

HERBAL REMEDIES

Helping Patients Make Informed, Healthy Decisions

Studies of patients in family practice settings have reported use of herbal remedies as high as 50 percent. A recent article in the Journal of the American Medical Association reported that 15 million Americans spent \$21 billion on alternative therapies in 1997 alone. Herbal therapy is often used in conjunction with over-the-counter and prescription medications; interactions between medications and herbal products can occur.

Herbal products are not regulated by the FDA. There is no guarantee that the product purchased contains the promised herb or that the contents are free from unknown additives or other adulterants. Toxic ingredients such as pesticides, undeclared drugs, heavy metals and prescription drugs have all been found in herbal remedies. The words **standardized**, **USP** (United States Pharmacopoeia) or **True Label Program** on the label offer some assurance that the product has met some preparation guidelines.

Nearly 600 botanicals available on the U.S. Physicians should be routinely asking their patients about herbal products they may be taking and be prepared to openly discuss the pros and cons of herbal products with their patients but reliable information about herbal remedies can be difficult to find; most books on the subject are neither complete nor evidence-based.

***Note:** Much of the clinical evidence reported here is equivocal, antithetical and controversial. Ambiguities are most evident in the contraindications, interactions, side effects and dosing. The German E Commission Monographs, a compendium of research done in Germany on herbal therapies, is the gold standard for much of the information on dosing; unfortunately, this information is in the European style and often reported as infusions, tinctures and injectables. The newly issued PDR of Herbal Medicine uses the information from the German E Monographs but provides relevant literature citations. Further research, especially randomized trials in animals and humans, is needed to elucidate these issues.*

Ten Most Commonly Taken Herbal Remedies

Black Cohosh (*Cimicifuga racemosa*)

Primary Use: To relieve symptoms of menopause, PMS.

Mechanism of Action: Triterpene and flavonoid constituents bind to and presumably stimulate estrogen receptors.

Clinical Evidence:

A 1998 review of several German studies concluded that remifemin (the extract) is effective in reducing menopausal symptoms, and stimulating vaginal mucosa.

Contraindications and Side-Effects:

- Not to be taken by lactating women and women who cannot take birth control pills.
- Stimulates uterus; should not be taken by pregnant women.
- Can cause dizziness, nausea, vision problems, vomiting, hypotension.

Herb-Drug Interactions:

- Herb contains tannin which inhibits iron absorption.
- Concomitant use with estrogen replacement theoretically may cause nausea, bloating, hypotension, breast tenderness, migraine, edema. Best to avoid simultaneous estrogen use although no incidents of estrogen excess have been reported.

Dosage Recommended:

Bottle recommends 1 1mg capsule daily (standardized to be 1 mg triterpene as 27-deoxyactein). Should not be taken for more than 6 months because of lack of clinical data on effects of long-term use. Onset of action is about 2 weeks.³

Cost: \$10/60 capsules; 1 mg/capsule

Echinacea (*Echinacea purpura*)

Primary Use: To relieve symptoms of cold and flu.

Mechanism of Action: Immunostimulant response from alkamides, high molecular weight polysaccharides plus some caffeic acid derivatives stimulate phago-cytosis plus activation of T and B lymphocytes; alkamides and polysaccharides reduce inflammation; some polyacetylene compounds and caffeic acid (cichorin) have antibacterial plus antiviral activities.⁴

Clinical Evidence:

A meta-analysis of German in vitro studies found Echinacea possesses immunostimulating properties useful in treating and preventing colds and flu. An RCT of 302 healthy volunteers given *E. purpurea*, *E. angustifolia* or placebo for 12 weeks found no prophylactic effect for either extract, possibly due in part to small sample size. There is no clinical evidence supporting bactericidal or bacteriostatic claims in vivo.

Contraindications and Side-Effects:

- Little is known about toxicity and side-effects; no chronic or acute toxicity has been documented.
- Patients with systemic and autoimmune disorders or accelerating infection (MS, RA, SLE, HIV) should not use this herb.⁶
- Potential severe allergic reactions in those with atopy.
- Do not take if allergic to daisies.

