REVIEW ARTICLE

Drug Safety 2002; 25 (14): 1005-1019
0114-5916/02/0014-1005/$25.00/0

The Use and Safety of Non-Allopathic Indian Medicines

N.J. Gogtay, H.A. Bhatt, S.S. Dalvi, and *N.A. Kshirsagar*

Department of Clinical Pharmacology, Seth GS Medical College & KEM Hospital, Parel, Mumbai (Bombay), India

Contents

Abstract

Non-allopathic Indian medicines, referred to elsewhere in the world as complementary and alternative medicine have gathered increasing recognition in recent years with regard to both treatment options and health hazards. Ayurveda, Siddha, Unani and homeopathy are practiced in India as non-allopathic systems. These systems comprise a wide range of therapeutic approaches that include diet, herbs, metals, minerals, precious stones and their combinations as well as non-drug therapies. Ayurveda is the oldest system of medicine in the world and by far the most commonly practiced form of non-allopathic medicine in India, particularly in rural India, where 70% of the population lives.

The difference between modern medicine and these systems stems from the fact that the knowledge base of many of the above systems, unlike Western medicine, is based on years of experience, observations, empiricism and intuition and has been handed down generations both through word of mouth and treatises.

The focus on non-allopathic systems of medicine in India can be attributed to various causes including a need to revive a rich tradition, the dependency of 80% of the country's population on these drugs, their easy availability, increasing worldwide use of these medicines, the lack of focused concerted scientific research and the abuse of these systems by quacks. Elsewhere, the increasing use of herbal products worldwide and the growth of the herbal product industry has led to increasing concern regarding their safety. The challenges in these non-allopathic systems relate to the patient, physician, regulatory authorities, the abuse/misuse of these medicines, quality and purity issues. Safety monitoring is mandated by a changing ecological environment, the use of insecticides, new manufacturing techniques, an as yet unregulated pharmaceutical industry, the availability of combinations of herbs over the counter and not mentioned in ancient Ayurvedic texts, and the need to look at the active principles of these medicines as potential chemotherapeutic agents.

The Indian traditional medicine industry has come a long way from the times when it was considered unnecessary to test these formulations prior to use, to the introduction of Good Manufacturing Practice guidelines for the industry. However, we still have a long way to go. The conflict between the traditional practitioners and the purists demanding evidence of safety and efficacy needs to be addressed. There is an urgent need for the practitioners of the allopathic and non-allopathic systems to work together to optimise the risk-benefit profile of these medicines.

Non-allopathic medicines, referred to elsewhere in the world as complementary or alternative or complementary and alternative medicine (CAM) have gathered increasing recognition in recent years with regard to both treatment options and health hazards.[1] In India, these systems of medicine once formed the mainstay of treatment in the country, but were relegated to a secondary status following the colonisation of the country by the British during the nineteenth and first half of the twentieth century.[2] The gap widened with the scientific and systematic study of evidence-based analytical Western medicine as opposed to non-allopathic medicine, which had a more holistic approach. Today, 65–80% of the world's population depend on traditional systems of healthcare, as does 70–80% of India's population.[3] Non-allopathic medicines comprise a wide range of therapeutic approaches that include diet, herbs, metals, minerals, precious stones and their combinations, and non-drug therapies.[4] While the reasons for the use of these medicines are many and vary between countries; in many parts of the world, these are the only sources of treatment the population has access to. The WHO, based on the above findings, issued a recommendation to promote herbal medicine in order to fulfil a need unmet by modern systems.[5] However, medicinal plants contain powerful active principles that can both cure and induce toxicity.

Ayurveda, Siddha, Unani and homeopathy are practised in India as non-allopathic systems. Of these systems, the first two are Indian in origin. Siddha medicine is very similar to Ayurveda but basically originated and is practised more in southern India, whereas Unani is practised more in the northern and western parts of India. Ayurveda, Unani and Siddha are fundamentally similar in their approach to health and disease. The present article aims to provide an overview of the efficacy

and safety of non-allopathic Indian medicines, the extent of their use and differences from modern medicine, and give an insight into issues related to safety monitoring and means to resolve them. The primary focus of this paper will be safety monitoring in Ayurveda, since Ayurveda is the most widely accepted and practised form of non-allopathic medicine in the country. In view of the fact that the challenges resulting from the use of medicines from alternative systems are similar worldwide, the literature reviewed is both from India and elsewhere in the world.

1. The Principles and Practice of Non-Allopathic Systems: Differences from Modern Medicine

1.1 Ayurveda

Ayurveda is the oldest system of medicine in the world and by far the most commonly practiced form of non-allopathic medicine in India, particularly in rural India, where 70% of the population lives.[6] It is also widely practised in countries in Southeast Asia including Bangladesh, Sri Lanka, Nepal, and Pakistan. Ayurveda medicine dates back to 1500–2000 BC and the first written reports can be traced to 600 BC. It has its origins in two Sanskrit words; Ayuh meaning life and Veda meaning knowledge.[4,7] Ayurveda is a science which describes four means of getting knowledge: scriptural testimony (*apta*); perception (*pratyaksha*); inference (*anumaan*); and reasoning intellect (*yukti*). The practitioners of this system are called Vaidyas. Ayurveda has eight specialities similar to modern medicine; shalya (surgery), shalakya (diseases related to the part of the body above the clavicle, i.e ophthalmology, otorhinolaryngology), kayachikitsa (general medicine), graha badha (psychiatry), kaumara bhritya (obstetrics, gynaecology and paediatrics), agada tantra (toxicology), rasayana (rejuvenation) and vaji karana (aphrodisiacs and treatment of sexual diseases). Life is defined as the union of a healthy body, mind and soul. Every individual is believed to be unique with a unique combination of three basic doshas or functional units, viz. *vata*, *pitta* and *kapha*, which are in turn the representatives of the five basic elements of nature consisting of air, water, fire, earth and space in the body. This uniqueness of an individual is described as prakriti (basic constitution). Ayurvedic medicine differs from modern medicine in its holistic approach where the individual (microcosm) and the environment (macrocosm) are treated as a single unit and believed to be in harmony.[4] Examination of the patient's constitution precedes the disease history. The ultimate aim of Ayurveda is not just treating the diseased person but also maintaining health. Ayurveda also believes that treatment must be individualised (similar to the science of clinical pharmacology). Disease as well as health is thought to be multilevel and multifactorial, with disease resulting from an imbalance at the physical, social, psychological and spiritual levels.[8] Therapy is rarely drugs only, but a combination of drugs, diet, exercise, and lifestyle modification where necessary.[9] Therapy is almost never directed towards a specific organ or system, but rather promotes the body's own healing mechanisms and self repair processes.

