WISELEAF SCIENTIFIC VENTURES

Chapter 4: Pharmacological Activities of *Moringa oleifera*

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ABSTRACT

Moringa oleifera (M. oleifera) Lam., which is also known as the drumstick or the miracle tree, has been given a lot of attention because of its varying pharmacological heights due to a rich repertoire of bioactive phytoconstituents. The chapter covers an extensive review of the pharmacological potential of *M. oleifera*, its mechanistic activity and the emerging therapeutic potential. The biological effects of this plant are due to flavonoids (quercetin, kaempferol), phenolic acids, glycosylates, isothiocyanates, alkaloids, saponins and terpenoids. There is a lot of experimental and clinical evidence that *M. oleifera* is a strong antioxidant that stimulates the Nrf2 signaling pathway, which leads to the development of endogenous antioxidant enzymes including catalase, glutathione peroxidase, and superoxide dismutase. It possesses anti-inflammatory properties, inhibits the NF-KB signaling pathway, and reduces the production of pro-inflammatory cytokines such as IL-1 800) and TNF-800), among others. Furthermore, *M. oleifera* is an essential medicinal plant for diabetes management because of its capacity to regulate the AMPK and PI3K/Akt pathways, which promote insulin sensitivity and glucose absorption. It also exhibits a wide-spectrum antimicrobial activity against bacteria and fungi, and has various beneficial neuroprotective properties including anti-oxidant properties, microglial activation modulation and amyloid-2 aggregation inhibition. In addition to these proven activities, its main metabolic regulation pathway, the regulation of microbiomes and

the multi-target therapeutic effects have been recently identified. Recent advances in nano-pharmacology and new drug delivery systems are also involved in achieving the bioavailability and therapeutic activity of the phytoconstituents of *M. oleifera* and this is an important topic of current research. Although the medicine has favorable pharmacological characteristics, concerns such as lack of standardization, variability in phytochemical composition, and a lack of substantial clinical validation remain significant barriers to its effective clinical use in clinical practice.

Keywords: *Moringa oleifera*, pharmacological activities, antioxidant, anti-inflammatory, antidiabetic, antimicrobial, anti-neuro, nano pharmacology.

1. Introduction

1.1 Importance of *M. oleifera*

M. Oleifera is a very valuable plant because of its potential to treat malnutrition. *M. oleifera* Lam. Morning Glory (*Moringaceae*) is one of the most significant medicinal and nutritional plants due to its superior nutritional composition, high phytochemical content, and diverse biological activity. All parts of the plant (leaves, flowers, pods, seeds, roots, bark) are nutritionally and therapeutically valuable and are part of traditional medicine, and are increasingly used for producing medical products. This has resulted in many studies and scientific research interests around its high bioactive profile in disease prevention and management of chronic, metabolic, infectious and inflammatory diseases. The *M. oleifera* is particularly useful for its nutritive value, especially of its leaves. Along with a good number of vitamins, such as provitamin A (beta-carotene), B-complex vitamins (thiamine, riboflavin, niacin, pyridoxine, folic acid, choline), and vitamins C, D, and E, they are rich in minerals like calcium, potassium, magnesium, iron, zinc, phosphorus, copper, manganese, and sodium. The leaves are also rich in quality proteins, dietary fiber and essential amino acids, and have useful fatty acids like palmitic, oleic, linoleic and linolenic acids. Due to its impressive nutritional content, the *M. oleifera* is considered as a nutritional supplement to improve malnutrition and health conditions as well as immunity. In addition to its nutritional value, *M. oleifera* is a rich source of various phytochemicals like flavonoids, phenolics acids, alkaloids, tannins, saponins, terpenoids, sterols, anthraquinones, glycosides, glucosinolates, isothiocyanates, carotenoids,

tocopherols, polyunsaturated fatty acids, and other bioactive metabolites. Together these constituents put together demonstrate the antioxidant, anti-inflammatory, antimicrobial, anticancer, antidiabetic, antihypertensive, cardioprotective, hepatoprotective and immunomodulatory effects. The leaves, stems, flowers, pods and seeds contain the highest concentrations of the characteristic phytochemicals: glucomoringin 4-O-(α-L-rhamnopyranosyloxy)-benzyl glucosinolate and glucotropaeolin (benzyl glucosinolate) is predominantly found in the roots. Glucosinolates have been found to be most abundant in the leaves and seeds. These glucosinolates convert into biologically potent isothiocyanate, nitriles and thiocarbamates, which have antioxidant, anti-inflammatory, hypotensive, spasmolytic and anticancer effects, when they are hydrolyzed by the endogenous enzyme *myrosinase* and *glucosinolates*. The diverse pharmacological activities of *M. oleifera* arise from the synergistic action of its bioactive phytoconstituents, which collectively exhibit antioxidant, anti-inflammatory, antimicrobial, anticancer, antidiabetic, antihypertensive, cardioprotective, hepatoprotective, and immunomodulatory properties. These phytochemicals are distributed throughout different plant parts, including the leaves, stems, flowers, pods, seeds, and roots. Among the sulfur-containing compounds, glucomoringin [4-(α-L-rhamnopyranosyloxy) benzyl glucosinolate] is the predominant glucosinolate present in the aerial parts, whereas glucotropaeolin (benzyl glucosinolate) is primarily localized in the roots. The highest concentrations of glucosinolates are generally reported in the leaves and seeds. Upon tissue disruption, these glucosinolates are hydrolyzed by the endogenous enzyme myrosinase to generate biologically active metabolites, including isothiocyanates, nitriles, and thiocarbamates. These metabolites are largely responsible for the broad therapeutic potential of *M. oleifera* through their potent antioxidant, anti-inflammatory, vasorelaxant, antispasmodic, and anticancer activities.

