

Best Practice

CLINICAL EVIDENCE

An evidence-based review of the 10 most commonly used herbs

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Objectives

- Discuss the prevalence and use of herbal therapies in the United States
- Provide an evidence-based overview of the 10 top-selling herbs on the market
- Discuss general advice for patients who are interested in using herbal remedies
- Provide sources of information for doctors and patients

INTRODUCTION

Herbal therapies have been used throughout history but have recently undergone a renaissance. It is estimated that one in three Americans have used an herbal medication in the past year. Renewed interest in botanicals has pushed sales to an estimated \$4 billion a year, with sales increasing at 20% per year since the early 1990s.^{1,2}

About 25% of modern pharmaceuticals are derived from plants (see box).² Patients are often unaware of the similarities between medicinal herbs and prescription drugs, and they may mistakenly believe that these “natural” substances do not contain powerful bioactive ingredients. In addition, because herbs may be sold and marketed without FDA approval, there are concerns about the limited evidence on herbal side-effects, drug interactions, and product consistency. Recent reports have highlighted severe reactions to specific herbs and to contaminants in herbal preparations.^{3,4} The popular use of herbs may also lead to increases in patient self-diagnosis and to delays in the use of more effective therapy. Here we review the current evidence on the safety and efficacy of the 10 top-selling herbs in the United States in 1998 (see box).⁵

Medicines derived from plants

Atropine	Belladonna and Jimsonweed
Colchicine	Autumn Crocus
Digoxin	Foxglove
Etoposide	Mayapple root
Morphine	Poppies
Quinine	Cinchona tree bark
Salicylin	Willow bark
Scopolamine	Henbane
Tamoxifen	Pacific Yew Tree
Vincristine	Periwinkle

METHODS

Articles in our review were obtained through MEDLINE (1966 to March 1999) and the Cochrane Collaboration Database of Systematic Reviews, using a keyword search

of the common and Latin botanical names for each of the 10 herbs. The search was limited to English-language articles and human studies. Two authors reviewed the articles identified by the search, summarizing the evidence through a process of discussion and consensus. Statements regarding efficacy were based on the findings presented in systematic reviews and randomized controlled trials located by the search.

EVIDENCE ON THE TEN MOST COMMONLY USED HERBS

Echinacea

The species *purpurea* (purple coneflower) is believed to have immunostimulating effects and is most often used for the treatment or prevention of the common cold.⁶ A recent systematic review identified five randomized, placebo-controlled trials of echinacea for prevention of colds and eight for treatment of colds. The authors concluded that there was insufficient evidence to make conclusions regarding the efficacy of echinacea. For a more detailed discussion of this widely used herb, see also page 198.

St. John's wort

St. John's wort is derived from the plant *Hypericum perforatum* and has been used since ancient times for depression and anxiety. It blooms around St. John's Day (June 24th) and produces a red pigment when crushed, which is believed to represent the blood of St. John the Baptist. It is the most common antidepressant used in Germany, outselling selective serotonin reuptake inhibitors (SSRIs) by fourfold. Although the mechanism of action is only partially known, it is believed to inhibit the uptake of gamma-aminobutyric acid (GABA) and other neurotransmitters.

There are several studies examining the use of St. John's wort for depression. A meta-analysis of 23 trials involving 1757 patients showed that the use of St. John's wort significantly improved scores on the Hamilton depression scale by 4.4 points (95% confidence interval [CI] 1.78-4.01) compared with placebo. In eight of the studies, St. John's wort was also compared to low-dose tricyclic antidepressants and found to have equivalent efficacy with fewer side effects (19.8% of patients had side effects on St. John's wort compared with 52.8% on tricyclic antidepressants).⁸ Currently, the National Institutes of Health is funding a \$4.3 million multicenter randomized trial comparing St. John's wort to paroxetine. St. John's wort is relatively well tolerated, with only minimal side effects of gastrointestinal upset, fatigue, and phototoxicity. It is generally not recommended to be used in combination with other antidepressants.

