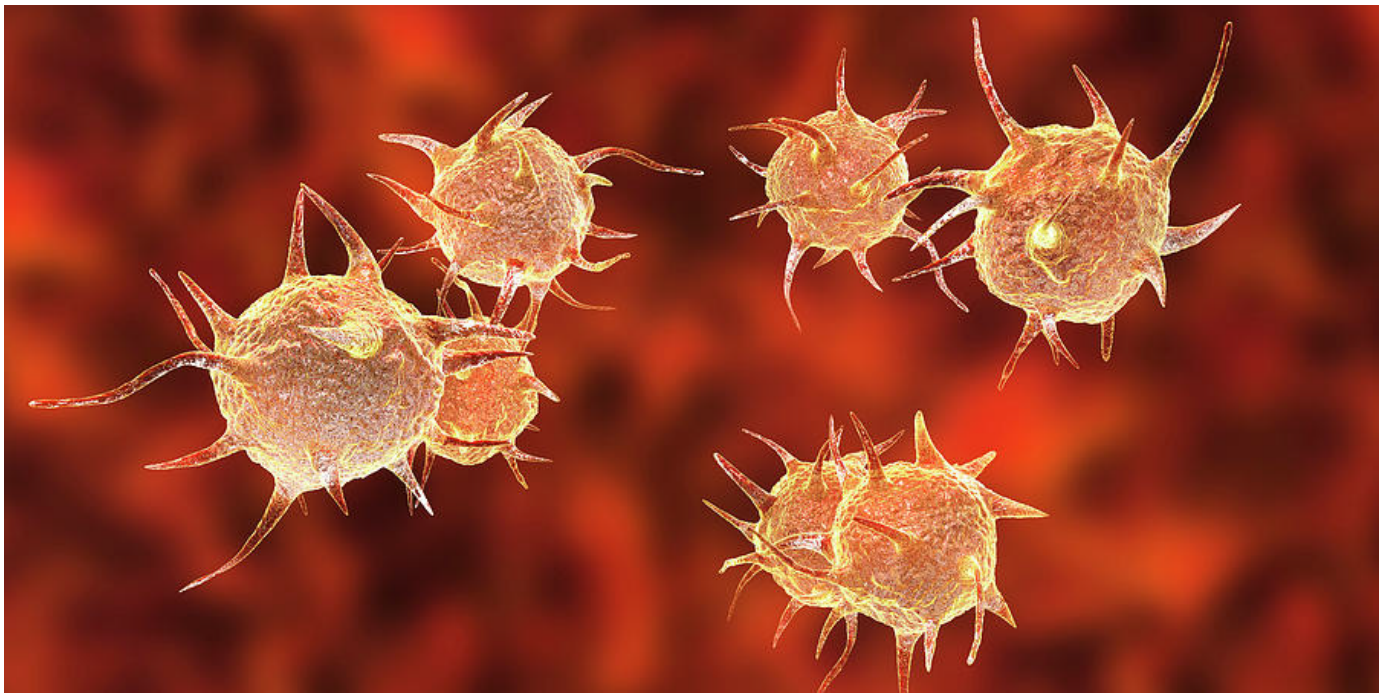
Are you looking for natural protection against viruses? We brought it to you!

Pick up the fight against viruses with our antiviral agent!

Humans have lived with viruses and bacteria for thousands of years. These microscopic creatures surround us, and even some beneficial strains of bacteria live in our bodies, while other - harmful - microorganisms get into the body causing diseases of varying severity.



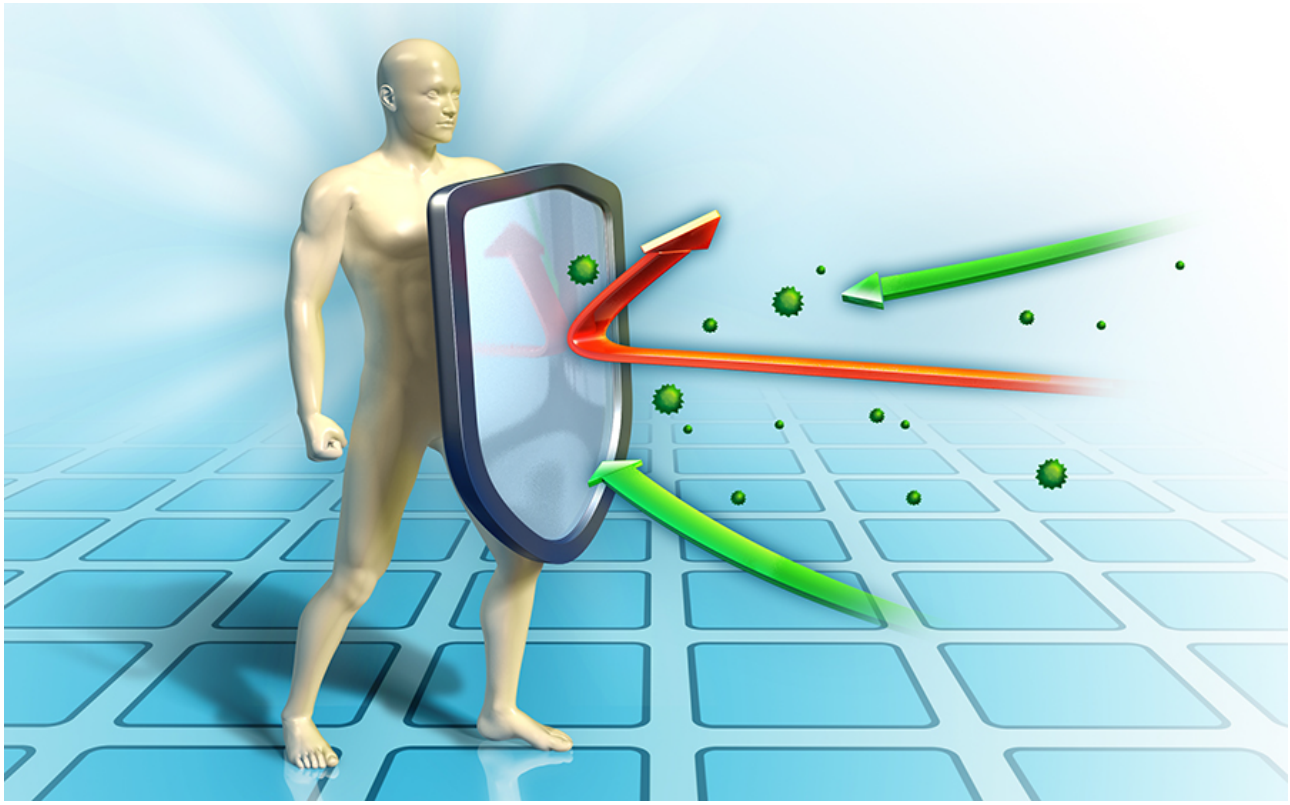
Unlike bacteria, viruses can only survive in a living organism. They can be spread by droplet infection, air, body fluids and possibly by insects. In the case of easily spreading viruses, epidemics can develop.

Elderly, chronic patients, people with weak immune systems are the most exposed to various infections and diseases caused by viruses.

Antibiotics are NOT effective against viruses.

How can we protect ourselves against viruses in a natural way?

As a first step, by strengthening our immune system. If we provide our bodies with the right antioxidants, vitamins and nutrients, our line of defense will be able to repel the attacks of these invading viruses.



With the consumption of herbs and active ingredients of extracts, antiviral properties can limit the growth of viruses,

reduce the risk of bacterial superinfection, and alleviate the course of the disease.

Virus OFF was developed in the spirit of building a natural defense against viruses.

Virus OFF supports the immune system with a powerful combination of vitamins, antioxidants and herbs. It promotes the production of immune bodies, neutralizes harmful substances and cell toxins.

In addition to its anti-inflammatory effect, it enhances immune protection and inhibits the growth of viruses and pathogenic bacteria.

