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SOME THOUGHTS ON THE STANDARDIZATION OF TRADITIONAL MEDICINES

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Abstract

Traditional medicine, the use of plants, animals, and minerals for human health needs must be brought to a new scientific level of sustainable development in order to accommodate future global health care needs.

Key words: Traditional medicine, safety, efficacy, standardization, intellectual property rights, sustainable development

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บทคัดย่อ

การพัฒนายาจากสมุนไพรทั้งที่มาจากพืช สัตว์ หรือ แร่ธาตุ จำต้องอาศัยความรู้และกระบวนการศึกษาวิจัยทางวิทยาศาสตร์อย่างถูกต้อง จึงจะนำไปสู่การใช้ประโยชน์เพื่อสุขภาพอนามัยของประชาชนอย่างยั่งยืน

คำสำคัญ : ยาจากสมุนไพร, ความปลอดภัย, ประสิทธิผล, มาตรฐาน, ทรัพย์สินทางปัญญา, การพัฒนาอย่างยั่งยืน

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Introduction

"Man and Nature are indissolubly joined." This quote from the American philosopher Ralph Waldo Emerson is even more relevant today than when it was written in a series of letters on "Nature" in 1836. It is a constant reminder that we are a part of Nature; not separate from the rest of our co-inhabitants of planet Earth. Our individual relationships with Nature are diverse and multifaceted. For some, it is an integral aspect of the daily routine to work in the fields or orchards tending crops. For others, it may be tending a garden or arranging flowers. It may be cooking a delicious meal with a myriad of fresh foods and spices, or it may be the preparation of medicines from plants or other natural sources for their family or for the health care of others. For those who live in the cities, health care may come in various forms, and drugs similarly. In most countries of the world, there are basically three forms of "drug" preparations: i) prescription products approved by a local regulatory agency after the evaluation of substantial, mandatory, chemical, biological, and clinical data; ii) "over-the-counter" drugs, which are also approved by the FDA and are regarded as being less dangerous (lower potential for side effects and abuse) than prescription products, and iii) phytotherapeutical products and traditional medicines. The absence of regulations regarding these products is a recent concern in many countries, and the question has been raised whether health care can be improved if the practices and policies with respect to traditional medicines can be standardized. This appears to be based on an assumption, which needs to be examined carefully, that enhancing the science behind the sale of traditional medicines will automatically provide health benefits.

Traditional Medicines and Phytotherapeutical Products

It was estimated many years ago that over 80% of the worlds' population in developing countries used plant materials as their source of primary health care[1]. This number is even higher today as populations in the developing world have continued to expand steadily in the past twenty years, and prescription drug costs have soared. Consequently, these products are even less accessible to the developing world. It must be recognized that the major pharmaceutical companies have a very different agenda for health care than responding to the day-to-day needs of the majority of the population. An examination of the major killer diseases of the world (Table 1) reveals that these are not

diseases that warrant much attention from the global pharmaceutical companies in their programs of research and drug development. Thus, all over the world, and at a variety of levels of health care, provisions are being made, using local resources, for the "treatment" of these disease states, as well as many other non-life threatening diseases. That is the societal role of what is referred to as traditional medicine. For most people in the world it is a critical health care role, and one which is not going to change in the next 20-30 years. Given the prominence of these traditional medicines it may be surprising for some to learn that at this point in time, there is scant chemical and biological evidence available in support of the safety and efficacy of these agents, and their quality remains unregulated.

Table 1. The Major Killer Diseases of the World*

AIDS:	3.1 million deaths per year, 5.5 million new cases
Tuberculosis:	2 million deaths, 8 million new cases
Diarrheal Diseases:	1.9 million deaths, 2.7 billion new cases
Malaria:	1 million deaths, 300-500 million new cases
Hepatitis B Virus:	1 million deaths, 10-30 million new cases
SARS:	to 04/04, 8,096 cases, 774 deaths
Tobacco-related deaths:	3.5 million

**Data from the websites of the Centers for Disease Control, Atlanta, and the World Health Organization, June 2004.*

We are all consumers -

From a consumer perspective, the absence of regulations supporting standardization results in a situation of "Buyer Beware". Whether you are going to your local health food store or to your local shaman, hakim, or curandero, you are "buying blind". Whether you go to a local market in Thailand and buy a medicinal plant preparation, or whether you buy a fancy package of capsules stated to contain a certain amount of a phyto-therapeutical agent in a health food store in Chicago, you, the consumer, have no idea what you are *really* buying. Maintenance of this situation, on a global basis, substantially undermines the credibility of natural product research and of the role that it should be assuming in health care now and in the future. We need to re-vision this role to regain

the scientific, moral, and societal stature of our science. How to begin? Let's start with the consumer, since we are all probably consumers of various phytotherapeutical products.

