



The Miracle Tree

Moringa oleifera

Second Edition

2019

Manuel C. Palada, Andreas W. Ebert, Ravindra C. Joshi

Editors

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- *Exodus 15:22-25: "So Moses brought Israel from the Red Sea; then they went out into the Wilderness of Shur. And they went three days in the wilderness and found no water. Now when they came to Marah, they could not drink the waters of Marah, for they were bitter. Therefore the name of it was called Marah. And the people complained against Moses, saying, "What shall we drink?" So he cried to the Lord, and the Lord showed him a **tree**. When he cast it into the waters, the waters were made sweet…"*
- *The "tree" in the Book of Exodus, maybe none other than the* ***Moringa tree.***

Dedication

11 December 1957 – 21 April 2010

Dedicated in memory of Dr. Lowell Fuglie, author of
The Miracle Tree – *Moringa oleifera*
First Edition, 1999

THE MIRACLE TREE

Moringa oleifera

Second Edition

by

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2019

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THE MIRACLE TREE

Moringa oleifera

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Foreword

Dennis P. Garrity

For thousands of years, moringa (*Moringa oleifera*) has been used as a food crop and as a medicinal plant. Almost all of moringa's plant parts have multiple uses, particularly the leaves and seed pods, which are highly nutritious. During the past several decades, more attention has focused on exploring and expanding the multiple uses and benefits of this miracle tree. Advances in research and development are rapidly progressing in the areas of botany and germplasm improvement, agronomy, nutrition, natural medicine, and its commercialization by the food and cosmetics industry. Recent developments are not only focusing on using moringa as a food crop, but also as an industrial commodity, with applications such as water clarification, livestock feed, and biofuel.

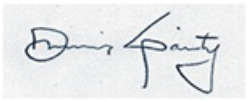
Earlier, the mainstream emphasis was on the nutritional and health benefits of moringa. It is a fast-growing plant and it produces large quantities of leaf biomass in a relatively short period of time. Research at the World Vegetable Center and other agricultural institutions has demonstrated its high yield potential, and its impact on alleviating poverty and malnutrition when produced and consumed as a vegetable. Moringa has a relative advantage compared to other food crops, as it provides high levels of protein, vitamins, amino acids and phytonutrients. Moringa leaves provide a rich source of β-carotene, protein, vitamin C, iron, calcium and potassium. It is also a good source of natural antioxidants such as ascorbic acid, flavonoids, carotenoids and phenolic substances.

Moringa can be grown in a wide range of climates. It has a very significant role to play in a world that is increasingly aware of the many who are undernourished and malnourished. During the 20th century, with the impact of the green revolution, agriculture fed the world with increased levels of protein and carbohydrates from high-yielding cultivars of dietary staple crops. In the 21st century, biofortification is seen by many funding agencies as the way to address malnutrition. But crop and diet diversification is in many ways a better, and more sustainable approach, to addressing hidden hunger than than the biofortification of staple crops. Moringa is a highly nutritious food crop that has the potential to play an enormous role in creating that dietary diversity and richness.

Many international scientific conferences have been convened in the past 20 years to highlight the current importance and future role of moringa around the world. The most recent was the ***First International Symposium on Moringa*** which was convened in Manila, Philippines, in November 2015, under the auspices of the International Society for Horticultural Sciences. The theme of the symposium was *"Moringa: A Decade of Advances in Research and Development"*. The symposium had 180 participants from 42 countries, sharing their experiences, expertise and knowledge on a wide range of topics, including the botany and germplasm, production technology, health and nutrition, industrial uses and cross-commodity issues.

The release of this book is very timely. It provides useful and comprehensive information about moringa that will be appreciated by readers across the globe. It adds to our knowledge and understanding of the importance and role of moringa for the benefit of all who may be interested in learning more about this miracle tree, as well as those that are engaged in using moringa for improved health, nutrition and income.

I heartily congratulate Prof. Manuel C. Palada, Dr. Andreas W. Ebert and Prof. Ravindra C. Joshi for their terrific effort in creating this new and improved edition, and for making it available to everyone. We owe them our warmest gratitude for their great dedication to the moringa world community.



Dennis P. Garrity
Former Director General, World Agroforestry Centre
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Chair, Landcare International

Foreword

Teodoro C. Robles

It has been my belief that the academe should not only limit its scope to student development or to producing globally competent graduates. An academic institution, it being one of the integral parts of the society, should also do its share of extending its reach to what is outside its gates, especially on programs that contribute to sustainable development.

In the recent years, Central Philippine University has been focusing on agriculture owing to the fact that it is an industry where the university can do its share in nation-building by tapping the potentials of our grassroots community, especially our farmers. In the recent times, the emerging economic profitability and undeniable health benefits of *Moringa oleifera* has caught the attention of CPU, seeing it as an avenue to extend help to others through research and development.

Moringa is found in almost all parts of the Philippines, thus, it is but fitting that this country takes advantage of its availability. Studies have been conducted to explore more on the benefits that we can get from Moringa, so that that this plant may be used to its full potential. The recent years have been good for the industry as government and private sectors have been providing the necessary assistance for it to grow locally and internationally.