Active ingredients:

Artemisinin extract (90%)

Artemisinin is an extract of Artemisia annua. It is a plant native to Asia that has long been used in traditional Chinese medicine for a variety of health problems. **Dr. Tu isolated an ingredient from artemisia that has also been shown to be effective against parasites, viruses, and certain cancer cell lines. Dr. Tu received the Nobel-prize in Medicine in 2015 for the isolation of Artemisinin, which had proven to be effective in treating even malaria.**

Besides malaria, Artemisinin copes with toxoplasma and flaviviruses, among others. It has anti-inflammatory and antioxidant properties. **Its antiviral effect is manifested by inhibiting the replication of the virus as well as increasing the production of interferons, which are responsible for activating the immune system and the defense mechanism of the surrounding cells.**

Moringa leaf meal-powder

Moringa oleifera is rich in vitamins and minerals. **Its leaf meal-powder contains more than 90 active ingredients and more than 46 antioxidants. It contains all the essential amino acids that are the building blocks of proteins.**

In addition, Moringa supports the immune system and strengthens the human body with two antibiotic-like molecules that inhibit the growth of harmful bacteria.

Vitamin C

Vitamin C contributes to the normal structure of bones and cartilage, teeth, the health of the gums, skin, blood vessels, and the maintenance of the immune system and the body's defenses. **As an antioxidant, it protects the body's cells from the damaging effects of free radicals, as well as inhibits cell aging.** It also contributes to normal metabolism, collagen formation and iron absorption.

Vitamin C reduces the risk of tumorous and cardiovascular disease. It strengthens blood vessel walls, enhances the protection of the skin and the mucous membranes against pus and other harmful organisms. **Vitamin C appears to prevent and treat upper respiratory and systemic infections caused by a virus infection.**

Virus OFF is recommended to:

- people wishing to be protected against viruses
- people infected by COVID-19
- people with immune weakness
- the elderly
- chronic patients, chronic drug users
- metabolic patients (diabetes, obesity, chronic renal failure)
- people working in high-risk environments

Virus OFF

- **Anti-inflammatory**
- **Inhibiting viral replication**
- **Immune defense enhancer**
- **All-natural**
- **Made in the EU**

Packaging: 30 Capsules

Dosage:
One capsule during breakfast with a glass of water

NEW PACKAGING COMING SOON!

Some of the most important studies regarding the ingredients of Virus OFF

We copied below the first pages of all the listed studies, we can provide the complete studies upon request

Artemisinin Inhibits the replication of flaviviruses by promoting the type I interferon production

Artemisinins: their growing importance in medicine

Moringa oleifera: A Review of the Medical Evidence for its Nutritional, Therapeutic, and Prophylactic Properties

The Nutrient content of Moringa Oleifera Leaves

Biochemical and functional properties of Moringa oleifera leaves and their potential as a functional food

Vitamin C and Immune Function

Anticoccidial effects of artemisinin on the Eimeria tenella

Anti-inflammatory, Antioxidant and Antimicrobial Effects of Artemisinin Extracts from Artemisia annua

The Role of Interferon in Viral Infections

Review of the Safety and Efficacy of Moringa oleifera

Health benefits of Moringa oleifera

The Medicinal Qualities of Moringa Oleifera

A double blind randomized controlled trial on the use of Moringa oleifera for augmentation of the volume of breastmilk among non-nursing mothersof preterm infants

Non Drug Delivery System of Plant Extract for the Management of Diabetes: An Antidiabetic Study

Antiproliferation and induction of apoptosis by Moringa oleifera leaf extract on human cancer cells

Moringa Oleifera aqueous leaf extract down-regulates nuclear factor kappaB and increases cytotoxic effect on chemotheraphy in panacreatic cancer cells

In vivo radioprotective effect of Moringa oleifera leaves

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Research paper

Artemisinin inhibits the replication of flaviviruses by promoting the type I interferon production

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ABSTRACT

Flaviviruses are considered to be major emerging human pathogens globally. Currently available anti-flavivirus approaches are ineffective, thus there is a desperate need for broad-spectrum drugs that can be active against existing and emerging flaviviruses. Artemisinin has been found to cause an antiviral effect against several viruses; however, its antiviral effect against flaviviruses remains unexplored. Here the antiviral activity of artemisinin against flaviviruses such as JEV, DENV, and ZIKV was evaluated by measuring the hallmark features of virus replication both *in vitro* and *in vivo*. Mechanistically, the artemisinin-induced antiviral effect was associated with enhanced host type I interferon response. The blocking of interferon signaling inhibited the artemisinin-induced interferon-stimulated genes expression and rescued the artemisinin-suppressed virus replication. This study demonstrated for the first time the antiviral activity of artemisinin against flaviviruses with a novel antiviral mechanism. The therapeutic application of artemisinin may constitute a broad-spectrum approach to cure infections caused by flaviviruses.

1. Introduction

The genus Flavivirus, belonging to the *Flaviviridae* family, comprises many important pathogens that pose a serious threat to the human population annually (Bradley et al., 2017; Carlo et al., 2014). Some flaviviruses, such as Japanese encephalitis virus (JEV) and West Nile virus (WNV), have the potential to infect the host central nervous system (CNS), deemed as neurotropic viruses (Gould and Solomon, 2008; Gregorius et al., 2012). In addition, Zika virus (ZIKV) has recently become a public health concern due to its association with microcephaly in infants and Guillain-Barré syndrome (GBS) in adults (Capasso et al., 2019; Hirsch et al., 2018). Dengue virus (DENV), a causative agent of dengue fever and dengue shock syndrome, also exhibits a potential of being a neurotropic virus (Amorim et al., 2019; Calderón-Peláez et al., 2019).

The pathogenesis of flaviviruses is complex and primarily classified into three distinct phases that include initial infection, viremia, and severe symptoms (Ye et al., 2013). Initial infection and viremia are associated with the replication of viruses in dendritic cells and macrophages (Diamond, 2003; Imran et al., 2019). Then, the host may exhibit various clinical symptoms and even death (Chen et al., 2018). Some flaviviruses such as JEV and WNV breach the blood-brain barrier, and subsequently infect the CNS wherein they trigger the host inflammatory response (Maximova et al., 2018; Mustafá et al., 2019) characterized by gliosis, rampant production of inflammatory cytokines, and eventually neuronal cell damage (Ashraf et al., 2016; Zhang et al., 2015). The interplay between flavivirus pathogenicity and the host innate and adaptive immune responses governs the neuropathogenesis and resultant effect of the flavivirus infection (Ngono et al., 2018; Olagnier et al., 2016).

Natural products serve as beneficial chemical scaffolds for the development of effective therapeutics (Wohlfarth et al., 2009). Artemisinin, for instance, is not only known to be active against malaria, but also to other diseases, including cancer (Wong et al., 2017) and some fungal (Denny et al., 2019), parasitic (Idowu et al., 2018), and viral (Efferth et al., 2008) infections. Several studies provided strong evidence for the antiviral activity of artemisinin and its synthetic analogues against herpesviruses, hepatitis C virus, and human immunodeficiency virus, whereas the pieces of evidence are weaker for papillomaviruses and polyomaviruses (Efferth, 2018; Sharma et al., 2014). However, their mechanisms of antiviral activity are largely unknown. Despite all these research progresses, the antiviral roles of

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Review

Artemisinins: their growing importance in medicine

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Artemisinins are derived from extracts of sweet wormwood (*Artemisia annua*) and are well established for the treatment of malaria, including highly drug-resistant strains. Their efficacy also extends to phylogenetically unrelated parasitic infections such as schistosomiasis. More recently, they have also shown potent and broad anticancer properties in cell lines and animal models. In this review, we discuss recent advances in defining the role of artemisinins in medicine, with particular focus on their controversial mechanisms of action. This safe and cheap drug class that saves lives at risk from malaria can also have important potential in oncology.

