

THE WORLD MEDICINES SITUATION 2011

TRADITIONAL MEDICINES: GLOBAL SITUATION, ISSUES AND CHALLENGES

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SUMMARY

- Traditional medicines, including herbal medicines, have been, and continue to be, used in every country around the world in some capacity. In much of the developing world, 70–95% of the population rely on these traditional medicines for primary care.
- The global market for traditional medicines was estimated at US\$ 83 billion annually in 2008, with a rate of increase that has been exponential.
- Regulatory status and the associated terminology varies widely. Traditional medicines are used as prescription or over-the-counter (OTC) medications, as self-medication or self-care, as home remedies, or as dietary supplements, health foods, functional foods, phytoproducts, and under any of many other titles in different jurisdictions, with only minimal consistency between the definitions of these terms from country to country and significant communication issues as a result.
- To control quality and to ensure safety and efficacy in production of traditional medicines is difficult. WHO, in cooperation with the WHO Regional Offices and Member States, has produced a series of technical documents in this field, including publications on Good Agricultural and Collection Practices (GACP) and Good Manufacturing Practices (GMP), along with other technical support, to assist with standardization and creation of high quality products.
- Regulation of traditional medicines is a complicated and challenging issue as it is highly dependent upon experience with use of these products. Model countries such as China, India, and South Africa present usable templates, as do the guidelines on regulation and registration of traditional or herbal medicines produced in the WHO African, Eastern Mediterranean, and South-East Asian regions and in the European Union.
- Evaluation of quality, safety and efficacy based on research is needed to improve approaches to assessment of traditional medicines, a situation made difficult to remedy in light of historically inadequate public and private funding to address this growing concern.
- World Health Assembly resolution 62.13, passed in May 2009 by the WHO Member States urges national governments to respect, preserve and widely communicate traditional medicine knowledge while formulating national policies and regulations to promote appropriate, safe, and effective use; to further develop traditional medicine based on research and innovation, and to consider the inclusion of traditional medicine into their national health systems. WHA 62.13 also urges Member States to cooperate with each other and to share knowledge while working to strengthen communication between conventional and traditional practitioners.

1.1**INTRODUCTION**

Traditional medicines include herbal medicines composed of herbs, herbal materials, herbal preparations, and finished herbal products, that contain as active ingredients parts of plants, or other plant materials, or combinations thereof. Traditional medicines may also use animal parts and/or minerals (1). They are used in every country in the world, and have been relied upon to support, promote, retain and regain human health for millennia (2-5). Traditional Chinese medicine (TCM), for example, is a completely defined medical system running parallel to allopathic medicine which has been used successfully to diagnose, treat and prevent illness for over 2500 years (6). Traditional medicines (products) are a part of the larger field of traditional medicine which includes procedures and practitioners, as well as products (1).

Despite the existence and continued use of traditional medical services and products over many centuries, the history of regulated use of traditional medicine is comparatively short. In many countries, in both the developed and developing world, traditional medicine products are still not officially recognized under the law (7,8). Although several national and regional organizations have created models for how to deal with this challenge, regulatory systems for traditional medicines have yet to be widely adopted. Countries which have taken steps to regulate production and use of such products include Brazil, China, Denmark, Ghana, Japan, Norway, the Republic of Korea and Saudi Arabia (8). The European Union is also developing methods for regulating the quality of traditional medicines and mechanisms for registering products (9).

