

Need to develop inter-cultural standards for quality, safety and efficacy of traditional Indian systems of medicine

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Traditional health sciences (THS) of various countries have evolved within different epistemologies and perspectives on disease, cause and cure. The epistemic framework, principles, concepts and practice are quite different from those of Western biomedicine. The traditional Indian sciences or shastras as they are called, possess qualitative standards that are derived by a subjective but impersonal approach to standardization. While there is a contemporary value in applying modern science and technology tools for creating objective and verifiable standards for traditional knowledge products and concepts, currently the approach to creating standards is one-sided. This is because it does not adequately consult the available qualitative THS standards and parameters. Furthermore, most therapies in THS involve both drug as well as non-drug interventions. Thus they also require a novel 'management trial' approach and compatible statistical designs in place of the conventional single- and double-blind drug trials to establish efficacy of treatment. This article cites constructive examples that illustrate the imperative for collaboration between scientists and traditional knowledge experts so as to promote mutual understanding and create relevant quality standards. It is such a collaborative approach involving in-depth consultation between traditional and modern health sciences that we refer to in this article as inter-cultural approach.

Keywords: Ayurveda, inter-cultural standards, medicinal plants, quality standards, traditional health sciences.

THE healthcare scenario in India and globally is undergoing dramatic transformation, evolving into a new emerging situation that emphasizes preventive health, customized care, body–mind medicine and the use of natural products¹. It is in this context that there is in recent decades a global and domestic resurgence of interest in the traditional health sciences (THS) because some of the requirements demanded by the emerging situation are inherent in them. Recent health-seeking behaviour studies testify the undeniable and widespread acceptance of Complementary and Alternative Systems of Medicine (CAM)². They suggest that any societal model of healthcare based on a single system of medicine will become obsolete in the next two decades, unless it broadens out to judiciously combine with complementary systems of medicine. This obsolescence will occur on account of the insufficiency of a single system to offer on its own, effective treatment for curative and preventive healthcare.

It is in this context of growing acceptance of THS products and therapies that questions regarding their efficacy and quality standards have become a matter of serious

concern to policy-makers, consumers and to the regulatory authorities in both the producing and importing countries. Today, government regulators do not take epistemological differences into account while setting standards to monitor quality in respect of consistency, safety and efficacy of THS products and services. Centuries of clinical evidence and practical methods for quality assurance that are available in the THS are thus overlooked. This unmindful neglect can be rectified by carefully translating the detailed and sophisticated traditional knowledge on identity, collection, processing and therapeutic applications into appropriate modern parameters, instead of setting standards *ab initio*.

A programme to develop modern inter-cultural standards for quality, safety and efficacy of traditional Indian systems of medicine is not only important for Indians, but also for global consumers. However, the project to develop such standards needs an appreciation of the epistemology of THS.

Epistemological differences between knowledge systems

In any knowledge system, scientific reason is applied in two ways. On the one hand, we can put several observa-

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tions together, thus building them up into broader objective pictures of the world. Through empirical evidence and systematic reasoning, these pictures can be integrated to create coherent fields of knowledge. On the other hand, scientific reasoning can function in reverse. Instead of building objective pictures, it can reflect inwards, in order to arrive at deep insights. This reflective reason is essentially subjective. In Sanskrit, this process is described by the word 'shastra', which implies making rules or laws. Shastra is often used as a traditional word for 'science'. These two ways of using reason have a long history of working together, since the beginnings of ancient science³.

In the last few centuries, the objective and analytical use of reason has developed well. Unfortunately, the development has been one-sided, and there has been a corresponding neglect of subjective reasoning. The neglect has gone so far that the word 'subjective' is routinely assumed to mean just 'personal', and a subjective use of reason is thus put outside the essential and proper functioning of science.

While an impersonal standardization is essential to all sciences, it can be approached in ways which are both objective and subjective. The objective approach is directed externally by prescribing standard techniques and instrumental analysis. The subjective approach is led through a reflective or inward investigation to discover qualitative parameters and principles that underlie natural phenomena.