Herb-Drug Interactions:

Hepatotoxic effects may be associated with persistent use; do not take with known hepatotoxic drugs (anabolic steroids, amiodarone, methotrexate, or ketoconazole).¹

Dosage Recommendation:

1-3 380 mg capsules 3 x daily with water at meals. Use for 5 days, stop for 2, repeat cycle for 15 days. Do not use for longer than 6-8 weeks because of lack of clinical data on long-term use and potential for reduced effectiveness.⁴ German guidelines discourage taking for >8 weeks. Prolonged use may suppress immunity.⁷

Cost: \$5-\$26/100 caps, 250-500 mg capsules

Feverfew (*Tanacetum parthenium*)

Primary Use: To prevent migraines

Mechanism of Action: Suppresses prostaglandin production; does not inhibit cyclo-oxygenase; principle active ingredient is parthenolide, a sesquiterpene lactone; spasmolytic; inhibits platelet aggregation;¹ constituents inhibit secretion of inflammatory mediators (arachidonic acid + serotonin) thought to down-regulate cerebrovascular response to biogenic amines.⁷

Clinical Evidence: Outside the U.S., feverfew has been approved for use in preventing migraine. Two randomized double-blind, placebo-controlled trials found feverfew effective in prevention of migraine.⁷

Contraindications and Side Effects:

- Contraindicated for those allergic to family compositae (*asteraceae*) e.g., chamomile, ragweed, harrow.⁴
- Feverfew should not be taken by pregnant women as it stimulates menstrual bleeding.⁷
- Sudden discontinuation can precipitate rebound headaches.⁷
- Oral preparations may cause mouth ulceration, inflammation and swelling of the tongue.⁷

Herb-Drug Interaction:

- NSAIDs may reduce effectiveness because of prostaglandin inhibition effects.
- Concomitant use of prescription medication for migraines not recommended due to lack of clinical data.
- Concomitant use of anticoagulants not recommended because of platelet aggregation inhibition.^{1,7}

Dosage Recommended:

Herbalists recommend gradual dose increase to 125 mg daily of encapsulated leaves (standardized to 0.2% parthenolide); no US products contain even half this dosage;⁷ no information on long-term clinical use; many commercial preparations may contain little if any of the active ingredient.⁷

Cost: \$8.50/60 caps; 80 mg/capsule

Garlic (*Allium sativum*)

Primary Uses: To reduce total cholesterol and triglyceride levels and increase HDL; to lower blood pressure.

Mechanism of Action: Some components have been found to be antibacterial and/or antimycotic; others inhibit platelet aggregation and enhance fibrinolysis. Mechanism of these actions and the purported lipid-lowering activity are unclear.

Clinical Evidence: 1994 meta-analysis of 5 controlled trials reported garlic effective in reducing triglycerides and total cholesterol. A more recent RCT of a commercial garlic oil preparation showed no effect on cholesterol synthesis or absorption and could not be recommended in the treatment of hypercholesterolemia. Another recent RCT of garlic powder tablets (Kwai) 900 mg/d for 12 weeks found no difference from placebo. However, an RCT in 41 moderately hypercholesterolemic men reported a modest reduction in both LDLs and diastolic blood pressure in response to an aged garlic extract.

Contraindications and Side Effects:

Dosage necessary to achieve physiological effects can produce diarrhea, flatulence, anti-platelet activity, dermatitis, anorexia and vomiting, hypotension, inhibition of iodine uptake.

Herb-Drug Interactions:

- Elevated INRs and prothrombin times in patients taking with warfarin.⁴
- Increases serum insulin levels and improves glycogen storage.¹⁴

Dosage Recommendations:

- Usual dose 300 mg 2-3 times/day standardized as above (equivalent to 3 g or 1 fresh clove daily).
- Heat and acid destroy active ingredients; enteric-coated products show best results. No research-based clinical information available on long-term use.

Cost: (not standardized) \$5-\$8/100 caps; 150-580 mg/cap

Ginkgo Biloba (*Ginkgo biloba*)

Primary Uses: To improve cognitive functioning in mild to moderate dementia; to reduce PMS and vertigo.¹⁴

Mechanism of Action: Only partially understood; flavonoids reduce capillary permeability and fragility, and serve as free radical scavengers; terpenes (ginkgolides) inhibit platelet activating factor, decrease vascular resistance, and improve vascular flow without affecting blood pressure.'

Clinical Evidence: Clinical and pharmacologic studies show Ginkgo extract promotes dilation of blood vessels and improves blood flow in arteries and capillaries. A double-blind, placebo-controlled, randomized study showed Ginkgo led to moderate improvement in symptoms of Alzheimer's type dementia at 1 yr.²¹

Contraindications and Side-Effects:

- Some may experience GI disturbances, headache, allergic skin reactions.
- Isolated reports of intracranial hemorrhages in patients using ginkgo.'