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environmental variations, indicating uniformity of nutritional value in different agroecological areas. Immature pods provide proteins and dietary fiber for gastrointestinal health, better digestion and decreased colorectal disorders. Besides, they're low in calories and contain lots of nutrients, making them a great addition to your diet and weight management plan. Synergic effect of phytochemicals from *M. oleifera* is well correlated with its medicinal property. The pharmacological properties of alkaloids include a wide range of effects, flavonoids possess strong antioxidant and hepatoprotective properties, saponins have immunomodulatory activity, tannins have antimicrobial and antiparasitic activity and isothiocyanates are widely known for their chemo preventive and anticancer activity. Quercetin has other medicinal properties such as antioxidant, anti-inflammatory, antiproliferative and antidiabetic. When combined these bioactive compounds all have immune modulatory properties and work together to prevent and manage many diseases. Due to its immense nutritional value and medicinal utility *M. oleifera* has been called as the “Miracle Tree”. It grows quickly and is drought and cold-tolerant, can withstand challenging environmental conditions and grow on poor soils, which makes it very useful in tropical and subtropical areas. Leaves, flowers, fruits and immature pods have all traditionally been consumed as very nutritious foods. The nutritional comparison indicates that *M. oleifera* can be considered as a functional food and nutritional supplement due to the content of vitamin C, vitamin A, calcium, potassium, iron and proteins compared to some common foods. In addition to being a medicinal and nutritional plant, *M. oleifera* has emerged as a much-valued plant for pharmaceutical, nutraceutical, cosmetic and food industries. Seed oil is broadly used in cosmetics for skin and hair care due to its excellent emollient properties and seed extracts have anti-bacterial activity and are extensively used as natural water-purifying agents. Experimental investigations have consistently demonstrated that *M. oleifera* possesses potent antioxidant, anti-inflammatory, antihyperglycemic, and antihypertensive activities, reinforcing its broad therapeutic potential. Owing to its exceptional nutritional composition, rich phytochemical profile, diverse pharmacological properties, industrial versatility, and ability to thrive under varied environmental conditions, *M. oleifera* has emerged as one of the most valuable medicinal plants of modern times. Its wide-ranging applications in improving nutritional status, addressing micronutrient deficiencies, and supporting the prevention and

management of numerous chronic disorders underscore its growing importance in public health. Consequently, *M. oleifera* represents a sustainable natural resource with considerable potential to contribute to healthcare and nutritional security, particularly in low and middle-income countries where affordable plant-based interventions are of substantial value.

1.2 Traditional Medicinal Significance

The most important medicinal trees that are utilized in traditional medicine systems are "Miracle Tree" or "Drumstick Tree" (*M. oleifera* L.). Since time immemorial, all parts of the plant-leaves, flowers, pods, seeds, roots, bark, gum and seed oil have been used to treat and prevent a wide range of illnesses. Many therapeutic properties and safe dietary application make *M. oleifera* a great importance in Ayurveda and other indigenous healings. In Ayurveda, *M. oleifera* is considered as rejuvenating and immunomodulatory herb and is believed to enhance overall health and vitality. All parts of the plant have been used traditionally as medicine in diabetes, hypertension, anaemia, arthritis, kidney stones, skin diseases, malnutrition, digestive and respiratory ailments, and inflammatory diseases. The plant is also claimed to have a favorable effect on cardiovascular, liver, urinary, digestive, respiratory and immune system. The roots are stimulant, diuretic, expectorant, anti-inflammatory, anti-spasmodic and are used traditionally in the treatment of asthma, epilepsy, urinary calculi, enlarged liver and spleen and sore throat. The leaves are most extensively used and used for diarrhea, dysentery, jaundice, conjunctivitis, as a diuretic for urinary disorders, bronchitis, asthma, influenza and tuberculosis. The leaves are also used topically in the treatment of acne, intestinal worms and skin infections. The flowers have traditionally been used as tonic, stimulant, cholagogue and diuretic and are believed to be useful for diabetes and reproductive health. The antimicrobial, antifungal, antiseptic and circulatory tonic properties of the bark are used in inflammatory disorders and for reproductive health. The seeds are used for urinary disorders, venereal diseases and diabetes, and have anti-inflammatory, antimicrobial, antispasmodic and diuretic properties. Furthermore, powdered seeds are known to have the natural power to cleanse water. *M. oleifera* has also traditionally been used for treating gastric ulcers, hemorrhoids, headaches, oedema, fatigue, nervous disorders, weakened immunity and cancer. All these are thought to be natural immunes, tonics and nutrients that enhance the

strength of the body, its nourishment, bone health and longevity. *M. oleifera* has been traditionally used in several cultures in a wide range of applications, indicating its significance as a multipurpose medicinal plant. Numerous of these ethnomedicinal properties have been confirmed by modern pharmacologic studies and make the plant an excellent source of bioactive compounds with valuable medicinal properties. *M. oleifera* is regarded as one of the most pharmacologically valuable medicinal plants owing to its remarkable diversity of bioactive phytoconstituents and broad therapeutic potential.

