

The quality and safety of traditional Chinese medicines

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SYNOPSIS

Modern chemical and pharmacological research has greatly contributed to our understanding of Chinese medicine. The quality of Chinese medicines may be controlled by understanding their pharmacognosy and applying pharmaceutical methods. Chinese medicines may have intrinsic toxicity. They can also be contaminated and adulterated. Interactions with prescription drugs are also possible. Regulation, backed by education and research, is needed to improve the quality and quality use of traditional Chinese medicines.

Index words: complementary medicines, herbal preparations, pharmacognosy.

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Introduction

Traditional Chinese medicine is a medical system based on theory, pathology, diagnosis, treatment and herbal pharmacology principles that differ from those of orthodox medicine or Western naturopathy. The practice of traditional Chinese medicine has developed from knowledge accumulated through clinical observation and treatment over several millennia. Traditional Chinese medicine has an established history in Australia and has expanded rapidly in recent years. Chinese medicines now account for 3.2% of the total use of complementary medicines.¹ The Chinese Medicine Registration Act was approved by the Victorian Parliament in 2000, to regulate the qualifications of traditional Chinese medicine practitioners and dispensers to encourage the safe use of traditional Chinese medicines in Victoria.

In parallel with the growth of Chinese medicine, serious issues have been raised about its quality and safety in Western countries. Chinese medicines have been contaminated with toxic heavy metals and adulterated with prescription drugs.² There is therefore a need for quality assurance of Chinese medicines in Australia.

Active principles and therapeutic effects of Chinese medicines

Modern research has revealed that many Chinese herbs act through one or more pharmacological mechanisms. Many active components have been isolated from herbs used in Chinese medicine and some are used in modern pharmaceutical drugs. They include ephedrine for hypotension (from ephedra (*Ephedra sinica* Stapf)), artemisinin for malaria (from Chinese

wormwood (*Artemisia annua* L.)), and berberine, an antibacterial component (from Chinese goldthread (*Coptis chinensis* Franch)). Active components have been defined in many other Chinese herbs, for example anthraquinone glycosides in rhubarb (*Rheum officinale* Baill), and gingerols in ginger (*Zingiber officinale* Rosc).

The chemistry of herbal medicines is the foundation of their pharmacology. It is also important for the manufacture and quality assurance of herbal preparations. For example, aconite (*Aconitum carmichaeli* Debx.) is an 'internal warming, hot and pungent herb' and is used to restore Yang deficiency in heart failure. Its cardiotoxic active substance has been isolated and identified as higenamine, a beta adrenergic agonist with an isoquinoline structure related to catecholamines. The active components responsible for analgesic and toxic effects are aconitine, mesaconitine and other diterpene esters, which are largely hydrolysed during processing and boiling. The toxicity of aconite is well understood in traditional Chinese medicine and the herb is only listable at very low concentrations in Australia. Red sage (*Salvia miltiorrhiza* Bunge) is a herb that is said to 'promote blood circulation and remove blood stasis'. It purportedly dilates the coronary arteries and increases the peripheral circulation so it has been used to treat angina pectoris. However, for most Chinese medicines the active components responsible for their pharmacological activities and clinical applications are not well defined.

The level of clinical evidence to support Chinese medicine does not generally meet the internationally accepted standards of clinical trials of new drugs. Many preclinical and clinical studies carried out in China have been published in the Chinese literature, but the results are not readily available to Western communities.

Quality control from agriculture to fingerprinting

As for pharmaceutical products herbal medicines require professional and government control to ensure their quality, safety and efficacy. The Chinese pharmacopoeia (2000)³ contains monographs and standards of *materia medica* and patent preparations. Australia relies mainly on imported herbal materials and has not developed a herbal pharmacopoeia.

The quality of a herbal medicine refers to the intrinsic properties of the herb, that is, the amount and range of medicinally useful or active constituents present. The correct identification of a plant with reference to its accepted scientific name(s) is a

primary step in the quality assurance process, as a single common name may often refer to different plant species, with potentially dangerous consequences. Other factors influencing the quality of herbal medicines are:

- agriculture
- harvesting
- processing
- good manufacturing practice.

Chinese herbal medicines are usually used as a decoction of a mixture of herbal materials defined in a formula, which therefore contains hundreds of components. The clinical application of Chinese medicines is related to the multiple chemical components and not a single component. A pharmaceutical approach to testing for the content of a single component may therefore not reflect the quality, safety and efficacy of a herbal preparation. Methods of chromatographic fingerprinting, such as high-performance thin layer chromatography and high-performance liquid chromatography, are being developed to define the profiles and variations between herbal medicines.