From the viewpoint of the consumer, it is necessary to consider what are some of the expectations that should be in place globally for traditional medicines? What should we, as consumers, be demanding from the natural product sciences for our traditional medicines?

As in any consideration of health care, and as clearly stated in the Oath of Hippocrates, to which physicians typically ascribe, the most important facet of health care is to do no harm. Thus a consumer should anticipate as the highest priority that their purchased traditional medicine will not jeopardize their health in any way. How can this be assured?

The past ten years have witnessed a very dramatic increase in the number of phytotherapeutical products from various traditional medicine systems around the world which are entering the commercial markets in developed and developing countries. Steadily, a global market for many of these products is emerging. This is both an economic opportunity for developing countries to market important traditional medicinal agents and a health care issue. The very diverse regulatory requirements being applied to these products in various countries are of great concern, and the quality of the science (botany, pharmacognosy, chemistry, and biology) which support their marketing offers an opportunity for improvement. As a result, there is an absence of clear and harmonious regulations regarding quality control and marketing, and the issues of safety and efficacy are being both understated and neglected. The WHO has issued a set of general guidelines for the study of traditional medicines in the form of a handbook[2]. The stated aims are to harmonize the terms being used, summarize the issues for developing research methodologies, improve the quality and value of research in traditional medicine, and provide appropriate evaluation methods to facilitate the development of regulation and registration of traditional medicines. An overall program for the development of more comprehensive standards for the safety and efficacy of traditional medicines is urgently needed in most countries in the world.

Currently, in the United States and elsewhere, substantial compromises with respect to consumer safety and product effectiveness are being made. One of these compromises is the use of a single marker compound to characterize a plant extract

chemically. These constituents may or may not be the active principle, but are frequently used to characterize extracts or plant materials giving an often false impression of standardization, without a demonstrated relationship to either safety and/or efficacy. Typically, consumers are unaware of this lack of assurance.

The first aspect of a medicinal plant to be assured is that the correct genus and species of plant material is being offered, and that the correct plant part is being used. Different plant parts of the same plant contain very different constituents, and thus to substitute a root part for a leaf, or a fruit for a twig, could result in toxicity rather than effectiveness. Consumers should be assured that the plant material or preparation is free of contaminants such as insects, (illegal) pesticides, solvent residues, heavy metals, aflatoxins and other toxic fungal metabolites, and radioactivity. Countries from which some plants are imported have different pesticide standards, and may be using illegal pesticides, herbicides, and even plant growth hormones to improve crop production.

Adulteration, the deliberate addition of biologically active materials to a plant preparation, has become a significant issue in the past few years. Several products have been withdrawn as a result of the demonstration of the presence of added ingredients to phytotherapeutical preparations. A recent report by Ernst[3] focused on the adulteration of Chinese medicinal herbal products with synthetic drugs. Some of the synthetic agents detected include: aminopyrine, indomethacin, phenylbutazone, and various corticosteroids.

When you buy a package of candy or a frozen food, there is usually a statement on the product which indicates "Best if eaten by", and then a date. Sometimes there is also a production date given, and often these are about a year apart; the "shelf-life" of the product. What is the "shelf-life" for a traditional medicine? How old is the traditional medicine that you are buying, and for how long will it be effective after you have bought it? More importantly, will it retain its safety and effectiveness? And when you buy the product a month or six months from now, will that material also be effective? Did it come from the same or a different plant sample?

There is a need for chemical and biological reproducibility and stability on a batch to batch basis. Thus, it will be necessary to have integrated chemical and biological systems developed which can correlate the stability of the active principle(s) with biological activity over time, and thereby establish a meaningful shelf-life. As the active principles become known, the authentication of primary reference standards will need to be improved substantially. In addition, there will be a need to develop quick, cheap,

accurate, and clinically relevant biological systems for the demonstration of biological activity for each batch of marketable product. The actual content of phytotherapeutic products versus the claimed content from a label has been an issue for many years. Routine analysis of marketed products is therefore an essential component of an effective regulatory program. We have shown that of 21 samples of capsicum cream, which is regulated as an over-the-counter product, less than half (43%) met the labeled content[4]. Five of the products had no capsaicin, only a synthetic substitute.

