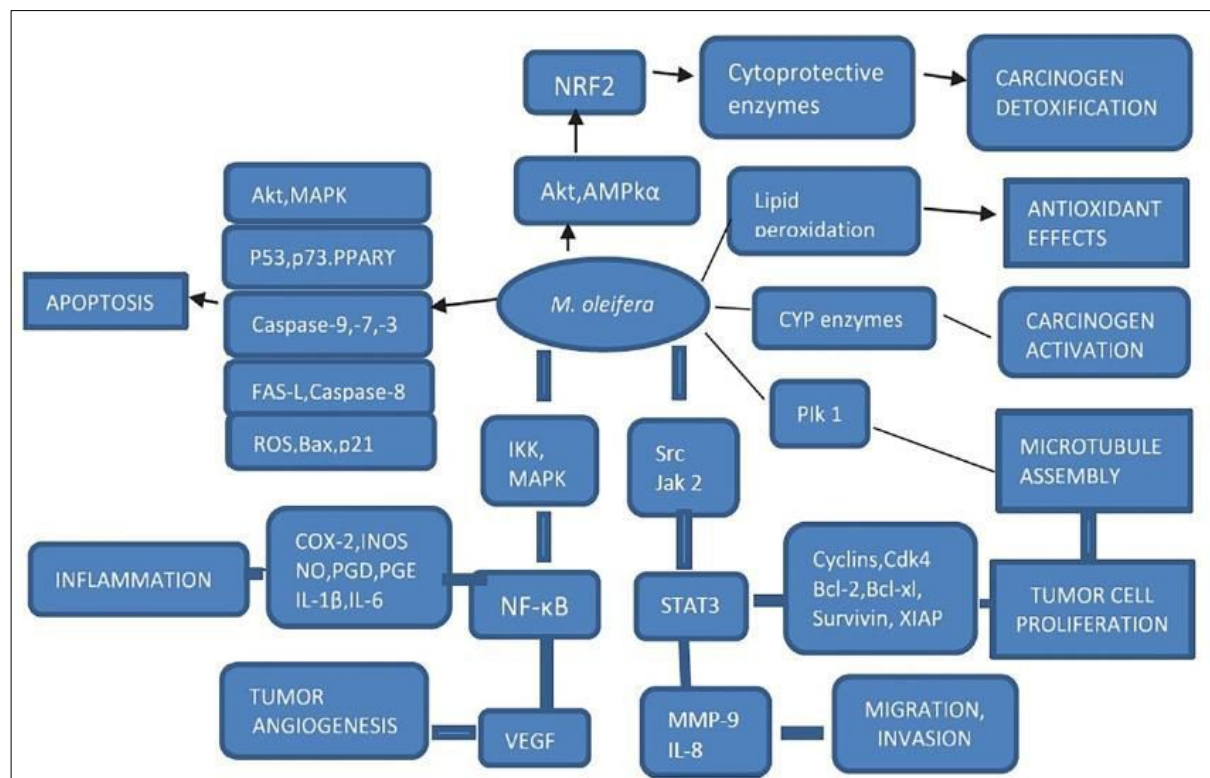


Fig 4: The anticancer potential and molecular targets of *Moringa oleifera* [67].

Antioxidant Properties

By defeating the cell's antioxidant defense system, reactive oxygen species oxidize biological molecules, resulting in damage to DNA, proteins, and carbohydrates as well as cell membranes (Figure 4). This oxidative stress is brought on by a number of clinical conditions, including diabetes, heart failure, and hypertension [68]. Consumers always choose natural antioxidants over synthetic ones since they are superior to them [69]. Strong antioxidants discovered in *Moringa oleifera* leaves include quercetin, kaempferol [70], ascorbic acid, β -carotene [71], isothiocyanates, polyphenols, and rutin [72]. Researchers have discovered that the extracts of leaves in a variety of organic solvents, including methanol, acetone, dichloromethane, water, diethyl ether, chloroform, and ethyl acetate, possess antioxidant capabilities [73, 74]. The superoxide anion radical (O_2^-) can be more effectively neutralized by the ethyl acetate extract of *Moringa oleifera*, which decreases tissue damage by preventing the interaction of free radicals with biological macromolecules. The linear association between phenolic chemicals and leaves' greater antioxidant activity [74] aids in the development of products that increase the oxidative stability of food goods. Due to the presence of a greater polyphenolic content, the extract of *Moringa oleifera*