1.2 Siddha

This system of medicine bears a striking similarity to Ayurveda and flourished around the same time in southern India. The word Siddha originates from the sanskrit word Siddhi meaning a 'goal to be attained' or 'perfection' or 'heavenly', and one of the definitions of Siddha medicine is conquest of death and measures for preventing mortality. The practitioners of this system are called Siddhars. Siddha medicine describes that the human body is composed of 72 000 blood vessels, 13 000 nerves and ten main arteries all in a network, and the body is liable to suffer from 4 448 diseases. Apart from prevention and cure of illness, this system also aims at rendering the body immortal, and hence uses metals such as mercury and sulphur, extensively. This is based on the premise that unlike plants and herbs, metals are not perishable. Disease diagnosis after examination of the pulse forms a special branch of Siddha medicine called Nadi Vidya or the science of the pulse, which is to date used for identification of various

diseases ranging from anaemia to cancer. Siddha differs from Ayurveda in that it includes fewer drugs (475 Siddha drugs as against 6 000 in Ayurveda), and uses extensive astrology and incantations. Otherwise, the differences are more linguistic than doctrinal.[10]

1.3 Unani

This system has its roots in Greek community medicine. The language of the text is Urdu and this system also has different modes of treatment; regimental therapy, diet modification, pharmacotherapy and surgery. The Greeks had the concept of three body humours – blood, phlegm and bile, and their concepts bore resemblance to Ayurveda. The practitioners of this system are called Hakims. The Arabs introduced the Unani system to India. This system is based on principles put forward by Hippocrates who established that disease is a natural process and its symptoms are the reaction of the body to the disease. In India, Unani is noted for the treatment of sexual disorders and diseases of the skin. It has its own pharmacopoeia and a well organised pharmaceutical industry.[11]

Medicines from these systems, although used as single drugs, are more often prescribed as combinations of drugs. They were formerly available as powders, juices of fresh plants, decoctions and pastes for local application, whereas today they are available in the form of powders, decoctions, extracts, tablets, capsules, syrups, creams, ointments, oil for local application and enemas. The difference between modern medicine and these systems stems from the fact that the knowledge base of all the above systems, unlike Western medicine, is based on years of experience, observations, empiricism and intuition, and has been handed down generations both through word of mouth and treatises in Ayurveda such as the Charaka Samita (for internal medicine) and the Sushruta Samhita (for surgery).[12] The principles on which these systems are based are not easy to comprehend. For instance, disease is believed to be an imbalance of energies that govern life. The practitioners also use terms and concepts that cannot be accurately translated into the English language. For example, Prakriti or the constitution of the person is categorised as either '*vata*', '*pitta*' or '*kapha*', or their combinations. These are loosely translated as air, acid and phlegm, respectively, and thus do not give an insight into the system or disease or the diagnosis and from the perspective of modern medicine are not easily verifiable.

2. Current Status of Non-Allopathic Indian Medicine

In 1997, CAM was defined as practices that are currently not part of the dominant (prevalent/conventional) medical system for managing health and disease.[13] In India, nearly every major city has an Ayurvedic college and hospital. Larger hospitals of the systems even have surgical, gynaecological and thoracic wards where the ancient principles are strictly followed. For traditional medical systems as a whole, there are 2 860 hospitals with 45 720 beds, 22 100 dispensaries, (clinics manned by a physician, with or without a pharmacist) and 587 536 registered practitioners. This system is also recognised under the Central Council of Indian Medicine Act of 1970. For Ayurveda, there are 154 undergraduate colleges and 33 postgraduate colleges, with an annual admission capacity of 6 117 and 462 students, respectively.[14] The number of registered Siddha practitioners is now over 11 000, and there are 28 382 registered Unani practitioners.[14] Systematic research in various systems of Indian medicine under the patronage of the Government of India commenced in the year 1969 and with the establishment of the Central Council for Research in Indian Medicine and Homeopathy (CCRIMH). In 1978, this body was split into four separate research councils; one each for Ayurveda and Siddha, Unani medicine, homeopathy, and yoga and naturopathy.[15] The present annual turnover of non-allopathic products manufactured by large pharmaceutical companies is estimated at approximately $US300 million, compared with a turnover of approximately $US2.5 billion for modern drugs.[15,16] Current insurance policies also cover the use of traditional medicines in the case of inpatients.[14] In every Indian state, about one-third of the government medical posts (allopathic)

are occupied by physicians belonging to the non-allopathic systems.[17]

3. Opting for Non-Allopathic Systems of Medicine

The reasons why people opt for CAM has been a subject of much debate.[18-20] In India, in addition, people use these systems because these are the only systems they have access to, and the fact that they have been in use for thousands of years. Adverse drug reactions are also perceived to occur less with non-allopathic medicines.[21-23] All non-allopathic products are available over the counter.[15] Failure of the allopathic system to cure some chronic disease conditions like rheumatoid arthritis, asthma, epilepsy, and recurrent infections has also led people to turn to non-allopathic systems.

4. Challenges in Safety Monitoring of Non-Allopathic Indian Medicines

4.1 Patient and Physician

All traditional medicines in India are available over the counter and their easy availability leads to their use by a large number of patients. However, in the perceived belief that they are 'safe', the patients need not necessarily inform physicians of their concomitant use. At our therapeutic drug monitoring clinic, we observed two patients taking phenytoin 300 mg/day who had well-controlled seizures who presented with sudden loss of seizure control. A close history taking revealed that they had started taking 'Shankhapushpi', a purported memory enhancer. Animal studies with rats were carried out both with single and multiple doses of the two drugs given alone and in combination. It was seen that on chronic administration, both the anti-epileptic effect and plasma levels of phenytoin were reduced by 'Shankhapushpi'. Single-dose administration of the drugs did not lead to any change in phenytoin levels but decreased its anti-epileptic effect. Thus, the interaction was found to be both pharmacokinetic and pharmacodynamic.[24,25] Another marketed memory enhancer 'Mentat' has been shown to increase phenytoin levels in rabbits.[26] Honey, which is used in Ayurveda both as a drug and vehicle, has been shown to decrease the bioavailability of carbamazepine.[27]

Worldwide, herb-drug interactions have been documented for St John's wort (*Hypericum perforatum*), Ginkgo (*Ginkgo biloba*), kava-kava (*Piper methysticum*), and Ginseng (*Panax ginseng*, *P. quinquefolius*).[28-32] The documentation of herb-drug interactions, however, still remains poor and under-researched, in part due to the variation in content of the herb in the marketed preparations.[33,34] Similar-sounding brand names can also create problems for patients. We found that an engineering student took a pain relief preparation 'Vedana Nigraha Ras' which translates as 'Pain relieving tonic', presuming it to be an Ayurvedic medicine based on its name. Examination of the bottle label revealed that it actually contained 530mg of aspirin and 100mg of paracetamol (acetaminophen).[35]

