



Herbal medicines

Moderators: Dr Dequan Ren, China, and Dr Konstantin Keller, Germany

The past two decades have seen a worldwide upsurge in the use of traditional medicine (TM) and complementary and alternative medicine (CAM) in both developed and developing countries. In Africa, up to 80% of the population in rural areas depend on traditional medicine to meet their primary health care needs, while in India the corresponding figure is 65%. The percentage of the population that has used TM or CAM at least once in the past 10 years is 42% in the USA, 48% in Australia, 49% in France and 70% in Canada.

With such widespread use, the development of national policies and regulations on TM/CAM has become an important concern for both health authorities and the public. There is a need for regulations that ensure the safety of TM/CAM therapies and products, promote recognition of these systems and modalities, and further define their role in modern health care systems.

Current status of traditional Chinese medicines in China Dr Dequan Ren, China

Traditional Chinese medicines (TCMs) play an important role in the Chinese primary health care system, with 1249 TCMs listed in the national Essential Drugs List. The sales of TCMs over the past year amounted to about US\$ 9.8 billion.

There are national quality standards for marketed drugs, including those of the Pharmacopoeia and Propharmacopoeia. The progress and achievements in respect of quality control are reflected in the current edition of the Pharmacopoeia.

Under the Drug Administration Law (1985), marketing authorization is required for all drugs; this authorization is issued by the drug regulatory authority after a strict evaluation process. In 1985, provisions for the approval of new TCMs were issued. Under these provisions, products marketed before 1986 can remain on the market if no adverse events have been reported. With effect from 1986, the process for approval of new TCMs is divided into two steps: approval for clinical trial and approval for marketing. In an application for drug registration, general data, pharmaceutical data, pharmacological and toxicological data, and clinical data have to be submitted.

All TCM manufacturers and commercial enterprises must be certified and registered by the local drug regulatory authorities. Good Manufacturing Practices (GMP) and Good Supplies Practices (GSP) are fundamental requirements for TCM manufacturers and commercial enterprises. GMP certification has been conducted since 1995. Currently, there are 1276 manufacturers with GMP certification, of which 184 are TCM manufacturers. As from 30 June 2004, manufacturers who fail to comply with GMP will not be allowed to manufacture medicines. GSP was promulgated in 2000 and is under trial implementation. The State Drug Administration (SDA) initiates GSP certifications for commercial enterprises. Currently, 67 commercial enterprises have been so certified.

Good Clinical Practice (GCP) was promulgated by SDA in 1999. All clinical trials should be conducted in line with GCP. There are 165 hospitals appointed as clinical trial sites, of which 40 are also TCM clinical trial sites. The applicants can choose the sites for their clinical trials.

Good Laboratory Practices (GLP) was formally promulgated by SDA in 1999. Toxicology and pharmacology studies of TCMs should be conducted in line with GLP. Institutions doing toxicology and pharmacology studies will be certified by SDA according to GLP. For applications for registration of new drugs, the toxicology and pharmacology data used must be from certified institutions only.

The following new measures are being taken to strengthen the management and to promote the development of TCMs:

- Good Agricultural Practices will be promulgated and implemented.

- A registration system for processed products and crude drugs will gradually be implemented. TCM quality standards should be improved.
- Quality standards of TCMs will be improved using fingerprinting technologies, such as fingerprinting chromatography.
- The efficacy of TCMs should be reviewed using modern techniques, not only in comparison with western medicine but also with TCM theory.
- International cooperation and communication should be improved.

Regulation of traditional Chinese medicines in Hong Kong, China

Dr Margaret Chan, Hong Kong SAR, China

The objectives of regulation of Chinese medicines in Hong Kong are: to safeguard public health, and to ensure the availability of good quality and effective Chinese medicines to the people of Hong Kong, China.

Traditional Chinese medicines have been used by the people of Hong Kong for more than 150 years. For historical reasons, no specific forms of regulation of TCM were in place in Hong Kong in the past.

