

# HERBAL MEDICINE THE GOOD, THE BAD, AND THE UGLY

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**Abstract:** *Increasing numbers of Americans are using herbal medicine. This article reviews the history and current use of herbs in the United States, their regulatory status, and approaches to reviewing information on herbs. The benefits and risks of 10 of the most commonly used herbs are described. The use of herbs by patients participating in clinical trials can impact the results of those trials. Issues in communicating with patients regarding their use of herbs are covered.*

**M**any of us are using herbs or have family members who are using herbs and many herbal studies are underway nationally. The biochemical potency of some of the most common herbs is impressive. The use of herbs by patients who are participating in clinical trials can impact the results of those trials.

Physicians are comfortable with herbal therapies such as using aloe on burns or eating cranberries for urinary tract infections. When a patient wants to use feverfew for migraines or goldenseal for upper respiratory infections, however, physicians frequently do not know or understand these herbal medicines. They may commonly lump all herbal medicines together under the category of “snake oil.”

The World Health Organisation estimates that four billion people—80% of the world’s population—presently use herbal medicine for some aspect of primary care (Table 1). Herbal medicine is not going to go away in the near future.

**Table 1**  
**The Use of Herbal Medicines is Increasing**

- 80% of the world’s population uses herbal medicine for some aspect of primary health care
- Americans are spending about \$6 to \$8 billion on herbal medicine
- Mainstream America is searching the Web for information about herbal medicine

Many people are using the Internet to research herbal medicines. For example, several years ago, Mayo Clinic’s Web site was getting about 450,000 hits per month. During the same time period, Dr. Andrew Weil’s integrative medicine Web site was getting 2,500,000 hits per month. Mainstream America is interested in herbal medicine.

Sales data show that Americans are spending about \$6 to \$8 billion on herbal medicines. If you think

people in your studies are not taking herbal medicines, you are mistaken. It is very important to ask patients if they are taking any herbal medicines, and if so, to get more information about their use of herbal medicines.

Many people point to Germany as a model for the use of herbal medicines. In 1978, the Germans established Commission E to gather information on herbs. Commission E has a standardized license

approach to herbs; if you buy an herb one day and go back three months later and buy the same herb from the same company, it will have the same chemical constituents.

The United States cannot follow this model because its regulatory environment for herbal medicines is very different. In 1994, Congress passed the Dietary Supplement Health and Education Act, which, instead of allowing the U.S. Food and Drug Administration (FDA) to bring some regulation and safety to herbal medicines, re-classified them as “dietary supplements.” Manufacturers do not have to prove the safety or efficacy of dietary supplements before marketing them. An herbal product can basically be put on the market with essentially no oversight and can only be removed if the FDA can prove it to be dangerous.

### The 10 Most Common Herbs

Table 2 outlines the 10 most commonly used herbs in the United States, according to recent sales data. Ginkgo biloba, used to prevent dementia, is probably one of the

best selling herbs worldwide. We know a lot about ginkgo. It crosses the blood-brain barrier and is a good antioxidant. It has several central nervous system effects, which could have some implications for clinical trials: increased cerebral arterial dilatation; increased oxygen, glucose, and neurotransmitter uptake; increased tolerance to hypoxia; decreased free-radical damage; and platelet aggregation inhibition.

Several studies have been published about ginkgo. In 1997, LeBars published a study of 202 patients with Alzheimer’s disease or multi-infarct dementia in the *Journal of the American Medical Association*. Half the patients received a standard ginkgo preparation and half received placebo; all were followed for a year. Researchers found that there was a modest improvement favoring the herb. Across clinical studies of ginkgo, you see this modest, questionably clinically significant, effect. If you are conducting a study related to cognitive development, if you do not ask participants about the use of herbs such as ginkgo, you will miss something important.

Most herbs have caveats. Many Americans still tend to think that herbs are natural, and thus, safe. For example, Ginkgo is a relatively good platelet inhibitor, like aspirin. There have been reports of people developing subdural hematomas with ginkgo. This is rare, but it is much more likely if ginkgo is mixed with high-dose aspirin, Coumadin, or Warfarin.

Is ginkgo a bad drug? No. Does it fix everything? No. Is there a role for it? Absolutely, but we must discuss how to use it with patients.

St. John’s Wort, used for depression, has gotten quite a bit of press lately. Many studies have been published about St. John’s Wort. In 1996, Linde published a meta-analysis of 23 studies of St. John’s Wort with 1,757 outpatients in the *British Medical Journal*. In 13 trials that compared St. John’s Wort to placebo, depression improved for 55% of the participants who took the herb and 22% of participants in the placebo group. In six trials that compared St. John’s Wort to TCA, researchers found a 64% response with the herb (side effects 20%), and a 59% response with TCA (side effects 53%). Thus, for mild-to-moderate depression, St. John’s Wort appears to be very effective. A more recent study suggested that it is not effective for severe depression. If you are conducting a study with an endpoint such as mood or depression, and the patient is taking St. John’s Wort unknown to you, the potential for confounding is high. Caveats about St. John’s Wort are phototoxicity, acute neuropathy, and drug reactions. Be especially cognizant of the profound effect St. John’s wort has on the cytochrome P450 system and the subsequent alteration of metabolism of a wide array of drugs.

