

Interactions Between Herbal Medicines and Prescription Drugs

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In recent years, the general public has embraced the practice of taking dietary supplements to help optimize health, slow the aging process or address specific health concerns. In addition to the use of vitamin and mineral supplements, the population has also acknowledged the potential health-promoting benefits of various herbal remedies.

Quoting from U.S. statistics, the percentage of the population using herbal products grew from 2.5% in 1990 to 12.5% in 1997.¹ This made herbal product use second only to relaxation techniques among various complementary therapies. In 1997, annual out-of-pocket expenditures for herbal medicinal products in the United States were estimated at \$5.1 billion.¹

Many patients are reluctant to disclose their use of alternative therapies to their physicians. In fact, 60% of patients fall into this category.¹

In the case of drug-nutrient interactions, this may raise some concern as certain natural agents can potentiate or modify the action of certain prescription medications. More specifically, drug-herb interactions may occur be at either the pharmacokinetic (pertaining to how our bodies process medicine, including the absorption of medicine, its distribution throughout the tissues of the body, and its elimination from the body through metabolism and excretion) or pharmacodynamic (how medicines affect the body) level.

Drug-herbal interactions are of greatest concern when patients are taking drugs with a narrow therapeutic window (the relationship between plasma concentrations that achieve therapeutic effects and those that result in toxic effects). Drugs with particularly narrow therapeutic windows are prone to adverse interactions with other drugs, and with herbal products. These include warfarin; digoxin; theophylline; phenytoin; and phenobarbital.

In general, the most important drug-nutrient interactions to guard against include bleeding disorders (including bleeding into the brain), upsetting brain chemistry (serotonin syndrome, cholinergic syndrome, triggering bipolar disease etc.), cardiac glycoside toxicity, and toxicity to internal organs (liver disease).²

Bleeding disorders can be caused by any herb that contains a significant concentration of anticoagulant active ingredients, when taken concurrently with anticoagulant medications such as aspirin, warfarin, coumadin, clopidogrel (Plavix), etc. Herbs such as red clover and dong quai (*Angelica* species) contain coumarins, which can potentiate the effects of anticoagulant drugs. Ginkgo biloba and devil's claw have also been shown to cause bleeding disorders in humans, sometimes in the absence of concurrent anticoagulant medication use. Their active ingredients are known to significantly interfere with normal platelet function. Feverfew (a herb used to treat migraine headaches), ginger, turmeric and white willow extract may also induce a mild anticoagulant effect, but to date, this and bleeding disorders have not been shown to occur to an

appreciable degree in humans.^{2,5}

Brain Chemistry Disturbances: As a rule, it is imperative not to recommend any natural health product that directly affects brain neurotransmitter concentrations if the patient is currently taking any medication aimed at altering mood (e.g., Prozac, tricyclic antidepressants, Alzheimer's medications, L-dopamine). The use of any herbal or accessory nutrient (such as St. John's wort or 5-hydroxytryptophan) that elevates serotonin concentrations, in conjunction with an antidepressant medication, can result in serotonin syndrome. This is a life-threatening condition characterized by excess serotonin concentrations, whose signs and symptoms include confusion; agitation; rapid heart rate; high blood pressure; muscle spasms; loss of coordination; sweating; shivering; fever; rapid breathing; coma; or even death.

Herbal supplements that elevate acetylcholine concentrations in the brain (huperzine A, bacopa monniera, phosphatidylserine, acetyl-L carnitine, DMAE-dimethylamino ethanol) have the potential to cause cholinergic syndrome, if taken concurrently with drugs used to treat Alzheimer's disease and dementia, which slow the break down of acetylcholine (acetylcholinesterase inhibitors - donepezil, tacrine). The signs and symptoms of cholinergic syndrome include vomiting, excess saliva and tear production, increased sweating and bradycardia.^{6-10,18}

Cardiac Glycoside Toxicity: The herbal agent hawthorn works in the body in a similar fashion as other cardiac glycoside drugs, such as digoxin and digitalis. Cardiac glycosides increase the intramuscular concentrations of cyclic AMP (cAMP), from which cardiac muscle synthesizes ADP and ATP. ATP is then used as the energy source to power the muscular contraction of the heart with each heart beat. Drugs such as digoxin and digitalis have a very narrow margin of safety, and thus the concurrent use of hawthorn may easily produce toxicity, with potentially life-threatening consequences.^{11,12,18}