Central Philippine University is truly honored for the opportunity to be involved in meaningful projects like this book, now on its second edition. With a heart full of optimism and faith, I hope and pray that, in the coming years, the university will be more involved in researches and endeavors that will impact not only the Centralian community but the country eventually. I am confident that by focusing our resources to undertakings promoting growth and development, we could help secure a better Philippines for the generations to come.

Teodoro C. Robles

TEODORO C. ROBLES, Ph.D.

President
Central Philippine University
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About the Editors

Dr. Manuel C. Palada

Dr. Manuel C. Palada obtained his B.S. in Agriculture from Central Philippine University, M.Sc in Agronomy from the University of the Philippines at Los Banos and a Ph.D. in Horticultural Science (Vegetable Crops) from the University of Florida. Dr. Palada has over five decades of working experience as international agronomist and horticulturist. He has worked with three international agricultural research centers in Asia (IRRI and AVRDC – The World Vegetable Center), and in Africa (IITA). Dr. Palada has made significant contributions to international horticulture as a researcher, teacher, and outreach specialist. He has made a genuine impact in developing sustainable crop production systems for resource-poor farmers across the globe, from the Caribbean basin to Eastern and Western Africa and throughout Asia and the Pacific. In 2005 he was an "Outstanding International Horticulturist" awardee of the American Society for Horticultural Science. Dr. Palada has been very active in the promotion of moringa both in the Philippines and abroad giving seminars and workshops on moringa. He has conducted agronomic and horticultural studies on moringa in the Caribbean, Africa, Asia and USA. Dr. Palada is also the President and Chief Executive Officer of the Farm Systems International Organization (FSI). He organized FSI upon his retirement as Head of the Crop and Ecosystems Management Unit at AVRDC -The World Vegetable Center in Taiwan.. His current research is focused on varietal evaluation for horticultural characteristics of moringa in the Philippines. He has published several technical and scientific papers on moringa and vegetable crops as well as book chapters and production guides. His journal article titled "Moringa (*Moringa oleifera* (Lam.): A Versatile Tree Crop with Horticultural Potential in the Southern United States" HortScience Vol. 3(5):794-797, 1996 was the first article on moringa published in American Society for Horticultural Science journal. Dr. Palada initiated the organization of the First International Symposium on Moringa at Crowne Plaza Manila Galleria Convention Center, November 15-18, 2015 in which he was the Convener. He is the co-editor of the *Proceedings of the I International Symposium on Moringa*. Acta Horticulturae # 1158, International Society for Horticultural Science. He also serves as Chairman of Moringa Working Group, ISHS. Dr. Palada is a free lance consultant on horticultural crops and presently serves as Visiting and Adjunct Professor of Sustainable Agriculture at the College of Agricultural, Resources and

Environmental Sciences, Central Philippine University, Iloilo City, Philippines.

Dr. Andreas W. Ebert

Dr. Andreas W. Ebert graduated in May 1976 from the University of Hohenheim, Stuttgart, Germany with a Diploma degree in Agricultural Sciences. In February 1980 he obtained his Ph.D. with distinction (magna cum laude) for his work on 'Hormonal aspects of crop regulation in apple' at the Institute for Fruit and Vegetable Production and Viticulture from the same University. Thereafter, he held a Postdoc position at the Glasshouse Crops Research Institute in Littlehampton, UK, where he conducted research on tomatoes. At a later stage, he worked on somatic embryogenesis of coconut at Wye College, University of London. Dr. Ebert dedicated his entire professional life to agricultural research for development in the tropics and subtropics, in Latin America, West Africa, East and Southeast Asia, and Oceania. From 2002 to 2008, he was Team Leader of an interdisciplinary plant genetic resources group at CATIE in Costa Rica, directed CATIE's genebank and served as Professor at its Graduate School. From 2008 until his retirement in December 2015, he held the position of Genebank Manager and Global Theme Leader – Germplasm at the World Vegetable Center's headquarters in Taiwan. Currently, Dr. Ebert is a Freelance Consultant in tropical agriculture and the management of plant genetic resources and genebanks. He is passionate about the conservation and sustainable use of plant genetic resources, especially landraces, farmers' varieties and crop wild relatives—key resources for crop improvement and adaptation to climate change. Dr. Ebert is author and co-author of numerous peer-reviewed journal articles and book chapters. He is senior author and editor of the bilingual book 'Securing our future: CATIE's germplasm collections – Asegurando nuestro futuro: Colecciones de germoplasma del CATIE. Dr. Ebert is senior editor of the *Proceedings of the I International Symposium on Moringa*. Acta Horticulturae # 1158, International Society for Horticultural Science.

