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Reviews

Moringa oleifera: A Review of the Medical Evidence for Its Nutritional, Therapeutic, and Prophylactic Properties. Part 1.

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Abstract

Moringa oleifera, or the horseradish tree, is a pan-tropical species that is known by such regional names as benzolive, drumstick tree, kelor, marango, mlonge, mulangay, nébéday, saijhan, and sajna. Over the past two decades, many reports have appeared in mainstream scientific journals describing its nutritional and medicinal properties. Its utility as a non-food product has also been extensively described, but will not be discussed herein, (e.g. lumber, charcoal, fencing, water clarification, lubricating oil). As with many reports of the nutritional or medicinal value of a natural product, there are an alarming number of purveyors of "healthful" food who are now promoting *M. oleifera* as a panacea. While much of this recent enthusiasm indeed appears to be justified, it is critical to separate rigorous scientific evidence from anecdote. Those who charge a premium for products containing *Moringa* spp. must be held to a high standard. Those who promote the cultivation and use of *Moringa* spp. in regions where hope is in short supply must be provided with the best available evidence, so as not to raise false hopes and to encourage the most fruitful use of scarce research capital. It is the purpose of this series of brief reviews to: (a) critically evaluate the published scientific evidence on *M. oleifera*, (b) highlight claims from the traditional and tribal medicinal lore and from non-peer reviewed sources that would benefit from further, rigorous scientific evaluation, and (c) suggest directions for future clinical research that could be carried out by local investigators in developing regions.

This is the first of four planned papers on the nutritional, therapeutic, and prophylactic properties of Moringa oleifera. *In this introductory paper, the scientific evidence for health effects are summarized in tabular format, and the strength of evidence is discussed in very general terms. A second paper will address a select few uses of Moringa in greater detail than they can be dealt with in the context of this paper. A third paper will probe the phytochemical components of* Moringa *in more depth. A fourth paper will lay out a number of suggested research projects that can be initiated at a very small scale and with very limited resources, in geographic regions which are suitable for* Moringa *cultivation and utilization. In advance of this fourth paper in the series, the author solicits suggestions and will gladly acknowledge contributions that are incorporated into the final manuscript. It is the intent and hope of the journal's editors that such a network of small-scale, locally executed investigations might be successfully woven into a greater fabric which will have enhanced scientific power over similar small studies conducted and reported in isolation. Such an approach will have the added benefit that statistically sound planning, peer review, and multi-center coordination brings to a scientific investigation.*

The following paper is intended to be useful for both scientific and lay audiences. Since various terms used herein are likely not familiar to the lay reader, nor are many of the references readily available to either scientific or lay audiences, we encourage active on-line dialog between readers and both the author and the journal staff. Both will attempt to answer questions and to direct readers to the experts in an open and public manner.

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PEER REVIEWED

Introduction

Moringa oleifera is the most widely cultivated species of a monogeneric family, the Moringaceae, that is native to the sub-Himalayan tracts of India, Pakistan, Bangladesh and Afghanistan. This rapidly-growing tree (also known as the horseradish tree, drumstick tree, benzolive tree, kelor, marango, mlonge, moonga, mulangay, nébéday, saijhan, sajna or Ben oil tree), was utilized by the ancient Romans, Greeks and Egyptians; it is now widely cultivated and has become naturalized in many locations in the tropics. It is a perennial softwood tree with timber of low quality, but which for centuries has been advocated for traditional medicinal and industrial uses. It is already an important crop in India, Ethiopia, the Philippines and the Sudan, and is being grown in West, East and South Africa, tropical Asia, Latin America, the Caribbean, Florida and the Pacific Islands. All parts of the Moringa tree are edible and have long been consumed by humans. According to Fuglie (47) the many uses for Moringa include: alley cropping (biomass production), animal forage (leaves and treated seed-cake), biogas (from leaves), domestic cleaning agent (crushed leaves), blue dye (wood), fencing (living trees), fertilizer (seed-cake), foliar nutrient (juice expressed from the leaves), green manure (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), rope (bark), tannin for tanning hides (bark and gum), water purification (powdered seeds). Moringa seed oil (yield 30-40% by weight), also known as Ben oil, is a sweet non-sticking, non-drying oil that resists rancidity. It has been used in salads, for fine machine lubrication, and in the manufacture of perfume and hair care products (158). In the West, one of the best known uses for Moringa is the use of powdered seeds to flocculate contaminants and purify drinking water (11,50,113), but the seeds are also eaten green, roasted, powdered and steeped for tea or used in curries (50). This tree has in recent times been advocated as an outstanding indigenous source of highly digestible protein, Ca, Fe, Vitamin C, and carotenoids suitable for utilization in many of the so-called "developing" regions of the world where undernourishment is a major concern.

