Traditional Chinese medicine authentication

For millennia, physicians' literature has addressed means of ensuring that purchased medicines are what they are claimed to be. Herbs are much more likely than cultivated vegetables to be accidentally confused: most botanicals are not highly modified in form and may closely resemble related or even unrelated species, and many are collected from the wild, where similar-looking species may also occur. Furthermore, inexpensive botanicals have sometimes been fraudulently substituted for or commingled with rare and costly botanicals. While most botanicals are correctly identified, substitution of the wrong species can cause serious harm. At worst, people have been poisoned after using a toxic species that was confused with an unrelated plant; in a relatively recent case, contamination of cultivated plantain with digitalis resulted in several reported illnesses. More commonly, the substituted plant may provide the consumer lesser benefits than the desired species, or none at all. In modern practice, every marketer of crude botanicals or manufacturer of botanical products should have explicit quality-control procedures to ensure that materials sold are correctly identified and of acceptable purity.

Traditional formulas. Traditional Chinese medicine was one of the first cultural medical systems to be codified in written form, and is probably the most complex. Its underlying philosophy relates health to a balance of vital and elemental energies and "pathogenic factors" (for example, "heat," "dampness") within bodily "organs" not corresponding precisely to the physical organs of the same name. Chinese healers usually use not single herbs but codified multiherb formulas that may contain a few to over two dozen ingredients, often including fungal, animal, or mineral products as well as botanicals. The primary herb in a formula is believed to act directly to correct an imbalance, whereas other herbs may increase the activity of the primary herb, reduce its side effects, or have a general tonic effect.

The official circumscription of a particular herb frequently includes more than one species: licorice root (*gan cao*) officially may be obtained from *Glycyrrhiza glabra, G. inflata*, or *G. uralensis*, while epimedium (*yin yang huo*) may include five species of *Epimedium*. Use of related species for similar purposes is common worldwide, and with reason as closely related species frequently share similar chemical constituents and activities; for example, in Western practice, several species of *Crataegus* (hawthorn) or *Plantago* (psyllium) may be used interchangeably. However, conflation of species from related genera occurs more frequently in traditional Chinese medicine, and in traditional practice unrelated herbs believed to have similar actions have occasionally been more or less freely substituted, depending upon local availability (see **table**). For example, in northern China the rhizome of *Menispermum dahuricum* (*bei dou gen* or "northern bean root") is sometimes substituted for the root of *Sophora tonkinensis* (*shan dou gen* or "mountain bean root"). Both of these botanicals have the primary activity of "clearing heat and eliminating toxins," but they are less likely to have similar chemical constituents as they are from very different plant families.

Health risks of Aristolochia substitution. *Aristolochia fangchi*, known as *guang fang ji* (family Aristolochiaceae), was believed by many traditional healers to be substitutable for the unrelated *Stephania tetrandra* (*fang ji* or *fen fang ji*, Menispermaceae); both have the actions of promoting diuresis and "dispelling wind and dampness." However, *A. fangchi* contains aristolochic acids, which can cause tubular interstitial fibrosis, a progressive kidney disease, and kidney cancer in both animals and humans. Worldwide case reports have documented instances of kidney failure following prolonged medicinal use of various *Aristolochia* species. Products sold as *Stephania* have repeatedly been found to contain aristolochic acids, proving that they were adulterated with *Aristolochia* species; consumers, believing the product to be the safer herb, might unknowingly consume hazardous amounts. (Contrarily, one survey has found that many "*Aristolochia*" products contain no detectable aristolochic acids.) Over 100 patients of a Belgian weight loss clinic developed interstitial fibrosis after using a regimen that combined apparently adulterated "*Stephania*" with other herbs and pharmaceutical drugs, including acetazolamide, which may have increased aristolochic acid toxicity. Western regulatory agencies have therefore banned both *Aristolochia* species and their harmless substitutes, unless those species are proven free of aristolochic acids.

Pharmaceutical drugs in herbal preparations. In recent decades, Chinese herbal medicines have also been adulterated with pharmaceutical drugs. One survey in Taiwan in the early 1990s found that 24% of sampled products were adulterated. Traditional philosophy may have condoned adding to a mixture any available substance that might improve its activity, but the unlabeled inclusion of potentially toxic drugs represents both fraud and a significant health hazard. Reported pharmaceutical adulterants with known health risks or contraindications include corticosteroids, appetite suppressants, acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), codeine, and diazepam; a number of consumer illnesses have been attributed to such adulteration. Because pharmaceuticals are added to an extract or finished product, they can be detected only by chemical analyses. Methods for detecting many potential adulterants by chromatographic methods, such as high-pressure liquid chromatography (HPLC), have been published.