1.3 Pharmacological significance of *M. oleifera*

Among its various parts, the leaves possess the highest medicinal value because they are particularly rich in flavonoids, phenolic compounds, alkaloids, tannins, carotenoids, β-sitosterol, vanillin, hydroxyleucine, moringine, moringinine, β-sitostenone, and 9-octadecenoic acid. The synergistic action of these phytochemicals contributes to a wide range of biological activities, supporting the traditional and scientific use of *M. oleifera* in the prevention and management of numerous diseases. Experimental studies have demonstrated that leaf extracts exhibit significant analgesic activity in both central and peripheral pain models, producing dose-dependent effects in hot-plate and acetic acid-induced writhing assays comparable to those of indomethacin. In addition, the extracts have shown promising efficacy in alleviating migraine-associated pain and reducing pain related to multiple sclerosis following topical application. The leaves also possess pronounced anti-inflammatory properties, as evidenced by significant inhibition of carrageenan-induced paw edema in experimental models. Collectively, these findings highlight the substantial therapeutic value of *M. oleifera* leaves and support their continued exploration as a natural source of analgesic and anti-inflammatory agents. This activity has been shown to be brought about by modulation of neutrophil function and inhibition of c-Jun N-terminal kinase (JNK) signaling pathway which results in the suppression of inflammatory mediator production. In addition to its anti-inflammatory and analgesic activity, the leaves of *M. oleifera* shows high activity in antipyretic activity. The extracts on the other hand proved to be effective in decreasing the elevated body temperature in Brewer's yeast induced pyrexia models which gave scientific justification for their traditional application in fever treatment. The pharmacological properties of *M. oleifera* such as its neuroprotective, anti-

pyretic, anti-inflammatory and anti-analgesic effects are noteworthy. This study has confirmed many of its traditional medicinal uses and has provided scientific support to its potential as a source for bioactive compounds for the formulation of safe, effective and evidence-based phytopharmaceuticals.

1.4 Scope and objectives

The Scope of the present chapter is to briefly describe a pharmacology of *M. oleifera* and to summarize the available scientific information regarding the traditional *M. oleifera* medicinal uses. It emphasizes the principle biological actions of various parts of plant like antioxidant, anti-inflammatory, antimicrobial, antidiabetic, hepatoprotective, cardioprotective, neuroprotective, anti-cancer and immunomodulatory activities. In addition, the bioactive phytoconstituents and therapeutic effects of the chapter are highlighted and their therapeutic potential of *M. oleifera* as a source of natural medicinal agents and future phytopharmaceuticals are discussed.

2. Botanical description of *M. Oleifera*

M. oleifera, widely known as the “miracle tree”, is extensively cultivated and naturalized throughout tropical and subtropical regions of the world, with particularly widespread distribution across Asian countries, including India, Bangladesh, Pakistan, and Afghanistan. The Moringa family contains 13 species and in recent years, *M. oleifera* is becoming popular in many applications as a fertilizer, biogas producer and source of nutrition. Moringa is especially drought resistant. Based on the research, *M. oleifera* is a good choice to achieve nutritional sufficiency at affordable cost and is reliable. For their vital nutrients, almost every component of the tree is used. *M. oleifera* is a tree that grows in tropical and subtropical regions around the world, and is a popular ingredient in various traditional dishes. Requires slightly acidic to alkaline soil, indirect sunlight and no water logging. After 6-8 months, the tree starts to bear fruit. Its dried leaves contain approximately 70% oleic acid, and are used to make moisturizers. The dried leaves of *M. oleifera* are commonly processed into powders that are incorporated into a variety of nutritional beverages and health supplements. In traditional medicine, the bark has been valued for its therapeutic properties and has been used to manage conditions such as gastric ulcers, dental pain, and hypertension.

2.1 Distribution of *M.* oleifera

M. oleifera Lam. is a fast-growing deciduous tree belonging to the family *Moringaceae* and is indigenous to the sub-himalayan belt of northern India. Renowned for its exceptional nutritional composition and medicinal value, the species has been cultivated for centuries and has subsequently spread throughout tropical and subtropical regions worldwide. Although its center of origin is associated with the Indian subcontinent, the Arabian Peninsula, and parts of the East Indies, *M. oleifera* is now extensively cultivated across Asia, Africa, the Caribbean, Central and South America, the Pacific Islands, and parts of North America. Its ability to thrive under diverse climatic conditions and in a wide range of soil types has contributed to its global cultivation and increasing agricultural and medicinal significance.

It is also commercially grown in India, Nigeria, Ethiopia, Mexico, Madagascar, Cuba, the Philippines and a few South American countries. In India the tree is cultivated for its delicious leaves, flowers and unripe pods, which are used in traditional food such as southern India. *M. oleifera* grows well under a range of agro-climatic conditions, but its phytochemical content and nutritional value could be different based on geographic region, soil properties, environmental factors and farming practices.

2.2 Taxonomy

Taxonomy of plants: *M. oleifera*

Kingdom: Plantae

Sub-Kingdom: Tracheobionta

Super division: Spermatophyta

Division: Magnoliophyta

Class: Magnoliopsida

Subclass: Dilleniidae

Order: Capparales

Family: Moringaceae

Genus: *Moringa*

Species: *oleifera*

2.3 Seed setting in *M. Oleifera*

A member of the *Moringaceae* family, *M. oleifera* Lam. is a deciduous tree that grows quickly and is prized all over the world for its remarkable nutritional and therapeutic qualities. The plant is native to northern India's sub-Himalayan plains, where it has been grown since antiquity. Because of its exceptional capacity to adapt to a wide range of climatic circumstances, *M. oleifera* has spread much from its original habitat and is currently grown across tropical and subtropical climates. It grows well in a variety of soil types and climates in Asia, Africa, Central and South America, the Caribbean, the Pacific Islands, and portions of North America. *M. oleifera* has become one of the most significant medicinal and nutritionally useful tree species due to its hardiness, ease of cultivation, and variety of uses. It is also commercially grown in countries like India, Nigeria, Ethiopia, Mexico, Madagascar, Cuba, Philippines and several South American countries. The tree is popular for its edible leaves, flowers and immature pods that are used in traditional Indian cuisine, especially in the southern part of the country. *M. oleifera* is a plant that can grow in diverse agro-climatic conditions, but its phytochemical content and nutritional value can be influenced by geographical location, soil type, environmental conditions, and cultivation methods.