From the physicians' perspective, the practice of Ayurveda today is vastly different from the ancient times. Formerly, vaidyas spent a minimum of one hour examining and diagnosing illness, grew herbs in their backyards under known soil and temperature conditions, and formulated their own medicines. Today, at least in the urban setting, a busy private practitioner or an Ayurvedic practitioner in a modern hospital like ours may see over 20 patients in 1 hour. Most of the medicines given to the patient by him are available preformulated from pharmaceutical companies, whereas the ancient texts mention that a physician must formulate his or her own medicines.[22] The current legislation of the country prohibit modern medicine practitioners from prescribing Ayurvedic medicines and vice-versa. However, this may not necessarily be followed. The practitioners of both allopathy and Ayurveda also believe that concomitant therapy is reasonably well tolerated. Practitioners of non-allopathic systems may give advice on continuing or discontinuing allopathic medicines. Discontinuation can lead to serious consequences particularly for diseases like asthma, diabetes, epilepsy

and cancer. A 15-year-old boy with stage IIA nodular, sclerosing Hodgkin's disease was recommended conventional treatment with multiagent chemotherapy and low-dose irradiation to the involved field. He progressed to stage IIB 4 months after the use of a dietary supplement and did not take the treatment advised. The dietary supplement contained the herb astragalus, dairy colostrum and whey supposed to elevate natural killer cell activity.[36] Continuation can lead to herb-drug interactions.[33,34] Low spontaneous reporting of adverse events is a worldwide issue. For Ayurvedic practitioners, without any training in their curriculum about the need to identify, document and monitor adverse drug reactions (ADR), this has become a big issue.

4.2 Regulatory Issues

Currently three categories of non-allopathic medicines are available for use in India: those formulated for the individual patient by the practitioners and containing only herbs; a combination of herbs and minerals individually formulated; and branded proprietary herbal medicines, containing single herbs and combinations. Their approval for marketing rests with the DCGI (Drug Controller General of India) and ISM & H (Indian Systems of Medicine and Homeopathy) who are the regulatory authorities for these medicines in India. Of these, the branded medicines are given marketing permission based on the fact that the manufacturing processes adopted by the company are identical to those mentioned in the Ayurvedic texts. Also, the marketed formulations often include medicines that have been formulated by combining individual plant extracts that have been mentioned as being effective in Ayurvedic texts.[15] For example, a formulation may have six ingredients each with a specific action. This combination is not described in Ayurvedic texts, only the individual plants have been mentioned as being effective. These formulations are thus new chemical entities with neither safety nor efficacy data even in the Ayurvedic texts. 'Geriforte' tablets are an example of a non-allopathic medication recommended for use in anxiety disorders and postmenopausal syndrome. These tablets contain a total of 49 herbs and two 'bhasmas' (organometallic compounds) of iron and zinc. 'Flu Five' is yet another preparation marketed for upper respiratory tract infections (URTI) which is a mixture of three formulations that have been mentioned as being individually effective for URTI but with no mention of a combination of these as per the Ayurvedic texts.

In India, there exist three centres for ADR monitoring, a National Centre in New Delhi, and two WHO special centres at Mumbai and Aligarh in North India (ours being a WHO special centre). These centres in turn report ADRs to the Drug Regulatory authorities. All centres are located in allopathic medical colleges and started in the late 1980s with a view to monitor ADRs to allopathic medicines, and hence over the last several years, this has been their major role. Occasionally, these centres do receive reports of ADRs associated with non-allopathic medicines, but as yet there is no concerted effort to monitor ADRs to non-allopathic medicines.

4.3 Quality and Purity Issues

The Charaka Samhita has given guidelines on the quality and purity of medicines and has mentioned that "all herbs should be stored in houses that are windless, and guarded against fire, water, moisture, smoke, dust, mice and quadrupeds".[37] Today, quality control of the crude plant materials is the most important and challenging issue of all. The major difficulty in this is the batch-to-batch variations in the medicinal herb. The reasons are several-fold, and include ecotype pharmacological variation, soil condition, status of nutrition, seasonal changes and climatic conditions. Because of lack of quality control, the amount of the active principle can vary between batches and manufacturers.[38,39] It has been shown with ginseng that the amount of ginseng varied widely between preparations, and some did not contain ginseng at all.[40] Also, the types of herbal material used by manufacturers and practitioners are different. The manufacturers use the crude (raw) materials, which are often cultivated near their own manufacturing units while the practitioners use material from the

market. Prabhu et al. found that the two botanical varieties of betel leaf (*Piper betle Linn.*) had two different actions; the Mysore variety lowered the activity of intestinal enzymes, whereas the Ambadi variety stimulated the enzyme activity.[41] The difference in quality is reflected in the vastly different pricing seen in the Indian market. For instance, the cost of bamboo used as an aphrodisiac and for upper respiratory tract infections ranges from Indian rupees (Re)80–100 to Re1500–2000 per kg. Similarly the cost of *Terminalia chebula* used for gastrointestinal disorders ranges from Re40–50 to 1600 per kg. Widespread use of pesticides, heavy metals and pollution also lead to adulteration of the ecotype. Misidentification of the plant, can also lead to toxicity. In the US, two cases of digitalis poisoning with a dietary supplement used for internal cleansing have been reported. None of the patients were actually taking digoxin.[42]

In India, currently, in addition to potency, purity is also not subject to monitoring by a regulatory agency. The use of *Aconitum ferox* (*Vatsanabh*) is a case in point. The roots of this plant are considered toxic as they contain the alkaloid aconitine. The detoxification procedure prior to the use of this plant includes boiling the roots with two parts of cow's urine (seven hours per day) for 2 consecutive days. The roots are then washed with water and boiled with two parts of cow's milk for the same duration. These are then washed again with lukewarm water, cut into pieces, dried and ground to powder. Aconitine containing preparations are consumed for their purported anti-inflammatory, analgesic or cardio tonic effects. However, there is no check on the alkaloid content in the various marketed preparations. Fatalities and life-threatening cardiotoxicity have been reported with this preparation in Hong Kong.[43]

4.4 Abuse/Misuse Issues

The Charaka Samhita has classified physicians into three categories; pseudo-physician, feigned physician and a genuine physician.[35] The non-allopathic systems are exploited by quacks that induce gullible patients into spending enormous amounts of money with little benefit, particularly for chronic diseases. Our analysis of so-called 'Ayurvedic' tablets given for the treatment of epilepsy showed that these tablets actually contained phenytoin and phenobarbital (phenobarbitone).[44] Likewise, our department carries out analysis of the corticosteroid content of so-called 'non-allopathic' tablets. Between 1997 and 2001, 73 samples were analysed and ten were found to contain corticosteroids by thin layer chromatography.(unpublished data). There are similar findings by Gupta et al.[45] Chopra.[46] reported deep burns after the use of unstandardised plant extract of *Semecarpus anacardium* (*Bhallatak*). Findings such as these bring disrepute to these systems when published, and shift focus away from the possible benefits.