Ayurveda shastra, the main THS of India has developed in a cultural milieu and through a methodology that is based on a subjective approach to standardization. At every level of the structure of the knowledge system such as principles, categories, concepts, logical framework, philosophy and worldview, there are major differences between Ayurveda and Western biomedicine. Ayurveda derives from a worldview that regards 'a living being as a microcosm of the macrocosm outside', thus accepting the unity between the two (*loka purusa samanya*)⁴. On the other hand, modern science is based on the observer-observed dualism, and on the Cartesian worldview⁵. The philosophical foundation of Ayurveda is derived from *sad-darsanas* (six philosophical traditions), mainly the *Samkhya darsana*. The Samkhya philosophy describes the devolution of the universe from the unmanifest which is a causeless state, to the mind, the sense organs and onto the five states of matter, with nine stages of devolution and twenty-four principles⁶. Modern science is based on logical positivism, which essentially advocates the idea that the ultimate basis of knowledge rests upon reproducible results. Another basic difference is the means of knowledge. Whereas Western science is mainly based on logical interpretation of empirical data, Ayurveda also gives importance to *apta vachan*⁴ i.e. impersonal subjective insights. In respect of understanding of health and diseases, Ayurveda has a systemic perspective based on a physiological theory that views the functioning of the body in terms of changes in energy fields (*doshas*) and their homeosta-

sis, whereas modern biomedicine is largely based on the study of changes in biological structures and their functions. Even though this is a simplistic portrayal of the differences in the two philosophies of science, it is evident that Ayurveda and modern science have different epistemologies and theoretical foundations.

It is important to appreciate these epistemological differences per se and not in terms of which is right or wrong or more superior or less. They represent different perspectives and ways of knowing and viewing nature and both have universal applications. Such cultural differences should be celebrated rather than give rise to conflicts.

It is thus challenging to develop tenable correlations between the concepts of Ayurveda and modern science. The bridging will however only happen when sensitive, open-minded scientists from the two knowledge systems dialogue in a sustained way and institutions devoted to inter-cultural research are specially created to pursue such interactions.

Traditional quality standards: Do they exist?

It is evident that any living, evolving system of traditional medicine which has served society for several millennia – such as we see in Asia, Africa and Latin America – could not have survived without possessing quality standards of its own. In most societies in these regions, health traditions remain undocumented because they are transmitted orally from generation to generation. This oral transmission despite its remarkable efficiency, outreach and cost-effectiveness, is poorly understood. In India and China, there are also codified medical traditions with extremely sophisticated theory and clinical practice documented in the form of thousands of medical manuscripts.

THS have their own sophisticated internal quality standards. They include standards for identity, collection procedures, processing technology, finished products, drug design and therapeutic applications. The criteria for collecting plants, for instance, may include the best time, season and stage of growth when the plant is most therapeutically active. It may include the best habitats for gathering the plants, in order to peak their medicinal potency. Standards also exist for safety and efficacy of 'pharmaceutical', 'nutraceutical' and 'cosmeceutical' products.

The inter-cultural approach to building quality standards

The evolution of inter-cultural standards is a complex task, as it requires deep understanding of both traditional and modern sciences. It involves the use of modern scientific tools of physics, chemistry and biology to establish universally verifiable standards. However, the identification of concepts, therapies, processes and products and the parameters on which they are to be standardized

needs help from THS from which they are originally derived; else the modern standards may be inadequate or even irrelevant to THS. The task of creating quality standards for THS products starts from establishing the identity of the medicinal herb, animal part or metals and minerals, and goes onto standardizing the process, product, pharmacological activity, clinical diagnosis and finally the therapeutic interventions.