2.4 Morphology

The fast-growing, drought-tolerant *M. oleifera* tree thrives at elevations of up to 500 meters above sea level in tropical and subtropical regions. Under ideal environmental circumstances, it may grow to a height of around 10 to 15 meters and requires a well-drained sandy loam soil profile. The tree features a slender, frequently straight trunk, pale corky bark, an open umbrella-shaped crown, and soft, light, spongy wood. It has a thin shape, branching irregularly and with gracefully drooping branches. The leaves are tripinnate with many small oval leaflets, and the creamy white scented flowers are in axillary panicles about 10-25 cm long. The fruit is a long pendulous, 3-sided capsule, often called a "drumstick" and filled with many rounded brown seeds, surrounded by a semi-permeable seed coat. Highly productive *M. oleifera* tree produces around 15,000-25,000 seeds per season, which facilitates propagation and propagation of this species in various agro-climatic zones.

Fig. 1: *M. oleifera* plant and its major morphological parts (whole tree, leaves, flowers, pods, and seeds).

3. Phytochemical profile

3.1 Major Phytochemical Constituents

Although not essential to plant primary metabolism, phytochemicals are secondary metabolites that are synthesized naturally in plants and are involved in defense mechanisms and adaptation to environmental stresses. Due to their various pharmacological properties and their potential in preventing and controlling many chronic diseases, these active ingredients have been a focus of scientific attention. Phytochemicals can be classified into two main groups according to their chemical properties: polyphenols and carotenoids, alkaloids, terpenoids, and sulfur-containing compounds. *M. oleifera* is an extraordinarily rich source of these phytochemical classes, which are even indispensable to explain the extraordinary nutritional and therapeutic value of the plant. Polyphenols, in particular, are the most abundant and best studied group of these, because of their high antioxidant and disease-modifying activities. Polyphenols have a phenolic ring in

their molecule structure and are primarily flavonoids, phenolic acids, and tannins. The leaves of *M. oleifera* contain the highest amount of these compounds, ranging from around 2,000 to 12,200 mg of gallic acid equivalents (GAE/100 g), while the flowers and seeds have relatively lower concentrations. Advanced chromatographic techniques have been used to identify various phenolic constituents across the various parts of the plant in the form of phytochemical profiling. The main flavonoids are quercetin and kaempferol glycosides-the former is present in all parts in higher amounts while the latter is present in higher amounts in most of the parts, except roots and seeds. Quercetin level in the leaves is 0.46-16.64 mg/g dry weight and kaempferol level is 0.16-3.92 mg/g dry weight. Other flavonoids such as myricetin, rutin and epicatechin have also been found, but in smaller amounts. The main phenolic acids are gallic, caffeic, chlorogenic, p-coumaric acids and ellagic acid, while the leaves are the richest source of tannins. The unique glucosinolate of *M. oleifera* is glucomoringin [4-(α-L-rhamnopyranosyloxy)benzyl glucosinolate] which is abundant in the leaves, stems, flowers, pods and seeds. The leaves contain the highest reported concentration of glucomoringin followed by the seeds which contain about 8,620 mg/100g. This glucosinolate is converted to biologically active isothiocyanate upon hydrolysis, which plays a major role in the antioxidant, anti-inflammatory, anti-microbial and anti-cancer properties of the plant. *M. oleifera* contains a wide range of phytochemicals, and is a rich source of minerals, including potassium, calcium, magnesium, and iron. Potassium is mainly stored in vegetative parts and immature pods while calcium and magnesium are highest in the leaves and seeds, respectively. Additionally, it has a significant amount of iron, which adds to the plant's nutritional value. In summary, the high nutritional value of *M. oleifera*, due to its rich phytochemical and mineral content, makes it a promising source of nutraceuticals and pharmaceuticals.

3.2 Plant parts and their phytochemicals:

The phytochemical composition of *M. oleifera* varies among its different plant parts, with each containing distinct bioactive constituents that contribute to its medicinal properties. A concise summary of the major phytochemicals identified in various parts of the plant is presented in the table below.

Table. 1: Phytochemical composition of different parts of *M. oleifera* and their therapeutic significance.

S. No.	Plant part	Extract	Phytoconstituents	Therapeutic Uses
1.	Leaves	Aqueous and Alcoholic	Niazirin, Niazirinin, Benzyl isothiocyanate, Niaziminin A, Quercetin, Kaempferol, Gallic acid.	Antioxidant, Anti-inflammatory, Free radical scavenging, Antimicrobial and Anticancer.
2.	Seeds	Aqueous and Hydro-alcoholic	Methionine, Cysteine, Niazimicin, Benzyl isothiocyanate, Moringine.	Antimicrobial, Antitumour and Antibacterial.
3.	Pods	Hydro-alcoholic	Benzyl carbamate, methyl-p-hydroxybenzoate, beta-sitosterol, Protein content and Vitamin C.	Nutritional, immune support, Antioxidant, immune function.
4.	Bark	Alcoholic	4-(alpha-L-rhamnopyranosyloxy) benzylgiucosinolate	Antimicrobial Activity
5.	Flowers	Alcoholic	Isoquercetin, kaemopherol, kaempferitin and ascorbic acid, protein, D-mannose.	Antimicrobial activity and Anticancer activity
6.	Root	Alcoholic	Moringine, moringinine and spirachin	Free radical scavenging.
7.	Stem	Alcoholic and Hydroalcoholic	Octacosonoic acid, beta-sitosterone and beta- sitosterol.	Antioxidants

3.3 Chemical structure of some primary active phytoconstituents

M. oleifera is a plant with an extraordinary pharmacological potential, which is mainly due to the presence of a wide range of bioactive phytoconstituents such as flavonoids, isothiocyanates, phenolic acids, alkaloids, glucosinolates and vitamins. Benzyl isothiocyanate, quercetin, niazimicin, and kaempferol **(Fig. 2)** are identified as important therapeutic constituents of these among which the former three are regarded as having a wide range of biological activities. The compounds have strong antioxidant, anti-inflammatory, antibacterial, antidiabetic,

cardioprotective, neuroprotective, hepatoprotective, and anticancer properties. These effects are due to the control of many cellular and molecular signaling pathways. Understanding the chemical structures of these phytochemicals is critical for understanding their biological functions, structure-activity relationships, and mechanisms of action. Additionally, structural characterization is a scientific basis for phytochemical standardization, quality control and the rational development of new nutraceuticals and phytopharmaceuticals from *M. oleifera* that can be used for the prevention and management of various chronic diseases.