Nutrition

Moringa trees have been used to combat malnutrition, especially among infants and nursing mothers. Three non-governmental organizations in particular—Trees for Life, Church World Service and Educational Concerns for Hunger Organization—have advocated Moringa as "natural nutrition for the tropics." Leaves can be eaten fresh, cooked, or stored as dried powder for many months without refrigeration, and reportedly without loss of nutritional value. Moringa is especially promising as a food source in the tropics because the tree is in full leaf at the end of the dry season when other foods are typically scarce.

A large number of reports on the nutritional qualities of Moringa now exist in both the scientific and the popular literature. Any readers who are familiar with Moringa will recognize the oft-reproduced characterization made many years ago by the Trees for Life organization, that "ounce-for-ounce, Moringa leaves contain more Vitamin A than carrots, more calcium than milk, more iron than spinach, more Vitamin C than oranges, and more potassium than bananas," and that the protein quality of Moringa leaves rivals that of milk and eggs. These readers will also recognize the oral histories recorded by Lowell Fuglie in Senegal and throughout West Africa, who reports (and has extensively documented on video) countless instances of lifesaving nutritional rescue that are attributed to Moringa (47,48). In fact, the nutritional properties of Moringa are now so well known that there seems to be little doubt of the substantial health benefit to be realized by consumption of Moringa leaf powder in situations where starvation is imminent. Nonetheless, the outcomes of well controlled and well documented clinical studies are still clearly of great value.

In many cultures throughout the tropics, differentiation between food and medicinal uses of plants (e.g. bark, fruit, leaves, nuts, seeds, tubers, roots, flowers), is very difficult since plant uses span both categories and this is deeply ingrained in the traditions and the fabric of the community (85). Thus, **Table 1** in this review captures both nutritional and medicinal references as they relate to Moringa, whilst avoiding most of the better known agro-forestry and water purification applications of this plant. The interested reader is also directed to the very comprehensive reviews of the nutritional attributes of Moringa prepared by the NGOs mentioned earlier (in particular, see references 47,123,157).

Phytochemistry

Phytochemicals are, in the strictest sense of the word, chemicals produced by plants. Commonly, though, the word refers to only those chemicals which may have an impact on health, or on flavor, texture, smell, or color of the plants, but are not required by humans as essential nutrients. An examination of the phytochemicals of Moringa species affords the opportunity to examine a range of fairly unique compounds. In particular, this plant family is rich in compounds containing the simple sugar, rhamnose, and it is rich in a fairly unique group of compounds called glucosinolates and isothiocyanates (10,38). For example, specific components of Moringa preparations that have been reported to have hypotensive, anticancer, and antibacterial activity include 4-(4'-*O*-acetyl-α-L-rhamnopyranosyloxy)benzyl isothiocyanate **[1],** 4-(α-L-rhamnopyranosyloxy)benzyl isothiocyanate **[2],** niazimicin **[3]**, pterygospermin **[4],** benzyl isothiocyanate **[5],** and 4-(α-L-rhamnopyranosyloxy)

benzyl glucosinolate **[6].** While these compounds are relatively unique to the Moringa family, it is also rich in a number of vitamins and minerals as well as other more commonly recognized phytochemicals such as the carotenoids (including β-carotene or pro-vitamin A). These attributes are all discussed extensively by Lowell Fuglie (47) and others, and will be the subject of a future review in this series.