Extraction techniques may change over time as the need to optimize the active principle(s) in the preparation becomes apparent and as solvent costs or alternative isolation techniques, such as supercritical fluid systems, are introduced. This will mean that safety issues regarding the new extract will need to be re-established, and thus monographs for specific drug preparations and their standardization will need to be developed and continuously updated as scientific techniques and the standards associated with them evolve. Efforts to enhance the bioavailability of herbal preparations will be increase through liposome preparations and other forms of controlled release formulation. At each of these changes and improvements, it will be necessary to re-establish the stability of the preparation chemically and biologically, as well as the shelf-life of the product, in order to assure consumers that the product is likely to be safe and efficacious on repeated purchases.

Educating the Public

A potentially dangerous situation regarding traditional medicines and other phytotherapeutical products has arisen in many countries because of the widespread belief in two myths. The first myth is that natural products are safe, when some of the most toxic agents known to humankind are from nature. This myth is particularly prevalent when applied to preparations of traditional medicines that may have been used for hundreds of years. There are several false assumptions underpinning this myth; one of which is that the "safe" plants can be distinguished from botanically similar, toxic plants. Another is that the dose of known toxic plants, such as aconite, can be modulated to a safe, effective level without specific scientific input. Yet another is that since the plant is regarded as safe, it is thought that two pills rather than one, or double the dose will work better. Finally, if two plants with different uses have the same local name there is a

serious potential for misidentification, and unknown health consequences.

The second common myth is that consumers think that the contents of a box or a bottle of a traditional medicine which contains plant or fungal products are somehow regulated or controlled for their quality. What is the role of natural product sciences in explaining these aspects of traditional medicines to the public?

A Long Scientific Road Ahead

The classical view of what constitutes an approved and regulated drug in much of the world, is a single chemical entity which, in its purest form, has been rigorously evaluated for its biological, pharmacological, toxicological, and clinical effects[5].

An alternative, natural product preparation, frequently derived from a traditional medicinal plant, is the multicomponent compound mixture. Such a preparation, which may be comprised of several closely related, biologically active compounds (e.g. gingko flavonoids, capsaicinoids, valepotriates), is marketed when the separation of the individual chemical entities is very difficult, or not cost-effective, and/or is not required by regulation. Mixtures of this type are usually characterized chemically (TLC, GC, or HPLC fingerprinting) or biologically, although one expectation is that standardization will, in the future, involve both chemistry and biology.

Another type of natural product preparation is that derived from a single plant. Sometimes, this is the pulverized plant part (roots, leaves, fruits, etc) which is then encapsulated, tableted, or prepared as a tea or a poultice. Alternatively, the preparation may be an aqueous or alcoholic extract which has been dried and powdered. Expressed oils and essential oils would also be included in this category. These preparations are comprised of very complex mixtures of compounds, and standardization chemically (other than a "fingerprint" HPLC or GC profile) is impossible, although cursory analysis is often important for the purposes of authentication and absence of adulterants[6]. Also marketed in some parts of the world are preparations which contain multiple plant extracts. Biological standardization is essential in all of these cases, but is almost never accomplished. At the local level, and thus often found in herb markets, fresh plant material is often regarded as being crucial for the preparation of teas, etc. in order to optimize effectiveness[7]. One of the greatest challenges for the natural product sciences is at the interface between these various preparations and the larger health care system.

The challenge is to establish those which are safe, those which are efficacious, and those which can be made available in a sustainable manner.

The diverse information regarding the uses of a particular plant as a medicinal agent may, therefore, come from a variety of sources. There are many Chinese, Middle Eastern, and Indian texts, and the various herbals prepared and used widely in Europe in the Middle Ages. There are a multitude of texts on various traditional medicine systems which have been published in English or in the respective native languages. There are numerous review articles and published surveys of local practices, often organized by disease state. There is on-going field-work, and there are hundreds of years worth of plant specimens collected and catalogued in the herbaria of the world which frequently are annotated with commentary regarding their ethnomedical uses. In addition, as phytochemical and biological work on plants is reported there are frequently references in the introduction of the article describing local uses which may not have been reported previously.