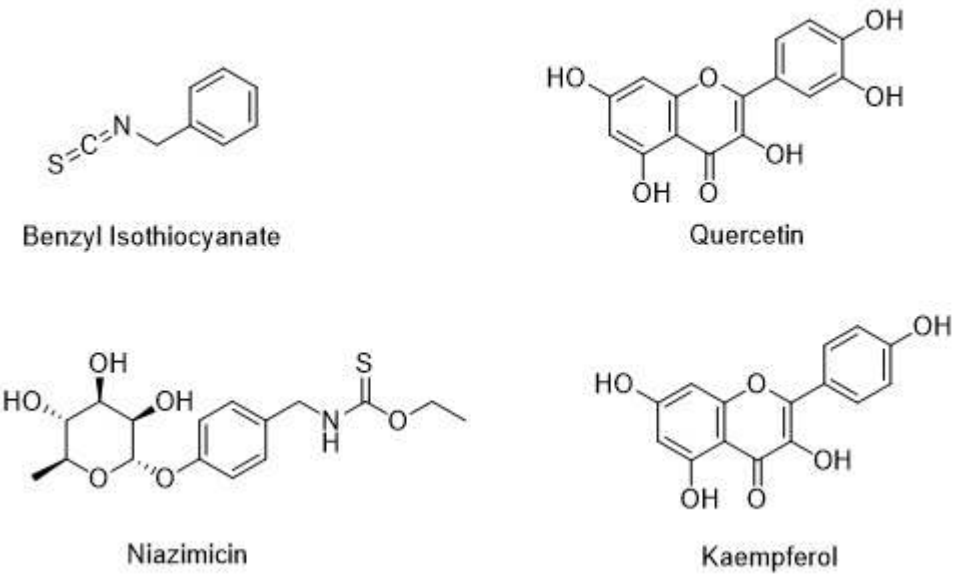


Fig. 2. Primary bioactive compounds found in *M. oleifera* and characterized as representative chemical structures, such as benzyl isothiocyanate, quercetin, niazimicin and kaempferol, which have been involved in the various pharmacological activities of *M. oleifera.*(1)

4. Pharmacological Activities

The *M. Oleifera* is a medicinal multi-functional plant rich in several active phytochemicals which include flavonoids, phenolic compounds, glucosinolates, isothiocyanates, alkaloids, tannins and vitamins. These bioactive phytochemicals have a synergistic effect because of their antioxidant, anti-inflammatory, and immunomodulatory properties, which help to prevent oxidative stress and cell damage. *M. oleifera* has been shown to have antioxidant, antimicrobial, antiviral, antidiabetic, anticancer, cardioprotective, hepatoprotective, nephroprotective, neuroprotective, gastroprotective, antihypertensive, wound healing and immunomodulatory properties in extensive preclinical and emerging clinical studies. Overall,

the results are indicative of the remarkable therapeutic activity of *M. oleifera*, and suggest that it is a promising natural source for future development as a nutraceutical or phytopharmaceutical.

4.1 Antioxidant Activity

The nutritional rich composition of *M. oleifera*, like the presence of phenolic compounds, flavonoids, vitamins, carotenoids, and other bioactive phytochemicals, is recognized as an excellent natural source of antioxidants. The leaves have the highest antioxidant activity among the various parts of the plant, and the ethanolic extracts consistently showed the highest free radical scavenger activity, as compared to aqueous and saline extracts. These phytoconstituents are effective inhibitors of generation of Reactive Oxygen Species (ROS), decrease oxidative stress and increase the endogenous antioxidant defense mechanisms of the cell, thus preventing the damage of cellular components due to ROS. Given these potent antioxidant properties, *M. oleifera* has become a subject of great interest as a functional food and natural therapeutic agent that could be used to prevent or delay the onset of oxidative stress-related chronic diseases, such as cardiovascular disorders, diabetes, neurodegenerative diseases, and cancer. However, more clinical trials of sufficient design need to be conducted to demonstrate its long-term efficacy and therapeutic benefits in humans.

4.2 Anti-inflammatory Activity

M. oleifera possesses potent anti-inflammatory activity owing to its rich content of flavonoids, isothiocyanates, polyphenols, and other bioactive phytochemicals. These compounds suppress key inflammatory mediators by modulating COX, LOX, NF-κB, and JNK signaling pathways while reducing oxidative stress through their antioxidant properties. Experimental studies have further demonstrated that *M. oleifera* extracts effectively alleviate inflammation, with bark extracts exhibiting efficacy comparable to diclofenac in carrageenan-induced edema models. These findings highlight the considerable potential of *M. oleifera* as a natural anti-inflammatory agent for the prevention and management of inflammatory disorders.