Dr. Ravindra C. Joshi

Dr. Ravindra C. Joshi is currently the SAFE-Network Pacific Islands coordinator; CABI-SEA Associate; Tropical Agriculture Association (UK) coordinator for the Pacific region; and technical adviser to Deltamed, Spain on invasive apple snail. He was also formerly visiting adjunct professor of Agriculture at the University of the South Pacific, Fiji; He was a former chief science research specialist at the Philippine Rice Research Institute (PhilRice) where he first started working on invasive apple snail in 1987. His central research over twenty-five years is on invasive alien species (IAS), important to agriculture sector, at the international, regional and national organizations, including the private and academic institutions, in Africa, Asia and Pacific Island countries. He published four manuals on IAS: Global Advances in Ecology and Management of Golden Apple Snails, Rice Black Bug: Taxonomy, Ecology, Management of Invasive Species, Philippine Rats: Ecology and Management, and Biology and Management of Invasive Apple Snails. In addition, he has also published over 150 research articles on IAS and their management. He has a PhD in Entomology from the University of the Philippines Los Baños in 1988. He has worked as a rice entomologist at the International Institute of Tropical Agriculture, Nigeria, and as a crop protection specialist under the auspices of the Cambodia-IRRI-Australia Project. He reviewed the crop protection research programs of the International Centre of Insect Physiology and Ecology in 1988 and of PhilRice in 1998. He was also visiting professor at the University of the Philippines, Baguio, and Pampanga State Agricultural University, the Philippines. He also served as a short-term bench consultant to the System-wide Program on Integrated Pest Management (IPM) / Consultative Group on International Agricultural Research Leafminer Flies Technical Working Group, and to the Food and Agriculture Organization's rice-fish IPM project in Surinam and Guyana. He was also the site coordinator in Solomon Islands with the World Vegetable Center; former senior adviser/consultant to the offices of minister and permanent secretary of Agriculture in Solomon Islands and Fiji, to advise on policy and research areas, and as former Non-OECD Representative to the CG Fund Council (formerly CGIAR) to represent the Pacific Island Countries and Territories. Dr. Joshi also served as member of the Scientific Committee of the First International Symposium on Moringa held in Manila, Philippines on November 15-18, 2015.

Acknowledgements

This book presents much information collected from various sources including field research studies conducted by organizations involved in developing and promoting moringa as one of the most useful plants, articles written by individuals with experience and knowledge about moringa, as well as other books and publications cited in this present edition.

Special appreciation is presented to the individual contributors of the chapters and sections which constitute the general and basic information on the various aspects of the moringa plant. They have been active in promoting moringa through research and publication.

Special acknowledgement goes to the World Vegetable Center in providing financial support during the initial writing of the book. Likewise, special thanks and appreciation are extemded to Central Philippine University for hosting and providing the first editor of this book a working office space and facilities.

Chapter 13
Medicinal Potential and Benefits of *Moringa oleifera*

13.1 *Moringa oleifer*a Medicinal Potential and Benefits

Jed W. Fahey

INTRODUCTION

The nutritional properties of moringa are now so well known that there seems to be little doubt stem 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. We have recently highlighted this need (Thurber, 2009).

Moringa oleifera is the most widely cultivated of the 13 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 (USA) and the Pacific islands. All parts of the Moringa tree are edible and have long been consumed by humans. According to Fuglie (1999), 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 as a food (in salads), for fine machine lubrication, and in the manufacture of perfume and hair care products (Tsaknis, 1999). In the West, one of the best known uses for Moringa is the use of powdered seeds to flocculate contaminants and purify drinking water (Berger, 1984; Gassenschmidt, 1995; Olsen, 1987), but the seeds are also eaten green, roasted, powdered and steeped for tea and used in curries (Gassenschmidt, 1995). 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.

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 (Lockett, 2000).

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. We consider phytochemical content separately herein, because it also impacts taste, palatability, consumer acceptance, and bioavailability.

Moringa belongs to a family of plants that is exceptionally rich in phytochemicals that are involved in detoxification. Evolving from the primordial soup about a half billion years ago, land plants first started the evolutionary process to develop biochemical detoxification mechanisms for their own protection. One of the beauties, or symmetries of nature, is that we inherited most of our biochemical detoxification mechanisms, from the very plants upon which we depended for a food supply, and those phytochemicals are as effective as anything modern pharmacology has developed, in assisting us in our own protection. Human beings have not just recently developed the need to detoxify air and water pollutants like pesticides, plasticizers, and volatile organic hydrocarbons. From the moment we (and our predecessor mammals) started eating, our survival depended upon our ability to detoxify toxins from fungal and bacterial food contaminants, and from the plants and animals we ate. When *Homo sapiens* emerged from Neanderthal man and first tamed fire about 40,000 years ago, we started living in highly polluted microenvironments, and charring our steaks to produce carcinogenic heterocyclic amines. As stated so eloquently by the populist writer Michael Pollan in The Botany of Desire (Pollan, 2001), *"While we animals were busy nailing down things like locomotion and consciousness, plants acquired an array of extraordinary and occasionally diabolical powers by discovering how to synthesize remarkably complicated molecules."*

The phytochemical content of moringa has implications with respect to its utility as a nutritional plant and as a source of micronutrients, as well as its medicinal effects (the application with which phytochemicals are most often associated). In particular, this plant family is rich in compounds containing the simple sugar, rhamnose, and it is rich in a fairly unique group of phytochemicals called glucosinolates, which are enzymatically converted to isothiocyanates (reviewed by Fahey, 2001). The isothiocyanates, in general, have tremendous anti-inflammatory, detoxification, antibiotic, and neuroprotective properties, to name just a few. Moringa is replete with some very potent glucosinolates that we and others have documented are influenced by both environment and genetics (Doerr, 2009; Bennett, 2003).