methanolic leaves demonstrated reasonable antioxidant activity (IC_{50} 49.86 g/mL) in comparison to ascorbic acid (IC_{50} 56.44 g/mL) [75]. Additionally, it has been claimed that leaves' antioxidant profile agrees with plants' ability to preserve themselves from freezing [76] and that its components are employed as a natural preservative for fat [77]. The antioxidant capacity of *Moringa oleifera* tea (81% inhibition of DPPH radicals compared to vitamin-C (0.1 mg/ml) with 76.5% inhibition) may be useful in preventing chronic illnesses linked to stress [78]. In a recent study, Khalofah *et al.* [79] found that cadmium stress had a deleterious impact on *Lepidium sativum* but that *Moringa* leaf extract considerably lessened that impact. Intoxicated rats with aluminum phosphide experience an increase in antioxidant levels and a decrease in malondialdehyde after receiving a dose of 100 mg/kg body weight of *Moringa* extract (MDA). As a result, it can be utilized as adjuvant therapy to treat cardiotoxicity brought on by aluminum phosphide (AIP) [80]. Alavrez Roman *et al.* [81] prepared topical formulations (nanoparticles and gel) from the hydroalcoholic fraction of *Moringa* leaves and identified the phytochemical profile's moisturizing and antioxidant potential. The viscosity, pH, and particle size of both formulations were good, indicating that they were suitable

for use as a formulation. There were discovered to be seven distinct substances, including phenolic acids and flavonoids. Additionally, this formulation could be exploited as a new skin medication delivery system due to its increased antioxidant activity and positive skin biophysical evaluation results (higher stratum corneum water content and lower trans-epidermal water loss). *Moringa* leaves were substituted for alfalfa hay in a different trial to improve the milk and serum quality of goats [82]. Three diets containing alfalfa alone, 25% *Moringa oleifera* leaves, and 25% *Moringa peregrina* in the diet of goat's fodder are all included in their analysis. Each experiment used ten goats and lasted two weeks to acclimate to before collecting data for six weeks. In comparison to an alfalfa-only diet, goats fed with both types of *Moringa* leaves displayed higher fat content that was free from nitrogen extract and total phenols. Additionally, by increasing total antioxidant activity, Vitamin C, catalase activity, and lowering the quantity of thiobarbituric acid reactive substance (TBARS), goats fed *Moringa* have improved the oxidative status of serum and milk [82]. Saleem *et al.* [83] investigated the *in vitro* antioxidant activity of several extracts of *Moringa* leaves at doses ranging from 0.1563-5 mg/mL. They discovered that the greatest DPPH activity was present in the methanolic extract at all doses and that all the extracts had radical

scavenging activity at a low dosage of 0.1563 mg/mL. Likewise, at a concentration of 1 mg/mL, the methanolic extract displayed the best H₂O₂ scavenging activity (70.56±0.43%) and reducing power (925.48±0.45%). The methanolic extract has a higher total phenolic content (TPC) and total flavonoid (TFC) than other extracts, which accounts for its high antioxidant activity. Aju *et al.* [84] looked at the effects of a methanol extract from *Moringa* leaves on the heart of diabetic rats experiencing oxidative stress brought on by streptozotocin. For 60 days, rats were given *Moringa* leaves orally at a dosage of 300 mg/kg body weight. They were divided into six groups: normal control rats (group 1), normal rats treated with *Moringa* leaves (group 2), high-energy diet control rats (group 3), diabetic rats (groups 4 and 5), and diabetic rats treated with metformin and atorvastatin (group 6). According to the authors, rats from groups 3 and 4 had significantly lower activity levels of antioxidant enzymes like catalase (CAT), glutathione (GSH), glutathione peroxidase (GPx), and superoxide dismutase (SOD), whereas rats from group 2, 5 and 6 had significantly higher activity levels of antioxidant enzymes in their hearts. The antioxidant potential of *Moringa* leaves is due to a variety of antioxidant compounds, including hexadonic acid, DL- α -tocopherol, and other compounds.