Article 138 of the Basic Law of Hong Kong Special Administrative Region provides that the Government of the Region shall formulate policies to develop western and traditional Chinese medicines and to improve medical and health services. In 1989, the Working Party on TCM was formed. A consensus on the principles of TCM regulation has been reached. The principles are: to safeguard public health, to recognize TCM as part of the health care system, and to adopt an incremental approach to upgrade the standards of practice and the safety, quality and efficacy of herbal medicines based on evidence. In 1995, the Preparatory Committee on Chinese Medicines was formed and worked on the details of TCM regulation. The vision for TCM regulation and development was well summarized in the Policy Address of the Chief Executive of Hong Kong SAR in 1997, in which the Region's Government was committed to:

- regulate Chinese medicine to protect public health;

- promote the integration of Chinese medicine with western medicine;
- develop Hong Kong into an international centre for research, training, information, manufacture and trade of Chinese medicine.

In 1999, the Chinese Medicine Ordinance was enacted. The Chinese Medicine Council, which is an independent, statutory body responsible for implementing regulatory measures on Chinese medicine, was established under the Ordinance in September 1999. Working under the Council, the Chinese Medicines Board and its three committees are responsible for formulating and implementing the regulatory measures on Chinese medicines.

The Chinese Medicine Ordinance defines Chinese herbal medicine as any of the substances specified in Schedule 1 or 2 to the Ordinance. Schedule 1 is a list of 31 potent herbs which can only be dispensed on a prescription issued by a registered Chinese medicine practitioner. Schedule 2 includes 574 Chinese herbal medicines commonly used in Hong Kong. Wholesalers and retailers of Chinese herbal medicines will be required to obtain a licence. The import and export of every consignment of Chinese herbal medicines must be covered by an appropriate licence. Activities are in progress to develop standards for raw and processed herbs, with the assistance of experts and institutions in Hong Kong, other parts of China, and overseas.

Wholesalers and manufacturers of proprietary Chinese medicines will be required to obtain a licence. It will be compulsory for traders in proprietary Chinese medicines to report any adverse drug reactions (ADR) to the Chinese Medicines Board. Proprietary Chinese medicines sold or manufactured in Hong Kong will have to be registered with the Chinese Medicines Board. Registration will be based on evidence of safety, quality and efficacy. Initially, for practical reasons, provisions will be made for transitional registration; under these provisions, for a specified time, an application may be made to register any proprietary Chinese medicine that was sold or manufactured in Hong Kong on or before 1 March 1999. On receipt of the application, the proprietary Chinese medicine will be deemed to be registered. However, manufacturers or importers will be required

in due course to submit evidence of safety, quality and efficacy in order to obtain formal registration.

In future, in order to safeguard public health, Hong Kong SAR will:

- continue the work of regulation of Chinese medicines;
- develop regulatory standards for selected herbs;
- set up a monitoring system for adverse reactions to herbal products;
- support evidence-based clinical research in Chinese medicines;
- promote industrial development and protection of intellectual property;
- enhance regional and international collaboration.

Proposed regulations for natural health products in Canada Dr Peter Chan, Canada

The Natural Health Products Directorate (NHPD) of Canada is committed to ensuring that all Canadians have ready access to natural health products that are safe, effective, and of high quality, while respecting freedom of choice, and philosophical and cultural diversity. Natural health products are defined as natural products used to maintain or promote health, or prevent or treat diseases or conditions. These include listed herbs, homoeopathic and traditional medicines, and substances derived from botanical or animal materials or microorganisms, including isolates. However, natural health products exclude biologicals, tobacco, antibiotics, etc.

The Natural Health Products Regulations cover natural health products. Under these regulations, all natural health products will be licensed and authorized for sale by NHPD. The evidence required for a product licence will depend on the level of claims made for the product and its safety. The evidence might include:

- published monographs;

- prior knowledge about the product;
- additional toxicological data (if required).