4.3 Antidiabetic Activity

The rich phytochemical constituents, especially flavonoids like quercetin and kaempferol in *M. oleifera* have attracted a lot of attention as a potential natural agent for treating diabetes. The

extracts of *M. oleifera* are found to possess blood glucose lowering effect, increase insulin secretion and improve pancreatic β-cell function in diabetic animal models in the preclinical studies. These positive effects have been attributed to its strong antioxidant activity, which reduces oxidative stress, maintains the shape of the pancreas and regulates glucose homeostasis. In conclusion, all these results point to the possibility of using *M. oleifera* as a therapeutic approach in the prevention and management of DM, and suggest a strong scientific basis for the development of further well-designed clinical studies that could confirm its efficacy and safety. The natural isothiocyanate, MITC-12, extracted from *M. oleifera*, has shown to possess remarkable anticancer properties in various human cancers, such as brain, melanoma, skin, colon, cervical and breast cancers. Experimental results have shown that MITC-12 selectively inhibits the proliferation of the cancer cells, in a dose and time dependent fashion, with minimal toxicity to normal cells. The antitumor potential is mainly mediated by activation of the c-Jun N-terminal kinase (JNK) signaling pathway, modulation of the Bax/Bcl-2 ratio, activation of caspase-3 and regulation of cell cycle associated proteins. Interestingly, growth inhibition was found in glioblastoma (U251) cells, making it a potential therapeutic target. Overall, these findings suggest the possibility of MITC-12 as a potential natural anticancer agent and indicate that it should be explored in future preclinical and clinical trials to test its efficacy, safety, and therapeutic potential in cancer treatment.

4.5 Antimicrobial Activity

M. oleifera possesses broad-spectrum antibacterial activity, primarily attributed to its rich content of flavonoids, phenolic compounds, and isothiocyanates. Experimental studies have demonstrated that leaf extracts, particularly acetone extracts, effectively inhibit the growth of clinically important bacteria, including *Escherichia coli, Staphylococcus aureus, Enterobacter cloacae, Proteus vulgaris,* and *Micrococcus kristinae*. These extracts exhibit both bactericidal and bacteriostatic effects, reflecting their strong antimicrobial potential, whereas antifungal activity has generally been reported to be less pronounced. The collective evidence highlights *M. oleifera* as a promising natural source of antibacterial agents, although further investigations are required to identify the active constituents, elucidate their mechanisms of action, and establish their clinical efficacy.

4.6 Antiviral Activity

M. oleifera has attracted considerable attention as a potential source of natural antiviral agents owing to its rich phytochemical composition and long history of traditional medicinal use. Historically, various parts of the plant have been employed in the management of viral illnesses, including chickenpox and smallpox. Although these traditional claims require further scientific validation, growing experimental evidence suggests that the bioactive constituents of *M. oleifera* may interfere with viral replication, modulate host immune responses, and reduce virus-induced oxidative stress. These promising findings highlight the potential of *M. oleifera* as a complementary antiviral therapeutic and underscore the need for comprehensive mechanistic studies and well-designed clinical trials to establish its efficacy and safety against emerging and re-emerging viral infections.

4.7 Hepatoprotective Activity

M. oleifera possesses significant hepatoprotective activity, primarily through its potent antioxidant and free radical-scavenging properties. Experimental studies have demonstrated that *M. oleifera* extracts effectively protect against cadmium-induced liver injury by reducing serum hepatic biomarkers, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP). In addition, the extract attenuates lipid peroxidation, enhances the activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD), and preserves normal hepatic architecture. These protective effects collectively reduce oxidative stress and improve liver function, highlighting *M. oleifera* as a promising natural hepatoprotective agent with potential therapeutic applications in the prevention and management of liver disorders.

4.8 Cardioprotective Activity

M. oleifera exhibits remarkable cardioprotective potential owing to its abundance of bioactive phytochemicals, including quercetin, isoquercetin, and isothiocyanates. These naturally occurring compounds possess potent antioxidant, anti-inflammatory, and vasoprotective properties that mitigate oxidative stress, preserve myocardial integrity, improve endothelial function, and maintain vascular homeostasis. By attenuating inflammation and oxidative damage, *M. oleifera* contributes to improved cardiovascular health and may reduce the risk of

hypertension, atherosclerosis, and other cardiovascular disorders. These findings underscore the potential of *M. oleifera* as a promising natural cardioprotective agent and warrant further clinical investigation to establish its therapeutic efficacy and long-term cardiovascular benefits.

4.9 Neuroprotective Activity

M. oleifera seeds possess significant neuroprotective potential, largely attributed to the bioactive phytoconstituent niazimicin. Experimental studies using aluminum chloride-induced dementia models have demonstrated that seed fractions exert potent antioxidant and anti-inflammatory effects by reducing malondialdehyde, nitric oxide, acetylcholinesterase, and amyloid-β levels while restoring glutathione content. In addition, molecular docking studies suggest that niazimicin effectively interacts with key neurodegenerative targets, including caspase-3 and inducible nitric oxide synthase (iNOS), thereby mitigating neuronal apoptosis and oxidative damage. Collectively, these findings highlight the therapeutic promise of *M. oleifera* as a natural neuroprotective agent and support its potential application in the prevention and management of neurodegenerative disorders.

4.10 Nephroprotective Activity

M. oleifera exhibits promising nephroprotective activity, primarily through its potent antioxidant properties. Experimental studies have shown that methanolic leaf extracts protect against renal ischemia-reperfusion injury by reducing oxidative stress markers, including malondialdehyde, protein carbonyls, advanced oxidation protein products, blood urea nitrogen, and serum creatinine. Simultaneously, the extract enhances the activity of endogenous antioxidant enzymes such as glutathione peroxidase and glutathione S-transferase. Histopathological findings further confirm the preservation of renal tissue architecture, highlighting the ability of *M. oleifera* to mitigate oxidative damage and maintain normal kidney function. These findings support its potential as a natural nephroprotective agent for preventing oxidative stress-induced renal injury.