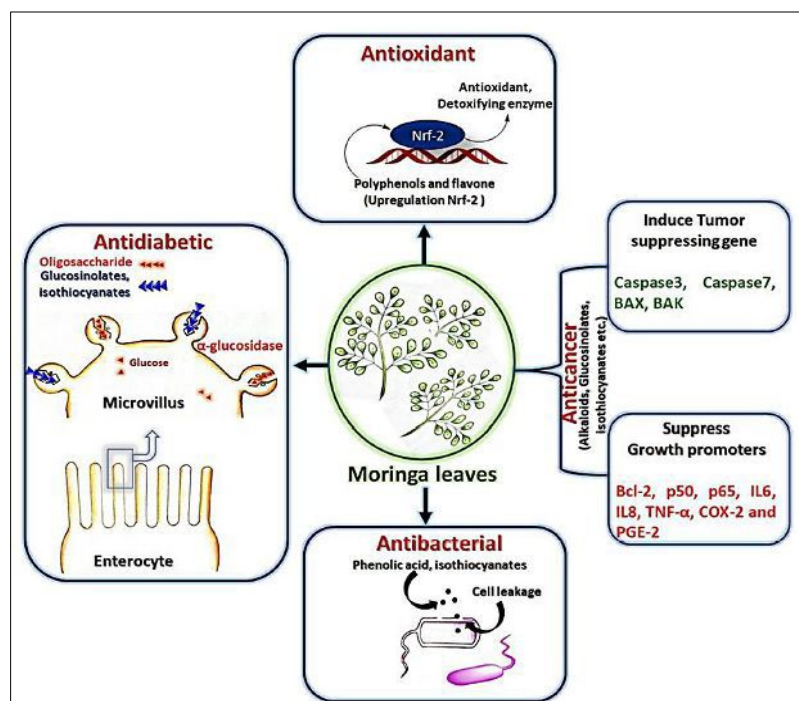


Fig 5: Pharmacological activities of *Moringa* with the mechanism of action [48].

Antimicrobial Activity

The main issue of the modern era is antibiotic resistance. Due to the widespread use of antibiotics without caution, the majority of infectious organisms have developed a permanent resistance to both chemotherapeutic drugs and antibiotics. Finding novel antibacterial agents with diverse functions is necessary. *Moringa* leaves contain a variety of bioactive substances, and the antibacterial, antifungal, antiviral, and antiparasitic properties of its many preparations have been thoroughly established. However, some studies claim that chemical compounds found in *Moringa* leaves, such as pterygospermin, moringine, and benzyl isothiocyanate, were what caused the plant's antimicrobial effects. Important studies are available on

crude extract [47]. Due to the enhanced activity of some apigenin derivatives, which have been found to be most effective against both Gram-positive and Gram-negative bacteria like *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa*, apigenin is thought to be a future green chemical to combat the problem of antibiotic resistance [85]. It was also mentioned as having possible antiviral properties against the HSV-1 and HSV-2 herpes simplex viruses, the hepatitis C virus, the influenza virus, the HFM virus, and the ASFV (African swine fever virus) [85]. There are numerous reports of catechin, epicatechin, Vallin phenols, vicinin-like anthocyanates, and glucosinolate in *Moringa* leaves. These chemicals are all lipophilic in nature, which may be the cause of the