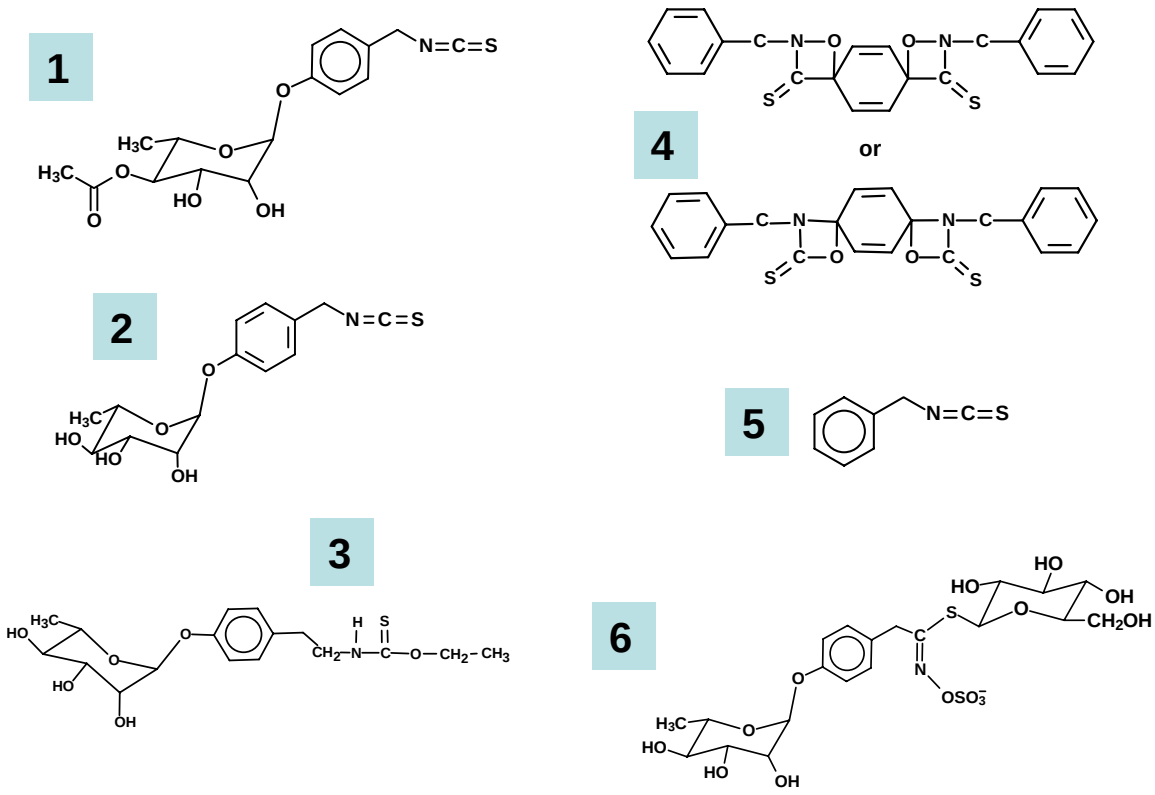

Figure 1. Structures of selected phytochemicals from Moringa spp.: 4-(4'-*O*-acetyl-α-L-rhamnopyranosyloxy)benzyl isothiocyanate **[1]**, 4-(-L-rhamnopyranosyloxy)benzyl isothiocyanate **[2]**, niazimicin **[3]**, pterygospermin **[4]**, benzyl isothiocyanate **[5]**, and 4-(α-L-rhamnopyranosyloxy)benzyl glucosinolate **[6]**

Disease Treatment and Prevention

The benefits for the treatment or prevention of disease or infection that may accrue from either dietary or topical administration of Moringa preparations (e.g. extracts, decoctions, poultices, creams, oils, emollients, salves, powders, porridges) are not quite so well known (116). Although the oral history here is also voluminous, it has been subject to much less intense scientific scrutiny, and it is useful to review the claims that have been made and to assess the quality of evidence available for the more well-documented claims. The readers of this review are encouraged to examine two recent papers that do an excellent job of contrasting the dilemma of balancing evidence from complementary and alternative medicine (e.g. traditional medicine, tribal lore, oral histories and anecdotes) with the burden of proof required in order to make sound scientific judgments on the efficacy of these traditional cures (138,154). Clearly much more research is justified, but just as clearly this will be a very fruitful field of endeavor for both basic and applied researchers over the next decade.