Table 1 A review of the evidence for the top 10 herbs

Herb	Common uses	Dose	Side effects and interactions	Bottom line
Echinacea	Treatment and prevention of upper respiratory infections, common cold	300-400 mg dried extract tid or 2-3 mls tincture tid	Rash, pruritis, dizziness, unclear long-term effects on the immune system	Inconclusive evidence
St. John's wort	Mild to moderate depression	300mg tid of extract standardized to 0.3% hypericin	Gastrointestinal upset, photosensitivity	Beneficial in mild to moderate depression
Ginkgo biloba	Dementia	40 mg tid standardized to 6% terpenoids and 24% flavonoids	Mild gastrointestinal distress, headache, may have anticoagulant effects	Beneficial in patients with dementia
Garlic	Hypertension, hypercholesterolemia, atherosclerosis	600-900 mg per day, standardized to 0.6%-1.3% allicin	Gastrointestinal upset, gas, reflux, nausea, allergic reactions, and antiplatelet effects	Probable modest effect for decreasing lipids and blood pressure
Saw palmetto	Benign prostatic hyperplasia	320 mg qid or 160 mg bid	Uncommon	Probably beneficial in benign prostatic hyperplasia
Ginseng	General health promotion, sexual function, athletic ability, energy, fertility, and others	200-300 mg/day of extract standardized to > 7% ginsenosides	High doses may cause diarrhea, hypertension, insomnia, nervousness, may interact with warfarin	No conclusive evidence for any indication
Goldenseal	Upper respiratory infections, common cold	Not established	Diarrhea, hypertension, vasoconstriction	No evidence for a beneficial effect
Aloe	Topical application for dermatitis, herpes, wound healing, and psoriasis, orally for constipation	Topical doses vary, oral dose 20-30 mg hydroxyanthracene derivatives daily	May delay wound healing after topical application, diarrhea and hypokalemia with oral use	Inconclusive evidence
Siberian ginseng	Similar to ginseng	2-3 g of root daily	May alter digoxin levels	No evidence for a beneficial effect
Valerian	Insomnia, anxiety	400 mg at night	Fatigue, tremor, headache, paradoxical insomnia— not advised with other sedative-hypnotics	Inconclusive evidence

Ginkgo

Ginkgo biloba has grown in China for over 200 million years and is one of the oldest surviving tree species in the world. It is typically used to treat cognitive deficits, including Alzheimer's-type and multi-infarct dementia, and peripheral vascular disease. The active ingredients, flavonoids and terpenes (ginkgolides), are believed to act as free radical scavengers, protecting vascular walls and nerve cells as well as inhibiting platelet-activating factors, thus reducing clotting.

A large multi-center randomized placebo-controlled trial of 2020 patients with dementia found that patients using ginkgo biloba showed improvements in both Alzheimer's Disease Assessment Scale Cognitive Subscale score by 1.4 points ($P=0.04$) and Geriatric Evaluation by Relative's Rating Instrument score by 0.14 points ($P=0.004$).⁹ There have also been two published meta-analyses, which concluded that ginkgo is effective for improving the memory and concentration of patients with cerebral insufficiency.^{10,11} Ginkgo is very well tolerated but should be used with caution in patients on anticoagulants, because there have been two case reports of subarachnoid hemorrhages and hyphemas in patients using ginkgo.^{12,13}

Garlic

Garlic (*Allium sativum*) has been cultivated worldwide for over 5000 years, not only to flavor food but also

because it contains a sulfur-rich derivative of cysteine felt to have medicinal benefits. Historically, garlic was used in China to lower blood pressure, in Egypt to increase physical strength, and in Europe to prevent the plague. Public interest in garlic was stimulated by two meta-analyses that demonstrated a decrease in total cholesterol by 9% to 12% after treatment of at least one month.^{14,15} However, eight subsequent clinical trials showed inconsistent results, with half showing no significant decrease in cholesterol and the remainder demonstrating a 6% to 13% decrease in total cholesterol.¹⁶⁻²³ Another meta-analysis of eight studies involving 415 patients revealed that garlic had a modest effect on blood pressure, with reductions of 7.7 mmHg in systolic blood pressure and 5.5 mmHg in diastolic blood pressure.²⁴ Garlic is also marketed for its antiplatelet, anti-atherosclerotic, and antitumor effects, although these indications have not been thoroughly studied. It is generally well tolerated but should probably be avoided in patients using warfarin, due to the possible antiplatelet effects.

Saw palmetto

Saw palmetto (*Serenoa repens*) is a dwarf palm tree native to the southeastern United States and the West Indies. Extract from the saw palmetto berry is widely used in Europe for the treatment of benign prostatic hyperplasia.



Aloe Vera

In Germany, for example, 90% of patients with this condition are treated with saw palmetto or other plant extracts.²⁵ The mechanism of action is unknown, but several theories have been proposed, including an antiandrogenic effect, an anti-inflammatory effect through action on prostaglandins, a direct inhibition of prostate growth, or an alteration in the available sex hormone-binding globulin.²⁵ A recent systematic review identified 10 randomized placebo-controlled trials and concluded that saw palmetto improved urinary tract symptoms and urinary flow. When compared with patients taking placebo, patients using saw palmetto showed improvement in peak urine flow of 1.9 milliliters per second (summary of eight studies) and improvement in urine symptom scores of 1.4 points (one study, 0-19 point scale). Adverse effects due to saw palmetto were mild and comparable with placebo. The studies were limited by their short duration, variability in design, and use of different preparations.²⁶

