Potential Herb-Drug Interactions for Commonly Used Herbs*

Herb	Drug	Potential Interaction	Basis of Concern	Recommended Action
Bilberry *Vaccinium myrtillus*	**Warfarin**	Potentiation of bleeding possible at very high bilberry doses.	Antiplatelet activity observed for high doses of bilberry in human volunteers.[1]	**Monitor** at high doses (> 100 mg/day anthocyanins, low level of risk).
Bladderwrack *Fucus vesiculosus*	**Hyperthyroid medication** eg carbimazole	May decrease effectiveness of drug due to natural iodine content.[2]	Theoretical concern, no cases reported.	**Contraindicated** unless under close supervision.
	Thyroid replacement therapies eg thyroxine	May add to effect of drug.	Theoretical concern linked to a case report where "kelp" caused hyperthyroidism in a person not taking thyroxin.[3]	**Monitor** (low level of risk).
Bugleweed *Lycopus virginicus* *Lycopus europaeus*	**Radioactive iodine**	May interfere with administration of diagnostic procedures using radioactive isotopes.[4]	Case report.	**Contraindicated.**
	Thyroid hormones	Should not be administered concurrently with preparations containing thyroid hormone.[5]	Theoretical concern based on deliberations of German Commission E.	**Contraindicated**.
Cayenne (Chilli Pepper) *Capsicum* spp.	**ACE inhibitor**	Cough induced by topical capsaicin.[6]	Theoretical concern since capsaicin depletes substance P.	**Monitor** (very low level of risk).
	Theophylline	Increased absorption and bioavailability.[7]	Clinical study.	**Monitor** (low level of risk).
Celery Seed *Apium graveolens*	**Thyroxine**	Reduced serum levels of thyroxine.[8]	Case reports.	**Monitor** (very low level of risk).
Coleus *Coleus forskohlii*	**Antiplatelet medication**	May potentiate effects of drug.	Theoretical concern based on *in vivo* animal studies of standardized coleus extract and the active constituent forskolin.[9]	**Monitor** (low level of risk).
	Hypotensive medication	May potentiate effects of drug.	Theoretical concern based on ability of forskolin to lower blood pressure *in vivo*.[10]	**Monitor** (low level of risk).
	Prescribed medication	May potentiate effects of drug.	Theoretical concern based on ability of forskolin to activate increased intracellular cyclic AMP *in vitro*.[11]	**Monitor** (low level of risk).
Dan Shen *Salvia miltiorrhiza*	**Warfarin**	May potentiate effect of drug: increased INR,[12-14] prolonged APTT.	Case reports.	**Contraindicated.**
Devil's Claw *Harpagophytum procumbens*	**Warfarin**	Purpura[15] possibly due to increased bleeding tendency.	One case report with very few details. Unlikely to occur.	**Monitor** (very low level of risk).
Dong Quai *Angelica sinensis* *Angelica polymorpha*	**Warfarin**	May potentiate effect of drug: increased INR and PT;[16] increased INR and widespread bruising.[17]	Case reports.	**Monitor** (low level of risk).
Echinacea *Echinacea angustifolia* *Echinacea purpurea*	**Immunosuppressant medication**	May decrease effectiveness of drug.[18,19]	Theoretical concern based on immune-enhancing activity of Echinacea. No adverse events reported.	**Contraindicated.**
Eleuthero *Eleutherococcus senticosus*	**Digoxin**	Apparently raised serum concentrations.[20]	Herb probably interfered with digoxin assay (patient had unchanged ECG despite apparent digoxin concentration of 5.2 nmol/L).	**Monitor** (very low level of risk).
Evening Primrose Oil *Oenothera biennis*	**Phenothiazines**	May decrease effectiveness of drug.	Reports of worsening epilepsy in schizophrenics. No causal association demonstrated and no effect observed in later trials.[21]	**Monitor** (very low level of risk).

