

Recent Advances on the Nutritional Effects Associated with the Use of Garlic as a Supplement

Global Harmonization of Herbal Health Claims¹

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ABSTRACT Over the past decade, herbal medicine has become a topic of increasing global importance, with both medical and economic implications. In developing countries, as much as 80% of the indigenous populations depends on traditional systems of medicine and medicinal plants as their primary source of healthcare. Within the European Community, herbal medicines represent an important share of the pharmaceutical market, with annual sales in the range of US\$7 billion. In the United States, the sale of herbal products has skyrocketed from \$200 million in 1988 to >\$3.3 billion in 1997. Such widespread use of botanicals throughout the world has raised serious questions concerning the quality, safety and efficacy of these products. Thus, accurate scientific assessment of herbal medicine is a prerequisite for global harmonization of herbal health claims. In 1995, as part of its overall global strategy of "Health for All" and due to numerous requests from the member states, the Traditional Medicine Program of the WHO began the extensive task of reviewing the world's scientific literature of commonly used herbal medicines and publishing this information in monographs. The WHO monographs are technical reviews of the quality, safety and efficacy of commonly used herbal medicines and are intended primarily to harmonize the proper use of herbal medicines throughout the world. *J. Nutr.* 131: 1120S-1123S, 2001.

KEY WORDS: • herb • botanicals • health claims

Over the past decade, herbal medicine has become a topic of increasing global importance, having repercussions on both world health and international trade. Recognition of the medical and economic benefits of plant-based medicines is growing in both developing and industrialized countries, although it varies greatly from country to country [WHO-Traditional Medicine (TRM) 1998]. In terms of world health, herbal medicines continue to play a central role in the healthcare systems of large portions of the world's population (Akerele 1988). This is particularly true in developing countries, where traditional systems of medicine have a long history of use. A good example is Traditional Chinese Medicine, an integral part of the Chinese culture that has served the health needs of the Chinese population for almost 5000 years (Mahady 1997, Shen 1996). This system of medicine has its own unique methods of diagnosis and incorporates >7000 species of medicinal plants into clinical practice (Medicinal Plants in China 1989, Shen 1996). In sharp contrast to developing countries, where herbal medicine has a long history of continued use, the United States has basically ignored botanicals

for almost 100 years. Nevertheless, as our history reveals, all medical systems were once botanically based, including the U.S. system of medicine, which is now considered by many to be one of the best in the world. The U.S. use of botanicals originated around 1620 AD, when the Pilgrims stepped off the Mayflower, bringing with them plants to use for both food and medicine. This was the beginning of what we now know in the United States as "conventional or Western medicine." In fact, botanical medicine in the United States was practiced relatively successfully for >300 years, from ~1620 to 1930. It was only during the 1940s to 1950s, with the advent of more potent synthetic drugs, coupled with a lack of clinical data to establish the safety and efficacy of botanicals, that herbal usage in the United States dwindled. However, even up to 1976 >25% of all prescription drugs dispensed in the United States were derived from plants (Farnsworth and Morris 1976).

During the past 10 years, herbal medicine has enjoyed a revival in many industrialized countries, including the United States, Canada and Australia (Eisenberg et al. 1993 and 1998, MacLennan et al. 1996, Millar 1997). In the United States alone, it is estimated that herbal usage increased by 380% between 1990 and 1997 (Eisenberg et al. 1998). This "herbal renaissance" has been fueled by strong consumer interest in preventative medicine, disappointment with allopathic medicine and the perception that botanicals are safe and free from side effects (Mahady 1998). Although few data exist to calculate the total global market for plant-based medicines with accuracy, it can be conservatively estimated that worldwide

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sales of herbal products are in the range of \$16–20 billion/y. Within the European Community, herbal medicines represent an important share of the pharmaceutical market, with annual sales in the range of US\$7 billion. To market herbal medicines in Europe, manufacturers must obtain a “marketing authorization” from the regulatory authorities; this requires the submission of a formal dossier providing scientific proof of safety and efficacy for each product (WHO-TRM 1998). The sale of herbal medicines in Europe has remained stable over the past number of years, whereas the sale of herbal supplements in the United States has increased dramatically. In 1988, annual retail sales of herbal products approached \$200 million. In 1997, the annual retail sales of herbal products was estimated at \$5.1 billion (Eisenberg et al. 1998). Thus, in just 10 years, a 24-fold increase in the sale of herbal products in the United States has occurred.

The situation in developing countries is somewhat different in that traditional systems of medicine have always played an important role in healthcare (WHO-TRM 1998). It has been estimated that as much as 80% of the population in these countries depend on traditional systems of medicine as a source of primary healthcare (Bennerman et al. 1983). If one assumes that the current world population is ~5.8 billion, then as many as 3 billion people rely on TRM. A common characteristic of all traditional systems of medicine is its reliance on plants as a source of medicine. In many cases, herbal medicines may be the only medicine available in these countries because modern pharmaceutical products are in great demand, making them unavailable to the general population due to the prohibitively high costs. Unfortunately, the use of medicinal plants in these countries is based primarily on empirical knowledge, and many of the plants have not been scientifically evaluated for their safety and efficacy.