In addition to their unique, rhamnosylated glucosinolates and isothiocyanates, moringa

contains a variety of related carbamates, thiocarbamates and nitriles (Faizi, 1992, 1994a, 1994b, 1995, 1998; Murakami, 1998). For example, specific components of moringa preparations that have been reported to have hypotensive, anti-cancer, and antibacterial activity are illustrated in **Figure 1**; they include 4-(α-L-rhamnopyranosyloxy)benzyl glucosinolate **[1]**, 4-(α -L-rhamnopyranosyloxy)-benzyl isothiocyanate **[2]** (also known as glucomoringin), 4-[(4'-O-acetyl-α-L-rhamnopyranosyloxy)benzyl] isothiocyanate **[3]**, benzyl isothiocyanate **[4]**, niazimicin **[5]**, niazirin **[6]**, and niazimin **[7]**. 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 (1999) and others, and are the subject of Chapter 13 of this volume.

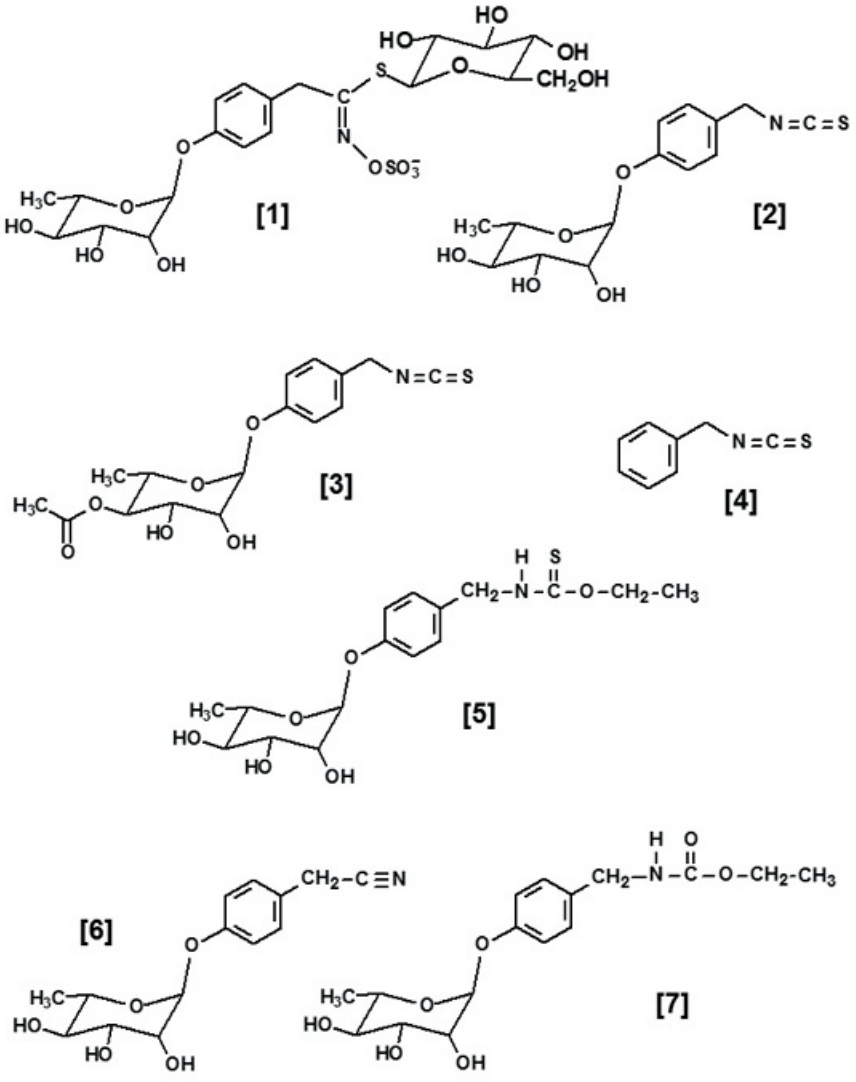

Figure 1. Structures of selected phytochemicals from *Moringa* spp.: 4-(α-L-rhamnopyranosyloxy) benzyl glucosinolate **[1]**, 4-(α-L-rhamnopyranosyloxy) benzyl

isothiocyanate **[2]**, 4-[4'-O-acetyl-α-L- rhamnopyranosyloxy)benzyl] isothiocyanate **[3]**, benzyl isothiocyanate **[4]**, niazimicin **[5]** (a thiocarbamate), niazirin **[6]** (a nitrile), and niazimin **[7]** (a carbamate).

DISEASE TREATMENT AND PREVENTION

Claims for ***medicinal uses*** are manifold, but are by-and-large less well documented than nutritional and micronutrient claims.

The following section was written 15 years ago (Fahey, 2005) and is paraphrased below. Unfortunately, whereas the volume of published work purporting medicinal benefits, and the number of papers repeating or newly reporting on *in-vitro* and animal model tests has ballooned over the past decade, the number of peer-reviewed papers that describe well done studies in human beings can still be counted on the fingers of one hand.

