



The Herbal Medicine Pharmacy: What Kaiser Permanente Providers Need to Know

Consumer use of herbal remedies in the United States is growing rapidly. As a result, many patients seen for routine or urgent care evaluation take herbal medication but might not inform their physician of this intake. Federal agencies do not evaluate herbal products and the Dietary Supplement Health and Education Act of 1994 defines herbal medications as dietary supplements. Patients may thus be misled into believing that herbal medicines are safe and effective. Although some herbal products have been anecdotally described as effective—and thus may be useful in treating some medical conditions for which traditional forms of therapy are contraindicated—many herbal products are toxic and should not be consumed.

This paper reviews several herbal and nutrient supplements that are most commonly used by consumers in the US. Physicians should determine whether their patients are taking herbal medicines and then carefully review the side effects of these substances so that patients can be alerted to potential problems.

Background

In November 1997, the American Botanical Council released the first English translation of the *German Commission E Monographs on Medical Plants for Human Use*,¹ a modern authoritative guide to over 300 biomedical remedies. Defining herbal medicines as dietary supplements, the 1994 Dietary Supplement Health and Education (DSHE) Act² expanded Americans' access to herbal remedies, and in 1996, Americans spent more than \$2 billion on herbal remedies.³ A recent statistical survey estimated that one third of all Americans use some form of alternative medicine.⁴

Many herbs may be useful as supplements and work well with many of the treatments used by physicians. However, not all physicians have necessarily kept up with recent advances and publications on this issue. In addition, many consumers who hear about the purported benefits of herbs from television, the Internet, or other sources, try these herbs before seeing the doctor. This sequence of events may fail to pro-

vide patients with the information they need for using herbal products safely.

This paper focuses on the herbs most commonly used in the community and discusses some herbs which may cause serious side effects and thus should be used with extreme caution. Information presented in this paper represents the result of literature review and should be used at reader's discretion. It must be remembered that herbal supplements today can be marketed with suggested dosages and are not subject to mandatory premarket scrutiny by any US governmental agency as to safety and efficacy. Most herbs are not manufactured in a standardized fashion and are not approved by the US Food and Drug Administration (FDA). Companies that market herbal remedies that have not been evaluated by the FDA are required by law to state this fact on package inserts along with the cautionary note that the products are not intended to cure or prevent any disease. The following sources of information are available to physicians:

1. National Institutes of Health (NIH) Office of Alternative Medicine (1-888-644-6226)
2. FDA consumer hotline (1-800-FDA-4010)
3. FDA: *Adverse reactions to herbal medications* (request by calling 1-800-FDA-1088)
4. Review of Natural Products. St. Louis, MO: Facts and Comparisons. [updated monthly]

Some Herbs may be Harmful under Certain Conditions

The top-selling herbs in the United States are echinacea, ginseng, ginkgo, saw palmetto, garlic, evening primrose oil, St. John's wort, kava-kava, feverfew, and milk thistle.⁵ These have been found to be relatively safe, but some carry warnings and should be used only with caution by patients who are pregnant or nursing as well as by those with a history of hypertension. Herbs whose use requires caution include ma huang, chaparral, comfrey, yohimbine, lobelia, and germander. The FDA suggests that these herbs may cause serious adverse reactions.^{6,7}

Ma huang (also known as *ephedra* or *ephedrine*) has had recent fame by being marketed with St. John's wort as "herbal fen-phen."⁸ Because this herb may cause high blood pressure, rapid heart rate, nerve and muscle damage, stroke, and memory loss, its use is not recommended. Chaparral is a desert shrub that has been marketed as a dietary antioxidant supplement. However, this herb has been associated with severe liver toxicity and should not be used.^{9,10} Comfrey is popular in some health stores as a remedy for cancer and ulcers. Like chaparral, comfrey has been associated with liver toxicity.⁹ Yohimbine

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"Herbalists may prescribe ma huang as a stimulant to decrease appetite or to increase energy, but I advise that patients avoid this herb."