Such widespread use of herbal medicines throughout the world has raised serious questions about their quality, safety and efficacy. There are further concerns over the perceived lack of adequate regulation of herbal medicines in many countries and the encouragement of the sale of unregistered products, which are not controlled by regulatory authorities (DeSmet 1995). The legal status of herbal medicines varies widely from country to country, and the regulation of these medicines has not evolved in any methodological manner (WHO-TRM 1998). Most countries have different ways of defining medicinal plants, herbs or the products derived from them and have adopted various approaches to licensing, dispensing, manufacturing and trading to ensure their quality, safety and efficacy (WHO-TRM 1998). In Europe, herbal medicines are well established and formally regulated, whereas in the United States, herbs are classified as dietary supplements and therapeutic claims are not allowed. The situation is even more precarious in many developing countries, where despite the great number of traditionally used herbal medicines and much empirical knowledge about their use, there are very few legislative criteria that can be employed to incorporate traditionally used herbal medicines into national drug policies (WHO-TRM 1998). Thus, in both industrialized and developing nations, the assurance of quality, safety and efficacy has now become a key issue (WHO-TRM 1999). Careful scientific evaluation of safety and efficacy is essential before herbal medicines can be officially incorporated into primary healthcare systems and before there can be global acceptance of their health benefits. What is required is a centralized, focused approach to providing accurate and up-to-date scientific information on commonly used herbal medicines.

As part of its overall global strategy of “health for all,” the

World Health Organization’s Traditional Medicine Program (WHO-TRM) has begun the extensive task of reviewing the world’s scientific literature of commonly used herbal medicines. The reviews will be published as a series of books entitled “WHO Monographs on Selected Medicinal Plants.” The groundwork for this project actually began in 1978 at the International Conference on Primary Healthcare convened by WHO and UNICEF in Alma-Ata, USSR. During this conference, the value of traditional systems of medicine was fully recognized, and the integration of safe and effective traditional medicine practices into primary healthcare was recommended (Akerele 1988). However, for this to occur, both traditional medicine practices and herbal medicines must be assessed on a scientific basis. In 1986, the participants of the 4th International Conference of Drug Regulatory Authorities (ICDRA) requested that WHO compile a list of medicinal plants and establish international specifications for the most widely used medicinal plants. The “Guidelines for the Assessment of Herbal Medicines” were prepared by WHO-TRM, and these guidelines were adopted by the 6th ICDRA held in Ottawa, Canada in 1991. During this meeting, the drug regulatory authorities further recommended that WHO develop model monographs based on the adopted guidelines (WHO-TRM 1999). As a result of these recommendations, and in response to the numerous requests by the Member States for assistance in assessing herbal medicines, WHO-TRM embarked on a long-term project to review selected medicinal plants commonly used around the world (WHO-TRM 1999). In 1994, at a WHO expert consultation held in Beijing, China, 31 medicinal plant species were selected. Plant selection was based on worldwide use, importance to each of the WHO regions and amount of sufficient scientific information to substantiate safety and efficacy. The WHO Collaborating Center at the University of Illinois at Chicago prepared the initial drafts of 31 monographs in 1995. The purpose of the WHO monographs is to provide accurate scientific information on the safety, efficacy and quality control/quality assurance of widely used medicinal plants. Because as many as 35,000 medicinal plants have been used worldwide (Farnsworth 1998), the monographs are also intended to provide models to assist the Member States in the development of their own medicinal plant monographs. The monographs were drafted on the basis of a systematic review of the global scientific literature from 1975 to 1995, including various pharmacopoeias, monographs such as the German Commission E Monographs, information from Medline, Napralert and Toxline, reference texts and peer-reviewed scientific journals. The initial draft of the book was circulated for review and comment to >120 experts in academia, government and industry in 40 different countries. Experts included members of WHO’s Expert Advisory Panels for Traditional Medicine, the International Pharmacopoeia and Pharmaceutical Preparations, and Drug Evaluation and National Drug Policies, as well as drug regulatory authorities of 16 countries. The book was revised on the basis of comments from the reviewers and then sent to a formal review at the WHO Expert Consultation on Model Monographs of Widely Used Medicinal Plants, which was held in Munich, Germany in 1996. After extensive discussions, 28 monographs were revised and adopted, one was rejected due to potential toxicity and two were revised for Volume II. The revised monographs were then presented at the 8th ICDRA congress held in Manama, Bahrain in November 1996, and the 28 monographs were adopted. During this meeting, the Member States further recommended that WHO-TRM should prepare a second volume of monographs.

