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11TH EDITION

COMPLEMENTARY MEDICINE INTERACTIONS GUIDE

For healthcare professionals

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Blackmores Institute

Blackmores Institute is the academic and research arm of Blackmores Group, established to support and drive an evidence-based approach to complementary medicine. With a focus on research and education, our primary purpose is to improve the safe and responsible use of complementary medicine by contributing to the evidence-base and translating this knowledge into practical healthcare education and clinical resources.

We partner with leading academic institutions and research bodies around the globe to investigate novel ingredient development, discovery and innovation, and legacy projects. We also proudly support the development of future leaders through academic and practice grants. Our diverse team consists of researchers, academics, healthcare professionals, educators and academic communicators, working together to enhance natural health literacy through:

- Research funding
- Education programs
- Industry advisory boards
- Interactions guidelines
- News and research updates
- White papers
- Academic projects

Education

Blackmores Institute offers award-winning CPD-accredited, evidence-based education for health professionals. We believe that education is the cornerstone for enabling pharmacists, doctors, and allied healthcare practitioners to apply research findings directly into their practice, and seamlessly integrating natural medicine safely into patient care.

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Healthcare Professional Advisory Service

Our Healthcare Professional Advisory Service has been providing free quality support and trusted advice in complementary medicine for over 30 years, to help guide the safe and appropriate use of natural medicines.

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Good Health Changes Everything

At Blackmores Institute, we believe that good health changes everything. This principle drives our dedication to advancing natural medicine through education and research. By providing healthcare professionals with access to the latest in natural medicine, we empower them to improve patient care safely and effectively. Join us in our mission to transform lives with informed, evidence-based healthcare practices, where good health is at the heart of all we do.

About this guide

This Complementary Medicine Interactions Guide is a concise and comprehensive reference resource designed to give healthcare professionals clinically relevant, evidence-based information about potential interactions between complementary medicines and pharmaceutical medications.

For the most part, complementary medicines can be used alongside conventional pharmaceutical drug treatments. However, some complementary medicines may interact with certain medications to reduce, or sometimes increase, their effect, or to cause potential adverse effects. In addition, some complementary medicines may have the ability to reduce drug side effects and also some common medications may adversely affect the nutritional status of individuals over time.

Severity, likelihood and level of evidence is provided in this guide to assist in assessment of risk and to support appropriate recommendations.

Key

LIKELIHOOD OF INTERACTION	**Theoretical**	**Unlikely**	**Possible**	**Likely**
	in vitro and/or animal evidence with unclear implications, However, it cannot exclude the possibility of occurring in humans	Evidence suggests this interaction can occur, but is not likely to occur in many patients	Evidence suggests this interaction might occur in some patients	Evidence suggests this interaction is likely to occur in most patients
SEVERITY OF INTERACTION	**Variable**	**Low**	**Moderate**	**High**
	Nature of interaction may vary	Healthcare professional intervention unlikely to be required	Intervention by a healthcare professional may be required	Clinical evaluation by a healthcare professional is recommended to assess the degree of intervention required
LEVEL OF EVIDENCE	**A**	**B**	**C**	**D**
	At least 1 good quality randomised, placebo-controlled trial or meta-analysis or systematic review	Lower quality human study	Case reports	*in vitro* or animal studies

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Note:

Blackmores has made every effort to ensure that the information in this guide is accurate and up-to-date but this does not guarantee that every possible interaction is included. Blackmores cannot be held responsible for any future changes that may occur in this constantly expanding area of study. The information in this guide is for informational purposes only and is not intended as a substitute for professional advice. Healthcare professionals who consult this document are cautioned that any medical or product-related decision is the sole responsibility of the healthcare professional. Blackmores advises that healthcare professionals should ask patients about both complementary medicine and drug use. Should an adverse event occur, send a 'blue card' adverse reaction reporting form to the TGA or go online to aems.tga.gov.au and inform the manufacturer of both the complementary medicine and the medication.

