

PERSPECTIVE



Herbal dangers

Traditional plant-based remedies are not risk-free. Doctors and patients need to be informed about the possible side effects, says **Masatomo Sakurai**.

Many modern medicines come with warnings of side effects, and some patients are understandably wary of their use. There is a trend for people to consider herbal medicines as natural and therefore 'healthier' than synthetic chemicals. In Japan, doctors are increasingly prescribing herbal medicines while more and more scientists investigate their efficacy.

Although herbal remedies work gently and typically cause milder side effects than modern medicines, they can still be dangerous. Adverse events can vary from the minor (gastric distress and appetite loss) to the serious (interstitial pneumonia or renal cancer), and even death. According to the Japanese Ministry of Welfare, in just two years from 1994 to 1996, herbal medicines caused at least ten deaths in Japan. The problem of herbal side effects is common elsewhere in Asia but is overlooked.

A SEVERE PROBLEM

In Japan, the first reported side effect resulting from the ingestion of herbal medicines was in 1989, from a traditional Japanese formula called syo-saiko-to prescribed to promote liver health (xiao-chai-hu-tang in Chinese)^{1,2}. Over the following 11 years, 35 cases of side effects related to syo-saiko-to were reported, including eight deaths. Because most of these cases involved hospitals or doctors that did not specialize in herbal medicine, it was generally believed that the deaths were attributable to the prescribers' lack of knowledge.

However, recent reports reveal that herbal formulae can cause side effects even when prescribed by experienced traditional medicine practitioners. Although no deaths linked to herbal formulae have been reported since 2000, there have been other side effects. In the seven years to 2009, the Center for Japanese Traditional Herbal Medicine at Kashima Rosai Hospital in Kamisu reported 503 cases of side effects out of 2,530 total prescriptions, with symptoms varying from poor appetite to 26 cases of liver disorder — half of which were caused by herbal medicine (4 in 1,000 cases)³. The Department of Herbal Medicine at Kitasato University in Tokyo has reported a similar rate: 21 cases of liver damage out of 20,271 prescriptions over 9 years (approximately 1 in 1,000)⁴.

Across Japan, the most common side effects from herbal formulae are gastrointestinal distress, often caused by *Rehmannia* root and *Ephedra* herb, and allergic reactions such as skin rashes, which can be caused by many different herbs. More serious side effects include interstitial pneumonia, which affects 1 in 25,000 patients taking any herbal remedy⁴, most commonly with syo-saiko-to, which contains *Scutellaria* root. This root, among others, can also cause liver dysfunction — a condition that affects 1–5 people out of every 10,000 taking herbal medicines, most notably women more than 50 years of age. Renal dysfunction and cancer of the urinary system can result from the consumption of aristolochic acid — a constituent of *Aristolochia manshuriensis* that is used in guan-mu-tong⁵.

Other common herbal formulae have also produced unwanted results. Up to 3% of people who consume liquorice, which is added to three-quarters of Japanese herbal formulae, develop pseudohyperaldosteronism, a condition that includes hypokalaemia (low potassium levels), convulsions, oedema, hypertension and weight gain. Medicines containing the root of *Bupleurum* can give someone an urgent need to urinate, a feeling of incomplete urination, and blood in the urine. These are also the symptoms of cystitis, a form of bacterial bladder infection. The *Bupleurum*-related cases, however, are thought to be an allergic reaction to the herb, as there are no signs of bacterial infection.

Side effects can be prevented to some extent if doctors are properly trained in the use of herbs and herbal formulae. For example, the *Ephedra* herb contains ephedrine — a stimulant often used in herbal medicine that should not be prescribed to patients with cardiovascular diseases.

Unfortunately, not all side effects can be predicted, even if they are prescribed by well-trained doctors. Here, however, is some simple and practical advice that could help prevent serious cases of side effects from occurring.

First, use a blood test to check liver and renal function before the first prescription, and every 3 months thereafter. This testing will enable early detection of dysfunction, which might not manifest before 12 months. Second, measure a patient's blood pressure at least once every 2 weeks. This helps to detect pseudohyperaldosteronism. Third, inform the patient about the early symptoms of the treatment's side effects, such as fever, oedema and shortness of breath, which might develop into a more serious condition. Advise the patient that if these symptoms occur, they should cease taking the herbal medicine and inform the prescribing doctor.

Building the education system is an urgent matter for countries looking to improve the safety and efficacy of herbal formulae. Japan has now made

it compulsory for medical students to take courses in the practice of herbal medicine, and in 2008 the first doctors graduated from this system. More importantly, doctors, researchers and government officials in Japan, China and South Korea should work together to decide the common name for each herb and create international rules concerning the use of herbal formulae to improve the sharing of information about side effects.

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1. Ito, T. *et al. Kampo Med.* **61**, 299–307 (2010).
2. Gono, Y. *Kampo Med.* **61**, 828–833 (2010).
3. Arai, S. *Kampouigaku* 124–130 (2009).
4. Vanherweghem, J. L. *et al. Lancet* **341**, 387–391 (1993).
5. Nortier, J. L. *et al. N. Engl. J. Med.* **342**, 1686–1692 (2000).



Aconite root is used to treat colds and can cause palpitations and blood rushes.