The best-known case of pharmaceutical adulteration is PC-SPES (PC for prostate cancer; *spes* is Latin for "hope"), a Chinese herbal mixture that gained

Several Chinese herbs for which unrelated or distantly related unofficial regional substitutes have been documented

Chinese name	Official or most common species	Substituted species
zi cao	*Lithospermum erythrorhizon* or *Arnebia euchroma* (family Boraginaceae)	*Onosma paniculatum* (family Boraginaceae)
guan zhong	*Dryopteris crassirhizoma* (Dryopteridaceae)	*Matteuccia struthiopteris* (Dryopteridaceae), *Osmunda japonica* (Osmundaceae), *Blechnum orientale* (Blechnaceae), etc. [class Filicopsida]
da qing ye	*Isatis indigotica* (Brassicaceae)	*Isatis tinctoria* (Brassicaceae), *Strobilanthes cusia* (Acanthaceae), *Polygonum tinctorium* (Polygonaceae), *Clerodendrum cyrtophyllum* (Lamiaceae)
shan dou gen	*Sophora tonkinensis* (Fabaceae)	*Menispermum dahuricum* (Menispermaceae)
jin qian cao	*Lysimachia christinae* (Primulaceae)	*Glechoma longituba* (Lamiaceae), *Desmodium styracifolium* (Fabaceae), *Hydrocotyle sibthorpioides* (Apiaceae), *Dichondra repens* (Convolvulaceae)
wang bu liu xing	*Vaccaria hispanica* (Caryophyllaceae)	*Ficus pumila* (Moraceae)

an impressive reputation for inhibiting prostate cancer. PC-SPES was noted to have estrogenic side effects, such as breast enlargement; further investigation revealed that early lots of PC-SPES were adulterated with synthetic estrogens, notably diethylstilbestrol (DES), which is used to treat prostate cancer. Some later lots included detectable amounts of the anticoagulant warfarin—perhaps added in the hope of preventing the blood clots that DES might otherwise cause. Discovery of these adulterants led to a product recall and a premature end to one clinical trial. Ironically, it is likely that the herbal ingredients actually worked, at least to boost the activity of DES. Case reports and preliminary clinical trial results indicated that PC-SPES was superior to standard DES treatment, even though the DES present in the PC-SPES had been a small fraction of the normal dose, and in-vitro studies also demonstrated anticancer activity in the herbal mixture alone. By hindering the study and use of promising herbal adjuvants, this manufacturer's lack of quality standards may have led ultimately to more deaths and illnesses than those directly caused by any contaminated botanical.

Good manufacturing practices. Good manufacturing practices for a modern herbal product must ensure, among other things, that the identity, purity, and quality of each raw material included in the product are confirmed. For most botanicals, authentication is most easily accomplished by observing morphological and organoleptic (taste, odor, fracture) characteristics before the material is processed. Preservation of voucher samples from each batch then permits identity to be reconfirmed later in case a question about product quality arises. Reference works are available in Chinese and English that provide descriptions and photographs of popular Chinese herbal drugs. If preprocessing identification is neglected, or if the intact material is not unambiguously identifiable (say, if the part harvested and supplied is a root without any unique features that distinguish it from similar-looking species), more elaborate methods can be used to confirm identity of extracted material. Chemical fingerprinting methods such as HPLC and thin-layer chromatography (TLC) are the most commonly used. These methods confirm the presence of expected marker compounds and thus simultaneously serve as a measure of quality.

However, it is virtually impossible to fully assess the quality of a finished multiherb formula by affordable chemical means. The number of compounds present becomes so great that peaks inevitably overlap and obscure one another; nor can any one HPLC protocol be expected to visualize appropriate marker compounds from a dozen different materials. Therefore it is particularly essential that the raw materials for such complex formulas be properly authenticated and documented, and that manufacturers scrupulously abide by label claims regarding content. Reputable Western dietary supplement manufacturers follow such practices as a matter of course. The Chinese government has taken laudable steps to promote quality control, such as issuing pharmacopoeial standards for commonly used botanicals, but these steps will not be fully effective so long as they coexist with traditional practices that tolerate contamination at levels from the wildcrafter to the factory floor. Sadly, at the moment, traditional Chinese medicine formulas compounded by foreign manufacturers may sometimes be of higher quality than Chinese-made products. To a significant extent, the message for the traditional Chinese medicine consumer remains *caveat emptor*.

For background information *see* AGRICULTURAL SCIENCE (PLANT); ARISTOLOCHIALES; BOTANY; INSPECTION AND TESTING; LIQUID CHROMATOGRAPHY; PHARMACOLOGY; PHARMACY; QUALITY CONTROL TOXICOLOGY in the McGraw-Hill Encyclopedia of Science & Technology.

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Bibliography. D. Bensky, A. Gamble, and T. Kaptchuk, *Chinese Herbal Medicine: Materia Medica*, Eastland Press, Seattle, 1986; J. K. Chen and T. T. Chen, *Chinese Medical Herbology and Pharmacology*, Art of Medicine Press, City of Industry, CA, 2004; J. P. Cosyns, Aristolochic acids and "Chinese herbs nephropathy": A review of the

evidence to date, *Drug Safety*, 26:33–48, 2003; E. Ernst, Adulteration of Chinese herbal medicines with synthetic drugs: A systematic review, *J. Intern. Med.*, 252:107–113, 2002; W. K. Oh et al., Prospective, multicenter, randomized phase II trial of the herbal supplement, PC-SPES, and diethylstilbestrol in patients with androgen-independent prostate cancer, *J. Clin. Oncol.*, 22:3705–3712, 2004.