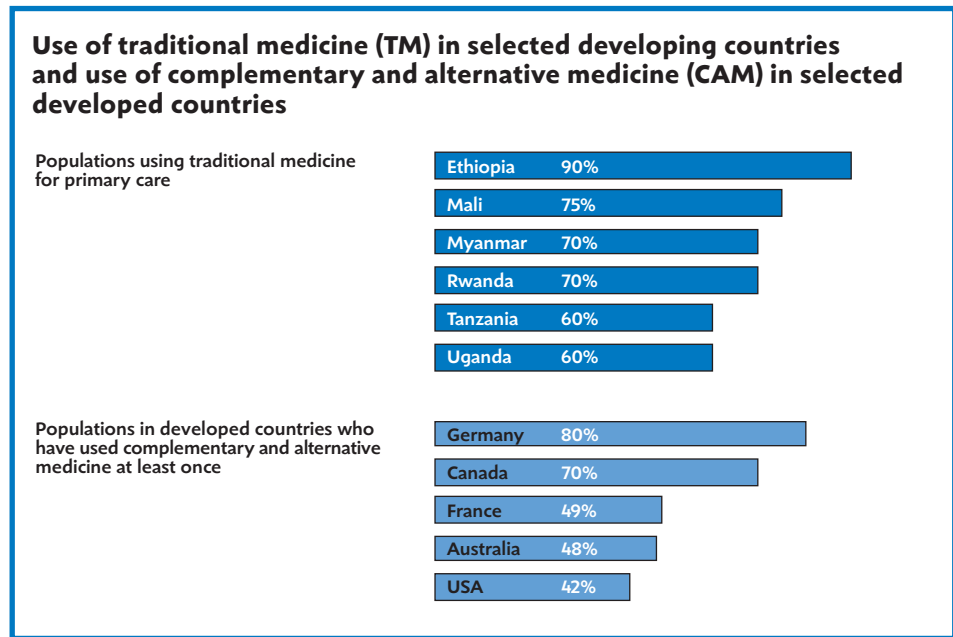
It is estimated that at least 25% of all modern medicines are derived, either directly or indirectly, from medicinal plants, primarily through the application of modern technology to traditional knowledge. In the case of certain classes of pharmaceuticals, such as antitumoral and antimicrobial medicines, this percentage may be as high as 60% (4,10). For example, in 1971 laboratory experiments verified the activity of extracts of a plant, *Artemisia annua*, against *Plasmodium berghei*, a mouse model of malaria (11). This discovery has since revolutionized the treatment of malaria around the world, but with little recognition for the traditional medicine practitioners of the African region who have used *Artemisia* spp. for centuries, but who lacked the technology or financing to prove its efficacy against malaria in a laboratory.

1.2**PRESENT SITUATION****1.2.1****Universal appeal**

Between 70% and 95% of citizens in a majority of developing countries, especially those in Asia, Africa, Latin America and the Middle East, use traditional medicine, including traditional and herbal medicines, for the management of health and as primary health care to address their health-care needs and concerns (1,12,13). In some industrialized nations, use of traditional medication is equally significant; Canada, France, Germany and Italy for instance, report that between 70% and 90% of their populations have used traditional medicines under the titles “complementary”, “alternative”, or “nonconventional” (1,14,15). This is perhaps not surprising given that until the middle of the 20th century and the advent of so-called “modern medicines” (starting with the commercial production of penicillin in 1943), traditional medicines were the only medicines (16). Figure 1.1 reflects the widespread use of traditional medicine in a number of representative countries worldwide.

In most developing countries, 70%–95% of population rely on traditional medicines for primary care.

FIGURE 1.1



Sources: References 9, 17–19.

Traditional medicines have always played a key role in world health and continue to be used to treat a vast array of conditions and complaints. A survey completed by WHO's Roll Back Malaria programme showed that in Ghana, Mali, Nigeria and Zambia, around 60% of all febrile cases in children, presumably due to malaria, are treated at home with herbal medicine (1,12). Information compiled by UNAIDS revealed that approximately two thirds of HIV/AIDS patients in a variety of developing countries seek symptomatic relief and manage opportunistic infections through the use of traditional medicines (1,12,13). TM/CAM use is also prevalent in the cities of San Francisco and London, as well as throughout much of South Africa, where a reported 75–78% of people living with HIV/AIDS use these interventions as well (1,6). Other conditions commonly addressed with traditional medicines include digestive or intestinal diseases, sickle-cell anaemia, hypertension, high cholesterol, headaches, insomnia, diarrhoea, microbial infections, bronchitis, diabetes, burns, rashes and menopause (10,12). In Brazil, a reported 89% of patients diagnosed with cancer use TM/CAM products to treat their conditions (6).

There is growing acceptance among policy-makers that there can be appropriate and effective treatment or control of certain diagnosed conditions via traditional medicine self-medication. In some settings, traditional medicine is actively being promoted as one way to reduce the health care burden on the public budget (20,21).