To identify the raw material (a plant, for instance), a reliable traditional source – texts as well as traditional knowledge holders – must be consulted. Tradition identifies materials by vernacular names and descriptions. It is therefore necessary to carefully link the vernacular names and descriptions of plants to the appropriate botanical entity. This could be a simple or complicated exercise. For example, *Tulasi* (Sanskrit) is the vernacular name of a plant which when pointed out to a botanist would be correlated to *Ocimum sanctum* or *Ocimum tenuiflorum*. In the case of certain vernacular names, however, one vernacular name may correspond to more than one botanical entity. For example, the plant referred to as *Brahmi* (Sanskrit), is correlated to two distinct botanical entities, namely *Bacopa monneri* (L.) Pennell (*Neer brahmi*) and *Centella asiatica* (L.) Urban (*Manduka Parni*)⁷. Other vernacular names like *Pashana bheda* and *Shankhapushpi* also have several botanical sources and regional substitutes, which are different species that possess similar pharmacological activity. For instance, the herb named *Ativisha* has been correlated to a rare and expensive Himalayan herb, *Aconitum heterophyllum* Wall. Ex Royle (Ranunculaceae). However, Ayurvedic texts also suggest that *Musta* (*Cyperus rotundus* L., Cyperaceae), a common weed, can be used as a substitute to *Ativisha*⁸. Many of the Ayurvedic drug-manufacturing units use *C. rotundus* as substitute. Preliminary HPLC studies conducted at the Foundation for Revitalisation of Local Health Traditions (FRLHT), Bangalore led to interesting findings: despite there being no botanical relationship between the two species, they possess similar chemical profiles (Figure 1). This indicates that Ayurveda

possessed schemes to identify different botanicals with similar pharmacological properties.

Another kind of complexity connected with vernacular names is the problem of synonymy, wherein a single, traditionally used plant entity has several vernacular synonyms. Therefore, one needs the help of traditional scholars to group all the vernacular synonymy that refers to a particular plant. This can be best illustrated by citing the case of an important Ayurvedic text called *Caraka Samhita*. In this text there is a mention of 12,000 plant names, which actually pertain to only around 620 unique plant entities after resolving the synonymy of names⁹.

Since biological materials possess genotypic and phenotypic variability, while establishing standards it is important to take note of traditional schemes for therapeutic classification of plants. In ancient Ayurvedic texts such as *Susrutha Samhita*, chapters have been dedicated to different kinds of classifications according to properties and contain advice about time and region of collection (*Kala and Desh Vichar*). Details on the different qualities of rice cultivated in different soils, milk from different animals, etc. have been described¹⁰. An interesting example pertains to the plant *Ipomea mauritiana* (Vidari). In traditional practice, the mature tubers of this plant are advised for preparation of medicine. It was found that mature tubers of the plant, *I. mauritiana* are richer in phytoconstituents (Figure 2) than their immature counterparts¹¹. A general bioactivity assay such as the Brine shrimp bioassay¹² indicated that the mature tubers were more active as determined by ED₅₀ value (Figure 3). Another interesting example of collection standards is the case of turmeric (*Curcuma longa* L.). It is called as *rajani* or *nisa* in Sanskrit, meaning 'night'. The rhizomes are traditionally collected during night for better therapeutic purposes. Brine shrimp bioactivity tests conducted at FRLHT indicated that turmeric collected at night was significantly more bioactive than that collected during day (Figure 4).

The more complex aspect of quality assurance arises in respect of standardization of the manufacturing process

