Antimicrobial and Immunomodulatory activities of *Moringa peregrine*- MINIREVIEW

Ibrahim Majali*, Osama Y. Althunibat, Haitham N. Qaralleh

Faculty of Pharmacy, Al-Zaytoonah Private University, Amman 11733, Jordan.

*corresponding author: majali201181@yahoo.com

Received: 17-5-2015

Revised: 11-6-2015

Published: 17-6-2015

Keywords:

Moringa peregrine
Antimicrobial
Immunomodulatory

Abstract: *Moringa peregrina* is considered as miracle tree. Extracts as well as some isolated compounds of *Moringa peregrine* show valuable biological activities, such as antimicrobial, antiviral, anticancer, antioxidant, immunomodulatory. On the other hand, *Moringa peregrina* is used traditionally as home cleaning agent, fertilizer, foliar nutrient, green fertilizer, gum, honey- and sugar cane juice-clarifier, biopesticide. In this review, the natural distribution and the general features for *Moringa peregrina* were discussed and the antimicrobial and immunomodulatory activities of *Moringa peregrine* extract were described. This review might guide researchers to undertake further investigation regarding this species and to use it as a source of active compounds.

INTRODUCTION

Medicinal powers in plants are an old idea. A small percentage of plants are used by human as food, even more are used for medicinal purposes. Medicinal plants are an important parts of the medicine background. Most of the populations in the world depend on herbal medicine for their health care needs (Manandhar, 1994). Phytochemicals in fruits, vegetables, spices and traditional herbal have been found to play protecting roles against human diseases (Schippmann *et al*., 2002). Crude or fractionated extracts and sometimes individual plant compounds are used for antibacterial, anti-inflammatory, antioxidant activities (Lev and Amar, 2002, Adam and Abdull Rasad, 2015).

Historically, man depends on the plants for medicine. The plant kingdom represents a rich store of traditional medicines and organic compounds that may lead to development of new agents that are considered as important drugs in one or more countries in the world. Unlike current drugs which are single active components that effect a specific pathway, medicinal plants may work in a way that depends on an synergetic effects. A plant contains a multiple different molecules may act synergistically on targeted elements of the complex cellular pathway (Durmowicz and Stenmark. 1999). In addition, the use of medicinal plants in medical synthesis becomes well-liked due to toxicity and side effects of synthetic drugs. Thus, medicinal plants play an important role in the enlargement of new healing agents (Verma and Singh 2008).

Jordan has a huge variation in wild plants due to the geographical and climatic diversity. It is known to have more than 2000 plant species belonging to about 700 genera. Among these plants, there are many of 485 species from around 99 plant families were categorized as medicinal plants (Oran and Al-Eisawi, 1998). Ethnopharmacological examination of

traditional drugs sold in Jordan showed that there are 236 local and imported plants used in Jordan traditionally for treatment of different disease (Lev and Amar, 2002).

Moringa has a direct impact on health, nutrition, agriculture, biodiversity and environment. *Moringa peregrina* is considered as miracle tree, because all of its parts are used. Thus, this review is prepared to highlighted the Antimicrobial and Immunomodulatory activities of *Moringa peregrine* extracts.

Moringaceae

The genus *Moringa* which is called miracle tree belongs to "*Moringaceae*" family with 14 known species (*Moringa oleifera* , *M. arborea, M. borziana, M. concanensis, M. drouhardii, M. hildebrandtii, M. longituba, M. ovalifolia, M. peregrine, M. pygmaea, M. rivae, M. ruspoliana* and *M. stenopetala*) (Oslon, 2002).

The *Moringaceae* tree is a full-grown mainly in semiarid, tropical, and subtropical areas, but, it grows best in dry soil. It tolerates poor soil, including coastal areas. It is a fast growing, drought resistant tree which tolerate a wide range of environmental conditions; it tolerates extremely high temperatures in the shade and can survive at light frost. *Moringaceae* is widely cultivated in Africa, central and south America, Sri Lanka, India, Mexico, Malaysia, and the Philippines. *Moringa* is planted either by direct seeding, transplanting, or using hard stem cuttings (Anbarassan *et al*., 2001). The name "Shigon" for *Moringa* was written in the "Shushruta Sanhita" which was written in the beginning of the first century, given a fact that the development used of this tree in India date back many thousands of years ago (Odee, 1998).