4.5 Use of Heavy Metals

In Ayurveda, an entire branch deals with metal-mineral studies termed as 'Rasashastra'. Seventy-five elements were in use during 8th century BC. Of a total of 6 000 medicines listed in the Ayurvedic texts, at least 35–40% contain heavy metals and about 20–25% of formulations contain more than one heavy metal.[15] The most commonly used heavy metals include lead, gold, iron, mercury, arsenic, copper, zinc and silver (table I). Metals are intended to be used as adjuvants to the primary herbal therapy and are commonly used for the treatment of chronic illnesses such as rheumatoid arthritis, epilepsy, haemorrhoides, insomnia and asthma, and other diseases that have an autoimmune basis. The rationale behind the use of metals is that in addition to exerting their own therapeutic effect, the metals help the drug in the formulation to reach its target site, and enhance the potency of the medication. After purification and oxidation by addition to herbs, the preparation containing the metal is now called a bhasma translated as 'ashes' (organometallic compounds). There are systematic step-wise procedures for the preparation of these bhasmas for mainly three reasons; to detoxify them, to convert them into an easily absorbable form, and to improve the potency and efficacy of the preparation. Bhasmas are contraindicated in pregnancy, lactation, in children

Table I. Commonly used metals and precious stones with indications, adverse events and dosage as per Ayurvedic texts

Metal	Indication	Adverse events	Maximum recommended daily dose (mg) as per Ayurvedic texts
Gold	As a cardiac and nerve tonic, memory enhancer, psychiatric disorders, poisoning, rejuvenation, chronic cough	Weakness, urticarial rash, death	15–30
Silver	Diabetes, anti-aging, nerve tonic	Weakness, urticarial rash, major diseases	30–60
Copper	Non-healing wounds, anaemia, haemorrhoides, bronchitis, chronic rhinitis, acid-peptic disease, worms, inflammatory conditions, hepatic dysfunction	Burning, excessive perspiration, anorexia, giddiness, fainting, diarrhoea, vomiting, death, hepatitis, cirrhosis, tremors, haemolytic anaemia, renal dysfunction	8–30
Iron	Anaemia, eye tonic, poisoning, haemorrhoides, splenomegaly, hyperlipidaemia, anthelminthic	Erectile dysfunction, cardiac disease, calculi, hiccups, death lethargy, coma, shock, liver injury, renal failure	30–240
Lead	Diabetes, as an aphrodisiac, worms	Dermatological conditions-pruritus, fistula-in-ano, anaemia, renal diseases, peripheral neuropathy with demyelination of long neurons, ataxia, convulsions, coma, death	30–125
Diamond	Cardiac tonic, chronic/recurrent infection, ascites, eye disorders, erectile dysfunction	Anaemia, dermatological conditions, paraplegia	12.5 (100mg costs ≈$US12.5)

(up to 5 years of age), and the elderly. The ancient texts mention two common tests for a perfect bhasma; one that is so fine that when pinched between the thumb and the index finger, it settles on the whorls of the fingers. Also when sprinkled on water, it should float. In addition, specific tests for specific metals are also mentioned. For example for copper, discolouration of yogurt 5–8 hours after addition of the bhasma is indicative of impurity. Lead bhasma, if kept in an iron vessel and heated at a high temperature, turns viscous and is indicative of an improper bhasma.[47]

The doses of metals used in practice are based on recommendations given in the ancient Ayurvedic text, which in turn is based on experience in treating patients. However, this is not a guarantee of safety as reflected by the fact that very few Ayurvedic physicians actually use or prescribe them in their practice. Bhasmas are often used as second line agents when first-line therapy fails. The toxicity of bhasmas relates to the fact that even Ayurvedic physicians who prescribe these in doses recommended in Ayurvedic texts, end up with patients who have toxic symptoms due to proprietary medicines themselves containing metals in amounts greater than the prescribed Ayurvedic dose. In one study, an analysis of 18 samples for lead and six samples for mercury revealed that all samples contained metals in excess of the permissible amounts (from 12–1500 ppm of lead and 1–7.5 ppm of mercury).[21] The patient usually presents with anaemia and basophilic stippling of the red cells is seen in a peripheral blood smear. In addition, medicines not supposed to contain lead, were also found to contain lead. In Singapore between 1990 and 1997 in a survey of 2 080 Chinese proprietary medicines that were screened for metals, 42 (2.1%) were found to contain metals in amounts exceeding the legal requirements.[48] Twenty of the 42 samples contained mercury as the contaminant. The reasons for the presence of metal in excess could be several-fold: addition as an intentional ingredient; deliberate adulteration; standards of purification not meeting those men-

tioned in the Ayurvedic texts; contamination during manufacture from grinding weights; use of metal utensils for preparation; and contamination of the soil in which the herbs were grown.

4.6 Use of Precious Stones and Marine Products

There are a total of nine precious stones used as drug therapy, of which pearl, coral and diamond are common. While diamonds are used as cardiac tonics, pearl is used as an aphrodisiac and for inflammatory eye conditions as a cooling and soothing agent. When purified and processed along with herbs, they too are classified as bhasmas.[49] Some marine products are also used as medicines; conch and oyster shell are purified and made to bhasma. Manufacturing of these medicines is a complex rigorous process that is temperature dependent. Toxicity is seen only with diamond. It is mentioned that, a stone should not be used if a portion of the stone is opaque or black in colour or if a part of the stone is of a colour other than the basic colour of the stone. If properly made, the bhasma should not produce a burning/tingling sensation when kept on the tip of the tongue. Methods of estimation of the content of these precious stones, though mentioned in the ancient texts, may or may not be carried out by Ayurvedic physicians who preformulate them or prescribe proprietary medicines. Toxicity can result if manufacturers do not comply with all steps listed in the ancient texts, and take shortcuts to save on costs and time.

