

Appendix 1. Commonly used herbs and herb-drug interactions

Herbs	Purported health benefits	Herb-drug interactions
Aconite	Analgesic, anti-inflammatory, cardiotonic	None reported
Alfalfa (<i>Medicago sativa</i>)	Arthritis, asthma, benign prostatic hypertrophy, diabetes, hyperlipidemia, urinary retention	↑ bleeding risk with warfarin ¹ ↓ effects of oral contraceptives ↑ effects of oral hypoglycemic, can cause hypoglycemia ↑ photosensitivity with trimethoprim/sulfamethoxazole, levofloxacin, tetracycline and TCA (amitriptyline)
Aloe vera	Dermatologic conditions (topical use), laxative (oral use)	↑ blood loss with anesthetic sevoflurane (oral); ² avoid before surgery ↑ risk of digitalis toxicity and arrhythmia by causing hypokalemia (oral) ³ ↑ effects of antidiabetics (aloe gel) causing hypoglycemia ⁴
<i>Angelica sinensis</i> (<i>dong quai</i>)	Appetite loss, dyspepsia, hypertension, infection, menstruation (dysmenorrhea, menorrhagia, premenstrual syndrome)	↑ bleeding risk with warfarin ⁵
Bilberry (<i>Vaccinium myrtillus</i>)	Diarrhea, eye disorders (cataracts, diabetic glaucoma, retinal disturbances), menstrual cramps, varicose veins, venous insufficiency	↑ bleeding risk with concomitant use of ginkgo biloba and ginseng ⁶ ↑ bleeding risk with warfarin ⁷
Bitter orange (<i>Citrus aurantium</i>)	Anorexia, indigestion, nasal congestion, weight loss	↓ effect of anti-hypertensive medications ⁸ Arrhythmogenesis ^{9,10} Hypertension and tachycardia with caffeine use & MAOI
Black cohosh (<i>Cimicifuga racemosa</i>)	Menopause, osteoporosis, premenstrual tension	↓ efficacy of CYP2D6 substrates (amitriptyline, codeine, metoprolol, trazodone) ↑ lung metastasis of pre-existing breast cancer ¹¹ ↑ potential for liver toxicity with acetaminophen, amiodarone, erythromycin, fluconazole and statins ¹²
Butcher's broom (<i>Ruscus aculeatus</i>)	Circulatory disorders, constipation, hemorrhoids (topical use), leg cramps, venous insufficiency, water retention	↓ effects of alpha blockers on lowering blood pressure ¹³
Cannabis (<i>Cannabis sativa</i> L.)	Anorexia, asthma, glaucoma, neuropathic pain	↑ bleeding risk with warfarin ¹⁴ ↑ CNS depressant effects with alcohol, benzodiazepines, narcotics, and antihistamine use ↓ maximum concentration of protease inhibitors: indinavir & nelfinavir ¹⁵ ↓ phenytoin concentration by CYP2C9 expression and increase hydroxylation of liver microsomes ¹⁶ Alters response to stress and anesthetic medications in oral surgery patients ¹⁷ Can cause myocardial infarction with sildenafil, tachycardia and delirium with TCA, manic symptoms with fluoxetine use ¹⁸ and ischemic stroke with cisplatin use
<i>Capsicum</i> (Peppers or bell peppers)	Analgesic, anti-inflammatory, diabetes, shingles, trigeminal neuralgia, weight loss	↑ bleeding risk with warfarin ¹⁹ Hypertensive crisis with MAOI
Cat's claw (<i>Uncaria tomentosa</i>)	Antiherpetic, anti-inflammatory, antimicrobial, antioxidant, endometriosis, immunomodulation	↑ bleeding risk with warfarin ²⁰ ↑ bleeding risk with ginkgo biloba, garlic, saw palmetto ↑ effects of antihypertensive drugs causing hypotension ↑ effects of benzodiazepines ²¹ ↑ plasma concentration of protease inhibitors (atazanavir, ritonavir, saquinavir) by inhibition of CYP3A4 ²² Disulfuram like reaction when used with metronidazole
Chamomile (<i>Matricaria recutita</i>)	Antiinflammatory, antispasmodic, anxiolytic, premenstrual syndrome, sedative, upper respiratory tract infections	↑ bleeding risk with aspirin or warfarin ²³ ↑ sedative effects of benzodiazepines and barbiturates ²⁴