In 2007, it was reported that 110 of the 193 WHO Member States had some type of policy in place regarding regulation and/or registration of traditional medicines, up from fewer than 15 who were able to make the same claim in 1986 (see Figure 1.2).

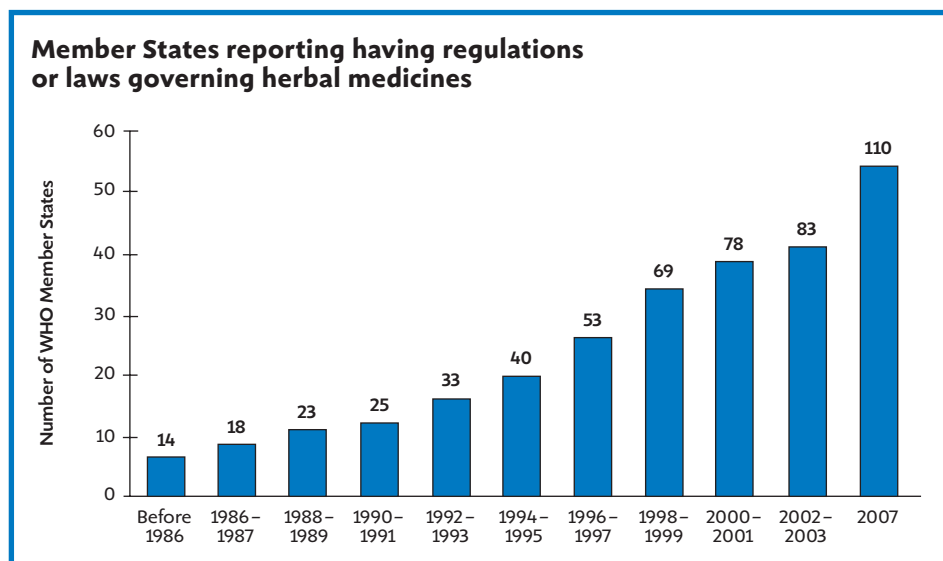
There is growing acceptance that traditional medicines are appropriate and effective in treatment or control of certain diseases.

1.2.2

Regulation/registration of traditional medicines

Traditional medicines are characterized in many different ways throughout the various jurisdictions around the world. They are commonly sold either as a prescription or over-the-counter (OTC) medicine (8) or may be variously described as self-medication, home remedies, dietary supplements, health foods, functional foods or phytoprotectants, or by some other title. The Canadians, for example, frequently use the term “folk medicines”

FIGURE 1.2



Source: References 8, 17, 22, 23.

(8,10). These types of products are variously marketed under the banner of traditional medicines, herbal medicines, herbal supplements, herbal pharmaceuticals, phytoprotectants or phytotherapeutic agents, or even simply as medicines or as a foodstuff (24). The array of classification options for herbal preparations is ably illustrated by the example of garlic (see Box 1.1).