antibacterial activity associated with leaf extract that has been described in several investigations. The lipophilic nature of phenolic compounds favors their interaction with the cell membrane and other lipophilic cell components, which increases their antibacterial activity^[86]. The contact leads to aggregates of cell components and long-lasting alterations to the cytoplasmic membrane, which impairs the function of channels and enzymes. According to reports, phenylpropanoid condensed cell content and tanning cause channels, membrane components, and crucial metabolic enzymes to become disrupted^[87-89]. According to Borges *et al.*, phenolic acids damage the integrity of the cytoplasmic membrane, which in turn causes the breakdown of the osmotic equilibrium and the integrity of the cell by leaking vital intracellular components. It was previously reported by Bouarab-Chibane *et al.*^[90] that plant polyphenols have antibacterial potential against a variety of food pathogens, including *L. monocytogenes* ATCC19115, *B. subtilis* ATCC6633, and *S. aureus* CNRZ3, as well as three Gram-negative ones, *P. aeruginosa* ATCC2785, *S. enteritidis* E0220, and *E. coli* ATCC25. This inhibitory effect might be brought on by polyphenol's capacity to change the outer membrane^[91]. The growth of Gram-negative pathogenic bacteria like *S. dysenteriae*, *E. coli*, *Klebsiella pneumoniae*, *Enterobacter sp.*, and *Salmonella sp.* was arrested in several solvent extracts of *Moringa oleifera*, according to Rahaman *et al.* and comparable to tetracycline in terms of antistaphylococcal potential^[92]. The ethanolic extract was reported to be effective against *Enterococcus faecalis*, *Vibrio parahaemolyticus*, and *Aeromonas caviae*. Additionally, these isothiocyanates were discovered in *Moringa* leaves^[93], and their biological activities, such as antioxidant and antibacterial properties, are well known. *Moringa oleifera*'s glucomoringin and other metabolites have been shown to have anti-inflammatory, antioxidant, antibacterial, antifungal, and antiviral properties^[94]. Numerous isothiocyanates demonstrated strong antibacterial activity through a variety of methods, including maintaining membrane integrity and preventing bacterial quorum sensing^[95, 96]. It has also been noted that the Iberian variety of *Moringa oleifera* inhibits *S. aureus*, *P. aeruginosa*, and *E. coli*. The antibacterial potential of particular pure chemicals extracted from *Moringa* leaves must still be determined. The antimicrobial activity of *Moringa* leaf extract in ethanol, water, and chloroform against *Staphylococcus aureus* and six Gram-negative bacteria (*Escherichia coli*, *Salmonella typhi*, *Enterobacter aerogenes*, *Salmonella typhimurium*, *Shigella spp.*), while no inhibition was seen at any tested concentration, is one of the contentious reports. Buker *et al.*^[97] reported this finding. But against *Mucor spp.* and *Rhizopus spp.*, the *Moringa* leaf extract showed substantial antifungal ability. The ability of *Moringa* leaf extract to suppress *Candida tropicalis* and *Saccharomyces cerevisiae* at high concentrations was also demonstrated by Pinal *et al.* in both aqueous and ethanol forms. *Candida albicans* nevertheless displayed resistance to these extracts. *Aspergillus flavus*, *Aspergillus fumigates*, *Aspergillus niger*, *Cryptococcus neoformans*, and *Candida albicans* all showed similar responses to *Moringa* leaf extract^[98, 99].

Wound Recovering Properties

In male Swiss albino mice, the aqueous extract of *Moringa oleifera* has the ability to heal wounds. Significant improvements in skin-breaking strength, granuloma-breaking strength, wound healing rate, granuloma dry

weight, hydroxyproline content, and scar area reduction were noted^[100]. V.I. Hukkeri^[101] revealed the antipyretic and wound-healing effects of the ethanolic and ethyl acetate extracts of *Moringa oleifera* leaves. Ethyl acetate extract of dried leaves exhibits considerable wound healing activity (10% extracts in the form of ointment) on excision, incision, and dead space (granuloma) wound models in rats, whilst ethanolic and ethyl acetate extract of seeds show significant antipyretic action in rats.

Antifertility Activity

Moringa oleifera root extract was tested for antifertility effects. Rats' pre and post-implantation uterine histoarchitecture has been examined in relation to the action of an aqueous extract^[102]. In female reproductive organs of rats, the aqueous extract of *Moringa oleifera* has an anti-implantation property, while the roots of the plant show antifertility activity. The moist weight of the uterus in rats with bilateral ovariectomies grew gradually after extract administration. This estrogenic activity was kept up by the uterus's histo-architecture. When the extract was administered along with estradiol dipropionate (EDP), there was a consistent decrease in uterine weight as opposed to the growth with estradiol dipropionate alone^[103]. Additionally, the histological configurations of the uterus were suppressed.

Hepato-protective Movement

Alaaeldin A. Hamza^[104] describes how the treatment of *Moringa oleifera* seed extract decreased the CC14-induced rise of serum aminotransferase activity and level of globulin. Treatment with *Moringa oleifera* also decreased the increases in myeloperoxidase activity and hepatic hydroxyproline levels. The oral treatment of 20% carbon tetrachloride (CC14) twice per week for six weeks promoted liver fibrosis. The findings of the histological and biochemical tests indicated that *Moringa oleifera* decreased liver fibrosis and symptoms of liver damage. In the case of an overdose, it is thought that oxidative stress triggers the onset of acetaminophen toxicities^[105]. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphate (ASP) levels, was significantly lower in the group treated *Moringa oleifera* than in the group treated with acetaminophen alone, according to histopathological examination. In animals treated with *Moringa oleifera*, the amount of glutathione (GSH) was discovered to be recovered. Using male Wistar rats as a protective and curative model, Eshwar Kumar demonstrated the *in vitro* antioxidant and *in-vivo* hepatoprotective effects of crude ethanolic extracts of *Moringa oleifera* seeds. *Moringa oleifera*'s capacity to scavenge superoxide, hydroxyl, and DPPH radicals were tested.