Clove (<i>Syzygium aromaticum</i>)	Antihelminthic, antiinflammatory, ant repellent, aromatherapy, digestive problems, food spice, fragrance (pomander) and multiple sclerosis	↑ bleeding risk with warfarin ¹⁹
Coenzyme Q10 (<i>Theobroma cacao</i>)	Antioxidant, cardiotoxic (angina, congestive heart failure, hypertension), infertility (improves serum quality and sperm count)	↓ anticoagulant effect of warfarin ²⁵
Cranberry (<i>Vaccinium macrocarpon</i>)	Blood and digestive disorders, diabetes, Helicobacter Pylori-induced gastric ulcers, urinary tract infections	↑ bleeding risk with warfarin ^{26,27}
Danshen (<i>Salvia miltiorrhiza</i>)	Angina, ischemic stroke, myocardial infarction	↑ bleeding risk with warfarin use ²⁸ Falsely ↑ or ↓ serum digoxin levels ²⁹ ↑ free salicylate concentration and toxicity ↑ metabolism of CYP substrates
Devil's claw (<i>Harpagophytum procumbens</i>)	Anorexia, atherosclerosis, bladder and kidney problems, difficult childbirth, dyspepsia, musculoskeletal (myalgia, back pain), osteoarthritis, palpitations	↑ bleeding risk of warfarin ³⁰ ↑ blood levels of drugs metabolized by P-glycoprotein by inhibiting its activity ³¹ ↑ increases blood levels of drugs metabolized by CYP3A4 substrates by inhibiting CYP3A4 enzyme (see Table 3)
Echinacea purpurea	Immune stimulant, upper respiratory tract infections	↑ hepatotoxicity with statins, fibrates, niacin ^{32,33} ↑ QT interval with amiodarone or ibutilide ↓ effect of cyclosporine, can cause transplant rejection ^{32,34} Inhibits hepatic CYP 3A4 enzymes elevating drug levels of drugs metabolized by CYP 3A4 enzymes (see Table 3) ^{35,36}
Ephedra (<i>Ma-Huang</i>)	Asthma, common cold/flu, enhanced athletic performance, headache, increased alertness, weight loss	↓ effect of β-blockers ↓ effectiveness of oral hypoglycemic ↑ heart rate and blood pressure with MAOI and caffeinated products Inhibits cytochrome P450. Caution advised with h drugs causing QT prolongation, antiarrhythmics and diuretics ³⁷
Fenugreek (<i>Trigonella foenum-graecum</i>)	Appetite simulant, diabetes, hyperlipidemia, indigestion, labor induction, lactation, menopausal symptoms, wound and leg ulcers(topical use)	↑ bleeding risk with warfarin ↑ risk of hypoglycemia with oral hypoglycemic ↑ risk of hypokalemia with diuretics ³⁸
Feverfew (<i>Tanacetum parthenium</i>)	Arthritis, dermatitis, migraine headaches, premenstrual dysphoric disorder, psoriasis and urticaria	↑ bleeding risk with warfarin, clopidogrel (Plavix), or aspirin ¹⁹ May interact with a variety of medications metabolized by the liver ³⁹
Fumitory (<i>Fumaria officinalis</i>)	Cholecystopathies, constipation, dermatologic conditions (eczema, scabies), inflammatory bowel disease	↑ effects of beta-blockers, calcium channel blockers and cardiac glycosides
Garlic (<i>Allium sativum</i>)	Antimicrobial, heart disease, HIV, hypercholesterolemia, hypertension, immunostimulant, prevention of stomach and colon cancers	↑ bleeding risk with warfarin ⁴⁰ and antiplatelet drugs ⁴¹ ↑ risk of hypoglycemia with oral hypoglycemics (chlorpropamide) ⁴² Severe gastrointestinal side effects with ritonavir ⁴³
Ginger (<i>Zingiber officinale Roscoe</i>)	Arthritis, hyperlipidemia, indigestion, motion sickness, muscular pain, nausea (chemotherapy-induced)	↑ risk of bleeding with warfarin ⁴⁴
Ginkgo biloba	Alzheimer's dementia, peripheral arterial disease, senile macular degeneration, tinnitus	↑ bleeding risk with warfarin, aspirin, ticlopidine or COX-2 inhibitors ⁴⁵⁻⁴⁸ ↑ effects of digoxin ⁴⁹ ↓ efficacy of antiviral agents (efavirenz) ⁵⁰ ↑ risk of hypotension with antihypertensive drugs ³⁰ ↑ risk of priapism with risperidone ⁵¹