Herb-Drug Interactions:

- Concomitant use with aspirin, NSAIDs, warfarin, heparin (anticoagulants) may cause spontaneous bleeding.
- May diminish effectiveness of anticonvulsants (carbamazepine, phenytoin, phenobarbital) because of presence of low levels of ginkgo neurotoxin.
- Concomitant use with medications that decrease seizure threshold (tricyclic-antidepressants not recommended).^{4,23}

Dosage Recommendations:

- 40 mg 3 times/day or 80 mg twice/day.
- One RCT used 240 mg of extract (Egb 761) daily.
- Herbalists suggest taking for at least 8 weeks + re-evaluate at 3 months. To avoid headache, start with low dose and titrate to recommended dose.³

Cost: \$7-\$20/60-100 cap bottle, 40-60 mg capsules.

Ginseng Korean or Asian (*Panax ginseng* C.A. Meyer).

NOTE: Do not confuse with Siberian ginseng (eleuthero senticosis) which contains no true ginseng.⁷

Primary Use: To relieve stress and related ailments.

Mechanism of Action: Principles believed to be responsible are triterpenoid saponins, called ginsenosides by Japanese and panaxosides by Russian scientists;¹⁵ contains at least 18 triterpenoid saponins, oligoglycosides that may act at different levels within the hypothalamic-pituitary-ovarian axis.

Clinical Evidence: Purported benefits include relief from effects of stress, aging, physical and mental fatigue. Little convincing scientific data exists substantiating the purported benefits. Clinical trials supporting its use were flawed and inconclusive. An RCT of healthy males found no evidence ginseng is an ergogenic aid to improve aerobic exercise. An Italian RCT, however, showed improved muscular oxygen utilization in subjects taking ginseng.

Contraindications and Side-effects:

- Potential side-effects include headache, tachycardia epistaxis, insomnia, diarrhea, hypertension, nervousness, depression, hallucinations, skin rashes, uterine bleeding, mastalgia.²⁵
- Do not take during pregnancy/lactation.⁷
- Can act as mild stimulant, so probably should be avoided in patients with cardiovascular disease.⁷

Herb-Drug Interaction:

- Can potentiate effects of CNS depressants
- May interfere with diabetic therapies
- Potential interaction between warfarin may be related to antiplatelet components.⁴
- Concomitant use with heparin, aspirin, NSAIDs should also be avoided.²⁶
- Not recommended for patients taking phenelzine (Nardil, a MAO inhibitor) because of reports of headache, tremulousness, manic episodes.²⁶
- May augment corticosteroid toxic effects in predisposed patients.²⁶
- May potentiate MAO inhibitor actions due to neurotransmitter effect.
- Avoid other stimulants - caffeine (coffee, tea, colas).⁷

Dosage recommendation: Difficult to find standardized amounts; often contain contaminants or may lack active ingredient.⁹ One source recommends 100-300 mg extract (standardized to 7% ginsenosides) 3 times/day for 3-4 weeks, then 1-2 week wash-out period.

Cost: \$12-\$16/100 caps; 100-110 mg/capsule

Kava-Kava (*Piper methysticum*)

Primary Use: To relieve mild anxiety.

Mechanism of Action: Contains Kava -pyrones (or kava-lactones; terms are used interchangeably);¹³ believed to directly affect limbic system in animal studies;¹³ believed to have mild sedative plus tranquilizing effects by adhering to different versions of GABA receptors than other CNS depressants such as alcohol, sedatives, etc.; relaxant effects may be due to dihydromethysticin.

Clinical Evidence: RCT of 101 patients diagnosed with non-psychotic generalized anxiety disorder by DSMIII-R criteria found significant reduction of anxiety after 25-weeks; subjects received 1 90-110 mg capsule of dry extract 3 times/day. (Each capsule was standardized to 70 mg kava-lactones.) Subjects experienced no significant side effects or withdrawal symptoms. Before recommending kava, care should be taken to distinguish anxiety disorder from other disease states such as hyperthyroidism, panic disorder, and endogenous depression.

Contraindications and Side Effects:

- Mild GI distress, allergic skin rxns, sedation.
- Ataxia, somnolence, difficulty in hearing and vision.
- Consistent and heavy use can produce dizziness and yellow discoloration of hair, skin and nails.
- Do not use if pregnant, nursing, diagnosed with depression, or operating heavy machinery.

Herb-Drug Interaction:

May potentiate CNS effects of barbiturates, alcohol, antidepressants (benzodiazepines), antipsychotics. One case of coma in a patient taking kava and alprazolam was reported.

Dosage recommendations:

RCT used 90-110 mg (standardized to 70 mg kava-lactones) 3 times/day.³¹

German E Commission recommends 60-120 mg kava -pyrones.¹⁰

No clinical data available on long-term use.