• Ginkgo biloba
• St. John’s Wort
• Echinacea
• Ginseng
• Garlic
• Saw Palmetto
• Kava-kava
• Valerian
• Milk Thistle
• Feverfew

Echinacea, used to fight colds, is another popular herb. Can Echinacea really help you fight colds? In animal data and small amounts of human data, Echinacea has some immune-stimulating effects. More than 350 very small studies, often sponsored by pharmaceutical or herb companies, have been conducted with Echinacea, primarily in Europe. Schoneberger randomized 108 subjects to Echinacea vs. placebo for eight weeks during cold season. He found a 36% reduction in risk of contracting a cold and one third of those who did get a cold said they had milder symptoms. Other studies of equal quality or size have suggested no effect. It is very difficult to get a handle on Echinacea's efficacy. Caveats to Echinacea are autoimmune disorders and problems with chronic use. If you buy it in the United States, you will generally not see these warnings. If you buy Echinacea in Germany, you will usually be told not to take it if you have a compromised immune disease and not to take it year-round.

Ginseng, claimed to enhance exercise and sexual performance, is one of the big sellers worldwide. In traditional Chinese medicine, ginseng helps bring balance to the body. Most studies of ginseng have been pretty unexciting. A few small studies have suggested that ginseng can improve quality of life, enhance memory, and improve diabetes control. Overall, ginseng has a great reputation, and has been around forever, but good current research is lacking. Caveats with ginseng are possible increased or decreased blood pressure, possible estrogenic effects in postmenopausal women, and Ginseng Abuse Syndrome (hyper-excitability caused by taking a lot of ginseng, especially by chewing raw root).

The active ingredient of garlic is allicin. Garlic modestly reduces cholesterol (about 10%), can modestly affect blood pressure in some patients, and inhibits platelet aggregation. Caveats are that garlic must be used with caution with anticoagulants, and can cause gastrointestinal upset and topical allergic reactions.

The berries of saw palmetto have long been used to control prostate symptoms. The berries are well characterized (sterols are probably the active ingredient). Studies have found saw palmetto to be about equivalent in efficacy to finasteride for BPH. Caveats are that saw palmetto causes mild side effects such as headache, gastrointestinal upset, and impotence/decreased libido. It does not affect libido as much as pharmaceuticals for BPH do.

Kava-kava, a very good anxiolytic, has been in the news for a while. It comes from the South Pacific islands, where it is used as a ceremonial drink. Kava-kava has proven efficacy as an anxiolytic for anxiety. In one study, it had an effect on anxiety that was basically equivalent to benzodiazepines. Kava-kava appeared to be relatively safe until winter 2002, when Germany reported several cases of severe liver toxicity. We do not know yet whether that is related to a kava preparation, compound, or a specific manufacturer. In the meantime, several countries have banned kava-kava (e.g., United Kingdom, Australia, Switzerland, and Germany). The United States has issued warnings not to start taking kava-kava if you are not already taking it. Caveats of kava-kava are mild gastrointestinal distress, a scaly skin rash, and numbness/an astringent effect in the mouth. Kava-kava can potentiate the effects of benzodiazepines and anesthesia.

Valerian is primarily used as a sedative and sleep aid. It has dramatic effects on sleep and can reduce sleep latency and decrease the time to REM sleep. It does not seem to be habit-forming or lose its efficacy over time. Side effects are pretty limited. There have been a few reports of liver toxicity and some people get a "hangover" (drowsiness, ataxia) when they first start taking it.

Milk thistle has been around for a long time as a treatment for liver disease. Is this plausible? Milk thistle is a pretty good antioxidant; it stimulates membrane synthesis in liver cells, and it provides membrane stabilization.

The results of studies of milk thistle have been all over the board. Some studies of milk thistle in Hepatitis A or B have shown that taking silymarin, the combination of lignans of the plant that are thought to be active, decreases the amount of time required to achieve normal liver enzymes. Other studies have not found that effect. Most studies show a modest effect. There is a lot of interest in milk thistle. Mayo Clinic is conducting several studies with milk thistle in patients with various liver diseases. Many patients are taking milk thistle either to prevent or reduce the severity of liver problems. A caveat of milk thistle is that loose stools occasionally occur at high doses.

Feverfew is a prophylactic agent for migraine headaches. Several good studies suggest that it works. Some patients take it as soon as they get a migraine headache. Feverfew is pretty benign. Taking a large amount can cause mouth ulcers. Stopping feverfew after long-term use can cause rebound headaches. Feverfew can cause indigestion and may be an abortifacient.

### **The Impact of the Use of Herbal Medicines on Clinical Trials**

All herbs are not bad or dangerous. FDA does not have the authority, however, to regulate herbal medicines. Using herbal medicines takes a lot more caveat emptor than most of our patients understand. Many patients will not tell their physicians that they are taking herbal medicines (Table 3). They probably will not be as forthcoming with you from a research standpoint. I try to make sure that my physicians, nurse colleagues, and anybody else who is talking to patients remember that patients are reluctant to talk about herbal medicines with healthcare providers. We must be very non-judgmental. Ask questions about herbal medicine in the same tone that you use for other medicines. Recognize that patients will take herbal medicines. Be alert and watch for adverse effects due to the use of herbs or drug-herb combinations.

Put some of the responsibility back on the patients. I try to get my patients to decide why they are taking an herbal medicine. If a patient is taking St. John's Wort, I ask what he is looking for. If he says depression, I suggest re-assessing the situation in a month, so we have an endpoint. Often, you see a patient with 10 or 20 herbs in a grocery bag; if one does not work, he adds another one, two, or three. That makes it really complex for physicians and researchers to manage.

**TABLE 3**

#### **The Impact of the Use of Herbal Medicines on Clinical Trials**

- Most patients will not tell their physicians that they are taking herbal medicines
- Most participants in clinical trials will not tell researchers that they are taking herbal medicines

**Researchers must:**

- Recognize that patients will use herbal medicines
- Be very non-judgmental about the use of herbal medicines
- Ask questions about herbal medicines in the same tone used for questions about other medicines
- Be alert and watch for adverse effects due to the use of herbal medicines or drug-herb combinations