Introduction

The remarkable story of the discovery of artemisinin (Figure 1a) and establishment of its antimalarial activity by Chinese scientists represents one of the great discoveries in medicine in the latter half of the 20th century [1]. Through a collaborative effort, collectively referred to as 'Project 523', the Chinese prepared dihydroartemisinin (DHA; Figure 1b), artemether (Figure 1c) and artesunate (Figure 1d) in the 1970s. It is these derivatives [with others, including artemisone (Figure 1e), arteether (Figure 1f) and artelinic acid (Figure 1g), generically known as 'artemisinins'] that are now making a crucial contribution to the management of malaria, one of our most important infections. The magnitude of the malaria problem is represented in the annual burden of 500 million cases. This fascinating class of drug, with structures so different from the classical quinoline antimalarials, is particularly valuable when used in combination with other antimalarials [2,3].

Artemisinins have also been submitted to studies aimed at exploring other uses for this drug class. Artemisinins are active against other parasite species *in vitro*, including protozoa that are phylogenetically unrelated to apicomplexan parasites such as the *Plasmodium* species that cause malaria. Artemisinins also act against metazoan parasites such as *Schistosoma* spp. Their anti-disease properties include potent anticancer activity in *in vitro* studies and in an *in vivo* model of colorectal cancer. Taken together with case reports describing benefits in diverse cancers, a recently published clinical trial of short-term use in lung cancer, their established record of safety in children and adults with malaria, and their permissive cost, there are compelling reasons to study their contribution to management of tumours that require adjuvant and neo-adjuvant therapies. This selective review focuses on rapidly advancing areas of artemisinin science and usage and illustrates why artemisinins have the potential to rival acetylsalicylic acid in the breadth of their anti-disease properties.

There is considerable debate regarding the mechanisms of antimalarial action of artemisinins. An endoperoxide bridge (Figure 1) lies at the heart of antiparasitic activity of artemisinins, although the chemical nature of the interaction between artemisinins (particularly the essential endoperoxide) and parasite target(s) is not well understood. The role of ferrous species in the antimalarial actions of artemisinins is also debated [4] because these cations can catalyse *in vitro* reactions of some artemisinins, including their decomposition in aqueous solutions.

One issue focuses further discussions: is there a single important target for artemisinins in *Plasmodium* spp. or are there multiple targets? Fully synthetic trioxolanes that contain an endoperoxide bridge but lack other features of artemisinins have increased complexity of the debate on mechanisms of action of artemisinins [5]. Many groups, including our own, have reviewed recent developments [6–9]. Clarifying mechanisms of action of artemisinins is important for understanding both how structurally related drugs, such as the fully synthetic trioxolanes, might work and the basis for the development of resistance by parasites to this class of antimalarial. Clearly, a structural appreciation of the putative targets should contribute to the design of derivatives that are not crippled by mutations in target, as exemplified by approaches used in the development of new dihydrofolate reductase inhibitors [10,11].

Rodent malarias are also useful models for understanding possible mechanisms of resistance to different classes of antimalarials [12,13]. Genetic analyses permitted by *Plasmodium chabaudi* infection in mice identified a locus linked to artemisinin resistance that is stable after mosquito passage [14,15]. Linkages to artemisinin resistance have been narrowed down to a de-ubiquitination enzyme (among others) that might function in the endoplasmic reticulum of parasites and be involved in the stress response. Other groups have established stable artemisinin-resistant strains, confirming that artemisinin resistance can develop through

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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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Trees for Life Journal 2005, 1:5

PEER REVIEWED

The Nutrient Content of *Moringa oleifera* Leaves

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Introduction and purpose

Despite considerable interest in the use of *Moringa oleifera* as a nutrient source, gaps and inconsistencies in the information on the nutrient content of this interesting plant remain. There are many reasons for this. The nutrient content of newly harvested plant material naturally varies with soil and climate as well as season and plant age. Differences in processing and storage procedures add more variation; and the use of different analytical techniques amplifies the variation further. For moringa leaves, additional variation has been created over time due to errors created as nutrient content values are incorrectly copied from source to source (30).

The purpose of this review is to summarize the more recent scientific information about the nutrient content of fresh *Moringa oleifera* leaves and dried *Moringa oleifera* leaf powder.

Methods

Literature Search: A search of the literature on the nutrient content of *Moringa oleifera* leaves was performed using PubMed as well as internet searches, with an emphasis on locating original sources of information reported in the last 20 years. Papers in professional publications where the methods were described, and analyses from university and commercial labs specializing in nutrient analysis were included. One unpublished analysis of a sample of moringa leaf powder by a professional laboratory in 2011 was also included.

Types of leaves and processing procedures included: This summary provides data on the nutrient content of mature leaves. For dried leaves, values for sun, shade, and oven dried were utilized; but values for leaves which had been blanched, sulfited, or freeze dried were omitted as these procedures are less commonly available. Several authors provided data for different cultivars or harvests. Some of these authors provided data for each sample, and others averaged the samples together. When the data for individual samples were provided, the individual samples were averaged and used as one value.

Table construction: The nutrient data was compiled into tables providing the nutrient content of 100 grams of fresh leaves or dried leaf powder. A number of papers provided data based on the dry matter content of the leaves only. For these papers, the nutrient values were converted to 100 grams of leaf or leaf powder using the moisture values provided in the paper. If the data were provided on a dry matter basis only and the percent moisture for that sample was not provided, conversion to a the amount in fresh leaves or leaf powder was done using the average moisture content of fresh or dried leaves. For nutrients where more than two independent data sources were identified, the average and standard deviation of the nutrient values provided was calculated. If only two values were available, both were included as a range. If only one value was available, it is provided. For fresh leaves the values were compared to those published in three current reference sources: The United States Department of Agriculture National Nutrient Database[3], Nutritive Value of Indian Foods from the National Institute of Nutrition[19], India, and the World Health Organization West African Food Composition Table[46].

Contribution to Nutrient Needs: The table values were used to estimate the percent of the nutrient needs of a 1–3 year-old child which would be provided by a typical serving—1 tablespoon of dried leaf powder or 1 cup of raw fresh leaves. When no original source data were available for a particular nutrient, the FAO West African Food Composition Table values were used.

Results

Fresh Leaves

There is considerable variability in the nutrient values reported, especially for minerals and fat-soluble vitamins (Table 1). For the B vitamins, no recently published values were identified. Nutrient values are provided on a 100 gram basis, but for practical purposes it is important to note that this is substantially more than one person would consume as a single serving.

Dried Leaves

As is the case for fresh leaves, the reported nutrient content of dried leaves varies considerably (Table 2). Dried leaves are not included in the United States Department of Agriculture National Nutrient Database[3],The Indian Council of Medical Research Nutritive Value of Indian Foods[18], or the Food and Agriculture Organization West African Food Composition Table[46]. Nutrient values are provided on a 100 gram basis, but for practical purposes 5 grams (15 mL or 1 tablespoon) is a reasonable serving size.

Contribution to Nutrient Needs

Table 3 provides a comparison of the nutrient content of one tablespoon (5 grams) of dried moringa leaf powder and 1 cup (20 grams) of fresh leaves to the nutrient needs of 1–3 year old children. Both dried and fresh leaves appear to contain a substantial amount of the magnesium, iron, folate, and vitamins B-6, A, C, and E young children need. They are also a moderately good source of calcium, niacin, protein and dietary fiber. A 1 cup serving of fresh, raw leaves appears to be a better source of a number of vitamins, especially vitamin C. However, vitamin levels will likely drop if the leaves are cooked. It is important to note that for many of these nutrients the data is limited or highly variable.