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taken by male patients to relieve impotency or achieve an erection is also available in prescription form. However, yohimbine has been associated with kidney failure, seizures, and even death, so patients should avoid yohimbine unless they take it under the direct supervision of a physician. Yohimbine is contraindicated in pregnant women or individuals with a history of renal insufficiency.⁹ Lobelia (also known as Indian tobacco) can produce sensations similar to those experienced with nicotine and has been associated with swelling of the lower extremities, tachycardia, hypotension, and coma. Germander, like ma huang, has also been marketed for weight control. The main side effect associated with this herb is liver toxicity.

As shown above, many herbs used medicinally can have serious, life-threatening side effects. Of particular concern are those that may cause irreversible liver failure, which can result in death.¹⁰⁻¹³ For these reasons, I recommend that physicians review carefully with their patients the possible side effects of herbs before advising their use. In general, herbs should not be prescribed to patients who are (or who are planning to become) pregnant, nursing mothers, infants, or who have any documented allergies to plants.

Beneficial Herbs That Can Complement Medical Treatment

Echinacea (*Echinacea angustifolia*, *Echinacea purpurea*) has been evaluated extensively,¹⁴ and many patients use this herb to prevent colds and other infections because it appears to boost the immune system and has shown activity against viruses, bacteria, and fungi. However, having heard that a major problem facing our medical establishment is the number of bacteria that have become resistant to antibiotics, some patients try echinacea themselves as first-line therapy for respiratory tract infections because they want to avoid long-term exposure to antibiotics. Without receiving available medical advice, these patients may thus be unaware of the side effects associated with *Echinacea*. These side effects may include fever, chills, nausea, and vomiting. Because of its potential to stimulate the immune system, *Echinacea* should not be used by patients with a history of multiple sclerosis, AIDS, tuberculosis, or other autoimmune diseases, and no patient should take this herb for longer than 6-8 weeks.¹⁴

Saw palmetto (*Serenoa repens*) has been widely used in Germany to treat benign prostatic hypertrophy. Extracts of this herb containing fatty acids and sterols may have antiandrogenic activity.¹⁵ Saw palmetto is relatively safe and has few side effects. Nonetheless, patients taking this herb should schedule routine appointments with their health care provider to allow appropriate long-term management of symptoms associated with prostate enlargement and to follow clinical guidelines for screening prostate cancer.

Ginseng, taken primarily to increase stamina and endurance, is relatively safe and may help in treating hypertension. Nonetheless, blood pressure should be monitored during its use.

Ginkgo biloba, too, is an interesting herb: The ginkgo is the sole survivor of the family *Ginkgoaceae* and can be dated back almost 200 million years.¹⁶ The herb *Ginkgo biloba* is used by many patients to manage tinnitus and to prevent age-related memory loss.¹⁶⁻²⁰ It is the most widely prescribed phytomedicine worldwide. This wide popularity arises from studies which suggest that *Ginkgo biloba* can slow the deteriorating effects of dementia.¹⁸ High concentrations of the herb's active ingredients enter the brain's circulation

and apparently improve blood supply to nerve cells.¹⁷ Side effects associated with use of *Ginkgo biloba* include dyspepsia, headache, and allergic skin reactions. In addition, because of its anticoagulant properties, use of this herb should be discontinued before surgery: Spontaneous bilateral subdural hematoma has been reported in patients taking *ginkgo biloba* for prolonged periods of time.²¹

Garlic (*Allium sativum*) has been used by patients because of reports suggesting that it has antibacterial, antifungal, anticoagulant, lipid-lowering, and vasodilative properties.²² Combined, the latter three properties may improve circulation to the heart and brain by preventing formation of blood clots, closure of blood vessels, and cholesterol deposits.²³ For this reason, garlic should be avoided before elective surgery.²⁴

Like other herbs, evening primrose oil has multiple beneficial properties. It is a good source of gamma linoleic acid (GLA), which promotes prostaglandin formation (helpful in reducing painful inflammation in arthritis).