Widespread claims of the medicinal effectiveness of various Moringa tree preparations have encouraged the author and his colleagues at The Johns Hopkins University to further investigate some of these possibilities. A plethora of traditional medicine references attest to its curative power, and scientific validation of these popular uses is developing to

support at least some of the claims. Moringa preparations have been cited in the scientific literature as having antibiotic, antitrypanosomal, hypotensive, antispasmodic, antiulcer, anti-inflammatory, hypocholesterolemic, and hypoglycemic activities, as well as having considerable efficacy in water purification by flocculation, sedimentation, antibiosis and even reduction of Schistosome cercariae titer (see **Table 1**).

Unfortunately, many of these reports of efficacy in human beings are not supported by placebo controlled, randomized clinical trials, nor have they been published in high visibility journals. For example, on the surface a report published almost 25 years ago (141) appears to establish Moringa as a powerful cure for urinary tract infection, but it provides the reader with no source of comparison (no control subjects). Thus, to the extent to which this is antithetical to Western medicine, Moringa has not yet been and will not be embraced by Western-trained medical practitioners for either its medicinal or nutritional properties.

In many cases, published *in-vitro* (cultured cells) and *in-vivo* (animal) trials do provide a degree of mechanistic support for some of the claims that have sprung from the traditional medicine lore. For example, numerous studies now point to the elevation of a variety of detoxication and antioxidant enzymes and biomarkers as a result of treatment with Moringa or with phytochemicals isolated from Moringa (39,40,76,131). I shall briefly introduce antibiosis and cancer prevention as just two examples of areas of Moringa research for which the existing scientific evidence appears to be particularly strong.

Antibiotic Activity. This is clearly the area in which the preponderance of evidence—both classical scientific and extensive anecdotal evidence—is overwhelming. The scientific evidence has now been available for over 50 years, although much of it is completely unknown to western scientists. In the late 1940's and early 1950's a team from the University of Bombay (BR Das), Travancore University (PA Kurup), and the Department of Biochemistry at the Indian Institute of Science in Bangalore (PLN Rao), identified a compound they called pterygospermin **[4]** a compound which they reported readily dissociated into two molecules of benzyl isothiocyanate **[5]** (23,24,25,26,77,78,79,80,81,108). Benzyl isothiocyanate was already understood at that time to have antimicrobial properties. This group not only identified pterygospermin, but performed extensive and elegant characterization of its mode of antimicrobial action in the mid 1950's. (They identified the tree from which they isolated this substance as "*Moringa pterygosperma,*" now regarded as an archaic designation for "*M. oleifera.*") Although others were to show that pterygospermin and extracts of the Moringa plants from which it was isolated were antibacterial against a variety of microbes, the identity of pterygospermin has since been challenged (34) as an artifact of isolation or structural determination.

Subsequent elegant and very thorough work, published in 1964 as a PhD thesis by Bennie Badgett (a student of the well known chemist Martin Ettlinger), identified a number of glyosylated derivatives of benzyl isothiocyanate **[5]** (e.g. compounds containing the 6-carbon simple sugar, rhamnose) (8). The identity of these compounds was not available in the refereed scientific literature until "re-discovered" 15 years later by Kjaer and co-workers (73). Seminal reports on the antibiotic activity of the primary rhamnosylated compound then followed, from U Eilert and colleagues in Braunschweig, Germany (33,34). They re-isolated and confirmed the identity of 4-(α-L-rhamnopyranosyloxy)benzyl glucosinolate **[6]** and its cognate isothiocyanate **[2]** and verified the activity of the latter compound against a wide range of bacteria and fungi.

Extensive field reports and ecological studies (see **Table 1**) forming part of a rich traditional medicine history, claim efficacy of leaf, seed, root, bark, and flowers against a variety of dermal and internal infections. Unfortunately, many of the reports of antibiotic efficacy in humans are not supported by placebo controlled, randomized clinical trials. Again, in keeping with Western medical prejudices, practitioners may not be expected to embrace Moringa for its antibiotic properties. In this case, however, the *in-vitro* (bacterial cultures) and observational studies provide a very plausible mechanistic underpinning for the plethora of efficacy claims that have accumulated over the years (see **Table 1**).