Moringa tree can reaches 3 meters in height, just after 10 months of planting. A tree can reach 12 meters in height with a stem of 30 cm wide. This tree can be found growing naturally at elevation of up to 1,000m over sea level. It can grow well on hillsides but is more often found growing on pastureland or in river sides (Morton, 1991). *Moringa* tree quickly flowering and fruiting; it is also called "nebeday" or the tree that never dies (D'souza & Kulkarni, 1993). Optimum leaves and pods production requires high average daily temperatures of 25- 30°C, well-distributed annual rainfall of 1000-2000mm, high solar radiation and well-drained soils (Odee, 1998).

Moringa is a perennial soft wood tree with wood of low value, but for many centuries it has been used for traditional medicine and industrial uses. In the Philippines, where the leaves of the *Moringa* were cooked and fed to babies, its called "mother's best friend" (Fuglie, 1999). *Moringa* trees have been used to combat starvation, especially among infants and tending mothers. Three non-governmental organizations, Trees for Life, Church World Service and Educational Concerns for Hunger Organization, have considered *Moringa* as natural nutrition for the tropics. Leaves can be eaten fresh, cooked, or stored as dried powder for many months without loss of nutritional value (Fahey, 2005; Mughal *et al*., 1999). The *Moringa* could become one of the world's most important plants, at least in humanitarian area.

The uses for *Moringa* include: crop (biomass production), animal feed (leaves and treated seed-cake), biogas (from leaves), home cleaning agent (crushed leaves), blue dye (wood), fence (living trees), fertilizer (seed-cake), foliar nutrient (juice expressed from the leaves), green fertilizer (from leaves), gum (from tree trunks), honey- and sugar cane juice-clarifier (powdered seeds), honey (flower nectar), medicine (all plant parts), ornamental plantings, biopesticide (soil incorporation of leaves to prevent seedling damping off), pulp (wood), cord (bark), tannin for tanning hides (bark and gum), water purification (powdered seeds) (Fuglie, 1999). Thus, *Moringa* promotes economic development (Kebreab *et al*, 2005).

Phytochemicals are those chemicals produced by plants. Chemicals which may have direct contact with health, taste, odor, and color of the plants, but are not required by humans as essential main nutrients. Test of the phytochemicals of *Moringaceae* species were afford to examine a range of exclusive compounds that it contains. *Moringaceae* family is rich in compounds containing the simple sugar, rhamnose, and it is rich in a compounds called glucosinolates and isothiocyanates (Bennett *et. al*., 2003; Fahey *et. al.*, 2001).

Moringa peregrina, is known in Arabic as "Habb El Yasar, Habb El Pan", the seeds are known as "Habba Ghalia". It is occur in nature in dry or semiarid countries neighboring the Red Sea, from Somalia and Yemen to Palestine and to Syria (Somali *et al*., 1984). Flowers appear before leaves in May. The pod is pendulous and contains slanting, nut-like white seeds which are of bitter sweet taste and rich in oil. Flowering and fruiting: February-April (Morton, 1991). When *Moringa peregrina* seedlings start out, they have broad leaflets and a large tuber. As the plant gets older, the leaves get longer and longer, but the leaflets get smaller and smaller and more widely

spaced. Adult trees produce leaves with a full complement of tiny leaflets, only to drop them as the leaf matures. However, the naked leaf axis remains, giving the tree a translucent look similar to *Tamarix* (Al-Kahtani, 1993).

Even though there is worry about the decline of *Moringa peregrina* especially where it collected for fuel, it is not listed in the IUCN Red List 2006. It is endangered in the Sinai in Egypt. Hard work to restore the local flora by restoring the stand of the dominant species, were resulted in an increase in the numbers of it. *Moringa peregrina* is included in a field gene bank of fodder plants in Oman (Olson., 2002).