Table 4 provides a comparison of the nutrient content of one tablespoon (5 grams) of dried moringa leaf powder and 1 cup (20 grams) of fresh leaves to the nutrient needs of pregnant and lactating women. Both fresh and dried leaves provide substantial sources

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Full Length Research Paper

Biochemical and functional properties of *Moringa oleifera* leaves and their potential as a functional food

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BACKGROUND: Moringa is a tree of a not well-understood plant since it has not been fully studied all over the world. Therefore, the aim of the present study is to evaluate the chemical as well as functional properties of the Egyptian Moringa oleifera leaves. Such leaves can be used as a functional food ingredient in the food and pharmaceutical applications. RESULTS: The proximate analysis showed that moringa leaves are rich in: fiber, protein, carbohydrate and energy contents (11.23±0.16, 9.38±0.23, 56.33±0.27 g.100g-1 and 332.68±0.06 KCal, respectively). Moringa is a good source for essential amino acids especially Lysine (69.13±0.13mg.100g-1), essential minerals such as Na (289.34±0.35), K (33.63±0.24), Mg (25.64±0.25) Ca (486.23±0.11), P (105.23±0.32) and Fe (9.45±0.16) mg.100g -1 respectively and vitamins (A=13.48±0.51, B1=0.05±0.28, B2= 0.8±0.25, B3= 220±0.42, C= 245.13±0.46 and E= 16.80±0.24 mg.100g respectively). It is appeared using HPLC that methanol 70% is the most suitable solvent for extraction of phenolic compounds from moringa leaves (. Scavenging activity results confirmed that Moringa leaves extract might be a potent source of natural antioxidants with a high human health benefits. Antimicrobial activity results indicate that Moringa leaves extracts may be used as an antimicrobial agent with reasonable safety margins to inhibit bacterial growth in pharmaceutical and food applications. CONCLUSION: Moringa is considered as a nutrient-rich plant especially in its leaves. Such leaves might be used to combat malnutrition, especially among infants and nursing mothers.

Keywords: *Moringa oleifera*, biochemical analyses, phenolic content, antioxidant, antimicrobial Pathogens.

INTRODUCTION

Moringa oleifera is a perennial tree, still considered as among underutilized plant and falls under Moringa ceae family. The plant is also known as Drumstick, Sahjan or Sohanjana in India. All plant parts are having remarkable range of some functional and nutraceutical properties (Singh *et al,* 2012) make this plant diverse biomaterials for food and allied uses. The leaves, flowers and fruits of this plant are used in the preparation of several delicacies in Indian subcontinent. Associated with high nutritional value of its edible portions pave a way in making this plant more popular as an important food source in order to combat protein energy malnutrition problem prevailed in most of the under developed and developing countries of the world. Presence of various types of antioxidant compounds make this plant leaves a valuable source of natural antioxidants (Anwar *et al,* 2007) and a good source of nutraceuticals and functional components as well (Makkar and Becker, 1996). There are considerable variations among the

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nutrients

MDPI

Review

Vitamin C and Immune Function

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Abstract: Vitamin C is an essential micronutrient for humans, with pleiotropic functions related to its ability to donate electrons. It is a potent antioxidant and a cofactor for a family of biosynthetic and gene regulatory enzymes. Vitamin C contributes to immune defense by supporting various cellular functions of both the innate and adaptive immune system. Vitamin C supports epithelial barrier function against pathogens and promotes the oxidant scavenging activity of the skin, thereby potentially protecting against environmental oxidative stress. Vitamin C accumulates in phagocytic cells, such as neutrophils, and can enhance chemotaxis, phagocytosis, generation of reactive oxygen species, and ultimately microbial killing. It is also needed for apoptosis and clearance of the spent neutrophils from sites of infection by macrophages, thereby decreasing necrosis/NETosis and potential tissue damage. The role of vitamin C in lymphocytes is less clear, but it has been shown to enhance differentiation and proliferation of B- and T-cells, likely due to its gene regulating effects. Vitamin C deficiency results in impaired immunity and higher susceptibility to infections. In turn, infections significantly impact on vitamin C levels due to enhanced inflammation and metabolic requirements. Furthermore, supplementation with vitamin C appears to be able to both prevent and treat respiratory and systemic infections. Prophylactic prevention of infection requires dietary vitamin C intakes that provide at least adequate, if not saturating plasma levels (i.e., 100–200 mg/day), which optimize cell and tissue levels. In contrast, treatment of established infections requires significantly higher (gram) doses of the vitamin to compensate for the increased inflammatory response and metabolic demand.

Keywords: ascorbate; ascorbic acid; immunity; immune system; neutrophil function; microbial killing; lymphocytes; infection; vitamin C

1. Introduction

The immune system is a multifaceted and sophisticated network of specialized organs, tissues, cells, proteins, and chemicals, which has evolved in order to protect the host from a range of pathogens, such as bacteria, viruses, fungi, and parasites, as well as cancer cells [1]. It can be divided into epithelial barriers, and cellular and humoral constituents of either innate (non-specific) and acquired (specific) immunity [1]. These constituents interact in multiple and highly complex ways. More than half a century of research has shown vitamin C to be a crucial player in various aspects of the immune system, particularly immune cell function [2,3].

Vitamin C is an essential nutrient which cannot be synthesized by humans due to loss of a key enzyme in the biosynthetic pathway [4,5]. Severe vitamin C deficiency results in the potentially fatal disease scurvy [6]. Scurvy is characterized by weakening of collagenous structures, resulting in poor wound healing, and impaired immunity. Individuals with scurvy are highly susceptible to potentially fatal infections such as pneumonia [7]. In turn, infections can significantly impact on vitamin C levels due to enhanced inflammation and metabolic requirements. Early on, it was noted that scurvy often

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Korean J Vet Res(1995) 35(1):123-130

Artemisinin의 *Eimeria tenella*에 대한 항콕시듐 효과

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(1994년 10월 18일 접수)

Anticoccidial effects of artemisinin on the *Eimeria tenella*

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Abstract : Artemisinin, a sesquiterpene lactone, is isolated from the leafy portion of the *Artemisia annua* and has been known to be effective against *Plasmodium* species. Since the genera of *Plasmodium* and *Eimeria(E) tenella* are included the same order, Eucoccidiidae, it is presumed that artemisinin may also be effective against *E tenella*.

In order to study the anticoccididal effects of artemisinin, the chickens inoculated with *E tenella* were treated with artemisinin at different concentrations as feed additive and the results were compared to those of non-medicated, infected control (NIC) and non-medicated, non-infected control (NNC) group.

Artemisinin demonstrated anticoccidial effects by showing, compared to NIC group, improved results in all parameters, such as bloody diarrhea, lesion scores, the numbers of excreted oocystis in feces, body weight gain and feed conversion rate. Anticoccidial index (ACI) of artemisinin treated group (5ppm~50ppm) was higher than that of NIC group. Improvements were greatest in the group treated with artemisinin 50ppm with an ACI of 147.6.

These results indicate that artemisinin has anticoccidial effects on the *Eimeria tenella*.

Key words : Artemisinin, *Eimeria tenella*, anticoccidial effects, anticoccidial index

서 론

사람을 포함한 모든 가축과 가금에 감염되는 *Eimeria*속 콕시디아는 특히 닭에 기생하는 종류가 병원성이 높아 양계농가에 커다란 경제적 피해를 가져다 주는 원충성 질병으로써, 이러한 질병은 국내에서도 만연되어 1959년에 5개종(*E tenella, E acervulina, E maxima, E necatrix, E mitis*)이 처음으로 이와 문에[22] 의해 보고된 후 *E praecox*가 장에[23] 의해, *E brunetti*와 *E mivati*가 최와 이에[25] 의해 보고되어 국내에서도 8종의 존재가

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Artemisinins: their growing importance in medicine

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Anti-inflammatory, Antioxidant and Antimicrobial Effects of Artemisinin Extracts from *Artemisia annua* L.

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The anti-inflammatory, antioxidant, and antimicrobial properties of artemisinin derived from water, methanol, ethanol, or acetone extracts of *Artemisia annua* L. were evaluated. All 4 artemisinin-containing extracts had anti-inflammatory effects. Of these, the acetone extract had the greatest inhibitory effect on lipopolysaccharide-induced nitric oxide (NO), prostaglandin E_2 (PGE_2), and pro-inflammatory cytokine (IL-1β, IL-6, and IL-10) production. Antioxidant activity evaluations revealed that the ethanol extract had the highest free radical scavenging activity, (91.0±3.2%), similar to α-tocopherol (99.9%). The extracts had antimicrobial activity against the periodontopathic micro-organisms *Aggregatibacter actinomycetemcomitans*, *Fusobacterium nucleatum* subsp. *animalis*, *Fusobacterium nucleatum* subsp. *polymorphum*, and *Prevotella intermedia*. This study shows that *Artemisia annua* L. extracts contain anti-inflammatory, antioxidant, and antimicrobial substances and should be considered for use in pharmaceutical products for the treatment of dental diseases.