Herb	Drug	Potential Interaction	Basis of Concern	Recommended Action
Garlic *Allium sativum*	**Aspirin**	Could increase bleeding time.[22]	Case reports of increased bleeding tendency with high garlic intake.[23-25]	**Monitor** at doses equivalent to > 5 g/day fresh garlic.
	HIV protease inhibitors eg saquinavir	Decreased serum levels of saquinavir.[26]	Clinical study.	**Monitor** (medium level of risk).
	Warfarin	May potentiate effect of drug: increased INR observed.[27] Large doses could increase bleeding tendency.	Case reports of possible interaction[27] and increased bleeding tendency.[23-25]	**Contraindicated** for doses equivalent to > 5 g/day fresh garlic unless under close supervision.
Ginger *Zingiber officinale*	**Antacids**	May decrease effectiveness of drug.	Theoretical concern since ginger increases gastric secretory activity.[18]	**Monitor** (low level of risk).
	Phenprocoumon	May increase effectiveness of drug: increased INR reported.	One case reported (dosage undefined).[28]	**Monitor** (low level of risk).
	Warfarin	Increased risk of spontaneous bleeding.	Inhibits platelet aggregation and thromboxane after high doses (5 g/day) in volunteers. No effect at 2 g/day. Mechanism reportedly involves inhibition of platelet cyclooxygenase.[18] One case reported for warfarin (ginger dosage undefined).[29] No effect demonstrated in a clinical trial (3.6 g/day).[30]	**Monitor** at doses < 4 g/day dried ginger. **Contraindicated** unless under close supervision at doses > 4 g/day dried ginger.
Ginkgo *Ginkgo biloba*	**Anticonvulsant medication** eg sodium valproate, carbamazepine	May decrease the effectiveness of drug.	Theoretical concern based on *in vivo* animal studies.[31] Two case reports.[32]	**Monitor** (medium level of risk).
	Antiplatelet and anticoagulant drugs eg aspirin, warfarin	Increased bleeding tendency. Ginkgo extract could have clinical antiplatelet activity.	Rare case reports of spontaneous bleeding, including concomitant intake of aspirin or warfarin.[33-35] Interactions with warfarin and aspirin are not supported by clinical studies.[30,36,37]	Aspirin: **Monitor** (low level of risk). Warfarin: **Monitor** (medium level of risk).
	Haloperidol	May potentiate the efficiency of haloperidol in patients with schizophrenia.[38]	Randomized, controlled trial.	Prescribe cautiously. **Reduce** drug if necessary in conjunction with prescribing physician.
Hawthorn *Crataegus monogyna* *Crataegus laevigata* (*Crataegus oxyacantha*)	**Beta-blockers** and other hypotensive drugs	May increase effectiveness of drug.	Clinical studies demonstrate hawthorn causes a slight reduction in blood pressure in patients with heart conditions.[18]	**Monitor** (low level of risk).
	Digoxin	May increase effectiveness of drug.	Clinical studies indicate a (beneficial) synergistic effect.[39,40] Pharmacokinetics not affected in a clinical study.[41]	**Monitor** (low level of risk).
Hypoglycemic herbs eg *Gymnema sylvestre*, goat's rue (*Galega officinalis*), fenugreek (*Trigonella foenum-graecum*)	**Hypoglycemic drugs and insulin**	Enhanced reduction of blood glucose.	Theoretical concern, no documented case histories.	Prescribe cautiously and monitor blood sugar regularly. **Warn** patient about possible hypoglycemia. **Reduce** drug if necessary in conjunction with prescribing physician.