BOX 1.1

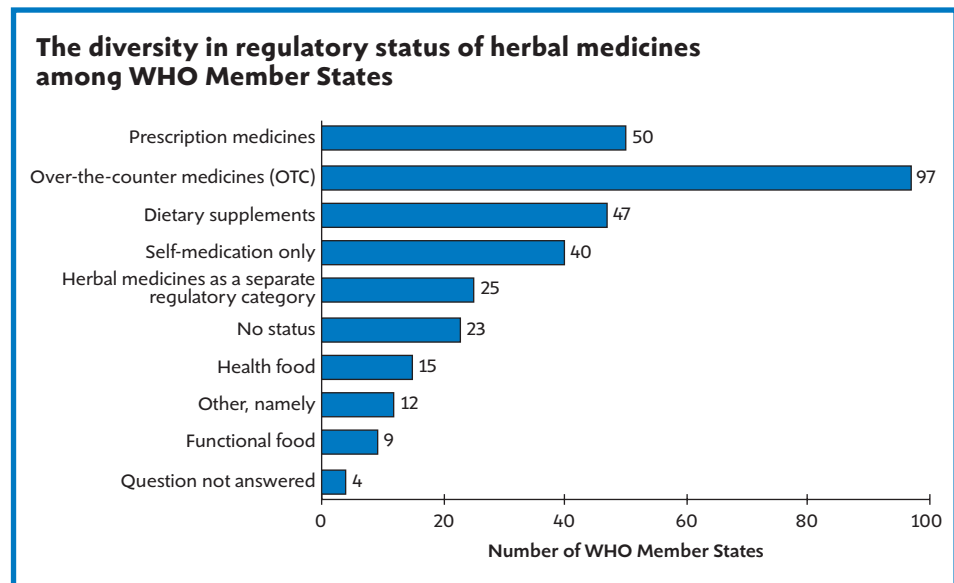
***Allium sativum* (garlic)**

Allium sativum (garlic) is a useful example when trying to understand the complicated regulatory environment for traditional medicines. Garlic is eaten as a food or spice all over the world, but it is also frequently used for health benefit, including to lower blood cholesterol and to inhibit some cancer processes (1,10,25). In Europe alone, garlic is marketed as a foodstuff, a herbal supplement, a herbal medicinal product, a food supplement, a health food or as a pharmaceutical preparation; however, it may not be marketed as a dietary supplement because European Union directive restricts use of that term to vitamins and minerals (25). In contrast, in the USA garlic is classed as a food or as a dietary supplement only. In Bangladesh garlic is sold as a “phytoprotectant”, as a “functional food” in Nepal, and as a “phytotherapeutic agent” in Brazil (10,25,26). This lack of consistency in terminology contributes to the complications inherent in the regulation of traditional medicines and quantification of their international economic role. Statistics on the sale of specific traditional medicines are understandably difficult to gather in light of the array of classification options.

The diversity in the description and classification of traditional medicines means that in many countries, herbal and other traditional medicinal products are often subject to multiple, concurrent levels of certification. In such situations, and depending to some extent on the level of sophistication of the regulatory framework, a single medicinal plant may be simultaneously defined and regulated under several different regulatory instruments. A few of these categories of regulation can be seen in Figure 1.3, and the complications just outlined begin to explain the greater number of responses than number of countries submitting a response. According to a WHO survey conducted in 2001, 57 countries currently have

regulations that require traditional medicines to meet the exact same safety assessment requirements as those in place for conventional pharmaceuticals, while another 82 list some special requirements which run parallel to non-traditional or “conventional” medicines. Seventy-three countries apply the same rules to traditional medicines manufacture as to conventional pharmaceuticals manufacture, while 28 countries reported that they have no requirements governing the manufacture of traditional medicines (8). The variety of levels to which traditional medicines are integrated into the pharmaceutical culture of each individual country serves to highlight the vastly different cultural understanding and priorities between countries.

FIGURE 1.3



Source: Reference 8.

It is clear from the preceding discussion that the degree to which the production and use of traditional medicines is regulated varies hugely between WHO Member States. More than 120 WHO Member States requested that WHO provide support to create a database and network for information sharing on regulatory issues (8). This led in 2006 to the creation of the International Regulatory Cooperation for Herbal Medicines (IRCH), coordinated by WHO. The mission of IRCH is to protect and promote public health and safety through improved regulation of herbal medicines. Currently, the membership of IRCH consists of 22 countries and three regional/sub-regional groups.¹