4.7 Use of Poisons as Medicines

The Charaka Samhita has said there is nothing in this world which does not have therapeutic utility in appropriate conditions and situations. All non-allopathic systems use several 'poisons' for therapy including 'Ahiphen' (opium), 'Kupilu' (strychnine), 'Dhattur' (Atropine), 'Vatsanabha' (aconite) and 'Bhallataka' (Semicarpol). The Charaka Samhita states that "even an acute poison can become an excellent drug if it is properly administered. On the other hand, even a drug, if not properly administered becomes an acute poison". It also states further that "a drug not known is likened to poison, weapon, fire and thunderbolt while the one known, to nectar". Toxicity with poisons occurs either after prolonged usage or overdose. Usually these preparations are available in combination and are contained in approximately 25% of the formulations.[15] This leads to their unregulated use and toxicity. Many of them are also advertised widely as 'safe' medicines.[50] They are to be prescribed only by a trained practitioner, under strict supervision, but this does not happen, as they are available over the counter. Until June 2000, these drugs did not have to be labelled as toxic but now under stringent Good Manufacturing Practice (GMP), they need to be labelled with the warning 'to be taken under medical supervision only'. In addition, following toxicity, the patient is often presented to an allopathic and not an Ayurvedic physician, who may miss taking a history of non-allopathic medicines.

4.8 Safety of Nonpharmacological Ayurvedic Treatments Such as 'Panchakarma'

Panchakarma is a combination of two Sanskrit words pancha (five) and karma (methods/measures), and is an integral part of Ayurveda. This modality of treatment is used on both healthy and diseased individuals, the basic principle being detoxification. In a healthy individual it serves the purpose of maintaining health, whereas in diseased states, the detoxification precedes drug therapy and is believed to be necessary for drug effectiveness. It purifies the body from gross to molecular levels and cleans all channels of the body for free flow of nutrients, drugs and metabolites. The procedures in Panchakarma involve body massage and application of heat as preparatory measures and the induction of emesis (vaman), purgation, enema, use of aerosols for nasal drug delivery and liquefaction of the toxins in the form of sputum induction and bloodletting (using leeches) as the main purificatory procedures.[51] A strict diet and life style is followed after the treatment under the physician's supervision. Since this procedure involves excessive fluid loss, anticipated adverse

events include dehydration, exhaustion, hypotension, loss of consciousness, cardiovascular collapse and even death. These procedures both in modern allopathic and Ayurvedic hospitals are carried out with adequate cardiovascular monitoring which includes half-hourly pulse, blood pressure and ECG monitoring. Hence, it is mandatory that these be carried out by trained staff and under adequate supervision. In view of the supposed safety of these medicines and the mushrooming of so-called 'Ayurvedic' clinics in the country, these are often carried out by untrained and non-qualified people with disastrous consequences.

4.9 Irrational Use of Ayurvedic Medicines

The Charaka Samhita has defined an ideal drug as one which requires to be taken in small doses, has a rapid onset of action, is easy to take, easy to digest, palatable, has a pleasing appearance, curative of a particular disease and relatively harmless. Individualising drug therapy in Ayurveda is one of its most critical components. Formulations that contain metals and poisons are contraindicated on an empty stomach. People residing in cooler climes are told to avoid pepper (*Piper longum/nigrum*) that has been cultivated in hot climates. These people are also requested to avoid the use of garlic, and ginger that are 'hot' in nature. For aconite, one is told to avoid the use of spicy, salty and sour food, which is believed to increase the potency of the active principle.[52] Irrational use of these medicines, which is not in line with the above principles, by both allopathic and non-allopathic physicians, results from their easy availability, availability of preformulated preparations and lack of knowledge thereby leading to unexpected toxicity.

5. The Way Forward

5.1 Regulations and Pharmaceutical Industry

There are over 7 000 manufacturers of Ayurvedic products in India. However, of these less than 200 are members of the Ayurvedic Drug manufacturing association and the remaining are largely unregulated. The total Indian Systems of Medicine industry has been rated as a $US840 million industry out of which $US700 million is from Ayurvedic and the remaining from the Siddha, Unani and other systems.[15] The current growth rate of this industry has been stipulated to be 13–14%. The export value of crude drugs from India to the international market has increased 2.76 times between 1985 and 1986 and 1994 and 1995 and now stands at Re53.2 million.[53] (Re49 = $US1). Today, Ayurveda, Unani, Siddha, naturopathy, yoga and homeopathy are both recognised by the Indian government as well as integrated into the national healthcare system. Schedule E-1 of the Drugs and Cosmetics Act lists all ingredients from Ayurveda, Siddha and Unani medicine, which are supposed to be toxic. The availability and sale of these drugs is not restricted. However, the labels of the formulations containing these medicines must include a warning stating "to be taken under medical supervision only".

In 1995, the Government of India created the Department of the Indian Systems of medicine and this department with its 4 000 personnel works towards standardisation, enhancement of the availability, quality of raw materials, research and development, information dissemination, and communication and involvement of the practitioners of alternative systems of medicine into national healthcare.[54] The development of GMP for non-allopathic systems of medicine aims to improve the quality and standard of Ayurveda, Siddha and Unani medicine. For the pharmaceutical industry, standards of quality are specified under GMP and these include sensory (e.g. colour, texture, odour, touch), microscopic (e.g. identification of the plant and any adulterant), physical (e.g. solubility, specific gravity) and chemical (e.g. alkaloid content) factors. Optional tests include techniques like nuclear magnetic resonance, high performance liquid chromatography and bioassays. The GMP guidelines were released in June 2000 and manufacturers have been given time, up to the 31st of December 2002, to comply with them.[55]

These rules of the Government of India form part of the Drugs and Cosmetics Act are listed under Schedule T, and contain requirements for essential infrastructure, manpower and quality control. It is hoped that the end result of this would be use of good quality, authentic and contaminant free raw material for making drugs for the country as well as permit their export, since quality is closely linked with safety. The manufacturing units have also been asked to develop standard operating procedures for reference and inspection. Exempt from these rules, however, are registered practitioners and teaching institutions that prepare their own medicines. The Indian Systems of Medicine is also working on strengthening its monitoring and surveillance systems to carry out regular inspections as well as surprise checks.