		↑ risk of seizure with anticonvulsants (valproic acid and phenytoin) ⁵²
Ginseng	Alleviation of menopausal symptoms, anti-aging, anticancer, antidiabetic, antifatigue, attention deficit hyperactivity disorder, immunomodulation, memory enhancement, sexual dysfunction (improves libido, erectile dysfunction and copulatory performance)	↓ anticoagulation effect of warfarin ^{53,54} ↑ risk of hypoglycemia with oral hypoglycemic (e.g. chlorpropamide) ⁵⁵ and herbs lowering blood sugar level (devil's claw, ginger, fenugreek, gum, guar) ↑ QTc interval, can potentiate arrhythmogenesis with antiarrhythmic agents ⁵⁶ Can induce liver enzymes and inhibit CYP3A4 (see Table 3); use with caution in CYP metabolized drugs Hepatotoxicity with antiretroviral raltegravir and imatinib mesylate ^{57,58} Interferes with digoxin assay, leading to falsely elevated levels ⁵⁹
Gossypol	Anticancer, antimicrobial, antioxidant, hypercholesterolemia, infertility, male contraception	↑ effects of diuretics
Grapefruit juice	Anticarcinogenic, cardiovascular disease, diabetes, hypercholesterolemia	↑ bleeding risk with warfarin ^{60,61} and antiplatelets (cilostazol) ⁶² ↓ efficacy of angiotensin receptor blockers ↑ effects of calcium channel blockers (tachycardia, flushing, hypotension) ⁶³ ↑ effects of nitrates and phosphodiesterase type 5 inhibitors (sildenafil, tadalafil or vardenafil) causing hypotension ↑ risk of hypoglycemia with oral hypoglycemics (repaglinide) ↑ risk of rhabdomyolysis with statins ^{64,65} ↑ steady state concentration of cyclosporine with potential side effects ↑ toxicity of antiarrhythmics causing QT prolongation and torsades de pointes ^{64,66} Causes hypertension and tachycardia with appetite suppressant sibutramine Inhibit CYP3A4 enzymes (see Table 3) and drugs metabolized by P-glycoprotein
Green tea (<i>Camellia sinensis</i>)	Endurance, weight loss	↓ anticoagulant effect of warfarin ^{67,68} Antithyroid (↓ T3, ↓ T4, ↑ TSH) and goitrogenic effect in high doses ⁶⁹
Guarana (<i>Paullinia cupana</i>)	Increased alertness, improved task performance, weight loss	↑ effects of caffeine ↑ risk of hypokalemia with diuretics
Hawthorn (<i>Crataegus sp.</i>)	Angina pectoris, atherosclerosis, bradyarrhythmias, congestive heart failure, hypertension	↑ effects of calcium-channel blockers or nitrates causing hypotension, angina and arrhythmias ⁷⁰ ↑ effects of digoxin ⁷¹
Kava (<i>Piper methysticum</i>)	Anxiety, insomnia, sleeping aid, stress	↑ bleeding risk with warfarin ⁷² ↑ the clearance of chlorzoxazone (a CYP2E1 substrate) ⁷³ Interacts with alprazolam, paroxetine and drugs used for Parkinson's disease ⁷³
Kelp (<i>Laminaria</i>)	Cancer, genitourinary infection, goiter, hypothyroidism, immune stimulation, indigestion, obesity, promotion of healthy growth of hair, skin and nails	↑ bleeding risk with warfarin and antiplatelet drugs ⁷⁴ ↑ effect of levothyroxine ⁷⁵ (due to high iodine content) causing tachycardia, tremors, acne and hypertension
Licorice (<i>Glycyrrhiza glabra</i>)	Catarrhs, cirrhosis, eczema, peptic ulcer, polycystic ovarian disease, prostate cancer, upper respiratory tract infection	↓ anticoagulant effect of warfarin ↑ effect of digoxin leading to digoxin toxicity and arrhythmogenesis ⁷⁶ ↑ effects of spironolactone ↑ plasma prednisolone concentration ⁷⁷ Induces cytochrome CYP3A4, ⁷⁸ use with caution when coadministered with other drugs that interact with CYP3A4 Use with caution in hormone-sensitive conditions (breast, uterine and ovarian cancer, endometriosis and uterine fibroids)