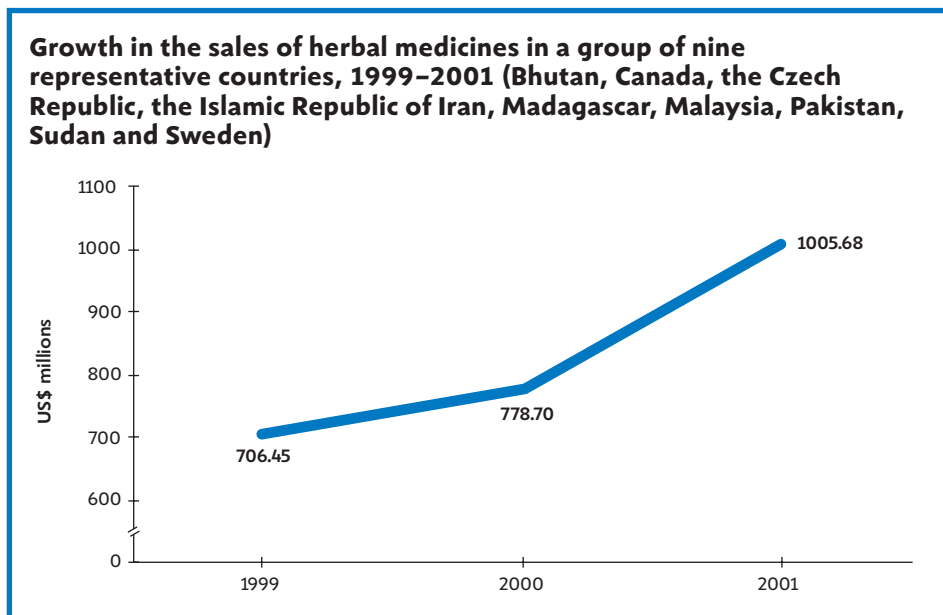
1.2.3

Economic importance

Given the inconsistent terminology and regulatory status of traditional medicines, it is difficult to put a precise figure on the economic value of such products. What data are available are generally considered to significantly under represent the actual economic impact of this branch of the health care marketplace. What is more certain is that the global market for traditional medicine products has expanded significantly over the last decade with growth

¹ Member Countries as of August 2009 include Armenia, Australia, Brazil, Canada, China, Ghana, Hungary, India, Indonesia, Japan, Malaysia, Mexico, Pakistan, the Republic of Korea, Saudi Arabia, Singapore, the United Arab Emirates, the United Kingdom and the United States of America. The three regional/sub-regional bodies are the Association of Southeast Asian Nations (ASEAN), the European Medicines Evaluation Agency (EMA) and the Latin American Parliament.

FIGURE 1.4



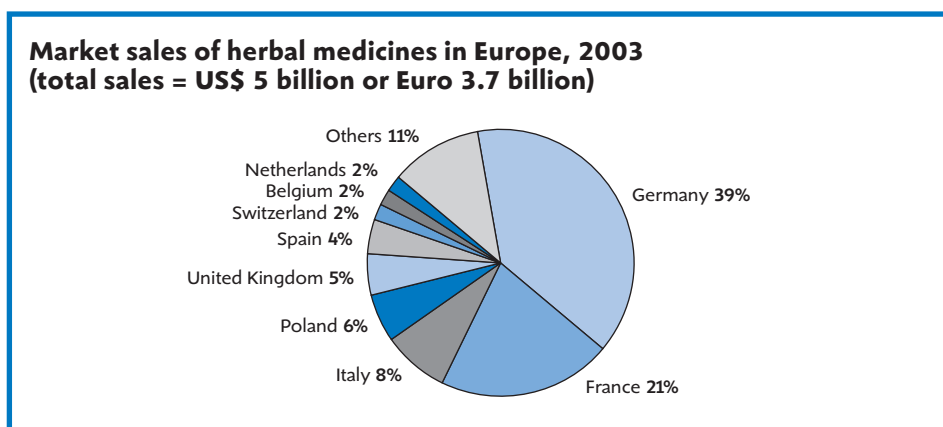
Source: Reference 8.

in demand, production and sales. Market estimates suggest that the rate of growth in traditional medicine product sales in recent years amounts to somewhere between 5% and 18% per annum (10).

Recent trends in annual sales of herbal medicines in a sample of nine countries, representing a number of world regions and a range of income levels, are shown in Figure 1.4, from which it can be seen that between 1999 and 2001 alone, the sales value of herbal medicines in this group of countries increased by more than 40% (8). In the absence of other information, however, it is difficult to put these data in historical context and to gauge what percentage of the increase is related to the rising costs associated with commercialization.

In China, traditional herbal medicinal preparations constitute between 30% and 50% of the total consumption of medicines, equating to a sales value of US\$ 14 billion in 2005 (up more than 28% from the previous year). In Japan, spending on traditional medicines (known as Kampo) in 2006 came to just over US\$ 1 billion (6) while in the period, June 2004–2005, Australians spent a total of US\$ 1.86 billion on herbal medicines (27). In the United

FIGURE 1.5



Source: Reference 28.