5.2 Establishing Safety and Efficacy in Clinical Trials

The 'gold standard' for the evaluation of efficacy of any therapeutic intervention is the randomised, controlled clinical trial (RCT), which can also detect type A adverse events.[56] For non-allopathic systems, which are considerably heterogenous, this presents significant problems.[57] The use of the placebo is one example. The concept of a placebo *per se* is not mentioned in the Ayurvedic texts. While it is easy to find placebos for trials on sleep, obesity and rheumatoid arthritis, finding a placebo for Panchakarma procedures may not be easy. Difficulty in blinding is yet another issue.[58] For instance, the use of neem oil (*Azadirachta indica*) in wound healing trials where the strong smell of neem would prevent blinding. Also the treatment used as comparator should be the most representative and the most appropriate for the disorder. While modern medicine practitioners are sceptical about their use, non-allopathic practitioners feel that evaluation of these time-tested remedies to satisfy Western thinking is not necessary. The solution probably lies in finding a middle path where some remedies that are amenable to a RCT be tested in such a manner. A study by Antarkar et al.[59] of the use of 'Aarogyawardhini' in acute viral hepatitis is one such example.[59] Likewise, a study by Bichile et al.[60] in rheumatoid arthritis has compared 'sallaki' (*Boswellia serrata*) with diclofenac sodium. These studies also show how modern medicine practitioners can work together with the non-allopathic physicians. For other drugs, open but parallel group comparative studies which may be assessor blind, with periodic checks on trial conduct would serve the purpose.

An analysis by Lodha and Bagga has shown that evidence-based studies on the efficacy and safety of traditional Indian medicines in patients are limited, and the data available is mostly experimental or in animals.[61-63] With a view to increasing concerted research in traditional medicine, the Indian Council for Medical Research (ICMR) has laid down guidelines for the conduct of clinical trials with medicines from non-allopathic systems.

These medicines can be evaluated by allopathic hospitals, provided that the collaborator or co-investigator is from the non-allopathic system. These products are divided into three categories; those that are in regular use by the practitioners of these systems and intended for use in identical indications as mentioned in the ancient texts, those that are plant extracts, intended to be evaluated for therapeutic effects not mentioned in the ancient texts, and an extract or a compound that is isolated from a plant but has not been mentioned in the ancient texts at all. For the first, no animal toxicity data are necessary, while the second and the third categories are treated as new chemical entities and animal toxicity data needs to be generated prior to approval for clinical trials.[64] It is also emphasised that prior to commercialisation, if the medicine is found to be effective then the legitimate rights/share of the tribe or community from whom the knowledge was gathered should be taken care of appropriately while applying for the Intellectual Property Rights and Patents for the product.

5.3 Ayurvedic Standardisation and Modern Correlates

The issues of quality and purity can only be resolved when there is consensus on the methodology used. For non-allopathic medicines, meth-

ods of assessing quality and purity need to be validated in the modern context. For instance, for bhasmas containing iron, sprinkling the final product on the fruits of *Emblica officinalis* checks purity. No change in colour of the fruit indicates a pure bhasma. Today, estimation of metals like iron, copper and lead can be done by atomic absorption spectrophotometry and the two methods compared.[65] Likewise, for aconite the high performance liquid chromatography method can be used to estimate batch-to-batch content. These checks on the pharmaceutical industry preparations available in the market can be carried out both by the personnel of the Indian systems of medicine as well as independently by departments like ours.

5.4 Sources of Drug Information

Successful safety monitoring is possible only if adequate information is available to the practicing physicians. The ancient Ayurvedic texts like Charaka Samhita, Sushruta Samhita, Ashtang Samgraha have been translated by several authors into English and other regional languages of India. A published encyclopedia also helps in understanding the science of Ayurveda.[66] Many of these publications have tried to explain the relevance of the science of Ayurveda, and how it can be integrated with modern medicine.[3,67,68] For Siddha, the central council of research in Indian medicine has developed a standardised formulary.[10] This contains 242 drugs and includes plants, metals, gems and shells. For the Unani system of medicine, there exists a National Formulary of Unani Medicine containing 441 formulations that is published both in English and the Urdu languages. It is important, however, that these be updated on a periodic basis. The Indian herbal pharmacopoeia has been recently published and contains at least 20 herbs with monographs devoted to them. Information on safety of commonly used plants is also available.[69] There are over 600 formulations in the Ayurvedic formulary and 80 single drugs are included in the Ayurvedic pharmacopoeia.[70]

5.5 The Patient and the Physician

The 'safe' use of non-allopathic medicines today rests both with the patient and the physician. Many allopathic practitioners tend to be dismissive of the use of non-allopathic medicines by their patients, which may deter a patient who may not then give a full history. Both need to realise that non-allopathic does not mean 'safe'. Patients should, as a matter of routine, inform their physicians about drugs from any other systems that they may be taking or may have been prescribed by non-allopathic physicians. Allopathic physicians should routinely take history of consumption of these medicines, and attempt to analyse the reasons why a particular patient may have opted for these medicines. They should be alert to the possibility of toxicity and herb-drug interactions. In the event of their occurrence, they should make an effort to elucidate the possible mechanisms. Whether allopathic practitioners should learn about non-allopathic systems and vice versa is debatable.

Currently, in India, many modern hospitals, including our own, have full-fledged units/divisions of non-allopathic systems in view of their wide scale use and a need voiced by several patients. Current sources of information on these systems include books, journals and Internet searches. We are looking soon to formalise this training. While this may not be necessary at the undergraduate level, postgraduate students can be trained to take a detailed history that includes history of medicines from non-allopathic systems. In addition, training can include a series of lectures on the current knowledge of toxicity with the systems and anticipated problems when the two systems are used together. For an individual patient, the decision to co-prescribe medicines from the two systems is a joint responsibility, with close monitoring of the patient. Joint collaborations by way of clinical trials between the physicians of the two systems are yet another way to optimise risk benefit.

6. Conclusions

The three main Indian systems of medicine Ayurveda, Siddha and Unani have since India's

independence, been receiving considerable encouragement from both the central and state governments.[10,11] The focus on non-allopathic systems of medicine can be attributed to various causes such as a need to revive a rich tradition, the dependency of 80% of the country's population on these drugs, the easy availability, increasing worldwide use of these medicines, the lack of focused, concerted scientific research, and the abuse of the non-allopathic systems by quacks. Elsewhere, the increasing use of herbal products worldwide and the growth of the herbal product industry has led to increasing concern regarding their safety. Safety concerns regarding rational drug therapies do exist in Ayurvedic literature, and are in no way different from those of modern medicine. However, since Ayurveda is an holistic discipline, allopathic practitioners find it difficult to analyse and interpret its principles and practice of drug therapy and fit it into the framework of modern medicine.

The issues related to safety monitoring of non-allopathic medicines include those of quality, irrational use, abuse/misuse, use of heavy metals and precious stones, a changing ecological environment, the use of insecticides, new manufacturing techniques, an as yet unregulated pharmaceutical industry, and the availability of combinations of herbs not mentioned in ancient texts. None of these issues existed 6 000 years ago, and today these have led to easy over-the-counter availability of these medicines, unregulated use by physicians and patients, drug interactions with allopathic medicines and serious toxicities. Addressing these issues is the combined responsibility of the patient, the physician and the government.