As recommended by the Standing Committee on Health, three types of claims will be allowed for natural health products:

- structure/function;
- risk reduction;
- treatment (some restrictions may be proposed depending on level of evidence).

In order to ensure safety and quality, all manufacturers, packagers and labellers of natural health products sold in Canada will be licensed, and will be required to employ GMP. Guidance on GMP appropriate for natural health products has been developed. All holders of licences for natural health products will be required to monitor and report any serious adverse reactions to Health Canada.

There will be specific requirements for the labelling of all natural health products, such as the product licence number, lot number, list of ingredients, directions for use and precautions, so as to allow consumers to make informed choices.

The Natural Health Products Directorate will:

- continue to involve stakeholders in the development of natural health products;
- build partnerships in the areas of research, education and awareness of the regulatory framework;
- put the natural health products regulations in the Canada Gazetteer, Part II by the end of 2002.

How regulation of herbal medicines was established in Thailand

Ms Yupin Lawanprasert, Thailand

Herbal medicines play an important role in the everyday life of the Thai people. The use of herbal medicines has increased remarkably in line with the global trend of people returning to natural therapies. The Government and authorities concerned have taken part in the promotion and regulation of local herbal medicines in order to ensure that their quality, efficacy and safety meet international requirements and that they are used rationally. Manufacturers are also encouraged by the Government to improve their production standards to meet the requirements of Good Manufacturing Practices (GMP) and to conform to the higher specifications needed for the global market.

Under the Drug Act, herbal medicines are classified into four categories:

- herbal household remedies;
- traditional herbal medicines;
- modern herbal medicines;
- new drugs.

The Drug Act requires that any person who wishes to produce, sell or import drugs into Thailand must obtain a licence from the Food and Drug Administration (FDA) of Thailand. Herbal medicinal products must be registered before they can be produced or imported for marketing. An applicant must hold a manufacturing or importing licence granted by the FDA. The procedures for registration of herbal medicinal products are in two stages:

- application for permission to manufacture or import drug samples;
- application for drug registration.

Every application is evaluated by an expert subcommittee; if it is found that the product is proven to be safe and effective, it is registered.

Thailand has participated in the development of the ASEAN Guidelines on GMP for Herbal Medicines. GMP for herbal medicine is currently being implemented. It is recommended that herbal medicinal products should be manufactured in a GMP environment to ensure acceptable quality.

The main problem affecting the quality of traditional drugs is microbial contamination, since the use of synthetic preservatives is not permitted. Herbal medicinal products must therefore comply with the accepted limits for microbial stability specified in the Thai Pharmacopoeia.

Under the Drug Act, all materials used in the advertising and promotion of medicines, including herbal medicines, are subject to approval by the FDA of Thailand.

Thai traditional medicine is a valuable heritage of the Thai people. The Royal Thai Government has tried to revitalize its significance as an effective alternative treatment.

Herbal medicine in the Islamic Republic of Iran **Dr A. Majid Cheraghali, Islamic Republic of Iran**

The Islamic Republic of Iran has a long and rich history of the use of traditional medicine, the most widely used type being herbal medicine. The Government of the Islamic Republic of Iran and the Ministry of Health (MOH) are strongly committed to promoting the use of traditional medicine in the health sector. Several departments in the MOH and in the Ministry of Agriculture are jointly involved in implementing Good Agricultural Practices for herbal medicines.

The National Herbal Medicine Expert Committee has been established under the Pharmaceutical Department of the MOH, and comprises representatives from the national regulatory authorities and university experts. The Committee is responsible for designing a national policy on herbal medicines, preparing guidelines for their use, and evaluating herbal drugs dossiers. Under the Secretary of Food and Drugs in the MOH, the Food and Drug Control Laboratory is responsible for the quality control of food products and pharmaceuticals, including herbal products. The Government of Iran

also focuses on the education of students of pharmacy and medicine in the use of traditional and herbal medicines.