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 (Palada, 1996). 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 (Sampson, 2005; Talalay, 2001). Clearly much more research is justified, but just as clearly this will be a highly 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, a report published almost 25 years ago (Shaw, 1982) appears on the surface 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 detoxification and antioxidant enzymes and biomarkers as a result of treatment with moringa or with phytochemicals isolated from moringa (Fahey, 2004; Faizi, 1994; Kumar, 2003; Rao, 1999). .

Table 1. Clinical evaluations of the anti-diabetic potential of *Moringa oleifera* leaf powder in 7 clinical studies.

Daily Dose	Durati-on of Interv-ention	Number of Subjects Taking Moringa (M) or Control (C)	Results	Comments	Reference
100g	3 months	20 – M 10 – C 20 – Other treatment	↓ FBG: (151 to 117.5)	"Control" group only measured once, but was just a baseline of non-diabetic patients. No control group of matched diabetic patients receiving placebo. Dose regimen unclear.	Sugunabai, 2014
50g	40 days	15 – M	↓ BG: (132.5 to 120.3) ↓ LDL: (45.8 to 31.5)	No controls. Dose regimen unclear ("All subjects were asked to use this [50g] powder with their food regularly"). Unclear how BG measured and whether it was fasting or post prandial	Kumar, 2013
?	?	45 – M	↓21.72 FBG ↓28.11 post-prandial	Other details not available	Kiranmayi, 2011
?	3 months	30 – M 30 - C	↓ PPG (210 to 150) (M) & (179 to 163) (C)	Significant differences in the experimental BG (post vs. pre), but initial levels very different between the experimental and control (210 vs 179). Dose not specified.	Giridhari, 2011

Daily Dose	Durati-on of Interv-ention	Number of Subjects Taking Moringa (M) or Control (C)	Results	Comments	Reference
8g	40 days	24 – M 9 – C 22 – Other treatment	↓FBG (162 to 117); ↓PPBG (219 to 163); ↓SC (261 to 224); ↓ST (130 to 112); ↓LDL (171 to 122), & ↓VLDL levels (26 to 22). No signif ↓ in any but ST in controls (138 to 133).	Randomization, masking and treatment allocation not indicated or specified	Kumari, 2010
4.68g	50 days	20 – M 20 - C	Significant ↓ in LDL/ HDL (3.27 to 2.99), TC/ HDL (4.58 to 4.28), TC (187.14 to 184.00) and NON-HDL (149.08 to 143.60)	Although directed at hyperlipidemic (not type 2 diabetes) subjects, there was no ↓ FBG in treatment, contrary to expectations.	Nambiar, 2010

Daily Dose	Durati-on of Interv-ention	Number of Subjects Taking Moringa (M) or Control (C)	Results	Comments	Reference
2.1g	30 days	33 – M 35 – C	Both the experimental and control groups had ↓ BG, but no significant diff. between the two.	Randomization, blinding and treatment allocation were all clearly stated, but study population was not type 2 diabetes and had normal glucose ranges at baseline.	Sandoval, 2013
*M – Moringa; C – Control BG – blood glucose; FBG – fasting blood glucose; PPG – post-prandial glucose; LDL – low density lipoprotein; HDL – high density lipoprotein; TC – total cholesterol; ST – serum triglycerides					

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.

In reviewing what has transpired in the scientific literature since the 2005 review was written, one comes up with the following metrics: A September 2014 keyword search in the database Scopus (an Elsevier product that credits itself as the world's largest abstract and citation database of peer-reviewed literature) reveals that there are now 1643 peer-reviewed papers in which "Moringa" is a key word, 1332 of them since 2005, and now being published at a rate of one per day. It is instructive to sort through not only the titles and abstracts of these thousand or so post-2005 studies, but to examine how they are sorted and categorized (according to titles and key-words). After ruling out those studies that deal with *plant anatomy* and *taxonomy*, *nutritional content*, *analytical methodology*, *biomass production*, and *water coagulation/purification* by moringa, one can get a vision of how studies dealing with the biomedical or medicinal effects of moringa are clustered:

- *Antioxidant activity* (including *lipid peroxidation*) accounts for between 100 and 200 of the remaining papers.
- *Drug screening*, *-isolation*, and/or *-efficacy* accounts for another 75-100.
- *Antibacterial activity*, *anti-inflammatory activity*, *anti-diabetic activity*, *anti-neoplastic activity* ("anti-cancer" effects) account for about 50, 50, 40, 30, and 30 of the remaining publications, respectively.

At first glance it appears that there has been a lot of research activity on the latter categories and there have been reviews, both critical and otherwise (most recently: Hussain, 2014). However, a more critical evaluation of the publications shows that some are very poorly done studies that reach spurious and highly debatable conclusions about their data, and almost all are

done on cell lines, in test-tube antibacterial assays, or in animal studies, and not in controlled human studies.

Although 383 of the 1643 papers identified are reported as "controlled studies", only 3 of them actually appear to be so. They are:

1. Anti-asthmatic activity of *Moringa oleifera* Lam.: A clinical study. (2008) B. Agrawal and A. Mehta. *Indian J Pharmacol.* 40(1), 28-31.
2. Effect of *Moringa oleifera* on undesirable skin sebum secretions of sebaceous glands observed during winter season in humans. (2013) A. Ali, N. Akhtar, M.S. Khan, M.T. Khan, A. Ullah, and M.I. Shah. *Biomedical Research* 24(1), 127-130.
3. Effect of malunggay (*Moringa oleifera*) capsules on lipid and glucose levels. (2013) M.A.S. Sandoval, and C.A. Jimeno. *Acta Medica Philippina.* 47 (3), 22-27.