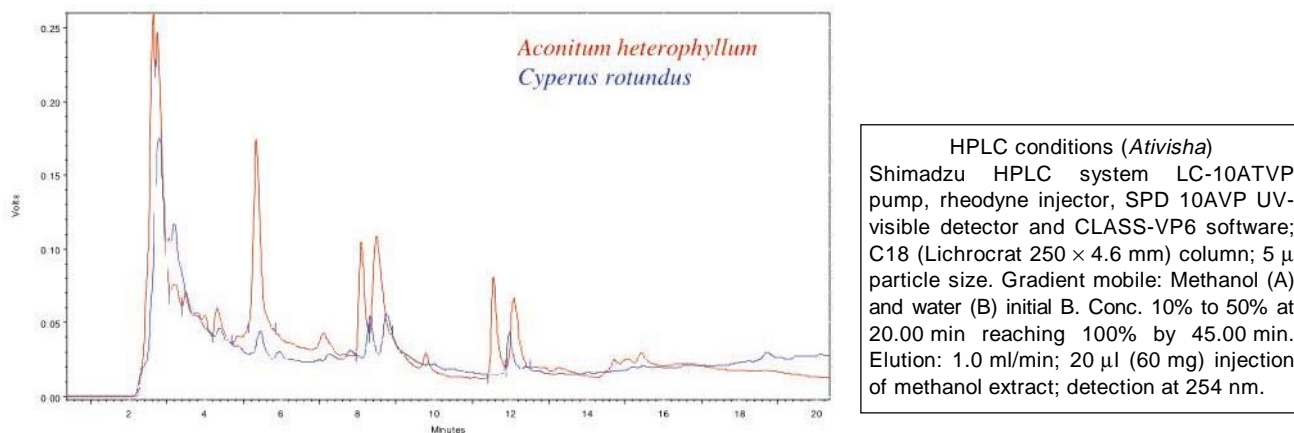
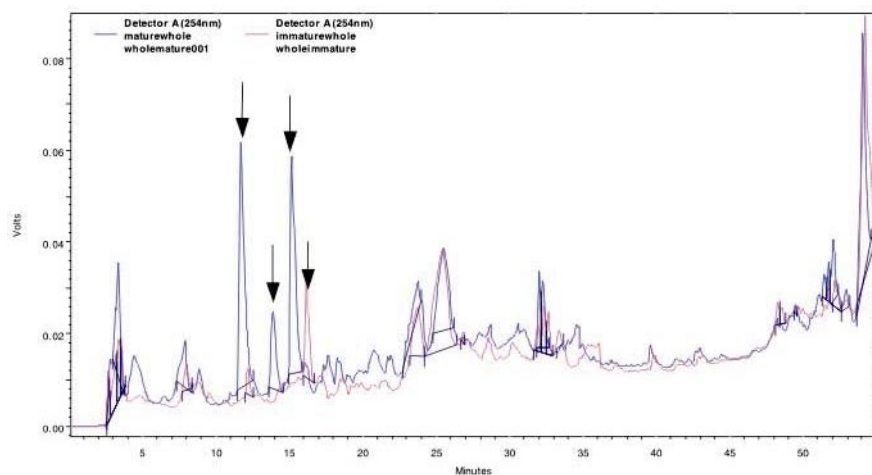


Figure 1. Similar HPLC profiles of *Aconitum heterophyllum* and *Cyperus rotundus*.



HPLC conditions (*vidari*)
 Shimadzu HPLC system LC-10ATVP pump, rheodyne injector, SPD 10AVP UV-visible detector and CLASS-VP6 software; C18 (Supelco 250 × 4.6 mm) column; 5 μ particle size. Gradient mobile: Methanol (A) and water (B) initial B. Conc. 10% to 50% at 20.00 min reaching 100% by 30.00 min. Elution: 1.0 ml/min; 20 μl (400 mg) injection of aqueous extract; detection at 254 nm.

Figure 2. Comparative HPLC profiles of mature and immature tubers of *Ipomoea mauritiana* (Vidari).

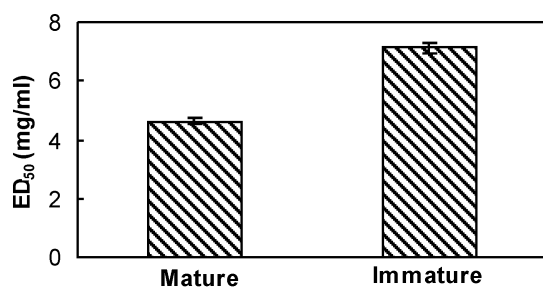


Figure 3. Comparative bioactivities of mature and immature tubers of *I. mauritiana* (Vidari).

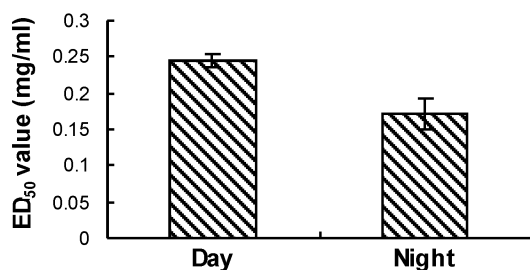


Figure 4. Bio-activity of night- and day-collected *Curcuma longa* (turmeric) rhizomes.

and finished product. The complexity arises because traditional products use a wide range of processing techniques and also dosage forms, from simple powders made from a single plant, to extracts made from many plants. The finished products may be aqueous extracts, herbal wines, herbal oils, baked products, plant starches or alkalis. These different dosage forms have been created because the end-products have differential rates and modes of bio-absorption in the body. Their design indicates appreciation of pharmaco-dynamics and kinetics in Ayurveda. Standardizing all these myriad processes and products poses a real challenge to modern scientists.