Herb	Drug	Potential Interaction	Basis of Concern	Recommended Action
Korean Ginseng *Panax ginseng*	**Antihypertensive medications**	May decrease effectiveness of drug.	Theoretical concern since hypertension is a feature of GAS. Clinical significance unclear.[18]	**Monitor** (very low level of risk).
	CNS stimulants	May potentiate effects of drug.[18]	Theoretical concern since CNS stimulation is a feature of GAS. Clinical significance unclear.	**Monitor** (low level of risk).
	Hypoglycemics	May potentiate hypoglycemic activity of drug.[19]	Theoretical concern based on clinically observed hypoglycemic activity of ginseng.[42] Clinical significance unclear.	**Monitor** (very low level of risk).
	MAO inhibitors eg phenelzine	Headache and tremor, mania.	Case reports.[43,44]	**Contraindicated.**
	Sildenafil	Potentiation of drug possible.	Theoretical concern based on *in vitro* studies which show ginseng increases nitric oxide release from corpus cavernosum tissue.[45,46]	**Monitor** (very low level of risk).
	Warfarin	May decrease effectiveness of drug: decreased INR reported.[47]	One case reported[47] but clinical significance unclear. No effect demonstrated in a clinical trial.[48]	**Monitor** (low level of risk).
Laxative (anthraquinone-containing) herbs eg aloe resin (*Aloe barbadensis*), senna (*Cassia* spp.), cascara (*Rhamnus purshiana*), yellow dock (*Rumex crispus*)	**Antiarrhythmic agents**	May affect activity if potassium deficiency resulting from long-term laxative abuse is present.	German Commission E and ESCOP recommendation.[5,49]	**Avoid** excessive doses of laxatives. Maintain patients on a high potassium diet.
	Cardiac glycosides	May potentiate activity, if potassium deficiency resulting from long-term laxative abuse is present.	German Commission E and ESCOP recommendation.[5,49]	**Monitor** (low level of risk at normal doses).
	Potassium depleting agents eg thiazide diuretics, corticosteroids, licorice root (*Glycyrrhiza glabra*)	May increase potassium depletion.	German Commission E and ESCOP recommendation.[5,49]	**Avoid** excessive doses of laxatives. Maintain patients on a high potassium diet.
Licorice *Glycyrrhiza glabra*	**Antihypertensive medications**	May decrease effectiveness of drug when consumed in high doses. Licorice can cause pseudoaldosteronism which includes edema and high blood pressure.[18]	Theoretical concern based on case reports of hypertension following intake of licorice-containing candy.[18]	**Avoid** long-term use at doses > 100 mg/day glycyrrhizin unless under close supervision. Place patients on a high potassium diet.
	Cortisol	Potentiation of drug possible by inhibition of drug metabolism.	Theoretical concern based on pharmacological studies and one early clinical study with the constituent (glycyrrhizin). No observed cases.[18]	**Monitor** (low level of risk).
	Digoxin	Excessive licorice intake causes hypokalemia which can potentiate the toxicity of the drug.[5]	Clinical studies of active constituents and case reports of hypokalemia from candy intake (large doses).[18] One case report of ingestion of herbal laxative containing licorice (1.2 g/day) and rhubarb (4.8 g/day).[50]	**Avoid** long-term use at doses > 100 mg/day glycyrrhizin unless under close supervision. Place patients on a high potassium diet.
	Prednisolone	Increases levels of drug by decreasing drug metabolism.[18]	Theoretical concern based on clinical studies of oral administration of active constituent glycyrrhizin.[51,52]	**Monitor** (low level of risk).
	Thiazide diuretics and other potassium depleting drugs	The combined effect of licorice and the drug could result in excessive potassium loss.[5]	Clinical studies of active constituents and case reports from candy intake (large doses).[18]	**Avoid** long-term use at doses > 100 mg/day glycyrrhizin. Place patients on a high potassium diet.
Marshmallow Root *Althaea officinalis*	**Prescribed medication**	May slow or reduce absorption of drugs.	Theoretical concern based on absorbent properties of marshmallow root.	**Take** at least 2 hours **away** from medication.
Meadowsweet *Filipendula ulmaria*	**Warfarin**	May potentiate effects of drug.	Theoretical concern based on *in vivo* animal studies demonstrating anticoagulant activity.[53]	**Monitor** (low level of risk).
Milk Thistle *Silybum marianum*	**Metronidazole**	May decrease absorption of drug, by increasing clearance.[54]	Clinical study (silymarin: 140 mg/day).	**Contraindicated.**