Interactions guide

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Acetyl-L-Carnitine	Antidepressant drugs (Serotonergic drugs)	May increase drug effect	May increase the serotonergic effects of these drugs when taken together	Level D *In vitro* study. No clinical studies in humans	Theoretical	Moderate	Significant interaction unlikely, however, monitor patient for signs of serotonin toxicity[a]
	Thyroid hormone	May decrease drug effect	L-carnitine blocks entry of thyroid hormone into the cell nucleus, so theoretically, acetyl-L-carnitine may also do the same	Level B Human study	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor the patient for signs of hypothyroidism[b]
	Warfarin	May increase drug effect	May have additive effect to drug	Level D Animal study	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Alpha Lipoic Acid	Anticoagulant and antiplatelet agents	May increase drug effect	May increase risk of bleeding when used alongside these drugs	Level D *In vitro* study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Anticonvulsants (Valproate)	May increase drug effect	May decrease the *in vitro* formation of VA-CoA in a concentration-dependent manner	Level D Animal study. ALA was shown to significantly decrease the *in vitro* formation of VA-CoA in a concentration-dependent manner	Theoretical	Moderate	Monitor patient. Clinical significance is uncertain until human studies are conducted
	Chemotherapeutic agents	May increase or decrease drug effect	Antioxidants may decrease the activity of chemotherapy or make chemotherapy more effective	Level D Animal study	Theoretical	Moderate - High	Avoid concomitant use
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect	Level A Clinical trials suggest ALA may affect glucose-lowering effect of these medications	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
	Thyroid hormone (Levothyroxine)	May decrease drug effect	Co-administration of levothyroxine with ALA may decrease conversion to active T3 form	Level D Preliminary animal studies	Theoretical	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypothyroidism[b]

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Andrographis *(Andrographis paniculata)*	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level D Animal and *in vitro* study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs	May increase drug effect	May increase the risk of hypotension when used with antihypertensive drugs	Level D Animal studies. Animal research suggests that andrographis has hypotensive effects	Possible	Moderate	Monitor patient for signs of hypotension[d]
	Anti-inflammatories (Etoricoxib, naproxen)	May decrease drug effect when co-administered, but has a synergistic pharmacodynamic effect	When co-administered with etoricoxib or naproxen, andrographis may decrease blood levels and increase clearance of these drugs. However, andrographis exhibits synergistic pharmacodynamic anti-inflammatory effects with these drugs; the clinical significance of this is unclear	Level D Animal studies	Possible	Low	If taking andrographis long-term, then monitor the effectiveness of the medication and consider alternative NSAIDs
	CYP450 enzyme substrates (CYP1A1, CYP1A2, CYP2B, CYP2C, CPY3A4)	May increase or decrease drug effect	May increase or decrease blood levels of substrates via inhibition of these enzyme activities	Level D Animal and *in vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient
	Immunosuppressants	May decrease drug effect	May have opposing effect to drug	Level C Case report	Possible	Moderate - High	Avoid concomitant use