4.11 Immunomodulatory Activity

M. oleifera exhibits significant immunomodulatory potential by enhancing both humoral and cell-mediated immune responses. Experimental studies have demonstrated that aqueous and ethanolic extracts significantly increase antibody production, augment delayed-type

hypersensitivity responses, and moderately enhance phagocytic activity in albino rats, indicating stimulation of both adaptive and innate immunity. The immunostimulatory effects were found to be comparable to those of levamisole, a standard immunomodulatory agent. These findings highlight the potential of *M. oleifera* as a natural immunomodulator for strengthening immune function and support its further investigation as a complementary therapeutic agent in immune-related disorders.

4.12 Antiulcer activity

M. oleifera has demonstrated promising gastroprotective and antiulcer activity in experimental models of gastric ulceration. Ethanolic extracts of its bark and roots significantly reduced gastric lesions induced by pylorus ligation and ethanol in rats. Treatment with *M. oleifera* (500 mg/kg) markedly decreased the ulcer index and provided approximately 78.5% protection against gastric ulcers, comparable to the standard antiulcer drug omeprazole. The gastroprotective effects are attributed to reduced gastric acidity, preservation of the gastric mucosal barrier, and enhanced mucosal healing. These findings suggest that *M. oleifera* possesses considerable therapeutic potential as a natural antiulcer agent and warrants further investigation to validate its clinical efficacy in the management of peptic ulcer disease.

4.13 Wound Healing Activity

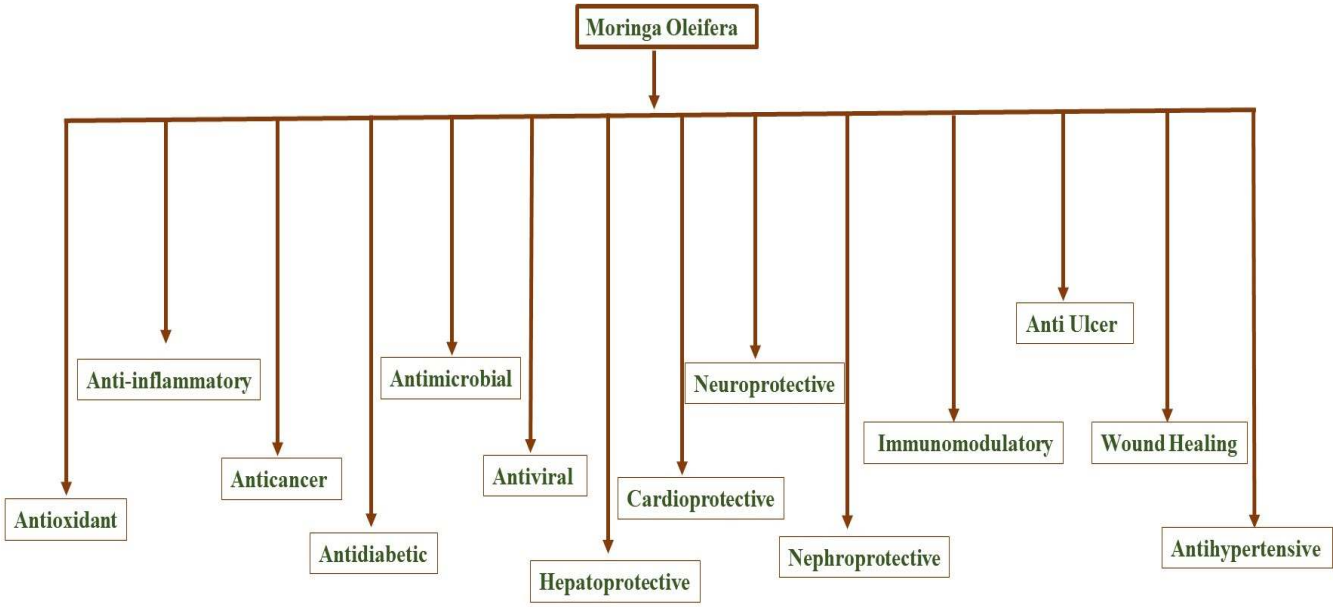
M. oleifera has demonstrated considerable wound-healing potential in both normal and diabetic experimental models. Treatment with leaf extracts, seeds, and dry pulp significantly enhanced hydroxyproline content, granuloma breaking strength, and collagen deposition, thereby accelerating tissue repair in incision, excision, and dead-space wound models. In diabetic wounds, the leaf extract promoted tissue regeneration, upregulated vascular endothelial growth factor (VEGF), reduced wound size, and suppressed inflammatory mediators, facilitating improved wound healing. Furthermore, in human fibroblast models, *M. oleifera* exhibited anti-migratory and anti-proliferative activities, highlighting its role in regulating cellular responses during tissue remodeling and wound repair.

4.14 Antihypertensive Activity

Aqueous leaf extracts of *M. oleifera* have demonstrated significant antihypertensive activity in N-nitro-L-arginine methyl ester (L-NAME)-induced hypertensive rats. Oral administration of

the extract produced a dose-dependent reduction in blood pressure, promoted vasorelaxation in methoxamine-precontracted arteries, attenuated adrenergic-mediated vasoconstriction, and improved acetylcholine-induced endothelial function. These protective effects are primarily attributed to its antioxidant properties, which reduce oxidative stress and preserve vascular integrity. Collectively, the findings of Aekthammarat *et al.* suggest that *M. oleifera* possesses promising cardioprotective and antihypertensive potential, supporting its development as a natural therapeutic agent for hypertension.