Antimicrobial activity

Since, there are increasing incidences of fresh and unwanted infectious diseases, appearance of unwanted side effects of certain antibiotics, as well as the increasing development of conflict to the antibiotics in clinical use, the nonstop search for a new antimicrobial compounds is highly needed. This search may yield to various chemical structures and new mechanisms of action for antimicrobial agents (Cowan, 1999).

Many previous studies were reported that various parts of *Moringa* roots, flowers, bark, and stem including seeds possess antimicrobial properties (Lockett *et al*., 2000; Anwar and Rashid, 2007). Powdered of *Moringa oleifera* seeds were traditionally used for water purification because of their ability to clot of suspended mud and other materials causing turbidity (Lalas and Tsaknis, 2002). During this process a decrease of the total microorganisms accounts of the purified water were observed, indicative of that the seeds contain substances with antimicrobial activity (Bhoomika *et al*., 2007).

Broin *et al*. (2002) reported that a recombinant protein in the seed of *Moringa* is able to flocculate gram-positive and gram-negative bacteria. In this case, microorganisms can be removed by settling in the same manner as the removal of colloids in properly coagulated water. On the other hand, the seeds may act directly upon microorganisms and result in growth inhibition. Antimicrobial peptides are acts by disrupting the cell membrane or by inhibiting essential enzymes (Suarez *et al*., 2003).

Moringa oleifera seed extracts were assayed for antimicrobial activity against bacterial strains: *Pasturella multocida, Escherichia coli, Bacillus subtilis* and *Staphlocuccus aureus* and fungal: *Fusarium solani* and *Rhizopus solani* strains. The crude, supernatant, residue and dialyzed samples inhibited the growth of all microbes at different variety. The zones of inhibition showed greater sensitivity against the bacterial strains as compared to the fungal strains. The *Moringa oleifera* extracts worked in dose dependent manner and resulted in distorted hyphae and apical branching in fungi. Minimum inhibitory concentrations (MIC) of *Moringa oleifera* extracts revealed that *Pasturella multocida and Bacillus subtilis* were the most sensitive strains to the extracts. However, the activity of the extracts was antagonized by cations (Na+, K+, Mg2+ and Ca2+). Maximum activity were found between temperature 4 -37 °C and pH 7 (Jabeen *et al.*, 2008).

Sutherland *et al.* (1990) reported that *Moringa* seeds could inhibit the replication of bacteriophages. The antimicrobial effects of the seeds are attributed to the compound benzyl isothiocynate. Jahn *et al*. (1986) identified the bactericidal substances in *Moringa* seeds as pterygospermin, moringine and the glycosides benzylisothiocyanate and 4-(α-L-rhamnosyloxy)-phenylacetonitrile. These substances inhibited mainly *Bacillus subtilis, Mycobacterium phei, Serratia marcescens, E. coli, Pseudomonas aeruginosa, Shigella* and *Streptococcus*. In addition, Harvey (2005) reported that Pterygospermin, a bactericidal and fungicidal compound contained in an aqueous extract made from seed of *Moringa oleifera* was effective against *Staphylococcus aureus* as the antibiotic neomycin.

The antimicrobial activity of the oil extracted with n-hexane from the seeds of *Moringa peregrina* was tested against *Staphylococcus aureus, S. epidermidis, Pseudomonas aeruginosa, Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae.* The oil proved effective against all of the tested bacterial strains (Lalas *et al.*, 2012). Furthermore, Spiliotis *et al.* 1997 tested the antimicrobial activity of seed water extracts and seed oil of three *Moringa oleifera* varieties on various microorganisms (including *S. aureus, S. epidermidis, P. aeruginosa, E. coli and C. albicans*).

Roots of *Moringa oleifera* have antimicrobial and anti-inflammatory compounds. The antimicrobial activity of isolated compounds from *Moringa oleifera* root extracts were against *Staphylococcus aureus* and gram negative *Shigella dysenteriae, Shigella boydii, Salmonella typhimurium* and *Pseudomonas aeruginosa.* All produced zone of inhibitions between 9 to 13mm in diameter (Nikkon *et al*., 2003).