In recent times there have been questions raised about the safety of herbo-mineral drug preparations based on the science of Ayurveda. This is because of the fear that such preparations may not be bio-assimilable and thus cause heavy metal toxicity. Herbo-mineral products are referred to in Ayurvedic pharmaceuticals as *Bhasmas*. Quoting Valiathan¹³, 'bhasmas have evoked extraordinary interest, if not concern, because they generally contain a metal or mineral apart from herbs. Mercury, gold, silver and lead among metals and sulphur and arsenic sulphide among minerals are common ingredients'.

Recent scientific studies suggest that the elaborate preparatory methods used in ancient texts to prepare *bhasmas* led to important microstructural changes in the finished product. Perhaps the ancient 'chemists' were aware of the higher reactivity of very fine metal powders. Dube¹⁴ showed that by following ancient techniques, silver powders of narrow size distribution could be obtained. A study by Wadekar *et al.*¹⁵ on microstructure of *Vanga Bhasma*, a drug administered for various types of genito-urinary tract disorder, points towards size-stabilization. The study revealed that elaborate preparation methods involving treatment of tin metal with plant extracts, followed by several cycles of calcination leads to stabilization of particle size to around 25 nm. These preliminary studies on herbo-metallic drugs, suggest that Ayurveda was perhaps the world's first medical science to have made use of nano-technology in pharmaceuticals.

Another interesting example of the relevance of traditional advice regarding processing of single plant drugs can be seen in the case of a medicinally active pepper (*Piper longum* L.). This species is widely used in Ayurvedic medicine. It is advised in Ayurveda that the fruits of this plant should be extracted as a milk decoction¹⁶. Brine shrimp-based bioactivity studies indicate that the extract of the plant in milk is 27 times more active than the aqueous extract (Figure 5)¹⁷.

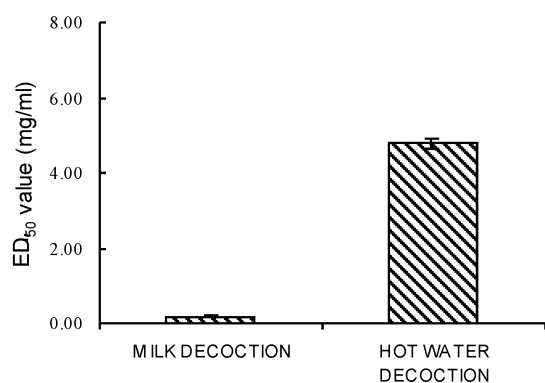


Figure 5. Comparative bioactivities of water and milk decoctions of *Piper longum* L.

There have been instances in the past when a traditional context of usage of a medicinal herb has not been taken into consideration and there have been serious consequences due to this. For example, kava-kava (*Piper methysticum*) is used in the preparation of a calming traditional beverage consumed by the Polynesians during festivals, due to which the herb was picked up by drug companies for use as an anxiolytic drug. However, the drug backfired in terms of safety and led to hepatotoxicity in several patients, forcing it to be withdrawn. On closer inspection the reason for the toxicity observed only in the modern derivative was pinned down to the solvent used for extraction. While the traditional preparations were water-based, the modern extraction was done in acetone. In addition to kava lactones, another compound glutathione, which was found to have a role in hepatoprotection, gets extracted in the water extract while it is significantly missing from the acetone extract. Glutathione reacts with the kava lactones and opens the lactone rings, thus reducing the side effects¹⁸.

The challenge of creating inter-cultural quality standards

The first step in building a bridge between traditional and modern scientific quality standards for traditional health sciences is to create databases on traditional knowledge with respect to identity, collection, processes, products, dosage form, diagnosis, therapeutic indications and end-outcomes. The second step is to study the relevance of the traditional concepts and approaches using modern scientific tools of chemistry, biology and physics. The third step is to identify the important physical, chemical and biological differences that are reflected when the traditional methods are followed, and demonstrate their relevance in establishing the quality, safety and efficacy of the products.