In the Islamic Republic of Iran, there are more than 100 registered herbal medicines, which are locally produced, and several hundred non-registered, but regulated, herbal medicines on the market. Importation of herbal medicines is not allowed at present. There are 32 producers of herbal medicine, mainly of oral and topical dosage forms. There is no herbal medicine for injection on the market. Although the sale of herbal medicine is growing sharply, at present its share in the drug market is less than 5%.

In November 2001, the regulatory authorities of Member States of the WHO Eastern Mediterranean Region met in Cairo to discuss various topics, including herbal medicines. Traditional medicines are widely used in the Eastern Mediterranean Region. While most of the countries in the region do not have any law on herbal medicines, they do have regulations on quality control of herbal medicines. Some countries, such as the Islamic Republic of Iran, the Syrian Arab Republic and Yemen, have monographs for herbal medicines. Regulatory authorities in the Region are generally more concerned about the safety of herbal medicines than about their efficacy. There is a great need for training of national authority experts in controlling the producers of herbal medicines. Regional priorities in the area of herbal medicines include training of health professionals, public education, exchange of information and expertise, training of national experts on registration of herbal medicine and Good Manufacturing Practices, availability of references for herbal medicine in national languages, and an effective strategy to protect natural resources.

Traditional herbal medicines: an update on European Union activities

Dr Konstantin Keller, Germany

The herbal medicines market in the European Union (EU), which is currently worth about US \$3 billion and growing, is dominated by Germany and France. In some countries, the majority of these herbal medicines are prescribed by conventionally trained medical doctors, mostly general practitioners.

There are two different approaches to assessment of herbal medicines in Europe. One is through the European Pharmacopoeia, which includes two groups of herbal medicines. The European Pharmacopoeia provides standards for:

- production of herbal drugs by the pharmaceutical industry;
- quality control laboratories;
- regulatory authorities; and
- community pharmacists.

The second approach is through the EMEA in London, England. A permanent working party was established in EMEA and became a permanent working party of the Committee for Proprietary Medicinal Products (CPMP). The working party has the responsibility to:

- develop new guidance on quality, safety and efficacy of herbal medicines, and common criteria for interpretation;
- form and regularly update a common understanding of existing legislation and guidelines.

The following quality guidance documents for herbal medicinal products were submitted for scientific review by the Quality Working Party and endorsed by CPMP:

- Notes for Guidance on Quality of Herbal Medicinal Products;
- Notes for Guidance on Specifications;
- Notes for Guidance on Quality of Water for Pharmaceutical Use.

Guidance on Good Agricultural and Collection Practice for Starting Materials of Herbal Origin and Guidance on the Assessment of Safety/Pharmacovigilance are also under consideration.

Currently, in the European Union, there are two ways to submit data on the safety and efficacy of herbal medicinal products. For herbal

medicinal products that have not previously been marketed in the EU, or for a new therapeutic use of an existing product, full documentation on new tests and trials must be provided, as required for any new drug application. For established products that have already been on the market in the EU for at least 10 years, full bibliographic documentation is needed.

The European Commission has proposed new legislation on traditional herbal medicinal products, which is still in draft form. The main provisions in the draft legislation are:

- herbal medicinal products may only be used orally, externally or for inhalation;
- there should be a history of at least 30 years of traditional use (at least 15 years within the EU and 15 years outside);
- there must be sufficient data on traditional use and the products should not be harmful;
- the only indications allowed are those that do not require the intervention of a medical practitioner for diagnosis or monitoring;
- efficacy must be plausible on the basis of long-term use and experience;
- there must be specific labelling that the product has not been clinically tested.

A committee for traditional herbal medicinal products at the EMEA will establish community herbal monographs with full information on certain herbs and lists of traditional uses of herbal substances.

With regard to quality, a full documentation dossier will be required for traditional herbal medicines, equal to that for full registration. Regarding safety and efficacy, a bibliographical review of safety data and bibliographical or expert evidence on traditional use for at least 30 years will be required. However, this evidence will not be required for products that are included in the lists or covered by the monographs published by the committee.