Unfortunately, there is no single place in the world where an effort is being made to acquire and correlate this plethora of intensely valuable information for future generations. There is a substantial collection of information in the NAPRALERT (Natural Products Alert) database at the University of Illinois at Chicago[8]. This database was founded in 1975 and has information available on the ethnomedical uses, biological (*in vitro, in vivo,* and in human) evaluation and chemical constituents of plants from all over the world. It presently contains information on 46,766 species of higher plant. Of these, 14,301 species have ethnomedical data associated with them, and they represent 3,701 genera and 272 plant families. Given that there are about 275,000 species of higher plant, then at least 17% have been used ethnomedically. However, for 5,705 (ca. 40%) of these ethnomedically used plants, no compound has been isolated. Thus, even beginning to consider standardization based on a chemical constituent may well involve substantial initial research.

Standardization from a biological perspective is significantly more challenging. Some traditional medicines are used for specific disease states, whereas others are used prophylactically in situations related to maintaining life-style, such as anti-aging. In the latter instance, bioassays are more difficult to define and the end points are frequently less clear. Bioassays for antimalarial or antimicrobial activities on the other hand are well-characterized and established and can be used quantitatively. Any assay that is

developed has to be robust, i.e. capable of use on a day-to-day basis in a variety of labs without very expensive equipment and with a high degree of efficiency and quantitative reproducibility. New enzyme-related bioassays are under constant development also, and the same caution applies with respect to relevance to the disease state. One new approach currently under development is the application of liquid chromatography-electrospray mass spectrometry (or NMR) coupled with a bioassay to simultaneously monitor both the chemical and biological aspects of a traditional medicine preparation. In this instance quantitation is an issue to be addressed. The impact of traditional medicines on the modulation of genes in the human genome is also now being studied, and one development for the future will be to evaluate where a particular traditional medicine operates and use a specific microarray system to evaluate plant materials in this manner on a batch-to-batch basis. At present, the cost of such microarray systems is prohibitive for routine analytical work, but one can envisage that in the near future these costs will diminish substantially.

One of the most important inferences from the burgeoning sales of phyto-therapeutical products is that the scientific literature associated with them is expanding correspondingly. Consequently, continuous evaluation of the literature relating to analytical procedures, to biological and chemical information, and to clinical trials on phytotherapeutic and traditional medicinal agents everywhere in the world, becomes a very important aspect of safety and standardization.

Intellectual Property Rights

In the past twelve years, the area of intellectual property rights has become a highly contentious and difficult area of natural products chemistry and biology. The implementation of the Convention on Biological Diversity (CBD) codified a myriad of intellectual property issues. It instructed sovereign nations to develop plans to catalog and preserve their indigenous knowledge and their biodiversity[9]. With respect to the issues of accessibility, it proposed that Contracting Parties "endeavor to create conditions to facilitate access to genetic resources for environmentally sound uses..." In response to this suggestion, some countries chose to impose strict regulations and an overarching bureaucracy to control access to their biome[10]. Other countries chose to strongly encourage external interested parties to work with local personnel and try to develop

relationships at the scientific level which could foster development without exploitation.

The impact of the CBD on the scientific and clinical study of traditional medicine is very profound. Protecting and compensating local groups for their indigenous knowledge, and for providing access to the biome, is a reasonable expectation for both those who hold the resources and those who are seeking them[11]. Compensation may take any one of a number of forms, including developing training programs for individual personnel, developing laboratories through the provision of equipment, and providing symposium programs[12]. Longer term forms of compensation may include sharing in any royalties or productivity payments and offering first right of refusal for indigenous crop development.

These protections and considerations for the source of the knowledge and for compensation, including the timeframe and the nature of the compensation, are required because of the potentially significant impact on the commercial aspects of the knowledge and its development. A native plant cannot be patented. However, a particular extract of a plant, with a defined biological use can. There are several recent examples where this has occurred; even in instances where the knowledge was previously well-documented. Thus standardization protocols should be evaluated in light of these considerations.

Traditional Medicine - Drug Interactions

As mentioned earlier, there is a continuing notion among many users of traditional medicines that they are safe for human consumption. It is thought that the accumulated experience of extensive use has eliminated from ethnomedical practice, those plants which consistently proved toxic or variably effective. However, because of the complexity of the preparations that are being interwoven, and the concomitant use of over-the-counter and prescription products, the use of traditional medicines is in need of a substantially more carefully considered botanical, chemical, and biological scientific approach.