Modern tools of chemistry and biology are indeed capable of objectifying the traditional standards that already

exist. Microscopy is useful to the herbal sector in authenticating plant drugs. Chromatography techniques, such as HPTLC and HPLC are efficient for 'fingerprinting' herbal products. The flame photometer and atomic absorption spectrophotometer, electron spectroscopy for chemical analysis and electron microscopy are useful for studying traditional medicines that contain metals or minerals. Volatile materials are generally measured using gas chromatography. Higher-end research tools such as nuclear magnetic resonance, and mass spectroscopy can be used to characterize compounds in traditional medicines. Molecular DNA-based techniques have become an important tool to study intraspecific and interspecific genetic variation in raw drugs derived from plants and animal species. *In vitro* biological assays have also been used in the research, standardization and quality control of traditional medicines. There is also scope for engineering new equipment and analytical instruments as well as devising new techniques in this field, since the current scientific instruments have been designed for allopathic drugs and for single molecules. These may not fully address processes and products that involve extracts of multiple herbs and measure parameters related to systemic functions.

While using modern tools one should not expect perfect correspondence between the traditional qualitative and modern quantitative parameters, because the correlations will be limited by the difference of epistemologies. Western biomedicine assumes a one-to-one cause and effect of diseases and therefore, the medicines are usually targeted to alleviate the single assumed cause. Ayurvedic pharmacology evaluates the overall systemic effects of drugs. The study of the systemic effects of a drug will always reveal wide-ranging action on several apparently unconnected aspects of the biological system. For example, systemic activity of the plant, *Commiphora wightii* (Guggul) is described in Ayurveda by the term *meha*, *meda*, *granthi* and *sopa hara*¹⁹. These terms when translated into English, could roughly be correlated to several apparently unrelated biological phenomena like poly-urea, fat metabolism, anti-tumour and anti-oedematous activity. Thus far modern pharmacologists have mainly tried to correlate its action to lowering of lipid levels. They have in fact successfully established the cholesterol-lowering activity of a particular fraction of the plant because of the tenability of this particular correlation²⁰.

This correlation, however, is not complete because the plant as traditionally understood has multi-faceted systemic effects.

New insights from inter-cultural research to the world of medicine

While the inter-cultural approach is essential for interpreting and understanding THS, it can also help pioneer new contributions to the medical world. One exciting

field that is opening up due to inter-cultural research is pharmacogenomics.

This field is well recognized as a critical futuristic area for drug research. It is now understood that no drug acts uniformly on every individual; its action depends on the genetic make-up of the person. Correlating phenotypes with genotypes is a major challenge in this emerging field. Attempts to correlate phenotypic characters associated with ethnicity, geographical divisions or diseases to genotypes have limited success, as commonly used ethnic labels are inaccurate representations of genetic clusters and do not reflect the underlying genetic make-up. A proposed 'human phenome' project based on the Ayurvedic concept of *Prakriti* by Bhushan Patwardhan's group at the Interdisciplinary School of Health Sciences, University of Pune, anticipates efforts to create comprehensive phenotypic datasets from different populations to find broad-based genomic representation. However, there is no consensus on how to define phenotypes and what phenotypic features are to be included in the database. Classifying human population thus remains a major challenge to medical sciences²¹. It is in this context that the phenotypic classification scheme of Ayurvedic science called *Prakriti*, which can categorize all human bodies into seven phenotypes, can serve to lead the human phenome project. PCR-based gene polymorphism studies on *HLA DRB1* gene carried out by Patwardhan's group support the Ayurvedic basis of classifying human population and provides a proof of concept for its putative genetic basis²².

Pharmacological and clinical studies

A big challenge lies in setting modern standards for evaluating the efficacy of a traditional drug. This calls for a paradigm shift in design of clinical trials because the THS adopt a customized and multi-pronged strategy in treatment. This involves drugs, diet and non-drug therapies such as yoga. They aim at improving systemic functioning and both mental and physical well-being. Furthermore, the causes of diseases and their classification in the THS do not have a one-to-one correlation with Western biomedical categories. Traditional treatments are designed to achieve homeostasis, rather than to eliminate a specific agent(s).