Antibacterial activity of aqueous and ethanolic extracts of *Moringa oleifera* seeds were tested against *Staphylococcus aureus, Vibrio cholerae, Escherichia coli* and *Salmonella enteritidis.* Antibacterial activity were as inhibition zones >13mm in diameter against *Staphylococcus aureus, Vibrio cholerae* and *Escherichia coli* (Vieira *et al*. 2010).

Balanites aegyptiaca and *Moringa oleifera* aqueous and organic leaves extracts traditionally used for the treatment of infectious disease, they tested for their activity against *Salmonella typhimurium* by Doughari *et al*., (2007). Extracts of *Moringa oleifera* resulted in 8mm zone of inhibition at 100 mg/ml. Three solvents were used and ethanol extracts of both plants demonstrated the highest activity, whereas the aqueous extracts showed the least activity at 100 mg/ml. The activities of these plant extracts were comparable to those of antibiotics, ciprofloxacin, cotrimoxazole. The antibacterial activity appears to increase when extracts of the two plants were used in combination at 100 mg/ml each (18 mm zone of inhibition). The antibacterial activities of the extracts on *Salmonella typhimurium* was reasonably stable when treated at 4, 30, 60 and 100 °C for 1 hour, however it is reduced significantly when the pH was changed to more than 8 (Doughari *et al*., 2007).

Moringa oleifera isolated compounds have wide band of antimicrobial activity which recorded by Eilert *et al*. (1981). These compounds were screened for antimicrobial activity against six gram positive and seven gram negative bacteria and were found that water extract, ethanol and petroleum, ether extracts possess high antimicrobial activity. The water extract of *M. oleifera* leaves inhibited the growth of *Escherichia coli* and *Enterobacter aerogenes.* The zone of inhibition of *Escherichia coli* were 7 mm for 200 mg/ml and 10 mm for 1000 mg/ml of the extract compared to 12 mm produced by the standard drug, tetracycline (250 mg/ml) *(*Thilza *et al*., 2010).

Nikkon *et al.* (2003) reported that the antimicrobial activity of aglycone of Deoxy-Niazimicine which is characterized as N-benzyl, S-ethyl thio-formate from the chloroform extract of *Moringa oleifera* roots barks. The compound was showed antibacterial activities against *Shigella boydii*, *Shigella dysenteriae* and *Staphylococcus aureus.*

Moringa oleifera roots have antibacterial activity and are rich in antimicrobial agents. The latter is mainly because they contain an active antibiotic principle, pterygospermin. Pterygospermin considered as the active compound in *Moringacaea* that causes its antibacterial action, once consumed, it break down into two separate benzyl isothiocyanate, a substance with known antimicrobial properties (Ruckmani *et al.,* 1998). Cáceres *et al.* (1991) reported the antimicrobial activities of *Moringa oleifera* leaves, roots, barks and seeds in vitro against bacteria, yeast, by a disk-diffusion method. The fresh leaf juice and aqueous extracts from the seeds inhibit the growth of *Pseudomonas aeruginosa* and *Staphylococcus aureus.*

Ethanol extract of fresh leaves were showed a wide antibacterial effect against all the tested gram-negative bacteria (*S. shinga, P. aeruginosa, S. sonnei, Pseudomonas* spp.) and some gram-positive bacteria (*B. cereus, B. subtilis, S. lutea, B. megaterium*) and their respective diameter zones of inhibition were 17.5, 21.21, 21.5, 21.25 and 16.25, 20.23, 19.50, 20.50 mm in diameter, respectively. The activity of the plant against both gram-positive and gram negative bacteria may be indicative of the presence of broad-spectrum antimicrobial compounds in the *Moringa oleifera* (Siddhuraju and Becker, 2003; Vaghasiya and Chanda, 2007).