A fourth paper appears to be such a study but is actually carried out *ex-vivo*, so would more properly be placed in the category of studies in cell culture (test-tube studies). However, it does provide encouraging results:

4. *Moringa oleifera* leaves as an inhibitor of human platelet aggregation. (2009) S. Arabshahi-Delouee, M. Aalami, A. Urooj, and T.P. Krishnakantha. *Pharmaceutical Biology*. 47(8), 734-739.

Furthermore, at the time this chapter was written, there were three studies with human subjects listed on www.clinicaltrials.gov, in which moringa was to be administered orally:

1. NCT01410058; *Moringa oleifera* – Antiretroviral pharmacokinetic drug interaction. *Sponsor*: University of Zimbabwe; *Status*: Recruiting (Aug 2013).
2. NCT02021799; The effect of under-nutrition on the human microbiota. *Sponsor*: Western University, Canada; *Status*: Completed (Dec. 2013)
3. NCT02234206; A clinical trial to study the safety and efficacy of Chandrakanthi Choornam on patients with low sperm count. *Sponsor*: Tamil Nadu Dr. M.G.R. Medical University; *Status* Completed (Aug 2014).

Thus, although the clinical studies highlighted above are commented upon herein, the fact remains that ten years further down the road, almost all studies of the biomedical or Thus, although the clinical studies highlighted above are commented upon herein, the fact remains that ten years further down the road, almost all studies of the biomedical or medicinal effects of moringa are still not the ultimate clinical trials that the Western medicine tradition requires for adoption of such therapies or preventive strategies. However, evaluating the overall quality of *in-vitro* and animal study findings for the most promising applications of moringa, these studies can be highly informative. Understanding what they say should focus research strategy and help scientists to prioritize their research goals. In particular, it should direct our attention to the clinical studies that have the highest likelihood of giving a definitive (e.g. ***Yes*** or ***No***) answer rather than simply generating more studies because the data were inconclusive. Therefore, we shall focus in the following sections, on the studies that address the areas of research which appear to have the most well-supported basis for further clinical efforts.

Anti-inflammatory and antioxidant effects, will be mentioned first. Antioxidant and anti-inflammatory studies by and large have been performed on cultured cells, and lead to general and overarching conclusions. Mechanistically, however, inflammation and oxidative stress are from a functional and pathophysiological perspective, at the very core of many chronic diseases (Fahey, 1999, 2012, 2013). These effects are absolutely central to many diseases, and these effects can be measured *in vitro*. Though traditional medicine has long observed this, the anti-inflammatory effects of *Moringa oleifera* roots were not well documented in the scientific literature until about two decades ago (Ezeamuzie, 1996). Most recently, for example, Waterman and colleagues (2014) showed the anti-inflammatory effects of isothiocyanate-rich extracts of *M. oleifera in vitro*, and Ndhlala and colleagues (2014) compared antioxidant variation between *M. oleifera* cultivars. However, associating antioxidative and anti-inflammatory measurements made in bodily fluids such as blood, urine, or sputum, with clinical symptoms of disease, are much more problematic. For example, Kushwaha et al. (2014) recently demonstrated changes in antioxidant profile and "oxidative status" upon monitoring blood/serum biomarkers in a trial in which 30 post-menopausal women were supplemented daily with 7 grams of *M. oleifera* leaf powder for 3 months, but no symptom measurement was reported. Reports on the use of moringa in rodent models of disease have increased in recent years. For example Galuppo et al. (2013) have reported that the isothiocyanates of *M. oleifera* repress the inflammatory component of experimental autoimmune encephalomyelitis.

Although much has been written on the antioxidant activity of moringa extracts and leaves, as well as many other food and herbal medicinal ingredients, the real benefits of such antioxidant activity remains highly controversial. Whereas the lay public and the companies that market products to them appear to have resolved the controversy in favor of eating lots of antioxidants, the real value of such a strategy is still hotly debated in the scientific literature (Moyer, 2013; Bjelakovic, 2007; Guallar, 2013). Antioxidant effects will not be directly addressed herein from the perspective of moringa's medicinal value.

From the perspective of more specific medical indications, there are five areas that are now well supported within the moringa literature, and they hold strong promise for future and more definitive animal model and human clinical trials: ***antibiosis***, ***chemoprevention*** (of cancer and other non-communicable diseases), ***diabetes***, ***hypertension,*** and ***asthma***.