Herb	Drug	Potential Interaction	Basis of Concern	Recommended Action
Polyphenol#- and flavonoid-containing herbs. especially chamomile (*Matricaria recutita*), green tea (*Camellia sinensis*), lime flowers (*Tilia cordata*), milk thistle (*Silybum marianum*), rosemary (*Rosmarinus officinalis*), vervain (*Verbena officinalis*) (See also Tannin-containing herbs)	**Iron**	Inhibition of non-heme iron$ absorption.	Clinical studies (chamomile, green tea, lime flowers, peppermint, rosemary, vervain, polyphenolic-containing vegetable, red wine, coffee):[55-59] (polyphenols per serving: approx. 30 mg[56] and 50-200 mg[55]). Results for green tea have been conflicting.[56,60-62] An iron chelating activity for the flavanolignan silybin is the suggested mechanism for the protection against iron-induced hepatic toxicity demonstrated *in vivo* (100 mg/kg).[63,64]	In anemia and where iron supplementation is required, **do not take simultaneously** with meals or iron supplements.
Schisandra *Schisandra chinensis*	**Prescribed medication**	May accelerate clearance from the body.	Theoretical concern based on *in vivo* studies demonstrating enhanced phase I/II hepatic metabolism.[65,66]	**Monitor** (medium level of risk).
Slippery Elm Bark *Ulmus rubra*	**Prescribed medication**	May slow or reduce absorption of drugs.	Theoretical concern based on absorbent properties of slippery elm.	**Take** at least 2 hours **away** from medication.
St John's Wort *Hypericum perforatum*	**Amitriptyline**	Decreases drug levels.[67]	Clinical study.	**Monitor** (medium level of risk).
	Anticonvulsants eg phenytoin, carbamazepine, phenobarbitone	May decrease drug levels via CYP induction.[68-70]	Theoretical concern. An open clinical trial demonstrated no effect on carbamazepine pharmacokinetics in healthy volunteers.[71]	**Monitor** (low level of risk).
	Antihistamine eg fexofenadine	Decreases drug levels.[72]	Clinical study.	**Monitor** (medium level of risk).
	Benzodiazepines eg midazolam	Decreases drug levels.[73]	Clinical study.	**Monitor** (medium level of risk).
	Calcium channel antagonists eg verapamil	Decreases drug levels.[74]	Clinical study.	**Contraindicated.**
	Cancer Chemotherapeutic drugs eg irinotecan, imatinib	Decreases drug levels.[75-77]	Clinical studies.	**Contraindicated.**
	Combined oral contraceptives	Breakthrough bleeding reported which was attributed to increased metabolism of drug.[78,79]	Clinical significance unclear. Cases of unwanted pregnancies have been reported.[80,81] Contradictory results demonstrated in clinical studies.[82] Preliminary results suggest extracts low in hyperforin may not affect plasma contraceptive drug levels.[83,84]	Hyperforin-rich extracts: **Monitor** (medium level of risk). Low-hyperforin extracts: **Monitor** (low level of risk).
	Digoxin	Decreases drug levels,[85-87] but is dependent upon dose of herb,[86] and the hyperforin content.[88]	Clinical studies.	**Contraindicated** at doses > 1 g/day dried herb, especially for high-hyperforin extracts.
	HIV non-nucleoside transcriptase inhibitors eg nevirapine	Decreases drug levels.[89]	Case report.	**Contraindicated.**
	Immunosuppressives eg cyclosporin	Decreases drug levels.	Case reports,[78,90-97] and case series.[98,99] Interaction may be dependent upon the hyperforin content.[100]	**Contraindicated** especially for high-hyperforin extracts.
	Other HIV protease inhibitors eg indinavir	Decreases drug levels.[101]	Clinical study.	**Contraindicated.**
	Phenprocoumon	Decreases plasma drug levels.[102]	Clinical study.	**Contraindicated.**
	Simvastatin$	Decreases drug levels.[103]	Clinical study.	**Monitor** (medium level of risk).
	SSRIs eg paroxetine, trazodone, sertraline **and other serotonergic agents** eg nefazodone, venlafaxine	Potentiation effects possible in regard to serotonin levels.[104-109]	Clinical significance of case reports unclear.	**Monitor** (very low level of risk).
	Theophylline	Decreases drug levels.[110]	Case report.	**Monitor** (low level of risk).
	Warfarin	Decreases drug levels and INR.[48,79]	Case reports and clinical study.	**Contraindicated.**