Quinones which are a group of naturally occurring phenol compounds are found in *M. oleifera* leaves and tend to have laxative effects. Terpenoids and steroids present in *M. oleifera* leaves were described as being active against bacteria such as *Staphylococcus aureus*. *M. oleifera* leaves contains alkaloids which are nitrogen-containing naturally occurring compounds, commonly found to have antimicrobial properties due to their ability to intercalate with DNA of the microorganisms (Bennett *et al*., 2003).

Moringa flavonoids, which are many in numbers, were found to be strong antimicrobial substances *in vitro* against a wide collection of microorganisms by inhibiting the membrane bound enzymes. They reported to possess substantial anti carcinogenic and anti mutagenic activities due to their antioxidant and inflammatory properties (Li-Weber, 2009).

Immunomodulatory

Immunomodulator is a substance which stimulates or regulates the immune system including both innate and adaptive immune responses. The modulation of immune system by various medicinal plant products has become a subject for scientific investigation. The immune system is the basic defense system of the body against pathogens and other foreign substances. Its function is to prevent foreign substances from invading the body and causing disease (Sherwood and Kinsky, 2004).

Immunomodulatory effect of ethanolic extract of *M. oleifera* leaves were studied in normal and immunosuppressed mice models. Pre-treatment of *Moringa* ethanolic extract inhibited cyclophosphamide bone marrow suppressive effect and phagocytic activity in mice (Anamika *et al*., 2010). Furthermore, different doses of *Moringa oleifera* caused significant increase in the level of white blood cell counts and immunoglobulin levels (Adedapo *et al.*, 2005).

Since *Moringa* is rich in ginseng and ginseng saponins were reported to have antioxidant, anti-inflammatory, anti-apoptotic and immune-stimulant properties, this raised theory that *Moringa* plant and its extracts could be play part in immunomodulation (Rausch *et al.* 2006). Furthermore, Sashidhara *et al.*, (2009) isolated aurantiamide acetate and 1, 3-dibenzyl urea, from roots of *Moringa oleifera* . Aurantiamide acetate showed significant inhibition on tumor necrosis factor (TNF-α) and interleukin two (IL-2) but not on interleukin (IL-6), while 1,3-dibenzyl urea showed to significantly induce analgesic activity in dose dependant manner and significant inhibition on IL 2. These results indicates that these compounds may be responsible for the anti-inflammatory, anti-arthritic and analgesic activity of *Moringa oleifera* root.

Moringa peregrina extracts exhibited antioxidant activity and the extracts could be considered as a source of natural antioxidants. *Moringa peregrina* has potential as an anti-inflammatory and antioxidant agent against inflammation and free radicals. Anti-inflammatory and antioxidant activities of *Moringa peregrina* seeds ethanolic and aqueous extracts were tested by Koheil *et al* (2011). The results indicated that *Moringa peregrina* ethanolic and aqueous extracts (100-300 mg/kg) inhibited significantly fresh egg albumin-induced acute inflammation. In addition, ethanolic and aqueous extracts of *Moringa peregrina* exhibited a strong reducing power, Fe2+ chelating effect, free radical scavenging activity, hydrogen peroxide scavenging ability, and hydroxyl radical scavenging activity. These latter effects were shown to be dose dependent.

The antioxidant properties of *Moringa* leaves allow the immune system to scrap infections and cancers more effectively, providing the body with a secondary line of defense against pathogens and offering hope to those pain from reduced immunity due to illness. The flavonoids such as quercetin and kaempferol were identified as the most potent antioxidants in *Moringa* leaves. Their antioxidant activity was higher than the conventional antioxidants such as ascorbic acid, which is also present in large amounts in *Moringa* leaves (Siddhuraju and Becker, 2003). *Moringa* is found to be rich in quercetin and glucosinolates. These phytochemicals are precursors of a wide range of bioactive compounds among established antibiotic, anticancer and antioxidant properties. Significant variations in antioxidant activity were reported in four *Moringa* species, with *M. peregrina* showing the maximum antioxidant activity (Ray *et al.*, 2006).

CONCLUSION

The consequences of this investigation suggest that *Moringa peregrina* can be used to discover antibacterial agent for developing new pharmaceuticals to control human pathogenic bacteria responsible for severe illness.

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