Safety and regulation of traditional Chinese medicines

The issues associated with the safety and quality of Chinese herbal medicines include toxic herbs, contamination with heavy metals, microbial organisms, and other contaminants, and deliberate combination or adulteration with pharmaceutical drugs. Chinese herbal products in Australia are regulated by the Therapeutic Goods Administration (TGA) and need to meet quality and safety standards (see page 130).

The importation and dispensing of raw herbs are not effectively regulated or closely monitored by the TGA. At present, raw herbs can be imported and dispensed legally over the counter without registration with the TGA. These herbs may not meet the standards for herbal products.

Toxic herbs

Some herbs or minerals are known to be toxic and, when appropriate, need to be used with care under the supervision of highly qualified practitioners. Aconite poisonings have occurred repeatedly overseas and in Australia. Aconite (*Aconitum carmichaeli* Debx., *Aconitum kusnezoffii* Reichb.) contains aconitine, a cardiotoxin and neurotoxin causing arrhythmia and ventricular fibrillation. Thornapple (*Datura metel* L.) and black henbane (*Hyoscyamus niger* L.) contain hyoscyamine, an antimuscarinic alkaloid. Other toxic herbs requiring special regulation include nux vomica (*Strychnos nux-vomica* L.) which contains strychnine, Chinese arum (*Arisaema erubescens* (Wall.) Schott), and tri-leaved pinellia (*Pinellia ternata* (Thunb.) Breit).

Some species of plants with similar Chinese names differ in their indication and toxicity and cannot be used interchangeably. Guang fang ji (*Aristolochia fangchi*) and han fang ji (*Stephania tetrandra*) have similar names and clinical indications in traditional Chinese medicine, but *Aristolochia fangchi* contains the highly toxic aristolochic acids. *Aristolochia fangchi* has

been found to cause renal failure and urothelial carcinoma. The nephropathy is characterised by extensive interstitial fibrosis leading to a severe atrophy of the proximal tubules.^{4,5}

Contamination or adulteration

Chinese herbal products have been found to contain heavy metals, such as mercury and arsenic, and non-prescription or even prescription drugs such as paracetamol, indomethacin, chlorpheniramine, aminopyrine, caffeine and hydrocortisone. The unapproved presence of these substances may have originated from mineral components, contamination or adulteration.² Currently quality monitoring relies on TGA post-marketing surveillance. Extra resources would be required to carry out routine surveys of the quality of Chinese herbal products in the Australian market to detect drug contamination or adulteration.

Drug-herb interactions

The combination of pharmaceutical drugs and Chinese herbal medicines is a common practice in China and must be considered when patients are using preparations obtained outside Australia. Similarly, patients in Australia may use Chinese medicines together with pharmaceutical drugs without informing their medical practitioners. The potential for drug-herb interactions remains to be investigated.

Regulation of herbal dispensers/pharmacists

Herbal medicines are usually dispensed by the practitioner who prescribes them, even though it is not accepted Australian practice for practitioners to have both prescribing and dispensing functions. It seems reasonable that dispensers should have sufficient training in the theory and properties of herbal medicines, equivalent to that found in pharmacy in Australia and traditional Chinese medicine pharmacy in China, in order for them to dispense herbal medicines safely according to best practice. This would require training in the pharmaceutical aspects of herbal medicines.

Recommendation

Best practice for Chinese medicines in Australia requires understanding both the traditional Chinese medicine system and modern orthodox medicine. There is a need to establish a quality testing system for raw herbs and their preparations and herbal products. This would detect any mislabelling or misidentification and the presence of undeclared components. Herbs with toxicities equivalent to prescription pharmaceutical drugs require a regulatory control system, such as a special schedule to enable registered practitioners to prescribe them under appropriate monitoring. Herbal dispensers should have an adequate qualification for dispensing, which includes knowledge of Chinese medicine and modern pharmaceuticals. Medical practitioners and pharmacists should have sufficient knowledge of traditional Chinese medicine and herbal medicines to allow them to discuss issues and give advice to patients, and to identify and manage drug-herb interactions. Education programs such as short courses on modern Chinese medicine or exposure to the subject in the undergraduate curriculum may be of benefit to healthcare practitioners.