Key Words: Anti-inflammatory effect, Anti-microbial activity, Antioxidant activity, Artemisinin

INTRODUCTION

There has been an increase is the reevaluation of traditional medicinal plants worldwide, with extensive research on various plant species and their therapeutic properties being carried out. Traditional medicinal plant remedies have been highlighted as alternative medicines that are less likely to cause adverse side effects, unlike synthetically generated chemical substances [1]. *Artemisia annua* L. (Asteraceae) is an annual herb native to Asia, and has been used for many centuries in traditional Asian medicine for the treatment and prevention of fever and chills [2]. A variety of compounds have been extracted from *Artemisia annua* L. such as sesquiterpenoids, flavonoids, coumarins, lipids, phenolics, purines, steroids, triterpenoids, aliphatics, and artemisinin [3].

The main component in *Artemisia annua* L., artemisinin, has the formula $C_{15}H_{22}O_{15}$ and contains a peroxide bridge (C-O-O-C) (Fig. 1). Artemisinin has been widely used for the treatment of malaria for the past two decades [4]. Additionally, artemisinin is known to have antibacterial, antifungal, antileishmanial, antioxidant, antitumor, and anti-inflammatory activity [5-7].

During inflammation, macrophages are key immune cells that regulate inflammatory responses. Inflammatory responses to pathogenic microbes rely on innate and adaptive im-

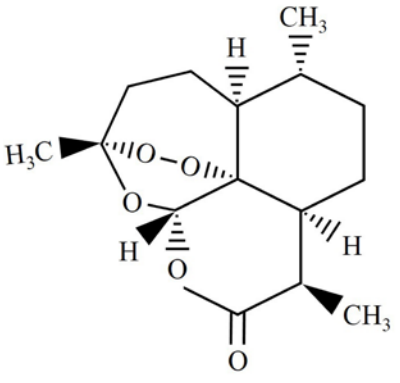

Fig. 1. The structure of artemisinin.

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ABBREVIATIONS: NO, nitric oxide; IL, interleukin; PGE_2, prostaglandin E_2; LPS, lipopolysaccharide; GAE, gallic acid equivalents; DPPH, 2,2-diphenyl-1-picrylhydrazyl hydrate; DMSO, dimethyl sulfoxide; DMEM, Dulbecco's modified Eagle's medium; ELISA, Enzyme-linked immunosorbent assay.

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The Role of Interferon in Viral Infections

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Summary. Interferon, a product of mammalian tissues, was originally described as an antiviral agent over twenty years ago. Only in the past few years has evidence started to accumulate that interferon actually played a role in vivo in natural virus infections.

Initially, evidence was accumulated showing that interferon could inhibit the replication of many viruses in vitro. The interferon, through induction of a second antiviral protein, could inhibit in vitro viral transcription or translation. Later, indirect evidence for an effect of interferon on in vivo viral infections was obtained by showing that (a) a temporal relationship existed between the appearance of interferon in viral infections and the progress of the infection and (b) treatment of virally infected animals with exogenous interferon or interferon inducer often resulted in less severe infections.

The most recent and direct evidence for a role for interferon in natural viral infections involves the use of an anti-interferon globulin. In several cases, injection of the anti-interferon globulin into animals infected with a wide variety of viruses resulted in a severely altered course of infection. These studies suggest that interferon is directly involved in the progress of viral infections. The involvement of the interferon in the viral infections could be a direct effect of the interferon on viral replication, or an interaction of the interferon with other host defenses, such as the immune system.

I. Introduction

Interferon was originally described over twenty years ago when Isaacs and Lindenmann observed an antiviral activity in media in which were suspended

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REVIEW

Review of the Safety and Efficacy of *Moringa oleifera*

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Moringa oleifera **leaves, seeds, bark, roots, sap, and flowers are widely used in traditional medicine, and the leaves and immature seed pods are used as food products in human nutrition. Leaf extracts exhibit the greatest antioxidant activity, and various safety studies in animals involving aqueous leaf extracts indicate a high degree of safety. No adverse effects were reported in association with human studies. Five human studies using powdered whole leaf preparations of *M. oleifera* have been published, which have demonstrated anti-hyperglycemic (antidiabetic) and anti-dyslipidemic activities. These activities have been confirmed using extracts as well as leaf powders in animal studies. A rapidly growing number of published studies have shown that aqueous, hydroalcohol, or alcohol extracts of *M. oleifera* leaves possess a wide range of additional biological activities including antioxidant, tissue protective (liver, kidneys, heart, testes, and lungs), analgesic, antiulcer, antihypertensive, radioprotective, and immunomodulatory actions. A wide variety of polyphenols and phenolic acids as well as flavonoids, glucosinolates, and possibly alkaloids is believed to be responsible for the observed effects. Standardization of products is an issue. However, the results of published studies to date involving *M. oleifera* are very promising. Additional human studies using standardized extracts are highly desirable. © 2015 The Authors Phytotherapy Research Published by John Wiley & Sons Ltd.**

Keywords: Moringa oleifera; leaf extract; anti-hyperglycemic; anti-dyslipidemic; antioxidant; chemoprotectant.

INTRODUCTION

Moringa oleifera Lam. is a tree that grows widely in many tropical and subtropical countries. It is grown commercially in India, Africa, South and Central America, Mexico, Hawaii, and throughout Asia and Southeast Asia. It is known as the drumstick tree based on the appearance of its immature seed pods, the horseradish tree based on the taste of ground root preparations, and the ben oil tree from seed-derived oils. In some areas, immature seed pods are eaten, while the leaves are widely used as a basic food because of their high nutrition content (Thurber and Fahey, 2009; Mbikay, 2012; Razis *et al.*, 2014). No human clinical trials have been conducted looking at the efficacy of *M. oleifera* for treating undernutrition.

Seeds, leaves, oil, sap, bark, roots, and flowers are widely used in traditional medicine. *Moringa* leaves have been characterized to contain a desirable nutritional balance, containing vitamins, minerals, amino acids, and fatty acids (Moyo *et al.*, 2011; Teixeira *et al.*, 2014; Razis *et al.*, 2014). Additionally, the leaves are reported to contain various types of antioxidant compounds such as ascorbic acid, flavonoids, phenolics, and carotenoids (Alhakmani *et al.*, 2013; Vongsak *et al.*, 2014). According to several commentaries (Anwar *et al.*, 2007; Mbikay, 2012; Razis *et al.*, 2014), various preparations of *M. oleifera* are used for their antiinflammatory, antihypertensive, diuretic, antimicrobial, antioxidant, antidiabetic, antihyperlipidemic, antineoplastic, antipyretic, antiulcer, cardioprotectant, and hepatoprotectant activities. The therapeutic potential of *M. oleifera* leaves in treating hyperglycemia and dyslipidemia was reviewed by Mbikay (2012). Razis *et al.* (2014) summarized potential health benefits of *M. oleifera*, focusing on their nutritional content as well as antioxidant and antimicrobial characteristics.

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SAFETY STUDIES

No adverse effects were reported in any of the human studies that have been conducted to date, and these studies will be described in more detail later in the text. Furthermore, various preparations have been and continued to be used around the world as foods and as medicinals without the report of ill effects. Several animal studies have specifically assessed the potential toxicity of various preparations on *M. oleifera*.

The safety of an aqueous leaf extract given orally to rats at doses of 400, 800, 1600, and 2000 mg/kg body weight was examined (Adedapo *et al.*, 2009). The treatment was either an acute single dose or given daily for 21 days except the highest dose. Various parameters were assessed including blood cell counts and serum enzyme levels. The authors concluded that consumption of *M. oleifera* leaves at doses of up to 2000 mg/kg were safe. A dose-dependent decrease in body weights of the rats occurred over the 21 days of the study.