ANTIBIOTIC ACTIVITY

This is clearly an 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 60 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 (B.R. Das), Travancore University (P.A. Kurup), and the Department of Biochemistry at the Indian Institute of Science in Bangalore (P.L.N. Rao), identified a compound they called pterygospermin, a compound which they reported readily dissociated into two molecules of benzyl isothiocyanate **[4]** (Das, 1954, 1957a, 1957b; Kurup, 1952, 1954a, 1954b, 1954c, 1954d; Narasimha Rao, 1953). 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 extracts of the moringa plants from which pterygospermin was reported to have been isolated, were antibacterial against a variety of microbes, the identity of pterygospermin was eventually challenged (Eilert, 1981) as an artifact of isolation or structural determination. Very recently, elegant computational chemistry and modeling performed by chemists at the University of Dayton (USA) concluded that pterygospermin would not be stable enough to exist in ambient conditions (Howarth, 2011). We must thus seek other phytochemicals to explain the very well documented antibiosis of moringa against certain environmental and clinical microbes.

*El*egant and very thorough work, published in 1964 as a PhD thesis by Bennie Badgett (a student of the chemist Martin Ettlinger), identified a number of glyosylated derivatives of benzyl isothiocyanate **[4]** (e.g. compounds containing the 6-carbon simple sugar, rhamnose) (Badgett, 1964). The identity of these compounds was not available in the refereed scientific literature until "re-discovered" 15 years later by Kjaer and co-workers (Kjaer, 1979). Seminal reports on the antibiotic activity of the primary rhamnosylated compound then followed, from Eilert and colleagues in Braunschweig, Germany (Eilert, 1978, 1981). They re-isolated and confirmed the identity of 4-(α-L-rhamnopyranosyloxy)benzyl glucosinolate **[1]** and its cognate isothiocyanate **[2]** and verified the activity of the latter compound against a wide range of bacteria and fungi. Since then, we and others have done much work to isolate, purify, and identify the antibiotic compounds in moringa, as well as isolating and characterizing the enzyme (myrosinase; E.C. 3.2.1.147) that is responsible for converting precursor glusosinolates such as **[1]** above, to isothiocyanates such as **[2]** (Bennett, 2003; Fahey, 2003, 2004, 2013b; Wade, 2007, 2015; Fisher, 2005; Haristoy, 2005; Waterman, 2014).

Extensive field reports and ecological studies (see Fahey, 2005) forming part of a rich traditional medicine history, claim efficacy of leaf, seed, root, bark, and flowers against a variety of dermal, internal, and parasitic infections including trypanosomiasis (Ayyani, 2014) dranunculaisis (Fabiyi, 1993) and mosquito-borne diseases (Pontual, 2014). 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, it would not be surprising if practitioners do not 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 and were reviewed a decade ago (Fahey, 2005).

Aware of the reported antibiotic activity of **[2-4]**, 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 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 (Fahey, 2002; Haristoy, 2005). 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 has been pursued in the clinic, and the prototypical isothiocyanate has already demonstrated some efficacy in pilot studies (Galan, 2004; Yanaka, 2005, 2009).

CANCER CHEMOPREVENTION

Since *Moringa* species have long been recognized by folk medicine practitioners as having value in tumor therapy (Hartwell, 1967), we examined compounds **[2]** and **[3]** for their cancer preventive potential (Fahey, 2004). Recently, **[3]** and the related compound **[4]** were shown to be potent inhibitors of phorbol ester (TPA)-induced Epstein-Barr virus early antigen activation in lymphoblastoid (Burkitt's lymphoma) cells (Guevara, 1999; Murakami, 1998). In one of these studies, **[4]** also inhibited tumor promotion in a mouse two-stage DMBA-TPA tumor model (Murakami, 1998). In a subsequent study, Bharali and colleagues examined skin tumor prevention following ingestion of drumstick (Moringa seedpod) extracts (Bharali, 2003). 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.

ANTI-DIABETIC ACTIVITY

Diabetes is the most common metabolic disorder worldwide. It has become endemic in industrialized counties and it is a major public health problem. In much of sub-Saharan Africa, access to pharmaceuticals is minimal or absent, and people rely on medicinal plants to resolve their health problems. A cross-sectional study in Senegal showed that out of 41 plants used for the treatment of diabetes, *Moringa oleifera* was the most common (Dieye, 2008). As indicated earlier, since reactive oxygen species are linked with the pathogenesis of chronic diseases such as hypertension and diabetes, plants with antioxidant properties are presumed to influence the etiology of these chronic diseases, and have been sought (Ogbunugafor, 2012).

Nine studies between 2003 and 2014 used moringa leaf extracts, in either aqueous or ethanolic solutions, to amelioriate glucose intolerance in rodent models of diabetes (Toma, 2012; Kar, 2003; Prakash, 2009; Momoh, 2013; Ndong, 2007; Jaiswal, 2009; Nardos, 2011; Divi, 2012; Yassa, 2014). In brief, these studies demonstrated reductions in fasting blood glucose, post

prandial blood glucose, and oral glucose tolerance tests.