In the developed world, and also in many developing countries, phytotherapeutical products and traditional medicines are frequently taken with other medicinal agents, both over-the-counter and prescription. When these latter products were originally approved by the cognizant regulatory agencies, there was no consideration of the concomitant use of possibly multiple herbal products. The interactions of prescription and over-the-counter

products with phytotherapeutical agents and traditional medicines has now become a very serious clinical issue. It is one which requires substantial scientific study and development from the perspective of public awareness and safety. There are numerous reports of these herb-drug interactions[13]. One of the common ones is that of St. John's Wort (SJW) and a broad range of drugs including indinavir, cyclosporin, digoxin, fluoxetine, clozapine, warfarin, and theophylline[14]. This is because a diverse array of constituents in the extracts of SJW are biologically active and can induce certain drug-metabolizing enzymes in the cytochrome P450 system, and possibly can alter serotonin concentrations[15]. Another example of an unintended clinical outcomes is that of the platelet activation inhibitors (gingko, grape seed, etc.), which may cause complications of excessive bleeding during surgery.

Sustainable Use of Medicinal Plants

Sustainability, with respect to both the use of solvents for primary extraction, as well as in the cultivation of the plant material, will become important future criteria. Already we have seen that once a traditional medicine (e.g. ginseng) or a phyto-therapeutical product (e.g. golden seal) becomes a major marketed entity, then wildcrafting of the plant (taking a plant from only wild sources such as the forests or the meadows) can almost eliminate that plant, if agricultural techniques for crop development are not introduced. In this regard, Shinwari and Gilani studied a small community in Astore, in northern Pakistan[16]. Thirty-three plant materials were being used by the local population. One plant, *Betula utilis*, had almost been driven to extinction. Two plants were recommended for rapid *in vitro* development, and another was suggested for a sustainable harvesting program. The need for education of the local populace regarding conservation and development of medicinal resources was emphasized. WHO has issued a set of guidelines for good agricultural and collection practices (GACP) for medicinal plants[17]. The guidelines are specifically aimed at the protection of medicinal plants, and the promotion of their cultivation, collection, and use in a sustainable manner which conserves the medicinal plant and the environment.

It is well-known that growing plants in different soil or climactic conditions can have a profound impact on the chemical profile. Thus, standardization of cultivation and harvesting techniques will also have an impact of the overall standardization of the

finished product. Sustainable development as a crop may also impact on the age of the plant material that is processed for sale. This is significant because the secondary metabolite profile will change substantially during the different phase of plant growth - a frequently unknown and poorly evaluated factor when safety and efficacy are concerned.

An Approach to Standardization

We can now begin to develop a strategy for the study of traditional medicinal plants which is focused on a safe, standardized preparation. This approach was first considered by Farnsworth and colleagues in 1985[1], and subsequently by Fabricant and Farnsworth[18], and is expanded on here (Figure 1).

If one begins with a previously documented or reported plant, the first consideration is to check for the correct spelling of the local name and see whether there are any known synonyms. Sometimes, the same local name is given to several plants which may appear to be the same plant, or which are different plants, but which have the same use. The next step is to verify the Latin binomial for the plant and also derive any synonyms for that binomial in the event that the literature may have data reported for the same plant under two (or more) binomial names. Review of the biological and chemical literature is next. This may involve other closely related plant species (the same genus usually) and should include *Chemical Abstracts*, *Biological Abstracts*, and *Index Medicus*. In addition, as many sources of ethnomedicine information should be consulted as possible, so that a clear picture of whether the plant has been used elsewhere in the world for similar or other purposes can be determined. It must be emphasized that this type of literature work, like any other literature work in science is an on-going process. The data obtained from the literature must now be analyzed for breadth, depth, and appropriateness. What compounds have been isolated? From which plant part? Are any of them possibly responsible for the observed activity? Has the biological and possibly clinical testing been carried out appropriately, with the necessary controls? Have the biological data been interpreted correctly? Based on this information, which can range from very extensive to almost non-existent, decisions will be needed with respect to the highest level of biological tests that can be applied to the chosen extract(s). Another aspect of biological activity which may be available from prior testing data relates to toxicity. Are there any reports of toxic side effects from the plant in question? Are

there specific extraction, preparation, or dosage issues (routes of administration) to be considered? Are there known toxic metabolites from related species?