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REFERENCES

1. MacLennan AH, Wilson DH, Taylor AW. The escalating cost and prevalence of alternative medicine. *Prev Med* 2002;35:166-73.
2. Ernst E. Toxic heavy metals and undeclared drugs in Asian herbal medicines. *Trends Pharmacol Sci* 2002;23:136-9.
3. The State Pharmacopoeia Commission of the People's Republic of China. *Pharmacopoeia of the People's Republic of China*. Beijing: Chemical Industry Press; 2000.
4. Nortier JL, Vanherweghem JL. Renal interstitial fibrosis and urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*). *Toxicology* 2002;181-2:577-80.
5. Nortier JL, Martinez MC, Schmeiser HH, Arlt VM, Bieler CA, Petein M, et al. Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*). *N Engl J Med* 2000;342:1686-92.

FURTHER READING

Quality control methods for medicinal plant materials. Geneva: World Health Organization; 1998.

Bensoussan A, Myers SP. *Towards a safer choice: the practice of traditional Chinese medicine in Australia*. Sydney: Faculty of Health, University of Western Sydney Macarthur; 1996.

Expert committee on complementary medicines in the health system. *Complementary medicines in the Australian health system*. Canberra: Commonwealth of Australia; 2003.

<http://www.tga.gov.au/docs/pdf/cmreport.pdf>

Conflict of interest: none declared

Editorial note:

Traditional Chinese medicines account for only a small part of the use of complementary medicines in Australia. The problems of quality mentioned in this article are not confined to traditional Chinese medicines. This year's recall of complementary medicines made by Pan Pharmaceuticals shows that problems can arise even when products are manufactured in a modern factory.

Self-test questions

The following statements are either true or false (answers on page 151)

3. Traditional Chinese medicines may contain therapeutic and toxic components.
4. The method of preparation of a Chinese medicine may alter its pharmacological effects.

The quality and safety of traditional Chinese medicines

Comment by John McEwen and Fiona Cumming, Therapeutic Goods Administration

It may seem strange that the Therapeutic Goods Administration (TGA) regulates the safety and quality of Chinese **herbal products**, but does not scrutinise the **raw herbs** dispensed by Chinese medicine practitioners in Australia. The explanation lies in the extent of federal powers under the Australian Constitution. The *Therapeutic Goods Act 1989* relies on federal controls of importations, infectious diseases (quarantine), interstate trade and corporations (companies) to regulate the supply of medicines. This Act does not control the behaviour of individual practitioners – indeed those who are unincorporated and do not trade across state boundaries are outside the federal powers.

Chinese medicine herbal products on lawful sale in Australia must have an AUSTR or AUSTL number on the label. All Australian and overseas manufacturers of these products are required to authenticate their starting materials and testing of final products, and their performance is audited. This is a more efficient mechanism than a customs barrier scrutinising documentation for, and on occasions testing, every import of a raw herb or manufactured Chinese herbal medicine. It does mean, as the authors point out, that raw herbs can be imported and dispensed without any TGA control, but that situation is not absolute. A number of herbs with recognised toxicity are prohibited imports or are subject to State and Territory poisons controls, or both. These herbs should not be being dispensed by herbal practitioners.

Toxicity can occur through substitution of a toxic herb for a relatively non-toxic herb. There are 11 herbs which are vulnerable to substitution by the nephrotoxic, carcinogenic herb *Aristolochia*, because of confusion over their similar names and appearance. In the few instances where such substitution has occurred, in herbal products regulated as therapeutic goods, the TGA has required the affected products to be recalled. The TGA maintains a regular testing program for potential *Aristolochia* substitution, and has stringent pre-market regulatory controls in place to help ensure such substitution cannot occur. Although raw herbs are outside the TGA's powers, the TGA has worked with the Australian Customs Service and the States and Territories to put in place additional scrutiny of herbs which may be at risk of substitution with *Aristolochia*.

The possibility of deliberate adulteration is very real, as illustrated by the experience in Singapore and Malaysia in 1992, with a herbal product for weight loss. Slim 10 was manufactured in China and promoted heavily. Adverse reaction reports of serious illness and death led to the identification of not one, but two, adulterants – dried thyroid gland extract, presumably of animal origin, and a fenfluramine derivative. In recent years the TGA has not identified any instances of a conventional pharmaceutical being used to adulterate herbal products with AUSTR or AUSTL numbers. In contrast, there has been a small number of instances of clinically significant adulterants being found in herbal products unlawfully supplied in Australia or purchased overseas.

Even when not surreptitiously adulterated, there can be dangers.