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MINI-REVIEW

Health Benefits of *Moringa oleifera*

Ahmad Faizal Abdull Razis[1,2]*, Muhammad Din Ibrahim[2], Saie Brindha Kntayya[2]

Abstract

Phytomedicines are believed to have benefits over conventional drugs and are regaining interest in current research. *Moringa oleifera* is a multi-purpose herbal plant used as human food and an alternative for medicinal purposes worldwide. It has been identified by researchers as a plant with numerous health benefits including nutritional and medicinal advantages. *Moringa oleifera* contains essential amino acids, carotenoids in leaves, and components with nutraceutical properties, supporting the idea of using this plant as a nutritional supplement or constituent in food preparation. Some nutritional evaluation has been carried out in leaves and stems. An important factor that accounts for the medicinal uses of *Moringa oleifera* is its very wide range of vital antioxidants, antibiotics and nutrients including vitamins and minerals. Almost all parts from Moringa can be used as a source for nutrition with other useful values. This mini-review elaborates on details of its health benefits.

Keywords: *Moringa oleifera* - anti-fibrotic - anti-inflammatory - anti-microbial - anti-hyperglycemic - antioxidant

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Introduction

Moringa (*Moringa oleifera* Lam). is a type of local medicinal Indian herb which has turn out to be familiar in the tropical and subtropical countries. The other terms used for Moringa are Horseradish tree, Mulangay, Mlonge, Benzolive, Drumstick tree, Sajna, Kelor, Saijihan and Marango. *Moringa oleifera* is shown in scientific division to become from Kingdom: Plantae, Division: Magnoliphyta, Class: Magnoliopsida, Order: Brassicales, Family: Moringaceae, Genus: Moringa, Species: M. oleifera (Fahey, 2005).

Moringa oleifera is one of the vegetables of the Brassica order and belongs to the family Moringaceae. The Moringaceae is a single genus family with 13 known species (Khawaja et al., 2010). *Moringa oleifera* is a small native tree of the sub-Himalayan regions of North West India, which is now indigenous to many regions in Africa, Arabia, South East Asia, the Pacific and Caribbean Islands and South America. Traditionally, besides being a daily used vegetable among people of these regions, the Moringa is also widely known and used for its health benefits. Among commoners, it has earned its name as 'the miracle tree' due to its amazing healing abilities for various ailments and even some chronic diseases. Several investigations were carried out to isolate bioactive compounds from various parts of the plant due to its various applications (Guevara et al., 1999). Therefore, herbal plants in medicine or known as phytomedicine are still trustworthy and widely applied as one of the alternative way in medicinal field due to its affordable cost (Abalaka et al., 2009).

For centuries and in many cultures around the world, the medicinal usage of the Moringa has been used to treat problems such as skin infections, anaemia, anxiety, asthma, blackheads, blood impurities, bronchitis, catarrh, chest congestion, cholera and many other illnesses (Khawaja et al., 2010; Hamza, 2010; Singh et al., 2012). *Moringa oleifera* also consists of anti-inflammatory, anti-spasmodic, anti-hypertensive, anti-tumour, anti-oxidant, anti-pyretic, anti-ulcer, anti-epileptic, diuretic, cholesterol lowering, renal, anti-diabetic, (Paliwal et al., 2011; Sharma et al., 2012) and hepatoprotective activities (Lai et al., 2010; Huang et al., 2012). It has also long been labelled for its great cosmetic value in which in recent years, the Moringa has commonly been found to be used in various health care products including body and hair moisturisers and conditioners. It was also discovered that Moringa oil was used in skin ointments ever since the Egyptian times. The Moringa was claimed to be 'the most nutrient-rich plant yet discovered' by Khawaja et al. (2010).

Nutritional Composition

The Moringa's incredible medicinal usage which is claimed by many cultures and communities based on real-life experiences are now slowly being confirmed by science. Through research, the Moringa was found to contain many essential nutrients, for instance, vitamins, minerals, amino acids, beta-carotene, antioxidants, anti-inflammatory nutrients and omega 3 and 6 fatty acids (Fahey, 2005; Hsu et al., 2006; Kasolo et al., 2010).

Nutrition content of a plant plays an essential function in medicinal, nutritional, and therapeutic properties (Al-

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FEATURES

The Medicinal Qualities of *Moringa Oleifera*

■ ***Bobbie Posmontier, PhD, CNM***

Moringa oleifera is an ancient tree that is historically known to possess numerous medicinal qualities. The purpose of this article is to familiarize nurses with the use of *Moringa oleifera* in traditional medicine, present the findings of evidence-based studies, and provide implications for clinical practice and further research. **KEY WORDS:** *complementary and alternative medicine*, *CAM*, Moringa oleifera, *traditional medicine*

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Moringa oleifera is a fast-growing tree indigenous to India, Pakistan, Bangladesh, and Afghanistan, known for its medicinal qualities for thousands of years.[1] It was first mentioned as "Shigon" in the Shushruta Sanhita, an ayurvedic medical text written in the first century AD.[2] *Moringa oleifera* was also used as a medicinal agent by the Romans, Greeks, and Egyptians.[3] In addition, it has been widely used in the Unani and Siddha medicine systems.[4] Now cultivated in many parts of the world, including the Philippines, the Sudan, the continent of Africa, tropical Asia, Latin America, the Caribbean, Polynesia, West Indies, Saudi Arabia, Madagascar, Sri Lanka and Florida, *Moringa oleifera* is commonly used as a traditional medicine in the treatment of a variety of illnesses. The National Center for Complementary and Alternative Medicine reported in 2007 that approximately 38% or 4 in 10 adults in the United States have used natural plant products such as *Moringa oleifera* for medicinal purposes in the past year.[5] In addition, the World Health Organization indicates that 80% of some African and Asian countries utilize herbal medicines for primary health care.[6] The purpose of this article is to familiarize nurses with its medicinal uses, summarize evidence-based studies on its risks and benefits, and suggest areas for further research.

ABOUT *MORINGA OLEIFERA*

Moringa oleifera, 1 of 13 species of the Moringaceae family, is a fast-growing, perennial, softwood tree that reaches a height of 10 to 50 ft.[1] It commonly grows in humid tropical or hot arid climates in hedges, sandy riverbeds, and near streams. Drought has little effect on its growth. *Moringa oleifera* is known by many names, including drumstick tree, horseradish tree, *Moringa pterygosperma*, benzolive, kelor, marango, mlonge, moonga, mulangay, nébéday ("never die"), saijhan, sajna, ben oil, Shigon, Mothers Best Friend, and Shagara al Rauwaq.[1,3] All parts of *Moringa oleifera* are edible, including the leaves, flowers, fruit, bark, gum, seed, seed oil, and root.[7] The mature fruit is a pod, approximately 1 ft in length, and contains 10 to 15 seeds.[3] The leaves can be eaten raw, cooked, or stored as a powder without loss of nutritional value. In addition to its medicinal uses, which will be reviewed later, *Moringa oleifera* has been used for correction of soil deficiencies, fertilizer, and as food for domesticated animals. Other uses include cleaning agents, biofuel, blue dye, living fence, honey and sugar clarifier, pesticide, pulp for making paper, rope, tannin for tanning hides, and water purification.[3] The essential oil (ben oil) from *Moringa oleifera* has also been used for its ability to resist rancidness, salad oil, machine lubricant, perfume, and hair-product ingredient.

NUTRIENT ANALYSIS

Moringa oleifera contains high levels of β-carotene, protein, vitamin C, calcium, iron, potassium, all essential amino acids, and antioxidants (ascorbic acid, flavenoids, phenolics, caratenoids, etc) (Table 1).[8] In

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A double-blind, randomized controlled trial on the use of *malunggay (Moringa oleifera)* for augmentation of the volume of breastmilk among non-nursing mothers of preterm infants

Ma. Corazon P. Estrella, M.D., Jacinto Blas V. Mantaring III, M.D., Grace Z. David, M.D., Michelle A. Taup, M.D.*

ABSTRACT

OBJECTIVES: To determine if there is a significant difference in the volume of breastmilk on postpartum days 3 to 5 among mothers with preterm infants who take *malunggay (Moringa oleifera)* leaves compared to those who were given placebo.