Lycium (<i>Lycium barbarum</i>)	Anti-aging, anticancer, antiinflammatory, antioxidant, diabetes, erectile dysfunction, hypertension, senile macular degeneration	↑ bleeding risk with warfarin ⁷⁹ ↑ hypoglycemic effects of oral hypoglycemic ↑ risk of hypotension with antihypertensive medications (inhibits effects on renin-angiotensin system)
Milk thistle (<i>Silybum marianum</i>)	Anticarcinogenic, antiinflammatory, cirrhosis, hepatitis, immunomodulation	Can interact with drugs metabolized with CYP enzymes ⁸⁰ Can potentiate digoxin toxicity ⁸¹

Mother wort	tachycardia, anxiety, insomnia, and amenorrhea, diuretic	↑ bleeding risk with warfarin ↑ platelet aggregation and fibrinogen levels (Intravenous) ³⁶ Synergistic effect with alprazolam may cause lethargy, disorientation, coma ⁸²
Oleander	Abortifacient, asthma, cancer, congestive heart failure, epilepsy, indigestion, leprosy, malaria, ring worms, venereal diseases including warts (topical use)	Can potentiate digoxin toxicity ⁸³
Peppermint (<i>Mentha piperita</i>)	Antimicrobial, antioxidant, antitussive, aroma, cancer, cold, digestive disorders, pain (headache, muscle ache, nerve pain)	↑ levels of CYP3A4 metabolized drugs, caution is advised with its co-use with CYP3A4 metabolized drugs ⁸⁴
Red clover (<i>Trifolium pratense</i>)	Anxiety, depression, high cholesterol, mastalgia, menstrual irregularities, osteoporosis, prostatic enlargement	↑ bleeding risk with warfarin ^{19,85} Can induce CYP enzymes; use with caution with CYP metabolized drugs ⁸⁶
Red yeast (<i>Monascus purpureus</i>)	Hyperlipidemia	↑ effects of statins including side effects
Saw palmetto (<i>Serenoa repens</i>)	Azospemia, benign prostatic hypertrophy, breast augmentation, decreased libido, edema, genitourinary conditions, mild diuretic	↑ bleeding risk with warfarin or antiplatelet agents ⁸⁷ Inhibits cytochrome P450 isoenzymes ⁸⁸
Soy (<i>Glycine max Merr.</i>)	Hot flushes, hyperlipidemia, osteoporosis	↓ anticoagulant effects of warfarin ⁸⁹⁻⁹¹ ↓ absorption of levothyroxine ⁹² Inhibits CYP3A4 and CYP2C metabolized drugs ⁹³
St. John's wort (<i>Hypericum perforatum</i>)	Anxiety, depression, insomnia, mental health conditions	↑ activity of clopidogrel with increased bleeding tendency ↓ anticoagulant effects of warfarin ⁹⁴ ↓ drug levels of ethanyl estradiol (breakthrough bleeding and unplanned pregnancies in women taking oral contraceptive pills) ⁹⁵ ↓ effectiveness of Class IA and III antiarrhythmics (precipitating arrhythmias) ↓ effectiveness of simvastatin, ↓ cyclosporine concentration (can cause transplant rejection) ↑ effects of calcium channel blockers and antihypertensive drugs causing negative chronotropic and dromotropic effects ↑ heart rate and blood pressure with MAOI ⁹⁶ ↑ plasma clearance of docetaxel (under treatment of cancer patients) ⁹⁷ ↓ plasma levels of indinavir (treatment failure in HIV patients) ⁹⁸ ↓ serum concentration of theophylline ↓ serum digoxin concentration ⁹⁹ Hypotension and delayed emergence from anesthesia ¹⁰⁰ Induction of CYP3A4 (see Table 3), reduces blood levels of drugs metabolized ⁹⁸
Yohimbine	Aphrodisiac, erectile dysfunction, impotence, orthostatic hypotension	↑ bleeding risk with warfarin or antiplatelet drugs ¹⁰¹ ↑ bleeding risk with angelica, clove, danshen, garlic, ginkgo biloba, ginger ↑ blood pressure and tachycardia with caffeine, ephedra and MAOI ↓ blood pressure reduction effect of centrally acting agents (clonidine, guanabenz), ACE inhibitors (hypertension) and beta blockers (hypertension and tachycardia)
ACE, angiotensin-converting enzyme; HIV, human immunodeficiency virus; MAOI, monoamine oxidase inhibitors; TCA, tricyclic antidepressant.		

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