OBG MANAGEMENT

Edzard Ernst, MD, PhD
Lang Chair in Complementary Medicine
Peninsula Medical School
Universities of Exeter and Plymouth, Exeter, UK

How to judge an herbal remedy

How do you determine usefulness? It's a matter of efficacy, safety, quality, and cost.

FAST TRACK

Do not prescribe or recommend herbal remedies without proven efficacy

IN THIS ARTICLE

How many of your patients take herbal preparations? More than you think, thanks to the proliferation of products. Between 1990 and 1997, the US population increased its use of herbal medicines by 380%, and total out-of-pocket expenditures in 1997 were $5.1 billion (**TABLE 1**).[1,2]

Safety issues surrounding herbal medicine are complex: possible toxicity of herbal constituents, presence of contaminants or adulterants, and potential interactions between herbs and prescription drugs. In addition, the preparations are often poor in quality. One reason: They are inadequately regulated, a problem many experts hope to change. Cost evaluations of herbal medicines are not available.

This article offers guidelines for prescribing herbal medications, as well as advice on when they are unwise.

TABLE 1

10 best-selling herbal medicines

RANK	HERB	RETAIL SALES ($ MILLIONS)*
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

* US, 2001 data

Is the herb effective for the patient's condition?

Although data are incomplete, some treatments have shown promise (**TABLE 2**), and findings indicate serious adverse effects of certain treatments (**TABLE 3**).

Besides safety, the critical question is: Does the remedy work for the patient's condition? Do not prescribe or recommend an herbal remedy if the answer is not a firm yes.

Herbal medicines usually contain a range of pharmacologically active compounds. In some cases, it is unclear which constituents produce 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 optimize the reproducibility of efficacy studies, extracts must be sufficiently characterized. This is often

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TABLE 2

5 herbal remedies: Systematic reviews and meta-analyses

COMMON (LATIN) NAME	ACTIVE INGREDIENTS	INDICATIONS	NO. OF TRIALS	METHODOLOGICAL QUALITY OF PRIMARY STUDIES	EFFICACY	MAIN RESULT
Feverfew *(Tanacetum parthenium)*	Parthenolide	Migraine prevention	5	Good	Likely	3 trials were positive, 2 were negative
Garlic *(Allium sativum)*	Alliin	Hypercho-lesterolemia	13	Good (some excellent)	Certain but effect small	Overall effect is signi-ficant but of debatable clinical relevance
Ginkgo *(Ginkgo biloba)*	Ginkgolides, bilobalide	Intermittent claudication	8	Good to excellent	Certain	Overall positive result
Horse chestnut seed extract *(Aesculus hippocastanum)*	Triterpene saponins	Chronic venous insufficiency	8/5*	Good	Likely	Active treatment more effective than placebo and equally effective as reference treatments
Peppermint oil *(Menta x piperial)*†	Menthol	Symptoms of irritable bowel syndrome	8	Good	Likely	Positive effect of peppermint oil com-pared with placebo

Sources: Ernst et al 2001[3]; Fugh-Berman 2003.[4]

*8 trials vs placebo; 5 trials vs reference treatments. †Am J Gastroenterol. 1997;93:1131–1135.

achieved by standardizing the amount of a single key constituent (eg, a pharmacologically active ingredient or a marker suitable substance if such an ingredient is unknown).

Once the dilemma of standardization is solved, herbal medicines are scrutinized in much the same way as other drugs. The literature contains several randomized, clinical trials and systematic reviews/meta-analyses of these studies.[3,4] The Cochrane database includes about 30 systematic reviews of herbal medicines, and several authoritative books recently were published.[3–6]

Unfortunately, systematic reviews are often limited by the paucity and varied methodological quality of the primary studies,[3,7] and research funds are generally scarce, in part because plants cannot be patented.