SETTING: Tertiary government hospital

STUDY DESIGN: Double-blind, randomized controlled trial

PATIENTS AND METHODS: A total of 68 postpartum mothers admitted at a tertiary government hospital and whose infants had pediatric ages of less than 37 weeks and admitted to the NICU for tube feedings were included in the study. The mothers were randomized to receive *Moringa oleifera* (encapsulated in a commercial preparation containing 250 mg of leaves) or an identical capsule containing flour as placebo. They were asked to pump their breasts using a standardized breastpump from day 1 to day 5 postpartum. The mothers were given capsules on postpartum days 3 to 5 . The contents of the capsules were unknown to both Investigator and subjects. T-test was used to determine differences in baseline variables. Chi-square was used to determine difference in baseline proportions between groups. One-way ANOVA was used to determine if there were significant differences in the volume of breastmilk between treatment and control groups. A p-value of <0.05 was considered significant.

RESULTS: There was a trend towards increased milk production among those on *Moringa oleifera* leaves (Day 3: 114.1 ml ± 62.9 vs. 87.2 ± 49.1; Day 4: 190 ml ± 103.5 vs. 128.8 ± 84.9; Day 5: 319.7 ml ± 154.10 vs. 120.2 ± 54.7). This was statistically significant on Day 4 ($p = 0.007$) and on Day 5 ($p = 0.000$).

CONCLUSION: Moringa oleifera leaves increase milk production on postpartum days 4 to 5 among mothers who delivered preterm infants.

KEYWORDS: breastmilk, *malunggay*

Feeding breastmilk to premature infants is of interest because of its potential nutritional and immunologic benefits. The prevailing consensus is that early milk produced by women who deliver prematurely is more appropriate for VLBW infants than is donor milk from later stages of lactation, and that is to feed each infant milk produced by his/her mother minimizes potential risks from contaminants. To implement this consensus, mothers of VLBW infants must produce sufficient milk to meet the nutritional needs imposed by the accelerated growth rates of their infants. More often than not, however, the biggest obstacle to the initiation of feeding breast milk is collection. Most mothers after initiating expression of breastmilk on the first few days after birth complain of insufficient volume of breastmilk. This complaint has prompted most mothers to use milk formula, shift to bottle feeding, and discontinue breastfeeding.

Little quantitative data are available with which to evaluate protocols for the initiation and maintenance of successful lactation during the long periods of infant-mother separation that commonly follow premature delivery. De Carvalho, et al (1985)[1] reported that the frequency of milk expression was associated positively with milk production in mothers of premature infants, but the mean volumes of milk produced by women in that study did not meet the nutrient needs of VLBW infants and declined production are common problems associated with premature delivery.

A pilot study was done by the authors among 10 mothers who delivered neonates whose pediatric ages were less than 37 weeks in a tertiary government hospital. The total amount of volume of breastmilk expressed for 24 hours was plotted from Day 1 to Day 7. Results showed that there was a steady increase in milk volume from days 1 to 3 after which a constant or lower volume was recovered from days 3 to 5. The authors determined that 3 to 5 days postpartum is critical for the success of implementing a breastfeeding program among mothers who deliver preterm

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Novel Drug Delivery System of Plant Extract for the Management of Diabetes: An Antidiabetic Study

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ABSTRACT. *Context: Moringa oleifera* leaves have been reported to have antidiabetic, antitumor, hypotensive, anti-inflammatory, and diuretic properties as well as antibiotic, antitryponosomal, hypotensive, and anti-inflammatory activities. They are outstanding source of vitamins A, B, C, and also rich in calcium and protein. *Objectives:* The aim of the study was to formulate *Moringa oleifera* powdered leaf tablets and to study the in vitro and in vivo properties of the herbal drug from the tablets. *Material and methods:* The *Moringa oleifera* powdered leaf was formulated into tablets by direct compression. The in vitro properties of the tablets were evaluated in terms of uniformity of weight, hardness, disintegration time, friability and dissolution rate. Also, the in vivo antidiabetic properties of *Moringa oleifera* tablets were studied using Wistar rats. *Results and discussion:* The results of the tablets' weight uniformity gave percentage deviation that was below 5%. Tablet disintegration time ranged from 11.50 ± 0.11 to 14.90 ± 0.27 min. The tablets exhibited friability results lower than 2% and exhibited about 82% to 83% release of the extract at 15 min. In vivo antidiabetic studies showed that at 8 hr, about 54.4% and 40% of glucose reduction occurred in groups that received *Moringa oleifera* tablets and glibenclamide (Daonil®) respectively, while the negative control groups showed increased blood glucose level with time. *Conclusions:* This study has shown that *Moringa oleifera* leaves formulated into tablets possess good physicochemical and antidiabetic properties in addition to being a supplement.

KEYWORDS. anemia, antidiabetic properties, direct compression, *Moringa oleifera*, tablets

INTRODUCTION

Moringa oleifera Linn. (Moringaceae) is native to the Indian subcontinent and naturalized in tropical and subtropical areas around the world and has been an ingredient of Indian diet for centuries (Alam, Singh, & Singh, 2011). This rapidly growing

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

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PEER REVIEWED

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Moringa appears to be a nutritional and medicinal cornucopia. The author, a Western-trained nutritional biochemist who has studied some of Moringa's phytochemicals for almost a decade, gives a brief commentary and extensive references, and presents a table introducing some of the tree's most intriguing features. This is the first article in a series, and will be followed by more detailed analysis of some of the strongest claims made regarding this edible plant.

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

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Antiproliferation and induction of apoptosis by *Moringa oleifera* leaf extract on human cancer cells

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ABSTRACT

Medicinal plants provide an inexhaustible source of anticancer drugs in terms of both variety and mechanism of action. Induction of apoptosis is the key success of plant products as anticancer agents. The present study was designed to determine the antiproliferative and apoptotic events of *Moringa oleifera* leaf extract (MLE) using human tumor (KB) cell line as a model system. KB cells were cultured in the presence of leaf extracts at various concentrations for 48 h and the percentage of cell viability was evaluated by MTT assay. MLE showed a dose-dependent inhibition of cell proliferation of KB cells. The antiproliferative effect of MLE was also associated with induction of apoptosis as well as morphological changes and DNA fragmentation. The morphology of apoptotic nuclei was quantified using DAPI and propidium iodide staining. The degree of DNA fragmentation was analyzed using agarose gel electrophoresis. In addition, MLE at various concentrations was found to induce ROS production suggesting modulation of redox-sensitive mechanism. Eventually, HPTLC analysis indicated the presence of phenolics such as quercetin and kaempferol. Thus, these findings suggest that the leaf extracts from *M. oleifera* had strong antiproliferation and potent induction of apoptosis. Thus, it indicates that *M. oleifera* leaf extracts has potential for cancer chemoprevention and can be claimed as a therapeutic target for cancer.

1. Introduction

Apoptosis, the process of programmed cell death, is now recognized as a vital process in the regulation of tissue development and homeostasis, which is highly conserved throughout evolution (Ghobrial et al., 2005). Homeostasis between cell death and cell proliferation is required to maintain normal state. Disruption of this cellular balance or dysregulation of controlling mechanisms can lead to human disease including cancer. Hence clinically many diseases are the ultimate result of either deficient apoptosis or excessive apoptosis (Thompson, 1995).Therefore apoptosis is necessary for normal developmental processes, maintenance of homeostasis, and elimination of damaged cells. During the past two decades, the molecular mechanism of apoptosis has been extensively studied and has gained recognition as an ideal way to eliminate precancerous and cancer cells. Many studies have reported associations between apoptosis and cancer, in as much as the apoptosis-inducing agents potent in the treatment of various cancer cells which are being appreciated as weapons for the management of cancer (Schmitt, 2003).