Antihypertensive, diuretic, and cholesterol-lowering properties

This plant is highly helpful in treating cardiovascular problems due to its potent mix of diuretic, lipid, and blood pressure-lowering components. Blood pressure can be stabilized by drinking *Moringa* leaf juice, which contains thiocarbamate glycosides and mustard oil glycosides that have been isolated from *Moringa* leaves^[106, 107, 108]. The majority of these compounds, which have carbamate, or nitrile groups, are fully acetylated glycosides, which are rare in nature. Four pure chemicals, niazimicin, niazinin A+B,

niazinin A, and niazinin B, which exhibit lowering of blood pressure in rats through a calcium antagonist effect, were isolated through bioassay-guided fractionation of the ethanolic extract of *Moringa* leaves. Additional research on the pulp, coat, and seed of whole pods and their component parts-aqueous and ethanol extracts found that the seed was more effective at lowering blood pressure, with similar outcomes in both water and ethanolic extracts demonstrating that activity is dispersed. Thiocarbamate and isothiocyanate glycosides were isolated from the ethanolic extract of *Moringa oleifera* pods using activity-directed fractionation, and these compounds are known to be the active ingredients in hypotensive medications. Examined in the pods of *Moringa oleifera*, methyl hydroxybenzoate and β -sitosterol also demonstrated encouraging hypotensive action. It has been discovered that the aqueous seed extract, flowers, leaves, roots, gum, and seeds of *Moringa* all have diuretic properties. These diuretic components may complement in lowering blood pressure. The presence of a bioactive phytoconstituent called β -sitosterol in the crude extract of *Moringa* leaves is likely what causes it to lower cholesterol in the serum of rats fed a high-fat diet [109]. In hypercholesteremic rabbits, *Moringa* fruit has been shown to lower serum cholesterol, low-density lipoprotein (LDL), phospholipids, triglycerides, very low-density lipoprotein (VLDL) cholesterol to phospholipid ratio, atherogenic index lipid, and affect the secretion of fecal cholesterol [110].

***Moringa* against Coronavirus Infections**

Surprisingly, experts recommended employing a large dosage of bitter and cold herbs to clear heat and detoxify the infectivity in its early beginning, as well as middle and late stages [111] in light of the novel universal and remarkable circumstances surrounding the coronavirus. The leaves of the *Moringa oleifera* plant have a sweet and bitter flavor as well as a cooling, ventilating, and dehumidifying effect. As a result, it makes for an excellent treatment option for the disease's profound overall immunological abnormalities. It is possible to imagine a sufficient and supportive therapy for coronavirus infection when combined with conventional medicine. Some of the *Moringa oleifera* constituents that function include kaempferol, pterygospermin, morphine, quercetin, and apigenin. The most effective anti-SARS agent against MPro-Cov-2 is apigenin [112]. In contrast to the well-known SARS-CoV-2 MPro inhibitor baicalein, three flavonoids-isorhamnetin, kaempferol, and apigenin demonstrated good binding empathy stable protein-ligand complexes with high binding energy and similar binding poses [113]. Rutin and isorhamnetin-3-O-rutinoside from the *Moringa oleifera* plant are powerful inhibitors of the SARS-CoV-2 designated target major protease (MPro), according to a dynamic study that was confirmed by *in vitro* and *in vivo* research [114].