Aware of the reported antibiotic activity of **[2]**, **[5],** and other isothiocyanates and plants containing them, we undertook to determine whether some of them were also active as antibiotics against *Helicobacter pylori*. This bacterium was not discovered until the mid-1980's, a discovery for which the 2005 Nobel Prize in Medicine was just awarded. *H. pylori* is an omnipresent pathogen of human beings in medically underserved areas of the world, and amongst the poorest of poor populations worldwide. It is a major cause of gastritis, and of gastric and duodenal ulcers, and it is a major risk factor for gastric cancer (having been classified as a carcinogen by the W.H.O. in 1993). Cultures of *H. pylori*, it turned out, were extraordinarily susceptible to **[2]**, and to a number of other isothiocyanates (37,60). These compounds had antibiotic activity against *H. pylori* at concentrations up to 1000-fold lower than those which had been used in earlier studies against a wide range of bacteria and fungi. The extension of this finding to human *H. pylori* infection is now being pursued in the clinic, and the prototypical isothiocyanate has already demonstrated some efficacy in pilot studies (49,168).

Cancer Prevention. Since *Moringa* species have long been recognized by folk medicine practitioners as having value in tumor therapy (61), we examined compounds **[1]** and **[2]** for their cancer preventive potential (39). Recently, **[1]** and the related compound **[3]** were shown to be potent inhibitors of phorbol ester

(TPA)-induced Epstein-Barr virus early antigen activation in lymphoblastoid (Burkitt's lymphoma) cells (57,104). In one of these studies, **[3]** also inhibited tumor promotion in a mouse two-stage DMBA-TPA tumor model (104). In an even more recent study, Bharali and colleagues have examined skin tumor prevention following ingestion of drumstick (Moringa seedpod) extracts (12). In this mouse model, which included appropriate positive and negative controls, a dramatic reduction in skin papillomas was demonstrated.

Thus, traditional practice has long suggested that cancer prevention and therapy may be achievable with native plants. Modern practitioners have used crude extracts and isolated bioactive compounds. The proof required by modern medicine has not been realized because neither the prevention of cancer nor the modification of relevant biomarkers of the protected state has been adequately demonstrated in human subjects. Does this mean that it doesn't work? No. It may well work, but more rigorous study is required in order to achieve a level of proof required for full biomedical endorsement of Moringa as, in this case, a cancer preventative plant.

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TABLE 1. REPORTED NUTRITIONAL, THERAPEUTIC & PROPHYLACTIC USES OF *MORINGA OLEIFERA*

Traditional Use Condition/Effect[a]	Plant Part[b]	References[c]
(ANT) Antimicrobial / Biocidal	**LFSPRBGO**	8, 13, 19, 24, 27, 31, 34, 64, 68, 100, 104, 114, 115, 126, 140, 151 160, 161, 162
Bacterial	LFS	25, 26, 55, 63, 77 - 81, 149
Dental Caries/Toothache	RBG	47
Infection	LF	47
Syphilis	G	47
Typhoid	G	47
Urinary Tract Infection	L	141
Fungal/ Mycoses	O	111
Thrush		88, 111
Viral		
Common cold	FRB	47
Epstein-Barr Virus (EBV)	L	104
Herpes Simplex Virus (HSV-1)	L	84
HIV-AIDS	L	1, 124
Warts	S	47
Parasites		
Dranunculiasis (guinea-worm)		36
Helminths	LFP	47
Schistosomes	S	113
Trypanosomes	LR	95
Other / Not Attributed to a Specific Pathogen		
Bronchitis	L	47
Earache	G	47
External Sores/Ulcers	LFRB	15
Fever	LRGS	47
Hepatic	L	6
Skin (Dermal)	O S	15
Throat Infection	F	47
Water treatment (general)	S	11, 50, 75, 86, 169