Herb	Drug	Potential Interaction	Basis of Concern	Recommended Action
Tannin- or OPC-containing herbs eg grape seed extract (*Vitis vinifera*), green tea (*Camellia sinensis*), hawthorn (*Crataegus* spp.), meadowsweet (*Filipendula ulmaria*), raspberry leaf (*Rubus idaeus*), sage (*Salvia officinalis*), St John's wort (*Hypericum perforatum*), uva ursi (*Arctostaphylos uva-ursi*), willow bark (*Salix* spp.) (See also Polyphenol-containing herbs)	**Minerals**, especially iron	May reduce absorption of non-heme iron from food.	Clinical studies[55,111-115] (black tea 2.5 g/150 mL).[111] Cases of iron deficiency/reduced iron absorption: heavy black tea drinkers[116,117] and those ingesting sorghum® (0.15% tannins).[118] In a clinical study tea consumption showed a small, non-significant adverse effect on zinc bioavailability.[119]	**Take** at least 2 hours **away** from medication.
Turmeric *Curcuma longa*	**Antiplatelet or anticoagulant medications** eg aspirin and warfarin	May potentiate effects of drug.	Theoretical concern based on *in vitro* and *in vivo* studies mainly of the active constituent curcumin demonstrating antiplatelet activity.[18]	**Monitor** (low level of risk at normal doses). Contraindicated in high doses (> 15 g/day dried tuber).
Valerian *Valeriana officinalis*	**CNS depressants or alcohol**	May potentiate effects of drug.	Theoretical concern expressed by US Pharmacopeial Convention. However a clinical study indicated no potentiation with alcohol.[120]	**Monitor** (very low level of risk).
Willow Bark *Salix alba* *Salix daphnoides* *Salix purpurea* *Salix fragilis* (See also Tannin-containing herbs)	**Warfarin**	May potentiate effects of drug.	Clinical study observed very mild but significant antiplatelet activity.[121]	**Monitor** (low level of risk).

CODE Contraindicated: Do not prescribe the indicated herb. **Monitor:** Can prescribe the indicated herb but maintain close contact and review the patient's status on a regular basis. Note that where the risk is assessed as medium, self-prescription of the herb in conjunction with the drug is not advisable.

* **Note:** This chart contains information the authors believe to be reliable or which have received considerable attention as potential issues. However, many theoretical concerns expressed by other authors have not been included.

The word tannin has a long established and extensive usage although it is considered in more recent years to lack precision. Polyphenol is the preferred term when considering the properties at a molecular level. Plant polyphenols are broadly divisible into proanthocyanidins (condensed tannins) and polyesters based on gallic and/or hexahydroxydiphenic acid and their derivatives (hydrolyzable tannins).[113] ξ Heme iron is derived from hemoglobin and myoglobin mainly in meat products. Non-heme iron is derived mainly from cereals, vegetables and fruits. ∑ Plasma concentration of pravastatin not effected. ⊗ Sorghum also contains phytate. Both phytate and polyphenol inhibit nutrients such as iron.[122,123]

Abbreviations: AMP: adenosine monophosphate; **APTT**: activated partial thromboplastin time; **CNS**: central nervous system; **CYP**: cytochrome P-450; **ECG**: electrocardiogram/graph; **GAS**: ginseng abuse syndrome; **INR**: international normalized ratio; **PT**: prothrombin time; **SSRI**: selective serotonin reuptake inhibitors; **>**: greater than; **<**: less than.

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