Kingdom and Brazil, out-of-pocket expenditure in 2007 was comparatively less, at only US\$ 230 million and US\$ 160 million, respectively (17). Among the European nations, the value of known market sales of herbal medicines in 2003 was estimated to be US\$ 5 billion (see Figure 1.5); this too is an under representation, as the total was based on the manufacturers' price to wholesalers, and as such does not reflect the actual cost to the end-user. Moreover, the statistics only refer to herbal medicines and do not include those traditional medicines which contain animal or mineral products (28).

1.2.4

The work of WHO

The impact of traditional medicines, in both the economic and health sectors, has resulted in a public demand for increased accountability in the traditional medicines marketplace. Consumers want to know that their products meet acceptable criteria to be considered both safe and effective. This has led to an increased interest among health authorities in research, regulation, international trade and marketing of traditional medicines (8,21).

Despite the many challenges, considerable progress has been made in recent years at the national, regional and international levels to create the institutional frameworks and regulatory environments necessary to support the registration, research and production of traditional medicines. Many countries continue, however, to seek technical assistance for producing and distributing quality traditional medicines that meet acceptable levels of efficacy and safety. To this end, WHO has produced several documents designed to assist national governments, including guidelines on methodologies for research and evaluation, good agricultural and collection practice (GACP), good manufacturing practice (GMP), and on the role of the pharmacist in traditional medicine (7,20,29,30). GACP serves to ensure that the raw materials selected for medicinal products are of assured quality, while GMP provides guidance on how to convert these components into assured quality traditional medicines. Some WHO Regional Offices, including those in the African, Eastern Mediterranean, and South-East Asian regions, have also produced more localized guidelines for regulation and registration of traditional medicines, as well as suggestions for marketing requirements (12,31,32).

WHO continues to monitor the status of traditional medicines around the world through regular surveys and other data gathering activities. The information so collected has formed the basis of several key reviews, including a worldwide review of the legal status of TM/CAM (22) and a global survey on TM/CAM national policy (8). The results of these exercises have been used to inform WHO's Traditional Medicine Strategy (1,24).

The WHO strategy for traditional medicine is currently in the process of being updated, and a second global survey is being undertaken to support this effort. This, and other work,(33) has culminated in a 2009 WHO World Health Assembly Resolution on Traditional Medicine (WHA62.13) which urges national governments to respect, preserve, and widely communicate traditional medicine knowledge while formulating national policies and regulations to promote appropriate, safe, and effective use; to further develop traditional medicine based on research and innovation and to consider the inclusion of traditional medicine into their national health systems. WHA 62.13 also urges Member States to cooperate with each other and to share knowledge while working nationally to strengthen communication between conventional and traditional practitioners (21).

1.3

FUTURE CHALLENGES AND PRIORITIES

Traditional medicines are not completely safe. There could be potential risks if not used appropriately.

The idea that just because traditional medicine products come from natural sources they are completely safe is dangerously false (10). Not everything that is natural is safe; traditional medicine products must be used judiciously and as indicated, just like any other medication, and with awareness of potential herb-herb and herb-drug interactions. The risks are relatively small when traditional medicines are used correctly, but they are still there, and consumer understanding is generally low. For example, a cross-sectional population survey conducted in Australia found that less than half (46.6%) of traditional, herbal medicine users were even aware that there could be potential risks associated with product use (34).

Most of the reported side effects associated with the use of traditional medicines are extrinsic to the product itself, arising instead from errors in plant identification, poor manufacturing practices and lack of product standardization, contamination of products, substitution or incorrect preparations or dosage. In addition, traditional medicine products are more likely to be affected by environmental factors such as light, temperature, soil quality, period and time of harvest, and age of the plant (2,35,36). These factors, and others, complicate the process of producing consistent products, let alone producing them in sufficient quantities for both use and testing purposes (37).

It is the issue of quality control in product manufacture, combined with a lack of understanding about the active ingredients of traditional medicines and their therapeutic mechanisms that has hitherto hindered their advancement. Research on safety and efficacy is of primary importance to the continued development of traditional medicines. However, each product may contain several different plants and potentially hundreds of chemical constituents, some of which may be present in very low concentrations; these factors combine to make laboratory investigation both complicated and expensive (10,31,38-41). Frequently, the combined action of the many constituents is considered crucial for the optimal therapeutic effect, even if the combination is only empirically known (42). To test each chemical independently, as well as in every potential combination, is impractical due to the amount of time which would be required to complete such a task.