Safety Studies

All of the up-to-date human investigations, which will be covered in more detail later in the text, have not revealed any negative consequences. Additionally, a variety of formulations have been utilized as both foods and medicines all throughout the world without any negative side effects being reported. Specific assessments of the possible toxicity of various formulations of *Moringa oleifera* have been made in several animal experiments. The security of an oral administration of an aqueous leaf extract to rats at doses of

400, 800, 1600, and 2000 mg/kg body weight was investigated [115]. With the exception of the highest dose, the medication was either administered as an acute single dose or every day for 21 days. A number of factors were evaluated, including serum enzyme levels and blood cell counts. The scientists came to the conclusion that up to 2000 mg/kg of *Moringa oleifera* leaves might be safely consumed. Over the course of the study's 21 days, the body weights of the rats decreased in a dose-dependent manner. In various experimental conditions, Asare *et al.* [116] investigated the possible toxicity of aqueous *Moringa oleifera* leaf extract. In one series of investigations, the cytotoxicity of the extract at various concentrations was tested on human peripheral blood mononuclear cells. Cytotoxicity was seen at a dosage of 20 mg/kg, which is insufficient for oral intake. In a further series of tests, rats received extract doses of 1000 and 3000 mg/kg and the animals underwent testing for as long as 14 days. Based on blood cell research, the *Moringa oleifera* leaf extract was proven to be genotoxic at a dose of 3000 mg/kg, which is still higher than most regularly used doses. Given to rats at a dose of 1000 mg/kg, which is still higher than most regularly used levels, it was determined to be safe and did not cause genotoxicity. Ambi *et al.* [117] fed 24 rats in four groups 25%, 50%, 75%, and control levels of *Moringa oleifera* powdered leaves along with regular livestock feed for 93 days. It is unknown how many *Moringa oleifera* leaves were ingested in total. After the experiment, the treated animals' organs had microscopic lesions that could be seen, while the 75% group exhibited necrosis of the liver cells, splenic blood vessels, and neural glial cells. In every organ inspected, the control animals lacked detectable microscopic abnormalities. No tissue photomicrographs were offered. Although the authors did not quantify the amounts of leaves consumed, they were far greater than the doses that would typically be used in either rats or humans. For instance, even at the modest dose of 25% of the chow, if the rats consumed an average of 15-20g of chow daily, the daily dose for an adult rat would be roughly 15-20 g of leaves per kilogram, which is equivalent to 195-260 g for an 80 kg human. Mice have also been used to test the toxicity of an aqueous extract of *Moringa oleifera* leaves [118]. Mice were given the extract in an acute trial at doses of up to 6400 mg/kg orally and 1500 mg/kg intraperitoneally. Mice were given oral doses of 250, 500, and 1500 mg/kg for 60 days in a subchronic study. The lethal dose of 50% LD50 was estimated to be 1585 mg/kg. No significant effects were observed with respect to hematological or biochemical parameters or sperm quality. A high degree of safety was observed during oral administration. The toxicological effects associated with the consumption of 50, 100, 200, or 400 mg/kg of methanol extract of *Moringa oleifera* for 8 weeks were performed in 30 rats [119]. The extract was a 30:1 concentration. All experimental animals that received *Moringa oleifera* had a significant increase in body weight in a dose-dependent manner, contrary to what is observed with an aqueous extract [115]. A substantial rise in serum levels of alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, and creatinine was observed in rats given *Moringa oleifera* at 200 and 400 mg/kg. It should be noted that methanol, not water, was used to create the extract. At a dose of 400 mg/kg, the 30:1 concentration of methanol extract would be equivalent to 12 g of leaves per kilogram, which is a very improbable dose. It is unclear how the methanol extract's composition compares to that of commonly used aqueous extracts because of the extract was not disclosed. According to Bakre *et al.* [120],