Acquisition of the plant material for study may require a number of levels of approval and negotiation depending on the whereabouts of the plant (forest or marketplace) and where and how the various aspects of the work will be conducted. In addition, licenses may be needed to export the plant material or the extracts derived from it to another country. Even if a plant is purchased in a local market, positive identification, some idea of the origin of the plant, and the preservation of a voucher sample with notes (or better a herbarium specimen) are needed. Negotiations to acquire plant material from the field may take some time as legally binding agreements are developed. Only when these formalities are completed, can field work with a local collaborator commence. Preferably, most or all of the scientific work should be done in the country of origin, with only minimal influence from outside laboratories. But in many countries of the world, that is simply not possible. Analysis of the extracts for pesticides, herbicides, heavy metals, and where considered important, known adulterants is the next step, so that when the biological data is determined in the selected assays, there is a high level of assurance that activity is due solely to the plant constituents. Bioactivity-directed fractionation is an important phase of the process because it may yield the compound, or group of compounds, responsible for the activity. In addition, it may demonstrate whether other compounds in the extract interfere with the potentiation of the activity. In other words, fractionation could afford clarification as to how to prepare a standardized preparation. Once there is good information regarding the active principles, investigations can begin as to what might be the nature of the preparation to be tested for potential marketing, which active compounds to use as chemical markers, and which tests to develop for batch-to-batch biological evaluation. Stability testing can start once a standard preparation has been determined and characterized, and this preparation is the one to be used for all *in vitro* and *in vivo* testing, prior to any testing in human subjects. Finally, it may be necessary to enlist crop specialists to develop methods for the sustainable production of the medicinal plant as a crop.