Thus, the legal framework within the EU has been consolidated, with a specific expert committee for herbal medicines. In future there will be three types of documentation: full documentation, bibliographic documentation and traditional documentation. We will also have two procedures: normal marketing authorization and registration of traditional herbal medicinal products.

Regulation of herbal medicines in Ghana

Dr Benjamin Kwame Botwe, Ghana

Traditional medicines are widely used in Ghana. Traditional medical practitioners cater for the health care needs of most of the 60-70% of the population who live in rural areas. The majority of practitioners are herbalists.

Since 1961, attempts have been made to regulate traditional medicines, starting with the formation of the Ghana Psychic and Traditional Healers Association. In 1975, the Centre for Scientific Research in Plant Medicines was established; in 1997, the Food and Drugs Board was established; and in 2000, a Traditional and Alternative Medicines Directorate was established in the Ministry of Health.

Under the Food and Drugs Law, the manufacture, import, export, distribution, use and advertisements of food, drugs, cosmetics, chemical substances and medical devices are controlled. No person may manufacture, prepare, supply, sell, distribute, export or import any herbal medicine or homoeopathic drug, unless it has been registered with the Food and Drugs Board. The Board seeks to ensure that herbal medicines are safe, of good quality and effective. Regulations may prescribe the information to be provided for the registration of herbal medicines and homoeopathic drugs.

Any person who labels or advertises any drug in contravention of any regulations under the Food and Drugs Law, or in a manner that is false or misleading as regards its character, constitution, value, potency, quality, composition or safety commits an offence.

Traditional medicinal products are defined under the Food and Drugs Law. The Traditional and Alternative Medicines Directorate, the practitioners, the research institutions and the universities were invited

to develop the guidelines for registration. University institutions are now offering courses in traditional medicines and the Government also facilitates training on quality assurance of traditional medicines.

In respect of safety data for product registration, basic toxicological studies are required. Product samples are submitted for testing for prohibited chemicals, heavy metals and microbial contamination.

In respect of quality data for product registration, the Government has introduced GMP inspection at the level of the manufacturer. Product samples are submitted for testing for adulterants, physical and chemical parameters, and orthodox drugs.

In respect of efficacy data for product registration, only evidence of long use with minimum side-effects is requested. The Government has also introduced a pharmacovigilance system to continuously monitor marketed products for possible adverse effects.

There are several challenges:

- Clinical assessment of the efficacy of the products needs to be improved.
- Comprehensive long-term toxicological testing of the products is needed.
- A National Herbal Pharmacopoeia should be developed.
- Postmarketing testing should be strengthened to eliminate products that are not useful.
- The concept of GMP should be promoted to the pharmaceutical industry.

Herbal medicines play a useful role in many countries. Stakeholders must integrate and coordinate efforts to provide accurate scientific evidence of their safety and efficacy, and to ensure that the products are of good quality.

Recommendations

1. Member States, together with WHO, should define criteria and standards for herbal medicines, health or functional foods, and dietary supplements. WHO should continue to develop guidelines on the assessment of safety, efficacy and quality control of herbal medicinal products and herbal combinations.
2. The safe use of herbal medicines is a major concern for governments and consumers. WHO should provide guidance to countries wishing to establish safety monitoring systems or to expand existing systems to monitor and report adverse reactions to herbal medicines. Member States should strengthen their post-marketing surveillance systems for herbal medicines. Such systems should involve health care providers, consumers and manufacturers.
3. WHO should support countries in developing sources of information on herbal medicines while facilitating information-sharing among countries. WHO should provide guidance to governments and nongovernmental organizations (NGOs) on how to develop information and educational programmes on the proper use of herbal medicines for the public.
4. WHO should provide guidance for governments and NGOs on training of traditional medicine providers, and promote communication with other health workers.
5. Member States should seek funds to support research on herbal medicines.
6. Progress should be reported back to the ICDRA.