mice required more than 6.4 g/kg of an oral ethanol extract of *Moringa oleifera* leaves to be fatal. Zvinorova *et al.* [121] studied the dietary benefits of *Moringa oleifera* leaves as a dietary supplement for liver function. The diets of normal rat feed fed at 20% and 14% of body mass or feed supplemented with *Moringa oleifera* fed at 20% and 14% of body mass were given to 32 weanling rats at random for 5 weeks. Supplementing with *Moringa oleifera* had no effect on the levels of blood metabolites, liver glycogen, or lipid storage. Rats were subjected to oral dosages of up to 1000mg /kg of an aqueous *Moringa oleifera* extract for 14 days and a single oral dose of 5000mg/kg of the extract, to determine any potential toxicological effects [122]. The authors reported that neither histological nor overt adverse effects were seen at these levels. Numerous liver enzymes showed small but statistically significant dose-dependent increases. A typical 400 mg dose of an aqueous extract in an 80 kg human is more than 30 times as powerful as a dose of 1000 mg/kg in rats. Three different assay techniques, including the Ames assay, were used to determine the genotoxicity of an aqueous *Moringa oleifera* seed extract [123]. Without metabolic activity, the seed extract was not genotoxic and did not endanger human health. A hexane extract of *Moringa oleifera* leaves was tested for its impact on male rats' reproductive systems [124]. For 21 days, the extract was administered orally at dosages of 17,170 and 1700 mg/kg body weight. Without affecting plasma gonadotropin levels, a dose-dependent rise in testis and epididymis weights, seminiferous tubule diameter, and epididymal epithelium thickness was seen. The authors concluded that spermatogenesis had increased as a result of the alterations. Several investigations on *Moringa oleifera* seeds and roots will be presented for the sake of completeness, even if the findings cannot be directly compared to or equated with those of studies on leaves. Arajo *et al.* assessed the cytotoxicity of an aqueous extract of *Moringa oleifera* seeds [125]. After 14 days of extract administration to mice (at doses of 500 and 2000mg/kg), no symptoms of systemic toxicity were seen, and every animal survived. Between the treatment and control groups, there were no differences in organ indices. Erythrocytes, platelets, hemoglobin, and hematocrit all underwent minor but not appreciable modifications. Every value stayed inside the acceptable range. Rats' acute and subacute toxicity tests were conducted using a methanol extract of *Moringa oleifera* seeds that had been phytochemically tested for chemical components [126]. Saponins, tannins, terpenes, flavonoids, carbohydrates, and cardiac glycosides were all found during the phytochemical screening, however, anthraquinones were not. Mortality was documented at a dose of 5000 mg/kg of the extract, even though indications of acute toxicity were visible at a dose of 4000 mg/kg. At dosages less than 3000 mg/kg, no unfavorable effects were noticed. The authors came to the conclusion that methanol extracts of *M. oleifera* are suitable for use in food. Paul and Didia [127] looked into the outcome of methanol extract of *M. oleifera* root on the liver and renal histoarchitecture of 24 guinea pigs. Daily intraperitoneal injections of the root extract at doses of 3.6, 4.6, and 7.0 mg/kg were used during the experiment, along with a control group, for three weeks. All treated groups' histological sections showed ballooning liver deterioration, which suggests time-dependent hepatotoxicity rather than a dose-dependent reaction. In the 4.6 mg/kg group, examination of the kidneys revealed little tubular damage and interstitial inflammation, whereas, in the 7.0 mg/kg group, the interstitium had been invaded by inflammatory cells and amorphous eosinophilic debris.

Regarding the extract's composition or level of concentration, nothing was said. Studies using aqueous leaf extracts cannot be compared to or comparable with the findings of this study. This study used an intraperitoneally administered, methanol-based root extract. In conclusion, numerous preparations of *M. oleifera* have been shown to be effective in human, animal, and *in vitro* research, as well as the extrapolation of results from animal studies to humans. *M. oleifera* leaves, including their aqueous extracts, seem to be incredibly safe at the dosages and quantities frequently used for thirty postmenopausal females. The results showed significant decreases in malondialdehyde (16.3%; lipid peroxidation), and increases in serum glutathione peroxidase (18.0%), superoxide dismutase (10.4%), and ascorbic acid (44.4%), markers of antioxidant capabilities. Additionally, it was shown that hemoglobin levels increased (17.5%), and fasting blood glucose levels significantly decreased (13.5%). There were no negative consequences noted. In conclusion, previous studies on humans have shown that whole-leaf powders of *M. oleifera* administered orally have significant anti-hyperglycemic, anti-dyslipidemic, and antioxidant effects in human subjects without producing any negative effects. Leaf extracts weren't used in any of these studies.

Conclusion

A lot of work is currently being done to identify, classify and understand the activities of the proteins found in *Moringa oleifera*. The qualities of the plant *Moringa oleifera* are constantly being studied. *Moringa oleifera* should therefore be thoroughly researched in order to better understand the action mechanisms. With a better understanding, *Moringa oleifera* can be used effectively in a variety of fortified nutraceutical and health-improving products. The use of *Moringa* as a natural complement to drugs may encourage the development of new drugs. By combining synthetic drug use with *Moringa*, the negative effects could be reduced. However, thorough risk assessment studies must be conducted to guarantee the security of the medications and items produced using *Moringa oleifera* products' dietary consumption could be planned based on insightful analysis and some legal safety regulations.

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