The chart above represents the most significant possible drug-herb interactions and the potential adverse effects:

Class/Drug	Possible Herbal Interaction	Possible Adverse Effect
Anticoagulants/ Antiplatelets (warfarin, ASA)	ginkgo	case reports of increased bleeding ¹³
	ginger, garlic, feverfew	increased bleeding potential ²
	ginseng	decrease in warfarin effectiveness ¹⁴
Anticonvulsants (phenytoin, phenobarbital)	<i>shankhapushpi</i>	decreased plasma levels of phenytoin ^{2,6}
	kava kava, valerian	decreased plasma levels of phenytoin ¹⁵ Herbs with sedative components could be additive to sedative properties of phenobarbital and phenytoin. ¹⁶⁻¹⁸

Antidepressants	St. John's wort	May bind to brain MAO receptors, making interactions with antidepressants unpredictable. ^{7,18}
	ginseng	case reports of euphoria and CNS stimulation between MAO inhibitors and ginseng ^{9,18}
	<i>ma huang</i> (ephedra)	potential for severe hypertension with MAO inhibitors ²
Antipsychotics	evening primrose oil, borage oil	possible exacerbation of temporal lobe epilepsy ²
Digoxin	licorice	mineralocorticoid activity may contribute to potassium depletion ²
	hawthorn, figwort, mistletoe	cardioactive properties may potentiate effects of drug ²
	Siberian ginseng	reported to elevate digoxin levels ²
Immuno-Suppressive Agents	echinacea	Can potentially counteract effect of drug ²

References

1. Eisenberg DM, et al. Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. *JAMA* 1998;280:1569-75.
2. McNeill J. Interactions between herbal and conventional medicines. *Can J Con Med Edu* 1999;12:97-113.
3. McRae S. Elevated serum digoxin in a patient taking digoxin and Siberian ginseng. *Can med Assoc J* 1996;155:293-5.
4. Matthews MKJ. Association of ginkgo biloba with intracerebral hemorrhage. *Neurology* 1998;50:1933-4.
5. Rosenblatt M, Mindel J. Spontaneous hyphema associated with ingestion of ginkgo biloba. *N Engl J Med* 1997;336: 1108.
6. Janetzky K, Morreale A P. Probable interactions between warfarin and ginseng. *Am J Health Syst Pharm* 1997;336:1108.
7. Dandekar UP, Chandra RS, Dalvi SS, et al. Analysis of a clinically important interaction between phenytoin and Shankhapushpi, an Ayurvedic preparation. *J Ethnopharmacol* 1992;35:285-8.
8. Bladt S, Wagner H: Inhibition of MAO by fractions and constituents of Hypericum extract. *J Geriatric Psychiatric Neurology* 1994;7:557-9.
9. Jones BD, Runikis AM. Interaction of with phenelzinc. *J Clin Psychopharmacol* 1987;7:201-2.
10. Shader RI, Greenblatt DJ. Bees, ginseng and MAOIs revisited. *J Clin Psychopharmacol* 1988;8:235.
11. D'Arcy PF. Adverse reactions and interactions with herbal medicines. Part 2-Drug interactions. *Adverse Drug React Toxicol Rev* 1993;12:147-62.
12. Fushimi R, Tachi J, Amino N, et al: Chinese medicine interfering with digoxin immunoassays. *Lancet* 1989;1:339.
13. Fushimi R, Yamanishi H, Inoue M, et al. Digoxin immunoassay that avoids cross-reactivity from Chinese medicines. *Clin Chem* 1995;41:621.
14. Rowin J, Lewis SL. Spontaneous bilateral subdural hematomas associated with chronic ginkgo biloba ingestion. *Neurology* 1996;46:1775-6.
15. Almeida JC, Grimsley EW. Coma from the health food store; interaction between kava and alprazolam. *Ann Intern Med* 1996;125:940-1.
16. Santos MS, Ferreira F, Faro C, et al: The amount of GABA present in aqueous extracts of

valerian is sufficient to account for [3H] GABA release in synaptosomes. *Planta Med* 1994;60:476-6.

17. Leuschner J, Muller J, Rudmann M: Characterization of the central nervous depressant activity of a commercially available valerian root extract. *Arzneimiteelforschung* 1993;43:638-41.
18. Consumerslab.com. www.consumerslab.com.

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