Development of conventional medicinal products (containing a single chemical entity) typically takes an average of 12 years, from discovery to finished product, and costs hundreds of millions of dollars (1,4). A traditional medicinal product, with its manifold additional complexities, could take significantly longer and cost a good deal more to research and develop fully. In the case of synthetic, chemical pharmaceuticals, the money spent on research and development is recuperated when the product is patented and brought to market. Plants, however, cannot be patented in the conventional sense - one cannot have proprietary rights over a tree or a flower, and there is no way to prevent another person from growing the same plant for medicinal purposes (43). In practice, this means that money spent on analysing and standardizing a specific traditional medicine cannot be recuperated through sales of the product. Investors are reluctant to invest when it is obvious that the ability to garner a return is limited or non-existent.

Development of criteria for unequivocal identification of the constituents of each product (but not necessarily the chemical composition of each of these constituents), together with documentation of the role of the constituent combinations, is a critical first step in achieving quality assurance. This is also a prerequisite for laboratory investigations into the products and their clinical applications (3,4,31,32,44). A second step will be to standardize the growing, harvesting and handling of the raw materials used in producing traditional medicines (44).

These, together with the establishment of appropriate specifications and standards, serve as the basis for consistency, quality control and the verification of safety (2,31,32). The creation or expansion of post-marketing surveillance system for the evaluation of potential toxicity and herb-herb/herb-drug interactions will be the next step in this process to ensure quality and safety (44).

Countries must formulate standards for quality and safety of traditional medicines as well as policies and regulations for production and use of traditional medicines.

Concurrent with efforts to create quality products that are both safe and effective, countries must formulate national standards, policies and regulations governing the production and use of traditional medicines; these are necessary to promote and maintain good practice among appropriately-educated producers and practitioners for the benefit of the population (1, 21). Although many nations have been moving swiftly towards the creation of national TM/CAM policies, mechanisms for sharing information and expertise, as well as the provision of the model guidelines, will facilitate this process and provide for greater international consistency and higher standards (24). Such moves will also facilitate reliable international trade in traditional medicine products through the creation of a set of globally acceptable criteria (41).

Moving forward, there are several things that can be done. While acknowledging that all traditional medicines must be subject to evaluation of safety, therapeutic efficacy, quality control and pharmacovigilance, according to prescribed criteria, we should, in conducting such evaluations, recognize the unique historical development of these products (32). Due weight should be placed on each of the primary methods of verifying efficacy – the history of long-term use, documentation of currently available knowledge and new/ongoing research and clinical trials on safety and efficacy. Although standardized laboratory work may be lacking, for many traditional medicines, there exists a long history of observations, field-testing and clinical trials in humans. This history of use should be included when considering the evidence base for use of traditional medicines; the prolonged and apparently uneventful use of a substance can supplement verification of safety and, potentially, add weight to claims of efficacy as related to traditional use (6,11,40). For example, European Union legislation passed in 2004 allows the registration of traditional medicines if, among other criteria, there is sufficient data on traditional use to show that they are acceptably safe, that therapeutic effects are plausible, and that they have been in use medicinally for at least 30 years, including at least 15 years within the member countries of the European Community (9,28).

While all of this development is going on, it will be important to preserve the historical knowledge together with the newly acquired data. This can best be done through the creation of a global database for traditional medicine information. This will consolidate the existing research to best determine priority needs for the immediate future. This database should also include documentation of the knowledge of traditional healers, while respecting intellectual property rights (7,44).

These challenges, while intimidating, are not insurmountable. Although the development of traditional medicines will likely require national legislation, the huge economic impact of, and the overwhelming public support for, these products, will ensure the continued focus on the investigation and development of traditional medicines in the future.

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ABBREVIATIONS

CAM	Complementary and alternative medicine
GACP	Good agricultural and collection practices
GMP	Good manufacturing practices
IRCH	International Regulatory Cooperation for Herbal Medicines
OTC	over-the-counter
TM	Traditional medicine