AST Asthma	**RG**	47
CAN Cancer Therapy / Protection	**LFPBS**	12, 17, 28, 39, 45, 59, 61, 64, 104, 115
Anti-tumor	LFSB	45, 48, 57, 61, 87
Prostate	L	47, 48
Radioprotective	L	132
Skin	P	12
CIR Circulatory/Endocrine Disorders	**LFSPR**	56, 93
Anti-anemic	L	47, 125
Anti-hypertensive	LP	40, 41, 42, 43, 44, 53, 83, 137
Cardiotonic	R	47
Diabetes/hypoglycemia	LP	6, 45, 71, 87, 101, 167
Diuretic	LFRG	6, 14, 62
Hypocholestemia	L	52, 94
Thyroid	L	153
Tonic	F	47
Hepatorenal	LR	93, 120
DET Detoxification	**BO**	76, 135, 166
Antipyretic		148
Purgative	O	47
Snakebite	B	47
Scorpion-bite	B	47
DIG Digestive Disorders	**LSRBG**	53
For TRTMNT of:		
Colitis	LB	47
Diarrhea	LR	47, 62, 64
Digestif	B	47
Dysentery	LG	47
Flatulence	R	47
Ulcer / Gastritis	LS	3, 115, 136
INF Inflammation	**LFSPRG**	14, 28, 35, 45, 62, 64, 68, 110, 131, 160, 161
Rheumatism	LFSPRG	28
Joint Pain	P	47
Edema	R	47
Arthritis	S	47
IMM Immunity	**SO**	69
Immune-stimulant	S	69
Lupus	O	28
NER Nervous Disorders	**LFRBGO**	58, 59, 62, 96
Anti-spasmodic	SR	14, 53
Epilepsy	RB	47
Hysteria	FRBO	47
Headache	LRBG	47
NUT Nuritional	**LSBO**	6, 7, 18, 22, 28, 30, 31, 32, 46, 47, 48, 51, 65, 66, 67, 70, 92, 102, 112, 116, 133, 163
Antinutritional factors	B	88, 89, 90, 110, 127, 128, 139, 156, 164, 165
Antioxidant	LO	110, 147
Carotenoids	L	29, 105, 152
Energy	LSO	85
Goitrogen	S	2
Iron deficiency	LS	16
Oil quality	O	5, 98, 110, 158, 159
Protein	LS	47
Vitamin/Mineral deficiency	LS	7, 9, 54, 56, 85, 119

REP Reproductive Health	**LFPRBGO**	44, 53, 64, 121, 122
Abortifacient	FRBG	106, 107, 155
Aphrodisiac	RB	47
Birth Control	B	45, 53, 142 - 146,
Lactation Enhancer	L	47
Prostate function	O	47
SKI Skin Disorders	**LRSG**	160, 161
Antiseptic	L	47
Astringent	R	47
Pyodermia	S	15
Rubefacient	RG	47
Vesicant	R	47
GEN General Disorders/Conditions	**LFSPRBO**	4, 6, 8, 20, 21, 45, 48, 64, 66, 67, 68, 73, 74, 82, 91, 92, 99, 102, 103, 109, 116, 117, 118, 123, 125, 128, 129, 130, 134, 150, 163
Bladder	OS	47
Catarrh	LF	47
Gout	RO	47
Hepatamegaly	R	47
Lactation	L	47
Low.Back/Kidney Pain	R	47
Scurvy	LSRBO	47
Splenomegaly	R	47
“Tonic”	LFPSO	47

[a] It is very difficult in some cases to separate the effects of severe nutritional deficiencies (e.g. Vitamin C) from sequelae (e.g. scurvy) which transcend categorization by organ systems or classification into single disease states.

[b] Plant parts are designated by their first letters (in bold):
Leaves
Flowers
Seeds
Pods (drumsticks)
Roots
Bark
Gum
Oil (from seeds)

[c] Many of the original citations have been collected by Lowell J. Fuglie, [and can be found in his excellent treatise entitled The Miracle Tree, (47)] and by Manuel Palada (116), Julia Morton (102), and Trees For Life (157). Most other compendiums in recent publications or on commercial websites appear to be highly derivative of these seminal works.

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(3-letter code in yellow at end of reference indicates major classification in Table 1)

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