The contents of the monographs, including the sections on microbiological quality, are in compliance with well-established standards for safety, efficacy and quality control (WHO-TRM 1999). In particular, there should be no toxicity of such plant preparations within the range of the recommended dose. The monographs were not written to replace other compilations such as those found in pharmacopoeias, formularies or legislative documents, but to provide further accurate scientific information to facilitate proper usage.

Each herbal monograph is composed of two parts. The first part includes pharmacopoeial summaries of quality assurance, including a definition, a description of botanical features, geographical distribution, identity tests, purity requirements, chemical assays and a listing of the major chemical constituents. The second part summarizes medical uses, pharmacology, contraindications, warnings, precautions, adverse reactions and dosage.

In each pharmacopoeial summary, the "Definition" section provides the correct Latin binomial of the plant, the most important criterion in quality assurance. A list of Latin synonyms and selected vernacular (common) names is also provided. The detailed botanical description is intended for quality assurance during collection and production, whereas the detailed description of the drug material is provided to facilitate manufacturing of products and commerce. General identity tests, purity criteria and chemical assays are all normal compendial components and are included under their own headings. Because each medicinal plant and the specific plant part used contain a characteristic chemical profile that can be used for chemical quality control and quality assurance, these constituents are described under the section heading of "Major chemical constituents."

The second part of each monograph contains information necessary for the practicing healthcare professional. Part two of each monograph begins with medicinal uses that are categorized on the basis of the level of scientific data to support the claims. Medicinal uses are defined as: *uses supported by clinical data*; *uses described in pharmacopoeias and traditional systems of medicine* (not supported by clinical data, but having some experimental pharmacology to support the use); and *uses described in folk medicine* (uses that are not supported by either experimental or clinical data). This section is written specifically for the healthcare professional and will enable a practitioner to quickly ascertain which therapeutic indications are supported by clinical data without having to read through all of the relevant experimental and clinical pharmacology. Part two of each monograph also includes a list of contraindications, warnings, precautions [general, drug interactions, drug and laboratory tests, carcinogenesis/mutagenesis/impairment of fertility, pregnancy (teratogenic or nonteratogenic effects), nursing mothers and pediatric use]. This section also covers adverse reactions and a dosage section entitled "Posology." Each monograph is fully referenced, enabling the reader to access further information when necessary. The "WHO Monographs on Selected Medicinal Plants, Volume I" contains 28 technical monographs, and provides details of quality, safety and efficacy for 39 species of plants, including aloe, aloe vera gel, astragalus, chamomile, echinacea, ephedra, garlic, ginkgo, ginseng, senna and valerian. Publication of Volume I of the WHO Monographs was published in 1999. The first draft of the "WHO Monographs of Selected Medicinal Plants, Volume II" has now been completed and will be published in 2001. The second volume includes 32 monographs, including black cohosh, dong qui, *Eleutherococcus*,

evening primrose, feverfew, hawthorn, kava, saw palmetto, St. John's wort and stinging nettle, among others. Volume II is scheduled to be reviewed at a WHO expert consultation to be held in Milan, Italy in March 1999.

The "WHO Monographs of Selected Medicinal Plants" were written to provide up-to-date scientific information on the safety, efficacy and quality of widely used herbal medicines and to promote the proper use of herbal medicines throughout the world. In developing countries, a positive scientific assessment of a medicinal herb used in traditional medicine will facilitate its integration into national healthcare systems, thus resulting in widespread use of that herb for a valid therapeutic indication. The proper use of herbal medicines has a twofold benefit in that it will not only promote health, but also protect consumer safety. In addition to medical benefits, there is a potential for the establishment of industry and international trade in developing countries. New industry and trade will bring employment to these countries and thereby promote a better standard of living.

Industrialized nations will also benefit by harmonization of herbal health claims. Accurate scientific assessments will provide assurance of safety, establishment of efficacy and standards for quality, which will contribute to the overall health and safety of these populations. Accurate scientific assessments of herbal medicines will give healthcare professionals the confidence to employ these products in their everyday practice, thereby facilitating the incorporation of safe and effective herbal medicines into our medical armamentarium.

Summary

Global harmonization of herbal health claims is inevitable and desirable from both an economic and medical standpoint. The free movement of safe and effective herbal medicines throughout the world will bring better standards of living by enhancing capacity building in developing countries, improve healthcare and promote WHO's goal of "health for all." Harmonization of herbal health claims is achievable only for those herbal medicines having sufficient scientific data to support the claims of safety and therapeutic efficacy. However, for others, more scientific information will be required in the form of well-designed, controlled, clinical trials and basic scientific research. However, such a global enterprise requires a global response. What is needed is a coordinated, forthright and determined initiative to unite the expertise of healthcare professionals and scientists from industry and academia from around the world, with the financial resources to do the job. Our collaborative efforts with WHO-TRM toward this goal represent a step in this direction.

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