Cancer is the largest single cause of death in both men and women. Recently, resistance to anticancer drugs has been observed. Therefore, research and development of more effective and less toxic drugs by the pharmaceutical industry has become necessary. Chemical as well as biological agents that induce apoptosis have been reported to be promising interventions in the management of malignant cancer. Many substances derived from dietary or medicinal plants are known to be effective and versatile chemo preventive and antitumor agents in a number of experimental models of carcinogenesis. There is an increasing evidence for an association between a high consumption of fruits and vegetables and reduced risk of cancer (La Vecchia et al., 1997; Morse et al., 2000). Antiproliferative screening of models *in vitro* provide important preliminary data to help select plant extracts with potential antineoplastic properties for future study.

Moringa oleifera Lam. (Family: *Moringaceae*) is the most widely cultivated species in tropics and subtropics of Asia and Africa. Also known by the names as drumstick tree, horse radish tree and kelor tree was utilized by the ancient Roman, Greeks and Egyptians. There are many distinct species with distinct morphological types. Only *M. oleifera* is cultivated widely in tropics. India has the prime position in the cultivation and production of *M. oleifera* (Ramachandran et al., 1980).Traditionally, almost all parts of this plant have been

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Moringa Oleifera aqueous leaf extract down-regulates nuclear factor-kappaB and increases cytotoxic effect of chemotherapy in pancreatic cancer cells

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Abstract

Background: Fewer than 6% patients with adenocarcinoma of the pancreas live up to five years after diagnosis. Chemotherapy is currently the standard treatment, however, these tumors often develop drug resistance over time. Agents for increasing the cytotoxic effects of chemotherapy or reducing the cancer cells' chemo-resistance to the drugs are required to improve treatment outcome. Nuclear factor kappa B (NF-kB), a pro-inflammatory transcription factor, reportedly plays a significant role in the resistance of pancreatic cancer cells to apoptosis-based chemotherapy. This study investigated the effect of aqueous *Moringa Oleifera* leaf extract on cultured human pancreatic cancer cells - Panc-1, p34, and COLO 357, and whether it can potentiates the effect of cisplatin chemotherapy on these cells.

Methods: The effect of *Moringa Oleifera* leaf extract alone and in combination with cisplatin on the survival of cultured human pancreatic cancer cells was evaluated by XTT-based colorimetric assay. The distribution of Panc-1 cells in the cell cycle following treatment with Moringa leaf extract was evaluated by flow cytometry, and evaluations of protein levels were via immunoblotting. Data of cell survival following combined treatments were analyzed with Calcusyn software.

Results: *Moringa Oleifera* leaf extract inhibited the growth of all pancreatic cell lines tested. This effect was significant in all cells following exposure to ≥0.75 mg/ml of the extract. Exposure of Panc-1 cells to Moringa leaf extract induced an elevation in the sub-G1 cell population of the cell-cycle, and reduced the expression of p65, p-IkBα and IkBα proteins in crude cell extracts. Lastly, *Moringa Oleifera* leaf extract synergistically enhanced the cytotoxic effect of cisplatin on Panc-1 cells.

Conclusion: *Moringa Oleifera* leaf extract inhibits the growth of pancreatic cancer cells, the cells NF-κB signaling pathway, and increases the efficacy of chemotherapy in human pancreatic cancer cells.

Keywords: Moringa Oleifera, Pancreatic cancer, NF-kB, cisplatin

Background

Natural products from plants provide an important source of new drugs and potential pharmaceutical "lead" compounds. Natural products or natural product-derived drugs include 28% of all new chemical entities launched between 1981 and 2002, and 24% of them are semi-synthetic natural product analogues or synthetic compounds based on natural product pharmacophores [1]. Furthermore, many anti-tumor agents in current clinical use are of natural origin, among them taxanes (docetaxel, paclitaxel), Vinca alkaloids (vindesine, vinblastine, vincristine), anthracyclines (idarubicin, daunorubicin, epirubicin), and others. Thus, there is a promising future for the use of natural products derived from plants as anti-tumor agents.

Adenocarcinoma of the pancreas, the most common form of pancreatic cancer, is the fourth commonest cause of cancer-related mortality worldwide [2]. This cancer is often diagnosed at advanced stages and has a poor prognosis, with fewer than 6% of those patients living as long as five years after diagnosis [2]. The basis of current pancreatic cancer therapy is targeting DNA

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In vivo radioprotective effect of *Moringa oleifera* leaves

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Radioprotective property of *Moringa oleifera* leaves was investigated in healthy adult Swiss albino mice. Animals were injected (ip) with 150 mg/kg body weight of 50% methanolic extract (ME) of *M. oleifera* leaves, as a single dose, or in 5 daily fractions of 30 mg/kg each, and exposed to whole body gamma irradiation (RT, 4 Gy) 1 hr later. Five animals from each group were sacrificed at 1, 2 and 7 days after treatment. Bone marrow protection was studied by scoring aberrations in metaphase chromosomes and micronucleus induction in polychromatic erythrocytes and normochromatic erythrocytes. Pretreatment with a single dose of 150 mg/kg ME significantly reduced the percent aberrant cells to 2/3rd that of RT alone group on day 1 and brought the values to normal range by day 7 post-irradiation. A similar effect was also seen for the micronucleated cells. Fractionated administration of ME (30 mg/kg x 5) gave a higher protection than that given by the same dose administered as a single treatment. ME also inhibited the Fenton reaction-generated free radical activity *in vitro* in a concentration dependent manner. These results demonstrate that pretreatment with the methanolic leaf extract of *M. oleifera* confers significant radiation protection to the bone marrow chromosomes in mice and this may lead to the higher 30 day survival after lethal whole body irradiation.

A major problem associated with cancer radiotherapy is the severe side effects resulting from normal tissue damage. Consequently, agents which protect normal tissues against radiation damage can increase the patient tolerance to radiotherapy. Several chemicals have been found to provide good radiation protection in experimental animals, but their clinical utility is limited by the drug toxicity on repeated administration[1]. The only drug approved for clinical use in cancer therapy patients is amifostine, a synthetic phosphorothioate compound, which also produces side effects of its own, like nausea, vomiting and hypotension[2,3]. Moreover, amifostine is very expensive. Therefore, there is a need to find nontoxic and inexpensive drugs for clinical radiation protection. Recent studies have indicated that some of the commonly used medicinal plants may be good sources of potent but nontoxic radioprotectors[4-7]. But research on the radioprotective property of plant products has not received the attention it deserves.

Moringa oleifera (family: Moringaceae, English: Horseradish-tree, Drumstick-tree, Sanskrit: Shigru) has been an ingredient of Indian diet since several centuries. Its constituents have been shown to possess antitumour[8,9], hypotensive[10], antifungal[11], antispasmodic and anti-inflammatory activities[12]. Its antioxidant property and possible anticarcinogenic action have also been investigated[13]. However, no study has been reported on its radioprotective effect. The present investigation was undertaken to study the radioprotective property, if any, of *M. oleifera* leaves.

Materials and Methods

Preparation of extract—Fresh leaves were collected locally during the month of July and shade dried for 2 days. About 200 g of powder was obtained from 4 kg of leaves. Fifty percent methanolic extract of dried leaves (ME) was prepared in a Soxhlet apparatus[14], and concentrated under vacuum using a Speedvac System (SC110A, Savant, USA). The extract was dissolved in double distilled water (DDW, pyrogen free) freshly before injection. This solution had a pH of 8.0.

Animals—Six to eight weeks old Swiss albino mice of both sexes, weighing 25-30 g, bred and maintained under standard conditions of light (14 hr dark; 10 hr light), temperature (23°±2°C) and humidity (50-60%) in the animal house of our department, were used for the experiments. The animals were fed on standard mouse feed (composition given by the Cancer Research Institute, Bombay) and acidified water *ad libitum*.

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