Today, in India, the focus on safety is easily visible. With governmental support, the Indian traditional medicine industry has come a long way from the times when it was considered 'unnecessary' to test these formulations prior to use, to the introduction of GMP guidelines for the industry. English translations of ancient texts are freely available. ADR monitoring centres like ours whose focus earlier was primarily safety monitoring of allopathic medicines, now work closely on safety monitoring of non-allopathic medicines as well. However, we still have a long way to go. The conflict between the traditional practitioners and the purists demanding evidence of safety and efficacy needs to be addressed. Practitioners of non-allopathic systems believe that these medicines that have been used for several centuries, should not be treated or tested as new chemical entities since this would mean loss of several years in animal toxicity testing and rigorous clinical trials. Rather the focus should be on standardisation, and quality control within the various practitioners and regulation of the pharmaceutical industry. It is important to remember that much of the development of modern medicine originated from plant-based formulations including quinine, salicylates, digoxin, reserpine, colchicine, vincristine, docetaxel, and the artemisinin derivatives. Although drugs such as vincristine and colchicine are potentially toxic, these are used. Vagbhata in his text Ashtang Samgraha has said that of all means of knowledge, the one gained from interaction between physicians in a *Tadvidyasambhasha parishad* or 'scientific conference' is the best. China is the only country to encourage the concomitant practice of allopathic and traditional Chinese medicine.[71] Today more than ever, there is an urgent need for the practitioners of the two systems to work together to optimise the risk benefit profile of these medicines (table II).

Table II. Factors to improve safety of non-allopathic Indian medicines

Adequate drug history taking, which includes both allopathic and non-allopathic systems
Training of non-allopathic physicians in recognising and reporting adverse events
Introduction of package inserts for non-allopathic medicines
Public education
Incorporating non-allopathic safety monitoring as part of routine safety monitoring
Stringent regulations regarding quality and purity

Acknowledgements

The authors have provided no information on sources of funding or on conflicts of interest directly relevant to the contents of this review.

References

1. Stickel F, Seitz HK. The efficacy and safety of comfrey. Public Health Nutr 2000; 3: 501-8
2. Srinivasan P. National Health policy for traditional medicine. World Health Forum 1995; 16: 190-3
3. Lele RD. Ayurveda (ancient Indian system of medicine) and modern molecular medicine. J Assoc Physicians India 1999; 47: 625-8
4. Singh RH. The holistic principles of Ayurvedic medicine. 1st ed. Varanasi (India): Chaukhamba Sanskrit Pratishthan, 1998
5. Trevelyan J. Complementary medicine: herbal medicine. Nurs Times 1993; 89: 36-8
6. Mishra L, Singh BB, Dagenais S. Ayurveda: a historical perspective and principles of the traditional healthcare system in India. Altern Ther Health Med 2001; 7: 36-42
7. Lenora RB. Ayurveda medicine. Clin Pediatr (Phila) 1968; 7: 239-42
8. Bhishagaratna KK. Sushruta Samhita. Vol 1, 1st ed. Varanasi (India): Chowkhamba Sanskrit Series Office, 1998
9. Dahanukar SA, Thatte UM, Rege NN. Pharmacology in Ayurveda: introduction. Indian Pract 1998; 5: 409-11
10. Subbarayappa BV. Siddha medicine: an overview. Lancet 1997; 350: 1841-4
11. Satyavati GV. Some traditional medical systems and practices of global importance. Indian J Med Res 1982; 76: 1-26
12. Mahabir RC, Son-Hing J, Tam AL, et al. Ancient Indian civilization: ahead by a nose. J Invest Surg 2001; 14: 3-5
13. Zollman C, Vickers A. What is complementary medicine? BMJ 1999; 319: 693-6
14. Legal status of traditional medicine and complementary/alternative medicine: a worldwide review. Geneva: World Health Organization, WHO/EDM/TRM/2001.2
15. Nayak B. Ayurmedline. Ayurvedic drug index. Ayurmedline, Bangalore (India). Jan-Jun, 2001
16. Vaidya AB, Vaidya RA, Nagral SI. Ayurveda and a different kind of evidence: from Lord Macaulay to Lord Walton (1835 to 2001 AD). J Assoc Physicians India 2001; 49: 534-7
17. WHO. Regulatory situation of herbal medicine: a worldwide review. Geneva: World Health Organization, WHO/TRM/98.1
18. Astin JA. Why patients use alternative medicine. JAMA 1998; 279: 1548-53
19. Furnham A. Why people choose complementary medicine. In: Andritzky W, editor. Yearbook of cross cultural medicine and psychotherapy. Berlin: VWB, 1994: 165-8
20. Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990-97. JAMA 1998; 280: 1569-75
21. Dahanukar SA, Thatte UM, Rege NN. Pharmacology in Ayurveda: VI. Adverse reactions to Ayurvedic drugs. Indian Pract 1998; 51: 815-21
22. Chopra A, Doiphode V. Ayurvedic medicine. Med Clin North Am 2002; 86: 75-89
23. Okamato T, Hino O. Drug development with hints from traditional Indian Ayurveda medicine: hepatitis and rheumatoid arthritis as an example. Int J Mol Med 2000; 6: 613-5
24. Dandekar UP, Chandra RS, Dalvi SS, et al. Analysis of a clinical important interaction between phenytoin and shankhapushpi, an ayurvedic preparation. J Ethnopharmacol 1992; 35: 285-8
25. Kshirsagar NA, Dalvi SS, Joshi MV, et al. Phenytoin and Ayurvedic preparation-clinically important interaction in epileptic patients. J Assoc Physicians India 1992; 40: 354-5
26. Garg SK, Islam AS, Kumar N, et al. Effect of Mentat on the pharmacokinetics of single and multiple doses of phenytoin in rabbits. Neurol India 1999; 47: 104-7
27. Koumaravelou K, Adithan C, Shashindran CH, et al. Effect of honey on carbamazepine kinetics in rabbits. Ind J Exp Biol 2002; 40: 560-3
28. Greeson JM. St John's wort (Hypericum perforatum): a review of the current pharmacological, toxicological and clinical literature. Psychopharmacology (Berl) 2001; 153: 402-14
29. Tomassoni AJ, Simone K. Herbal medicines for children: an illusion of safety? Curr Opin Pediatr 2001; 13: 162-9
30. LaFrance WC, Lauterbach EC, Coffey CE. The use of herbal alternative medicine in neuropsychiatry. J Neuropsychiatry Clin Neurosci 2000; 12: 177-92
31. Vaes LP, Chyka PA. Interactions of warfarin with garlic, ginger, gingko or ginseng: nature of the evidence. Ann Pharmacother 2000; 34: 1478-82
32. Ernst E, Pittler MH. The efficacy and safety of feverfew (tanacetum parthenium L): an update of a systematic review. Public Health Nutr 2000; 3: 509-14
33. Fugh-Berman A, Ernst E. Herb-drug interactions: review of assessment of report reliability. Br J Clin Pharmacol 2001; 52: 587-95
34. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs. Drugs 2001; 61 (15): 2163-75
35. Kshirsagar NA. Misleading herbal Ayurvedic brand name. Lancet 1993; 341: 1595-6
36. Coppes MJ, Anderson RA, Egeler RM, et al. Alternative therapies for the treatment of childhood cancer. N Engl J Med 1998; 339: 846-7
37. Sharma RK, Dash B. Charaka Samhita. 6th ed. Varanasi (India). Chaukhamba Sanskrit Studies, 1999
38. Subramaniam A. The problems and prospects of plant drug research in India: pharmacological evaluation of ecotypes in drug development. Indian J Pharmacol 2001; 33: 145-6
39. Marrone CM. Safety issues with herbal products. Ann Pharmacother 1999; 33: 1359-62
40. Cui J, Garle M, Eneroth P, et al. What do commercial ginseng preparations contain [letter]. Lancet 1994; 344: 134
41. Prabhu MS, Platel K, Saraswathi G, et al. Effect of orally administered betel leaf (Piper betle Linn.) on digestive enzymes of pancreas and intestinal mucosa and on bile production in rats. Indian J Exp Biol 1995; 33: 752-6
42. Slifman NR, Obermeyer WR, Aloi BK, et al. Contamination of botanical dietary supplements by *Digitalis lanata*. N Engl J Med 1998; 339: 806-11
43. Chan TY, Tomlinson B, Tse LK, et al. Aconitine poisoning due to Chinese herbal medicines: a review. Vet Hum Toxicol 1994; 36: 452-5
44. Gogtay NJ, Dalvi SS, Rane CT, et al. A story of Ayurvedic tablets and misled epileptic patients [letter]. J Assoc Physicians India 1999; 47: 1116
45. Gupta SK, Kaleekal T, Joshi S. Misuse of corticosteroids in some of the drugs dispensed as preparations from alternative systems of medicine in India. Pharmacoepidemiol Drug Saf 2000; 9: 599-602
46. Chopra A. Ayurvedic medicine and arthritis. Rheum Dis Clin North Am 2000; 26: 133-44
47. Joshi D. Rasamritam.1st ed. Varanasi (India): Chaukhambha Sanskrit Bhawan, 1998
48. Koh H, Woo S. Chinese proprietary medicine in Singapore. Drug Saf 2000; 23 (5): 351-62