These differences in the approach to treatment give rise to two issues. The first is that unconventional evaluation protocols are needed to assess an entire treatment 'package', rather than for one specific drug. The second is the need to use appropriate clinical, physiological, psychological and biochemical indices for evaluating outcomes which correlate well with the traditional understanding of cure. Customized and differential treatment is indicated by THS for patients who, from the Western biomedicine perspective, suffer from the same disease depending on their basic constitution or *Prakriti*. Ayurvedic concept of

classifying populations based on *Prakriti* may provide valuable insights into pharmacogenomics²² as well as in improving the design of clinical trials to test THS. The conventional double-blind, placebo-controlled clinical trials may not always be appropriate for THS. Case studies and observational studies – in which a clinical investigator monitors the effectiveness of a treatment package – can be valuable^{23,24}. Thus clinical trials need to be innovatively designed to evaluate 'management regimes', although in the case of OTC (over-the-counter) drugs, the conventional design of drug trials remains relevant.

The Inter-cultural gap in pharmacopoeias

Western-knowledge based pharmacopoeias – official handbooks on medical treatments – of traditional medicine like *British Herbal Pharmacopoeia*, *WHO Monographs* and even the *Ayurvedic Pharmacopoeia of India*, largely fail to adopt a comprehensive inter-cultural approach in setting quality standards. The quality standards they lay out for drugs are limited to the presence of major ingredients that are 'active', although no rigorous investigations have been carried to study the role of a whole range of compounds that may be present in smaller quantities, but whose therapeutic actions are unknown. Most pharmacopoeias list aspects such as morphology, microscopy, physico-chemical characteristics, nature of phyto-constituents and chromatography profiles, but are not as yet much informed by, or sensitive to collection protocols related to season, habitat stage of maturity, processing techniques and storage and shelf life that are critical for the quality standards established by traditional health cultures. They are usually silent on the standards for several traditional dosage forms, on-line quality control processes involved in their preparation and therapies. One of the reasons for such gaps is perhaps because detailed information on traditional knowledge parameters is not available in one place as a 'ready reckoner'. The other being the absence of an inter-cultural perspective in the development of pharmacopoeial standards.

International regulations on traditional medicine based on inadequate research investments

Globally, most of the pharmacopoeia on THS products have been restricted to single drugs or single plant extracts or at the most extracts of five herbs as fixed combinations²⁵. This is because not enough investment has been put into designing appropriate tools and methods to rapidly assess the quality of poly-herbals. While with respect to safety, traditional remedies will definitely need to be assessed within the same parameters now used for modern pharmaceutical, nutraceutical and cosmeceutical products, WHO has accepted that traditional medicines may need

less rigorous preclinical toxicological evaluations since their safety of use has been documented historically²⁴.

Conclusion

It is important for world-class pharmacognosy and pharmacology laboratories dealing with traditional knowledge products to have modern quality assurance standards based on the sophisticated qualitative standards built up over centuries within traditional health cultures themselves. Databases on TQS (Traditional Quality Standards) of major THS of the world need to be created for this purpose. These laboratories also need to engage in sustained dialogue with traditional medicine experts.

New scientific tools, methods and appropriate parameters need to be developed and research funding provided to rapidly evaluate the different pharmacologically active dosage forms like oils, wines, *bhasmas* (metal preparations), aqueous extracts made from poly-herbals, etc. Global customers are being unnecessarily denied the benefits of safe and effective traditional nutraceuticals, cosmeceuticals and pharmaceuticals due to poor investments in R&D.

The design of statistically significant schemes for conducting 'management trials' needs to be developed as a high priority task by bio-statisticians to evaluate efficacy of holistic treatment interventions.

Well-endowed schools for fundamental research into the theoretical foundations of THS as well as for intercultural research need to be created. The study of concept of *Prakriti* in the context of pharmacogenomics is a clear example of the potential.

Policy-makers and medical researchers should understand that authentic modern standards for products and services of THS can only be established through intercultural research. This is a vital pursuit, as it can enrich the field of medical pluralism, which holds the key for the advancement of world medicine.

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Received 6 December 2006; revised accepted 14 February 2007