Seven studies have been conducted on humans, and six of these demonstrated an effect of moringa in reducing blood glucose in patients with type 2 diabetes (**Table 1**). Unfortunately, though, three of these six studies did not report including placebo controls (Sugunabai, 2014; Kumar, 2013; Kiranmayi, 2011) thus reducing their potential impact and increasing the urgency for randomized controlled trials. Five of the seven studies enrolled type 2 diabetes patients as their study population, and the two that did not, report no reduction in blood glucose levels following treatment (Sandoval, 2013; Nambiar, 2010). Further, upon examining the three clinical studies in which placebo controls were used:

1. Giridhari and colleagues (2011) in Tamil Nadu, India, enrolled untreated controls, however there was a large difference between the initial blood glucose of the controls (179) and the experimental group (210). Further, it was unclear precisely what the dose was (2 "tablets" of *M. oleifera*/day), how these groups were allocated, or whether there was randomization.
2. Kumari and colleagues (2010), in Andhra Pradesh, India, were also not clear whether there was blinding, randomization, or how the treatments were allocated. However, in this study significant differences in fasting blood glucose, post prandial blood glucose, and lipid levels (LDL/HDL) were reported. Dose (8 g of dry *M. oleifera* leaf powder per day, for 40 d) was described, and the baseline glucose levels were similar for treated and control diabetic participants.
3. Vanisha Nambiar (2010) and colleagues in Gujurat, India, randomized 40 hyperlipidemic patients to either 4.68 g of dry *M. oleifera* leaves per day or a "no-supplementation" control. It was not made clear whether the study was blinded. Study subject allocation appeared reasonable (based on extensive baseline data), and investigators reportedly observed the subjects eat half of their dose during dinner every day. In the experimental group there were significant decreases in the total cholesterol (TC), LDL/HDL ratio, TC/HDL ratio and non-HDL (total cholesterol minus HDL). There were no changes in any other parameters of the experimental group, including no change in fasting blood glucose. No significant differences were reported in the control group.

ANTI-HYPERTENSIVE ACTIVITY

In the mid-1990s Faizi and colleagues in Karachi, Pakistan, followed up on moringa ethnobotanical observations of Caceres (1992) and others, and on some of the early German phytochemical investigations (Eilert, 1982). They performed extensive isolation and characterization of both the 4-(α-L-rhamnosyloxy)benzyl isothiocyanate (**[4]**) and a series of related rhamnosyloxybenzyl compounds (partial list below), and demonstrated substantial hypotensive activity from many of these compounds using an anesthetized normotensive Wistar rat blood pressure bioassay (Faizi, 1992, 1994a, 1994b, 1995, 1998). The compounds, named somewhat confusingly, include the following:

The first naturally occurring thiocarbamates (Faizi, 1992)

Niaziminin A & B

Niazinin A & B
Niazimicin (e.g., **[5]** in **Fig. 1**)
Nitrile glycosides (Faizi, 1994b):
Niazirin (e.g., **[6]** in **Fig. 1**)
Niazirinin
The first naturally occurring carbamates (Faizi, 1994a):
Niazimin A & B (e.g., **[7]** in **Fig. 1**)
Niazicin A & B.

Certain of these anti-hypertensive rhamnosyloxybenzyl thiocarbamates and isothiocyanates were subsequently shown to be anti-trypanosomal (vs. *Trypanosoma brucei rhodesiense*), as well as cytotoxic against cultured rat skeletal myoblast (L6) cells (Ayyari, 2014). Aqueous and ethanolic leaf extracts containing a presumptive alkaloid have been used to demonstrate hypotensive effects on isolated frog hearts and guinea pig ilea, reducing chronotropic and ionotropic effects (Dangi, 2002). Similarly, studies with spontaneously hypertensive rats concluded that a *Moringa oleifera* leaf extract significantly reduced blood pressure (Kajihara, 2008; Chen, 2012), as did a similar study with normotensive guinea pigs (Mengistu, 2012). Although widely cited in the ethnobotanical and ethnopharmaceutical literature as an anti-hypertensive, as of this writing, there are no relevant clinical studies for this indication.

The second study, performed in India, demonstrated robust cardioprotection by a rhamnopyranosyl vincosamide (an indole alkaloid) from *M. oleifera* leaves, using an isoproterenol induced cardiotoxin model in rats (Panda, 2013). They provided evidence that cardioprotection involved preventing the disruption in cardiac myofibrils by reduction of oxidative stress, leading to improved cardiac contractile function.

CONCLUSIONS

There are thus a plethora of studies that have been published in the decade or so since this author's last review. However, there is still a dearth of well-designed and executed clinical trials in the Western medical tradition. Anecdotes continue to abound, and in the last ten years the popularity of moringa as a "miracle tree" has skyrocketed. The sheer volume of information on ***nutritional benefits*** – coming from all over the world – has indeed given credence to claims of proponents, silenced some critics, and likely saved lives or improved health span of many people who otherwise might not have ingested moringa. The same case cannot, and probably should not be made for moringa's ***medicinal benefits***. Preclinical investigations, and a few small clinical trials are now beginning to support a short list of claims (anti-diabetic, anti-hypertensive, cardioprotective, anti-asthmatic, anti-inflammatory, antioxidant, chemoprotective). The antibiotic claims and studies stand alone, in that many such indications do NOT have an absolute requirement for clinical trials, although modification of clinical outcomes is at the root of many such claims. The author's erstwhile appeal to commercial purveyors of all things moringa NOT to raise false hope in regions and situations where hope is in short supply, still stands. No new evidence suggests anything but positive effects which, if applied in moderation will support overall healthy living. All recent evidence supports the need for further well-designed and

rigorous clinical experiments to validate the most promising claims in human beings.

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