Cost: \$17/60 caps; 128 mg/capsule

St. John's Wort (*Hypericum perforatum*)

Primary Uses: As an anti-depressant for mild to moderate depression; seasonal affective disorder.⁹

Mechanism of Action: Mechanism of action unknown; MAO inhibition has not been demonstrated; other actions possibly include inhibition of protein kinases and effects on cytokine production by peripheral blood mononuclear cells; extract contains naphthodianthrone (hypericins), flavonoids (quercetin), xanthones, and bioflavonoids; has high affinity for GABA which when stimulated has antidepressant effects, activates dopamine receptors and inhibits serotonin receptor expression.⁷

Clinical Evidence: NIH is sponsoring an RCT by Duke University to compare the effectiveness of St. John's Wort, fluoxetine and placebo in the treatment of moderate to severe depression.⁷ No evidence exists to support use of St. John's Wort in cases of severe depression. Meta-analysis of 23 RCTs found hypericum significantly superior to placebo and as effective as standard low-dose antidepressants (e.g., imipramine 50 mg/day) in treating mild to moderately severe depressive disorder.³⁴

Contraindications and Side Effects:

- Long-term use is not advised, can cause skin photosensitivity
- Other infrequent side effects include dry mouth, dizziness, GI complaints and confusion.¹⁴
- Do not use if pregnant (uterotonic) or lactating.

Herb-Drug Interactions:

- St. John's Wort found to have SSRI effects, concomitant use with SSRI's (fluoxetine, paroxetine) may result in serotoninism (headache, sweating, dizziness, agitation).⁴
- In vitro studies demonstrated MAO inhibition at concentrations unattainable in vivo; no reported side effects related to MAO inhibition in vivo.⁸
- Safety in combination with other antidepressants is unknown;³³ Until MAOI status defined, avoid concomitant use with known MAOI's (phenelzine) or with beta-sympathomimetic amines (ma huang, pseudophedrine HCL)⁴ avoid taking with other photosensitizing drugs such as piroxicam or tetracycline hydrochloride.

Dosage Recommendation:

300 mg extract (standardized to 0.3% hypericin) 3 times daily for 4-6 weeks.^{7,33} No clinical data available on long-term use.

Cost: \$12-\$20/120 caps; 150-900 mg/capsule

Saw Palmetto (*Serenoa repens*)

Primary uses: To relieve symptoms of benign prostatic hyperplasia (BPH); anti-inflammatory.

Mechanism of action: Mechanism of action may include alteration of cholesterol metabolism, antiestrogenic, antiandrogenic, and anti-inflammatory effects.

Clinical evidence: Systematic review of 18 RCTs found it produced similar improvement in urinary tract symptoms and urinary flow with fewer adverse events compared to finasteride. Average study duration was 9 weeks.

Contraindications and side-effects:

- erectile dysfunction
- mild headache, nausea, and dizziness
- possible hypertension

Herb-Drug Interaction:

- No serious drug interactions have been reported but clinical trials usually excluded men taking diuretics, alpha blockers and anti-coagulants.

Cost: \$6-\$15/60 caps; 150-160 mg/capsule

Valerian Root (*Valeriana officianlis*)

Primary Use: Sedative, hypnotic, anxiolytic.

Mechanism of Action: Unknown; herb believed to be combination of volatile oil components, valepotriales or their derivatives, and unidentified water-soluble constituents;¹⁵ constituents of the root bind -A receptors in similar fashion to benzodiazepines and barbiturates;¹³ valerian weakly binds these receptors when compared to valium and Xanax suggesting little addictive potential.¹³

Clinical Evidence: Two randomized double-blind clinical studies showed valerian extract produced a mild, subjective improvement in sleep quality and decreased sleep latency. '

Contraindications and Side-effects:

- Pregnancy
- Regular use may cause headaches, excitability, insomnia; GI disturbance; hepatitis if taken with skullcap;³⁰ however, skullcap may be the culprit and its use should be discouraged.¹⁵ **Note: many books on herbal healing recommend blending valerian with skullcap to enhance efficacy. Patients should be warned to avoid skullcap.**
- hallucinogenic
- Some may experience paradoxical stimulation including restlessness and palpitations.⁷

Herb-Drug Interaction:

- Do not take concomitantly with barbiturates as it prolongs thiopental -and pentobarbital-induced sleep.⁴
- May potentiate effects of sedatives and antidepressants.
- Some sources warn against concomitant use with alcohol.⁴

Dosage recommended:

Herbalists recommend 300-500 mg of valerian (standardized to at least 0.5% essential oils) 1 hour before bedtime for insomnia; for mild anxiety, may take morning dose of 150-300 mg. Herbalists recommend taking for only 2-3 weeks then wash-out.¹³ RCT studies used 400-405 mg before bedtime.^{37,38}

Cost: \$8/100 caps; 530 mg/capsule

References:

- 1 Spencer J, Jacobs J. *Complementary Alternative Medicine-An Evidence-Based Approach*. St. Louis: Mosby, 1999.
- 2 Lieberman S. *J Womens Health* 7(5):525-9, 1998.
- 3 Wong A, Smith M, Boon HS. *Arch Gen Psychiatry* 1998;55:1033-1044.
- 4 Miller LG. *Arch Intern Med* 1998;158:2200-2211.
- 5 Houghton P. *Pharm J* 1994; 253:342-43.
- 6 Melchart D, et al. *Arch Fam Med* 1998; 7:541-545.
- 7 O'Hara M, et al. *Arch Fam Med* 1998; 7:523-536.
- 8 Mullins RJ. *Med J Aust* 1998; 168(4):170-171.
- 9 Shaughnessy AF. *Fam Pract Recert* 1997; 19:53-56.
- 10 Blumenthal M (Ed). *The Complete German Commission E Monographs. Therapeutic Guide to Herbal Medicines*. Austin: American Botanical Council, 1998.
- 11 Murphy JJ, Heptinstall S, Mitchell JRA. *Lancet* 1988; 8604 (II):189-192.
- 12 Johnson ES, et al. *BMJ* 1985; 291:569-573.
- 13 Brown, D. *Herbal Prescriptions for Better Health*. Rocklin, CA: Prima Pub, 1996.
- 14 Zink T, Chaffin J. *Am Fam Phys* 1998; 58:1133-1140.
- 15 Tyler, VE. *The Honest Herbal: A Sensible Guide to the Use of Herbs and Related Remedies*. 3rd Ed. New York: Pharmaceutical Products Press, 1993.
- 16 Warshafsky S, Kamer RS, Sivak SL. *Ann Intern Med* 1993; 119(7):599-605.
- 17 Berthold HK, Sudhop T, vonBergmann K. *JAMA* 1998; 279(23):1900-1902.
- 18 Isaacsohn JL, et al. *Arch Intern Med* 1998; 158:1189-1194.
- 19 Steiner M, et al. *Am J Clin Nutr* 1966; 64(6):866-70.
- 20 Sorrentino M. *Alt Med Alert* 1998; 1(9):97-99.
- 21 LeBars PL, et al. *JAMA* 1997; 278(16):1327-1332.
- 22 Mashour, NH, Lin, GI, Frishman, WH. *Arch Intern Med* 1998; 158(9):2225-2234.
- 23 Vale S. *Lancet* 1998; 352(9121):36.
- 24 Kanowski S, et al. *Pharmacopsychiatry* 1996; 29:47-56.
- 25 Scheidermayer D. *Alt Med Alert* 1998; 1(7):77-78.
- 26 Engels H-J, Wirth JC. *J Am Diet Assoc* 1997; 97:1110-5.
- 27 Pieralisi G, Ripari P, Vecchiet L. *Clin Therapeut* 1991; 13(3):373-382.
- 28 Tsang D, et al. *Planta Medica* 1985; (3):221-224.
- 29 Harvard Women's Health Watch. August, 1998, pg 6.
- 30 D'Arcy PF. *Adverse Drug React Toxicol Rev* 1991;10(4):189-208.
- 31 Volz HP, Kieser M. *Pharmacopsychiatry* 1997; 30:1-5.
- 32 Almeida JC, Grimsley EW. *Ann Int Med* 1996;125:940-941.
- 33 Hornig M. *Alt Med Alert* 1998; 1(1):4-7.
- 34 Linde K. et al. *BMJ* 1996; 313:253-8.
- 35 Lowe F, Ku JC. *Urology* 1996; 48(1):12-20.
- 36 Wilt T, et al. *JAMA* 1998; 280(18):1604-1609.
- 37 Lindahl O, Lindwall L. *Pharm Biol Behav* 1989; 32:1065-1066.
- 38 Shulz H, Stolz C, Muller J. *Pharmacopsychiatry* 1994;27:147-151.
- 39 MacGregor FB, et al. *BMJ* 1989;299:1156-1157.
- 40 Hoffman D. *The Complete Illustrated Holistic Herbal*. Rockport, MA: Element Books, 1996, pg. 159.
- 41 Winslow L, Kroll DJ. *Arch Intern Med* 1998; 158:2192-2199.