Ginseng

Ginseng, or the man-root, is the most popular and most expensive herb sold worldwide. Its scientific name, *Panax ginseng*, alludes to its purported panacea-like quality. Because the shape of the root resembles a human being, it has been believed to benefit all aspects of the human body, with presumed effects ranging from its being an immunomodulating agent to its ability to improve sexual and athletic function. As with garlic, it is difficult to substantiate ginseng's

efficacy, especially given the inherent difficulty quantifying vague benefits such as "vitality" and "youthful vigor." There have been a few small poor quality studies on ginseng's effects on athletic ability, fertility, the immune system, and glucose control, but the evidence remains inconclusive.²⁷⁻³⁰

Adverse reactions from ginseng itself are quite rare, but there have been several case reports of side effects to contaminants in the preparations.³¹ There has also been one case report of ginseng interfering with warfarin.³²

Goldenseal

Goldenseal root (*Hydrastis canadensis*) was originally used by American Indians as an antiseptic. It is believed to have an immunostimulant effect and is currently used for upper respiratory tract infections, often in combination with echinacea. Although it accounts for 6% of all sales of herbal products in this country and approximately \$240 million in out-of-pocket expenditures, there is no evidence from randomized controlled trials to support its use for this indication. High doses and prolonged use may cause diarrhea, hypertension, and vasoconstriction.

Aloe

Aloe vera (*Aloe barbadensis*) is indigenous to the Sudan and the Arabian peninsula but is now grown in many parts of the world, including the United States. Aloe may be dried into capsules or formulated into gels for topical application. Aloe is most widely used for a variety of dermatologic conditions, but studies examining efficacy are limited. One study found aloe to be beneficial for more rapid healing of genital herpes,³³ and another showed a positive result in the treatment of psoriasis.³⁴ Conversely, aloe was found to be ineffective for prevention of radiation-induced dermatitis,³⁵ and it was found to delay the healing of surgical abdominal wounds.³⁶ Aloe ferox, a different plant, is used in oral tablets to treat constipation, but data on effectiveness are of poor quality. Overall, the evidence for efficacy for any indication for aloe is too limited to make recommendations for clinical use.

Siberian ginseng

Siberian ginseng (*Eleutherococcus senticosus*) is not of the *panax* (true ginseng) genus, but is a popular and inexpensive substitute for ginseng. Although Siberian ginseng is touted to have the same adaptogenic and androgenic properties as true ginseng, no randomized studies substantiate its use.³⁷ There has been one small study on the lack of androgenicity of Siberian ginseng and a few case reports on side-effects from adulterated products.^{38,39}

Valerian

The pink-flowered perennial *Valeriana officinalis* is commonly used as an anxiolytic and sleeping aid. Although initially approved in the United States to flavor foods such as root beer, valerian has over 100 constituents that are

thought to inhibit the degradation and reuptake of GABA, which may play a role in stress and anxiety. Despite valerian's popular use, there are few studies on its efficacy, safety, or interactions. Only two small randomized studies have been conducted, showing that valerian root caused decreased sleep latency and improved sleep quality without residual fatigue in the morning.^{40,41} These studies were poorly done, however, and definitive conclusions cannot be drawn from them. Because it binds the same receptors as benzodiazepines and causes sedation, valerian root should not be combined with benzodiazepines, barbiturates, or other sedative-hypnotics. In addition, some reports cite paradoxical stimulation, including tremor, headache, and cardiac disturbances in patients using valerian in high doses or for a prolonged period of time.

Advice for patients and doctors

Consumers should be aware that physicians are not able to guarantee the safety or consistency of products. More reliable products will likely have a label clearly stating the botanical name of the herb, milligram dose, batch or lot number, expiration date, and name and address of the manufacturer. Standardized extracts should be used whenever possible, and patients should avoid using a large variety of herbs, since herb-herb interactions are poorly described. Patients should start with the lowest effective dose and avoid using products over a long period of time, since long-term effects are generally unknown. Women who are pregnant or lactating should always avoid using herbal products unless they have been specifically tested for use in pregnancy. Moreover, all adverse effects should be reported to the Food and Drug Administration's Med-watch program (phone number 800-FDA-1088). Finally, patients and healthcare providers should educate themselves as much as possible about herbal therapeutics. Sources of information are shown in the right margin.

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Sources of information

See also page 201

Systematic reviews

The Cochrane Library.
Update Software Inc.
936 La Rueda Drive,
Vista, CA 92084.
Web URL:
<http://www.updateusa.com/cochrane.htm>

On-line resources

American Botanical
Council
<http://www.herbalgram.org>

Federal Drug
Administration
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