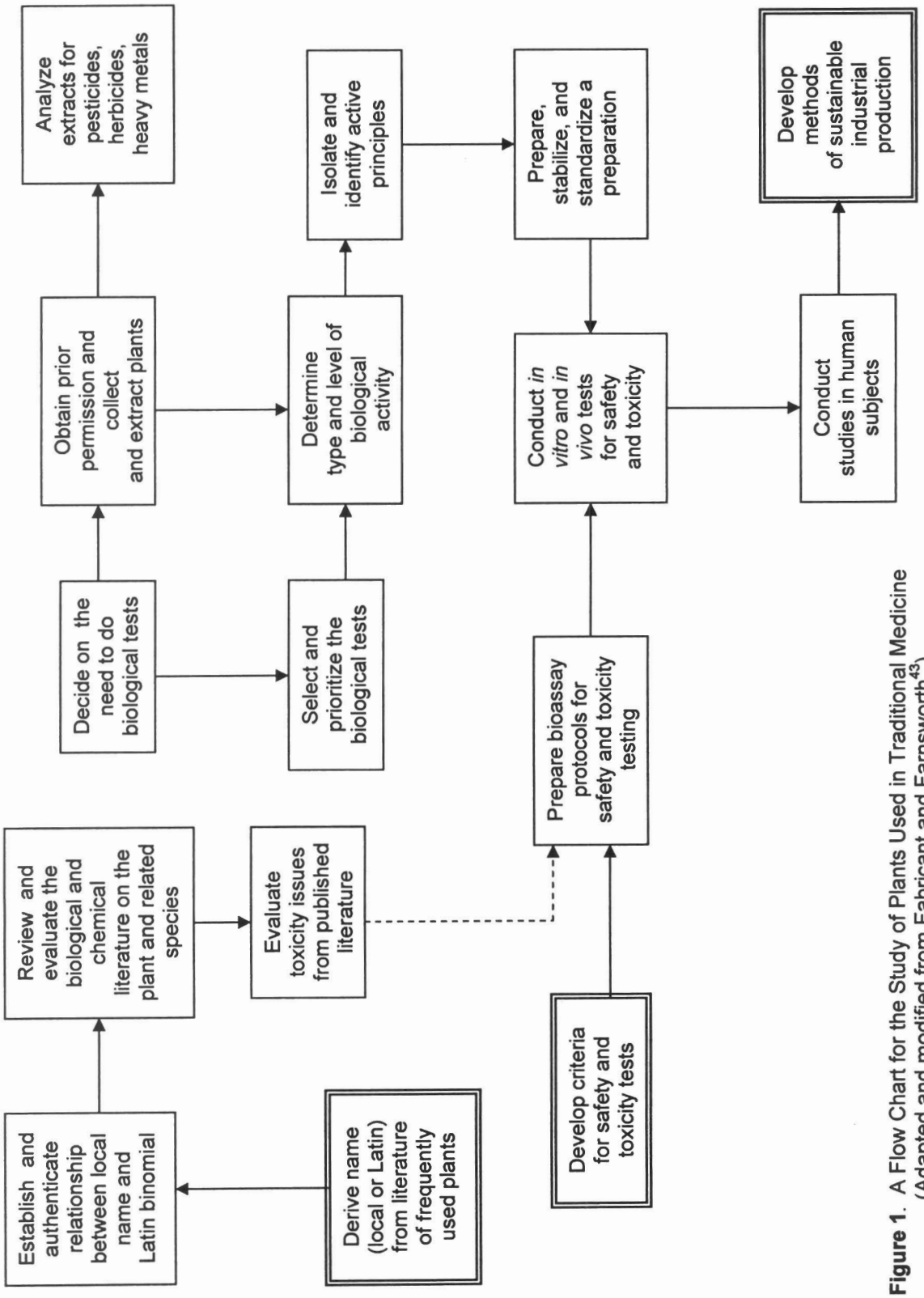


Figure 1. A Flow Chart for the Study of Plants Used in Traditional Medicine (Adapted and modified from Fabricant and Farnsworth[43])

An instantaneous, comprehensive set of standards for the acquisition, processing, production, sale, and marketing of traditional medicinal plants is clearly impossible. However, with careful planning and a long-term commitment a stepwise process can evolve to provide a solid system of regulation for the health and welfare of Thai citizens and for people in those countries to which Thai medicinal plants are exported.

Economic Development and Export Potential

The costs and environmental concerns relating to the discovery and production of synthetic drugs will continue to rise in the next fifty years. Therefore, as we consider the enhanced scientific study of traditional medicines from the aspect of the identification of the active agent for standardization purposes, there are other reasons, including drug discovery, and mechanism of action to be considered as justifications for the intense investigation of traditional medicines. Medicinal plants are the basis of 74% of the natural product prescription drugs, and there is a good possibility that the observed biological activity can be traced to a single compound or small group of related compounds. In an integrated pharmaceutical system, such a compound may be developed into a single compound drug, as well as being used as a marker compound for the traditional medicine. Consequently, there is the potential for countries to develop enhanced self-reliance and independence, resulting in a decrease in the importation of finished medicines from the north. Standardization with marker compounds, and assessment of their associated biological activity, can significantly add value to the product being marketed either locally or for export. Meeting a series of quality assurance parameters, some of which the buyer may not initially appreciate, will provide a consistent market advantage, particularly in a competitive export environment. A certified plant or plant preparation is simply more valuable. Thus, the necessity to develop the scientific foundations for understanding the scientific rationale traditional medicine in a given country is also economic. We have seen how the desperate needs for treatments for the major diseases of the world are being poorly served through the research efforts of the major pharmaceutical companies. Seizing this opportunity is therefore critical for long-term future health care.

One of the model approaches to this issue which was recently initiated in South Africa, is the in-depth scientific examination of local resources used as traditional

medicines for a variety of important diseases. The project is funded by the South African government and is a broad collaboration between a number of different groups representing different areas of botanical, chemical, biological, and pharmacological expertise. The program is aimed at searching for new medicines, and looking for "proof of principle" for traditional medicines.

Conclusions

There will be an increasing need for alternative, natural, sustainable sources of medicinal agents, compounds, derivatives, extracts, and teas. Because of the vast knowledge base that is the foundation of traditional medicine, those plants that are used in various traditional medicine systems will become critically important in the provision of primary health care in the future.

Overall, the scientific and regulatory situation regarding the currently marketed phytotherapeutical and traditional medicinal agents is no longer acceptable from a public health perspective in either the developed or the developing countries. A concerted effort by major international bodies, legislative groups, professional organizations, and industrial consortia is urgently needed to harmonize the regulations applying to the status and quality of these preparations which are, and will remain, the core of the global health care system.

Thailand is extremely rich in biodiversity, and many groups within the population make extensive use of this flora in their daily health care. Thailand also has a solid foundation of botanists, chemists, and biologists who can collaborate to establish standards for the safety and efficacy of traditional medicinal plants, which have the potential to lead to enhanced growth in local and export markets.

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