

Prescribing herbal medications appropriately

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Do you know how many of your patients are taking herbal preparations? With the proliferation of herbal products, the number could be greater than you think. Between 1990 and 1997, the US population increased its use of herbal medicines by 380%.¹ Total out-of-pocket expenditure for herbal medicines in 1997 was \$5.1 billion.¹ **Table 1** lists the 10 best-selling herbal medicines in the US.²

Safety issues related to herbal medicine are complex: possible toxicity of herbal constituents, presence of contaminants or adulterants, and potential interactions between herbs and prescription drugs. The quality of herbal medicines is often suboptimal. One reason for this is that they are not adequately regulated, and many experts are calling for a change in this situation. Cost-evaluations of herbal medicine are not available, so they cannot form the basis for clinical decisions.

This article provides guidelines for prescribing herbal medications appropriately.

■ EFFICACY

One of the first things to consider when a patient proposes trying an herbal medicine is efficacy. Data on efficacy of herbal medicines are incomplete, yet some treatments have shown promise.

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Medical herbalism here and abroad

Medical herbalism (ie, the medicinal use of preparations that contain exclusively plant material) once dominated our pharmacopeia but went into rapid decline when pharmacology established itself as a leading branch of therapeutics. During the last part of the 19th and the early 20th century, herbalism virtually vanished from the therapeutic map of the US and the UK. In contrast, many developing countries never abandoned medical herbalism (Ayurvedic medicine in India, Kampo medicine in Japan, and Chinese herbalism in China). In other countries (such as Germany and France), medical herbalism continued a “low-key” coexistence with modern pharmacology. More recently, herbal medicine has experienced a remarkable comeback.

The critical question is, Does the remedy work for the patient's condition? Clinicians should not prescribe or recommend herbal remedies if that question cannot be answered with a firm Yes.

Herbal medicines usually contain a range of pharmacologically active compounds. In some cases it is not known which of these constituents produces the therapeutic effect. Testing for efficacy in this situation is obviously more complex than with synthetic drugs. One approach is to view the entire herbal extract as the active component. To

TABLE 1

**10 best-selling herbal medicines
(United States, 2001)**

Rank	Herb	Retail sales
1	Ginkgo biloba	46
2	Echinacea	40
3	Garlic	35
4	Ginseng	31
5	Soy	28
6	Saw palmetto	25
7	St John's wort	24
8	Valerian	12
9	Cranberry	10
10	Black cohosh	10

Retail sales are rounded figures in million US dollars.

optimise the reproducibility of efficacy studies, extracts must be sufficiently characterised. This is often achieved by standardizing the amount of a single key constituent of the extract (eg, a pharmacologically active ingredient or, if such an ingredient is not known, a marker suitable substance).

Other than the dilemma of standardization, herbal medicines can be scrutinized in clinical trials in much the same way as are other drugs. Several randomized clinical trials of herbal medicines have been published, and systematic reviews/meta-analyses of these studies have become available (Table 2).^{3,4} The Cochrane database includes about 30 systematic reviews of herbal medicines, and several authoritative books have recently become available.³⁻⁶ The conclusions of systematic reviews are often limited by the paucity and varied methodological quality of the primary studies.^{3,7} Research funds in this area are generally scarce, not least because plants are not patentable.

Generalizations about efficacy of herbal medicines are not possible; each one must be judged on its own merits. Some herbal products have demonstrated efficacy for certain conditions, while others have not. Most products have not been submitted

to extensive clinical testing.³ "Clinicians should not prescribe or recommend herbal remedies without well-established efficacy...."⁷

■ SAFETY

Consumers are attracted to herbal medicines in part because they equate "natural" with "safe." Yet some herbal medicines pose serious risks.⁷

First, the active ingredients in herbal preparations can, of course, cause desirable as well as undesirable effects. Table 3 lists examples of commonly used herbal medicines that have been associated with serious adverse effects.³ Traditional use is no guarantee of safety and no acceptable substitute for data.⁸

A poignant example is kava (*Piper methysticum*), an herbal remedy that has been used for centuries apparently without problems. Numerous rigorous clinical trials have shown it to be a powerful anxiolytic medicine.⁹ Recently it has been associated with several cases of serious liver damage.¹⁰ Hence it has been withdrawn from the markets of several European countries, and the FDA has issued warnings about its hepatotoxic potential.