49. Srikantha Murthy KR. Bhavprakash of Bhavmishra. 1st ed. Varanasi (India). Krishnadas Academy, 1998
50. Rai J. The indigenous digestive treatments: useful/harmful. Indian Pract 2002; 55: 27-8
51. Shrikanthamurthy KR. Ashtanga samgraha of Vagbhata (English Translation) Vol. 1, 5th ed. Varanasi (India). Chaukhambha Orientalia, 2002
52. Gogate VM. The text book of Ayurvedic pharmacology and therapeutics of medicinal plants. Mumbai (India). Bharatiya Vidya Bhawan, 2000
53. Sairam TV. Home remedies. Vol. IV. India: Penguin Books, 2002
54. Sharma DC. India raises standards for traditional drugs [letter]. Lancet 2000; 356: 231
55. Notification of the Ministry of Health and Family Welfare (Department of Indian Systems of Medicine and Homeopathy). Jun 23, 2000
56. Angell M, Kassirer JP. Alternative medicine: the risks of untested and unregulated remedies. New Engl J Med 1998; 339: 839-41
57. Margolin A. Investigating alternative medicine therapies in randomized controlled trials. JAMA 1998; 280: 1626-8
58. Bhatt AD. Clinical research on Ayurvedic therapeutics: myths, realities and challenges. J Assoc Physicians India 2001; 49: 558-62
59. Antarkar DS, Vaidya AB, Doshi JC, et al. A double-blind clinical trial of Aarogyawardhini: an Ayurvedic drug in acute viral hepatitis. Indian J Med Res 1980; 72: 588-93
60. Bichile LS, Rajadhyaksha A, Kini S, et al. A double-blind randomized controlled trial of Sallaki (600mg) vs diclofenac sodium (50mg) in patients with rheumatoid arthritis. Indian Pract 2001; 54: 625-32
61. Lodha R, Bagga A. Traditional Indian system of medicine. Ann Acad Med Singapore 2000; 29: 37-41
62. Bajaj S, Vohora SB. Analgesic activity of gold preparations in Ayurveda and Unani. Indian J Med Res 1998; 108: 104-11
63. Kar A, Choudhary BK, Bandyopadhyay NG. Preliminary studies on the inorganic constituents of some indigenous hypoglycaemic herbs on oral glucose tolerance test. J Ethnopharmacol 1999; 64: 179-84
64. Indian Council of Medical Research. Ethical guidelines for biomedical research on human subjects. New Delhi: Indian Council of Medical Research, 2000
65. Uchil D, Rege NN, Dahanukar SA. Modern correlates for ayurvedic quality control tests for tamra bhasma. Indian Drugs 1996; 33: 384-9
66. Rao SKR. Encyclopedia of Indian medicine. Bombay (India): Popular Prakashan, 1985
67. Lele RD. Ayurveda and modern medicine. Bombay (India): Bharatiya Vidya Bhawan, 1986
68. Tripathi YB. Molecular approach to Ayurveda. Indian J Exp Biol 2000; 38: 409-14
69. Bharatiya Vidya Bhavan's SPARC. 111 selected medicinal plants of India. Bombay (India): CHEMEXCIL, 1992
70. Satakopan S. Quality control for Ayurvedic, Siddha and Unani drugs: attitudes and approaches. Ind Drugs 2000; 37: 114-8
71. Hesketh T, Zhu WX. Traditional Chinese medicine: one country, two systems. BMJ 1997; 315: 115-7

Correspondence and offprints: Dr *N.J. Gogtay*, Department of Clinical Pharmacology, New MS Building, 1st Floor, Seth GS Medical College & KEM Hospital, Parel, Mumbai (Bombay) 400 012, India.
E-mail: njgogtay@hotmail.com