Glucosamine sulfate is a chemical which naturally occurs in the body but may be deficient in some arthritic joints. It is therefore used by many patients to treat osteoarthritis. The main function of glucosamine sulfate is to stimulate production of glycosaminoglycans, a major structural component of cartilage. Some studies have shown that glucosamine sulfate helps to relieve pain and inflammation in osteoarthritis.^{25,26} The mechanism is not well known but may involve providing the natural substances needed to allow arthritic joints to heal.

Feverfew (*Tanacetum parthenium*)²⁷⁻³⁰ is an herb that may be useful for treating migraine headaches.²⁷ The plant contains a compound called parthenolide,²⁸ which is thought to prevent secretion of neurochemicals associated with vascular headache. Feverfew has been associated with mouth ulceration and contact dermatitis and is contraindicated in pregnancy.

Herbs which have important activity in the gastrointestinal tract include milk thistle (*Silybum marianum*), chamomile (active against pyrosis and intestinal spasm), and ginger (*Zingiber officinale*) (used to treat nausea and motion sickness). Milk thistle has been used for centuries to treat liver disease, but gastroenterologists are today noting many patients taking this herb. Milk thistle may be very helpful in treating various liver conditions and in protecting the liver from injury after exposure to toxins such as alcohol, chemical solvents, and poisonous mushrooms.³¹ Peppermint is an herb that has been used to treat symptoms of irritable bowel syndrome as well as spasm of the common bile duct.³² Oils of peppermint—often used in chewing gum—may relax smooth muscles that prevent physiologic spasm of the common bile duct and the lower esophageal sphincter. For this reason, patients should avoid products containing peppermint oil extract or peppermint oil if they have a history of gastroesophageal reflux disease or gallstones.

In Europe, many different herbs are used to manage anxiety and depression. Some of the most popular and safest include kava-kava for treating anxiety and St. John's wort for treating depression. When compared with other antidepressant agents in controlled studies, St. John's wort was found to effectively treat mild forms of depression at a third the cost with only a third as many side effects as standard treatment.³³ Because this herb is pharmacologically similar to



monoamine oxidase inhibitors, hypertensive patients who use St. John's wort should avoid foods that contain tyramine and other medications (eg, sympathetic amines and serotonergic agents) that may react with monoamine oxidase inhibitors.^{34,35}

Some women take herbs such as black cohosh to manage menopausal symptoms (hot flushes and mood swings). Black cohosh appears to have a mechanism of action similar to that of estrogen in that it prevents hormones from reaching the brain to cause menopausal symptoms.³⁶ The herb is safe and may represent an alternative option for women who refuse estrogen replacement therapy or in whom it is contraindicated.

Synthesis and Recommendations

Herbal remedies are commonly used by millions of Americans.^{37,38} Patients frequently ask their physicians about herbal remedies in the belief that certain herbs may be beneficial in treating acute and chronic diseases. The placebo effect is probably high with these natural products.

To consumers, herbal preparations may also represent a cost-effective natural alternative to some traditional medicines. Unlike Germany, however, where botanical medicines are approved by the government and physicians are given strict guidelines for prescribing these herbal medicines, herbal preparations are not well regulated in the US. Physicians should be aware of the potential toxicity of these herbal medicines. The table following this article summarizes the top-selling medicinal herbs in this country in a format that outlines many of the important issues discussed. ♦

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“Some studies have shown that glucosamine sulfate helps to relieve pain and inflammation in osteoarthritis.”^{25,26}