Fig. 3. Schematic representation of the major pharmacological activities of *M. oleifera*. (2)



5. Clinical studies and therapeutic potential

The clinical trials are the key to determining the safety, efficacy and translatability of medicinal plants before their use in clinical practice. Of the total, some 25 interventional studies have been registered at ClinicalTrials.gov, 15 of which have been completed and 10 are currently ongoing, for *M. oleifera*. The investigations cover a wide variety of applications such as dietary supplements, pharmaceutical formulations, functional foods and oral healthcare products, all demonstrating the scientific interest of validating the therapeutic potential of *M. oleifera via* evidence-based clinical research. The therapeutic effects of *M. oleifera* seed kernels were first demonstrated by *Agrawal and Mehta* (2008) in mild to moderate bronchial asthma patients. No

adverse effects were detected, and after three weeks of oral administration with 3 g/day of powdered seed kernels, there was a significant improvement in the respiratory function, asthma symptoms, hemoglobin level, and erythrocyte sedimentation rate (ESR). The results indicate that the kernels of *M. oleifera* can be used as a natural drug to enhance the pulmonary function and reduce the symptoms of asthma without causing severe side effects. Taweerutchana *et al*. (2017) investigated *M. oleifera* leaf capsules (8 g/day) for four weeks in therapy naïve people with type 2 diabetes mellitus (T2DM) in another randomized controlled placebo-controlled study. No significant difference was found in the fasting plasma glucose or glycated hemoglobin (HbA1c) levels between the groups, but there was a small non-significant drop in systolic blood pressure (SBP) for those who took *M. oleifera*. Importantly, it was well tolerated with no adverse events reported with treatment suggesting excellent safety and also requiring longer duration studies to determine the metabolic and cardiovascular benefits. In recent years the therapeutic potential of *M. oleifera* has been further expanded through investigations. El Masri *et al.* (2026) showed potent anticancer effects on lung cancer *in vivo* and *in vitro*. Bioactive phytochemicals showed antiproliferative effects by inducing apoptosis, regulating oxidative stress, downregulating oncogenic signaling pathways and blocking angiogenesis. In particular, formulations based on nanoparticles showed higher cytotoxic effects than crude extracts and animal experiments demonstrated a decrease in the tumor burden and an increase in antitumor immune responses. Still, detailed preclinical validation and proper clinical trials are necessary prior to clinical translation. Likewise, Suman *et al. (*2026) presented positive results from a Phase I, open-label pilot trial of a proprietary Ayurvedic formulation of *M. oleifera* leaf and seed extract. No adverse effects were observed and the formulation was safe and well tolerated. Significant reduction in anemia, fatigue, general weakness, muscular wasting and nervous debility were noted and almost 80% of the patients had clinically significant improvement. Based on these results, the study suggests that *M. oleifera* could be used as a nutraceutical in the management of conditions of nutritional depletion and physical weakness; however, larger RCTs with more patients and longer follow-up periods are needed to confirm the clinical effectiveness and mechanisms of action. In addition to systemic disorders, *M. oleifera* have also demonstrated significant potential in oral health care. Duarte

et al. (2022) conducted a randomized crossover, clinical trial to confirm that a *M. oleifera* based herbal dentifrice could be significantly more effective than a commercially available miswak dentifrice in reducing dental plaque and gingival inflammation among people suffering from mild to moderate gingivitis. In conclusion, *M. oleifera* provided promising anti-inflammatory activity and plaque reduction without any adverse effects, demonstrating the excellent safety profile of this valuable natural compound as an oral hygiene supplement for preventing periodontal disease. The clinical evidence available thus far suggests a relative safety, tolerability, and therapeutic potential for *M. oleifera* in a variety of clinical applications. However, most of the existing evidence is based on small sample sizes, short intervention duration and differences in formulation and study design. Hence, further multicenter randomized controlled clinical trials with standardized *M. oleifera* preparations and sound methodology are crucial to confirm the clinical efficacy of *M. oleifera* as well as to standardize dosage regime and promote it for incorporation in evidence-based medicine.

6. Toxicity and Safety

Although *M. oleifera* (3) is widely recognized for its exceptional nutritional value and diverse pharmacological activities, its successful translation into evidence-based therapeutic applications requires comprehensive scientific validation, standardized formulations, and thorough evaluations of its safety, efficacy, and long-term clinical outcomes. The toxicity data reported so far indicate that plant part used, method of extraction, phytochemical composition, processing conditions, dose and duration of exposure are factors that affect the safety profile of *M. oleifera*. Generally recognized as safe at recommended intakes, the root and bark contain bioactive alkaloids such as niazimin A, niazimin B and spirochin and have been reported to have hypotensive and neurotoxic effects in experimental studies. Moreover, some extracts were found to be cytotoxic and genotoxic, while some constituents of roasted seeds are known to be genotoxic due to the presence of glucosinolate. However, prolonged or excessive consumption of the leaves could also decrease the absorption of other micronutrients in the gut because of the naturally occurring saponins. The above observations emphasize the need to establish standard processing procedures, detailed phytochemical characterization of the species, optimization of doses, and detailed preclinical and clinical toxicological studies. Meeting

international standards of quality and providing evidence-based safety guidelines will be important for the success of integrating *M. oleifera* into the current evidence-based medicine (4).(5)

7. Future Perspectives

The plant *M. oleifera* has become a very promising candidate for medicinal purposes, due to its diverse pharmacological properties and phytochemical content. Although there are promising preclinical findings showing its antioxidant, anti-inflammatory, antimicrobial, antidiabetic, cardioprotective, neuroprotective, and anticancer properties, its clinical applications are still limited. Future research should also aim at standardization of the bioactive constituents, understanding the molecular mechanisms, extensive pharmacokinetic and toxicological studies, and extensive randomized clinical trials to validate its safety and therapeutic efficacy. The use of sophisticated drug delivery systems and cutting-edge analytical techniques could also be used to further improve the bioavailability and clinical benefits of *M. oleifera* phytochemicals. Furthermore, there is a need for harmonized quality control protocols and regulations to advance safe, effective, and evidence-based *M. oleifera* therapeutics. Together, these developments are likely to assist the integration of *M. oleifera* into the present-day health care and pave the way for its use as a source of novel therapeutic agents in the prevention and management of chronic diseases.

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