Second, the active ingredients in herbal medicines might interact with prescription drugs. For instance, extracts of St. John's wort (*Hypericum perforatum*) act as an enzyme inducer on the cytochrome P450 system and increase the activity of the P-glycoprotein transmembrane transporter mechanism. Both effects lead to a reduction of the plasma level of several conventional drugs.¹¹ Perhaps the most serious consequence could be insufficiently low cyclosporine levels in patients after organ transplantation, which jeopardize the success of this procedure.¹²

Third, some herbal medicines (particularly Asian herbal mixtures) have repeatedly been shown to be contaminated with heavy metals,¹³ or to contain misidentified herbal ingredients that turned out to be toxic,¹⁴ or to be adulterated with prescription drugs.¹⁵

Before prescribing or recommending an herbal medication, clinicians must ensure that it cannot generate undue harm.

TABLE 2

Examples of systematic reviews and meta-analyses of herbal remedies

Common (Latin) name	Active ingredients	Indications	No. of trials	Avg. methodological quality of primary studies	Efficacy	Main result
Feverfew (<i>Tanacetum parthenium</i>)	Parthenolide	Migraine prevention	5	Good	Likely	3 trials were positive, 2 were negative
Garlic (<i>Allium sativum</i>)	Alliin	Hypercholesterolemia	13	Good (some excellent)	Certain but effect small	Overall effect is significant but of debateable clinical relevance
Ginkgo (<i>Ginkgo biloba</i>)	Ginkgolides, bilobalide	Intermittent claudication	8	Good to excellent	Certain	Overall positive result
Horse chestnut seed extract (<i>Aesculus hippocastanum</i>)	Triterpene saponins	Chronic venous insufficiency	8/5*	Good	Likely	Active treatment more effective than placebo and equally effective as reference treatments
Peppermint oil (<i>Menta x piperia</i>)†	Menthol	Symptoms of irritable bowel syndrome	8	Good	Likely	Positive effect of peppermint oil compared with placebo

Sources: Ernst et al 2001³; Fugh-Berman 2003.⁴
 *8 trials vs placebo; 5 trials vs reference treatments. † *Am J Gastroenterol* 1997; 93:1131–1135.

■ QUALITY

The quality of an herbal preparation partly determines its efficacy as well as its safety. Herbal dietary supplements are not usually regulated as drugs and have repeatedly been found to vary in quality, sometimes being suboptimal.^{7,16}

In the US, such preparations have to meet the requirements set forth in the Dietary Supplement and Health Education Act (DSHEA) of 1994. Thus they are marketed without approval of their efficacy and safety by the FDA. The DSHEA does not allow medical claims to be made for such products. Structure or functional claims are, however, allowed. If safety concerns of a product arise, the burden of proof lies not with its manufacturer but with the FDA. Many experts find this regulation insufficient to guarantee consumer safety and argue for it to be changed.¹⁶ In Europe, new legislation will

soon regulate herbal medicines. Essentially the legislation will provide that efficacy be demonstrated on the basis of bibliographic data; safety, too, will be governed as it is with conventional drugs.¹⁷

■ COST

Clinicians should recommend treatments that save money for patients and the healthcare system. Many herbal medications are relatively inexpensive. However, very few proper economic analyses of herbal medicines exist.^{18,19} So far, only 1 cost evaluation of an herbal medicine has been published.²⁰ This study of symptomatic treatment of chronic venous insufficiency compared the cost-effectiveness of compression stockings with that of an extract of horse chestnut seeds. Its results implied that the treatments were similarly effective and associated with similar costs.

TABLE 3

Examples of herbal medicines associated with serious adverse effects

Common (Latin) name	Indication	Adverse effects (examples)
Aloe vera (<i>Aloe barbadensis</i>)	Various	Juice may cause intestinal pain and electrolyte loss
Feverfew (<i>Tanacetum parthenium</i>)	Migraine prevention	“Post-fever syndrome” after discontinuation (migraine, anxiety, insomnia, muscle stiffness)
Hawthorn (<i>Crataegus</i>)	Congestive heart failure	Additive effects with other cardiac glycosides
Kava (<i>Piper methysticum</i>)	Anxiety	Toxic liver damage
St. John’s wort (<i>Hypericum perforatum</i>)	Depression	Increased clearance of a range of prescribed drugs
Tea tree oil (<i>Malaleuca alternifolia</i>)	Skin problems (external)	Allergic reactions
Valerian (<i>Valeriana officinalis</i>)	Insomnia	Morning hangover

Without positive data demonstrating safety, herbal medications cannot automatically be considered safe for pregnant or nursing women.

For the prescribing physician, this means decisions cannot presently be based on conclusive cost-analyses. While waiting for such data to become available, decisions will have to be informed by our knowledge on the efficacy, safety, and quality of herbal medications.

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