Generalizations about the efficacy of herbal medicines are not possible. Each remedy must be judged on its own merits. Some herbal products have demonstrated efficacy for certain conditions, while others have not. Overall, few products have been subjected to extensive clinical testing.[3]

The bottom line? As a review in the *New England Journal of Medicine* concluded, "Clinicians should not prescribe or recommend herbal remedies without well-established efficacy."[7]

Tradition is no guarantee, as in the case of kava

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 cause both desirable and undesirable effects. **TABLE 3** lists examples of commonly used herbal medicines that have been associated with seri-

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Peppermint oil eases irritable bowel, according to 8 trials

TABLE 3

7 herbal medicines associated with serious adverse effects*

COMMON (LATIN) NAME	INDICATION	ADVERSE EFFECTS (EXAMPLES)
Aloe vera *(Aloe barbadensis)*	Various	Juice may cause intestinal pain and electrolyte loss
Feverfew *(Tanacetum parthenium)*	Migraine prevention	"Post-fever syndrome" after discontinuation (migraine, anxiety, insomnia, muscle stiffness)
Hawthorn *(Crataegus)*	Congestive heart failure	Additive effects with other cardiac glycosides
Kava *(Piper methysticum)*	Anxiety	Toxic liver damage
St. John's wort *(Hypericum perforatum)*	Depression	Increased clearance of a range of prescribed drugs
Tea tree oil *(Malaleuca alternifolia)*	Skin problems (external)	Allergic reactions
Valerian *(Valeriana officinalis)*	Insomnia	Morning hangover

* This is a sampling only. Also, without positive safety data, herbal medications cannot be considered safe for pregnant or nursing women.

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St. John's wort reduces plasma levels of several conventional drugs

ous 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 agent,[9] but it was recently associated with several cases of serious liver damage.[10] As a result, it was withdrawn from the markets of several European countries, and the US Food and Drug Administration (FDA) has issued warnings about its hepatotoxic potential.

Second, the active ingredients in herbal medicines can 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 would 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) are contaminated with heavy metals[13]; contain misidentified, toxic herbal ingredients[14]; or are adulterated with prescription drugs.[15] Be sure an herbal medication cannot cause harm before prescribing or recommending it.

Uneven quality marks herbal medicines

The quality of an herbal preparation contributes to its efficacy and safety. Herbal dietary supplements usually are unregulated as drugs and can vary widely in quality—to the point of being ineffective.[7,16]

In the United States, herbal preparations must meet the requirements set forth in the Dietary Supplement and Health Education Act (DSHEA) of 1994. Thus, they are marketed without FDA approval of their efficacy and safety. The DSHEA prohibits companies from making medical claims for dietary supplements, but does allow structure or functional claims. If safety concerns arise, the burden of proof lies not with the manufacturer, but with the FDA.

Many experts believe this regulation is insufficient to guarantee consumer safety and argue for it to be changed.[16] In Europe, new legislation will soon require

efficacy to be based on bibliographic data, and safety will be governed as it is with conventional drugs.[17]

Not enough data to base decisions on cost

As a general rule, clinicians should try to recommend treatments that save money for patients and the health-care system. Although herbal medications are relatively inexpensive, few proper economic analyses exist.[18,19] So far, only 1 cost evaluation[20] of an herbal medicine has been published. This study involved treatment of symptomatic chronic venous insufficiency and compared the cost-effectiveness of compression stockings with that of an extract of horse chestnut seeds; the treatments were comparable.

For the prescribing physician, this means decisions cannot be based on conclusive cost-analyses. Until such studies are available, decisions must be informed by our knowledge of the efficacy, safety, and quality of herbal medications. ■

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Herbal hazards: Heavy metals and undeclared ingredients

One of 5 Ayurvedic herbal medicine products may contain potentially toxic levels of lead, mercury, and/or arsenic, according to a study in the December 15 issue of *JAMA*. The Ayurvedic tradition is a holistic healing system that originated in India. When researchers tested Ayurvedic products produced in South Asia and sold in the Boston area, 14 of 70 contained heavy metals. If taken according to the package directions, the preparations would exceed published standards for the metals, some of them by a huge margin.

Pharmaceuticals in an herbal remedy?

Among other hazards detected in herbal products are undeclared prescription drugs mixed into the ingredients of some Chinese preparations, according to the FDA. And last May, *Consumer Reports* identified 12 dietary supplements "too dangerous to be on the market," yet all were readily available in stores or online. They include comfrey, androstenedione, chaparral, and kava.

Pose the question

All the more reason to ask patients what products they may be using. Ask specifically about herbal or natural remedies, since many people do not consider them drugs and fail to disclose them to physicians.

—The editors

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1 of 5 Ayurvedic herbal products may contain potentially toxic levels of lead, mercury, or arsenic

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