Table 1. Integrated Medicine Herbal Pharmacy

Substance	Botany	Medicinal use	Consumer information	Dosage
Glucosamine sulfate ^{25,26,39,40}	Substance classified as an amino sugar and made by cartilage cells in the body. This nutrient is important in production of glycosaminoglycans	Nontraditional analgesic agent for treatment of osteoarthritis	Rare side effects. Avoid buying this product in combination with other nutrients that may interfere with intestinal absorption	500 mg three times per day
Echinacea ^{14,41,42}	Active lipophilic component isolated from the leaves of Echinacea purpurea and Echinacea angustifolia	Supportive therapy for chronic respiratory tract infections (immune system stimulator)	No known drug interactions. Side effects include stomach upset and diarrhea. Contraindicated in autoimmune diseases (systemic lupus erythematosus and systemic illnesses (tuberculosis, AIDS, atopy, plant allergies and multiple sclerosis)	0.75 to 1.5 ml, two to five times daily. Do not take for periods greater than 8 weeks
Saw palmetto ^{15,43}	Active component isolated from berries of the plant Serenoa repens	Reduces symptoms of an enlarged prostate (difficulty with urination)	Mild gastrointestinal upset. Do not self-prescribe since symptoms of an enlarged prostate may mimic cancer	160 mg lipophilic saw palmetto extracts two times per day
Ginkgo ¹⁶⁻²¹	Active component is ginkgoloid, which is derived from leaves of the Maidenhair tree, Ginkgo biloba	Treatment of age-related malfunctions including general dementia and Alzheimer's Disease. Anti-oxidant that prevents cells from damage. Improves cerebral circulation by preventing blood platelet adhesion and subsequent blood clots (anticoagulant)	Use with caution in patients taking anticoagulant or NSAIDS. Mild, reversible side effects (nausea, headaches, and dizziness). Consult a physician if memory loss is persistent and progressive	60 to 80 mg of dried extract three times per day
Milk thistle ³⁰	Active component (silymarin) isolated from flower seeds of Silybum marianum	Supportive treatment for toxic liver damage and chronic inflammation of the liver. May protect the outer receptor sites of liver cells, preventing toxins from getting into the cells and causing genomic injury	Rare side effects include gastrointestinal upset and diarrhea	200 to 400 mg (70% silymarin) three times per day



Table 1 (cont.)

St. John's Wort ³³⁻³⁵	Active component (hypericin) isolated from parts of <i>Hypericum perforatum</i> dried above the ground	Treatment of mild depression. Monoamine oxidase and serotonin re-uptake inhibitor	Rare side effects include pruritus, gastrointestinal upset, fatigue. Do not use with foods containing tyramine, alcohol beverages, narcotics, and amphetamines. Consult a physician before use since symptoms may mimic bipolar disorder or hypothyroidism	300 mg of extract containing 0.3% hypericin, 3 times per day
Feverfew ²⁷⁻³⁰	Active component (parthenolide) isolated from dry leaves of <i>Tanacetum parthenium</i>	Prophylaxis and treatment of inflammatory conditions and migraine headaches. Parthenolide may block the release of serotonin and inhibits the production of inflammatory substances	Side effects include gastrointestinal upset and mouth sores. Do not use with NSAIDs, pregnancy and lactation, atopy or allergies to ragweed and yarrow. Stopping abruptly may cause withdrawal. Discuss abnormal symptoms with a physician	0.2 - 0.6 mg (0.2 percent parthenolide)
Kava-kava ^{44,45}	Active component (kavalactones) isolated from dried root of <i>Piper methysticum</i>	Treatment of mild anxiety	Rare side effects. Contraindicated during pregnancy and lactation. Monitor for sign of toxicity (drowsiness and lethargy)	100 mg (70% kavalactones) 3 times per day
Ginger ^{46,47}	Active component isolated from dried root of <i>Zingiber officinale</i>	Prophylaxis of nausea and vomiting associated with motion sickness	Rare side effects. Anti-coagulant properties but anti-thrombotic activity not confirmed in humans. Contraindicated in pregnancy and lactation or history of gallstones	1-2 g of dried root
Garlic ^{23,24}	Active component (alliin) isolated from bulb of <i>Allium sativum</i>	Cholesterol-lowering agent. Prevents platelet aggregation and enhances fibrinolysis	Large doses can be toxic if taken with other blood-thinning medication. Contraindicated in pregnancy and lactation	2-4 g dried bulb, 3 times per day

* eg. AIDS, multiple sclerosis
 ** Nature's Way, Inc., Raisin Rack, Westerville, Ohio

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