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Ashwagandha *(Withania somnifera)*	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect	Level D Animal study	Possible	Moderate	Monitor patient for signs of hypotension[d]
	Benzodiazepines (Diazepam)	May increase drug effect	May have additive effect to drug due to GABAergic activity	Level D Animal study (Co-administration of extract of *Withania somnifera* (50 mg/kg) and diazepam (0.5 mg/kg) increased the seizure threshold)	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Chemotherapeutic agents (Doxorubicin, cyclophosphamide, epirubicin, fluorouracil)	Herb effect on drug (May improve chemotherapy-induced fatigue)	Unknown mechanism of the interaction	Level B Human study (*Withania somnifera* 6 g/d throughout 6 months chemotherapy in breast cancer patients)	Possible	Low	Use with caution under supervision of a healthcare professional and monitor
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect	Level B Human study	Possible	High	Use with caution under supervision of a healthcare professional. Monitor for signs of hypoglycaemia[c]
	Psychotropic drugs (Olanzapine, typical antipsychotics, antidepressants, mood stabilisers, antianxiety, hypnotic)	Herb effect on drug (May improve negative, general and total symptoms and stress)	May improve neurotransmitter dysfunctions due to GABAergic and NMDA potentiating activity of withania	Level A Clinical trials (Adjunctive treatment with extract of *Withania somnifera* 1000 mg/d improved negative symptoms and stress in patients with recent exacerbation of schizophrenia. Another clinical trial showed extract of *Withania somnifera* 500 mg/d improved cognitive abilities without serious adverse effects)	Possible	Low	Use with caution under supervision of a healthcare professional and monitor. Mild to moderate and transient side effects were reported such as somnolence, epigastric discomfort or loose stools
	Thyroid hormone	May increase drug effect	May have additive drug effects and adverse drug effects	Level B Human study	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hyperthyroidism[e]

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Astragalus *(Astragalus membranaceous)*	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect	Level B Human study	Unlikely	Low	Monitor patient. Significant interaction is unlikely
	Chemotherapeutic agents (Cisplatin, vinorelbine, cyclophosphamide)	Herb effect on drug (May decrease drug side effect)	No direct interaction	Level A Clinical trials	Possible	Low	No significant adverse effect or reduction in the effectiveness of chemotherapy identified in studies. Supplementation may reduce side effects
	Diuretic drugs	May increase drug effect	May have additive diuretic effect	Level B Human study	Possible	Low	Monitor patient. Significant interaction unlikely
	Immunosuppressants	May decrease drug effect	Astragalus may have immunostimulant activity	Level D Animal and *in vitro* study	Theoretical	Moderate - High	Avoid concomitant use
	Lithium	May increase drug effect	Theoretically astragalus, through its diuretic action, might reduce excretion and increase levels of lithium	Level D Animal study	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of lithium toxicity[f]
	Oestrogen	May increase or decrease drug effect	Astragalus may cause a phytoestrogenic effect	Level D *In vitro* study	Theoretical	Low-Moderate	Monitor patient. Significant interaction unlikely
	P-glycoprotein	May increase drug effect	Astragalus may inhibit P-gp pump efflux	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient. Significant interaction unlikely
Beta-carotene	Orlistat and plant sterols	Drug effect on nutrient (May decrease nutrient effect)	Beta-carotene absorption may be decreased by these drugs	Level A Clinical trials	Likely	Low	Interaction may be minimised by separating dose of medication and beta-carotene by at least 2 hours. Supplementation recommended
Bilberry *(Vaccinium myrtillus)*	Antibiotics (Doxycycline and cephalosporins)	Herb effect on drug (The combination may have an immunostimulatory effect)	May improve the viability of thymocytes	Level D *In vitro* study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Anticancer agent (Erlotinib)	May decrease drug effect	Bilberry anthocyanins may modulate the growth-inhibitory effect of erlotinib	Level D *In vitro* study (Drug-herb interaction was not directly studied. Bilberry extract increased IC50 values of erlotinib)	Theoretical	Moderate - High	Avoid concomitant use

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Bilberry *(Vaccinium myrtillus)* *(cont)*	Anticoagulant and antiplatelet agents	May increase risk of bleeding	May have additive effect to drug	Level C Case report. (Rectal bleeding after taking warfarin with bilberry)	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs (ACE inhibitors)	May increase drug effect	May have additive effect to drug	Level D *In vitro* study (Drug-herb interaction was not directly studied. A significant dose-dependent inhibition of ACE activity was seen after incubation with bilberry extract)	Theoretical	Moderate - High	Monitor patient for signs of hypotension[d]
	Hypoglycaemic drugs	May increase drug effect	May have additive effect to drug	Level A Clinical trial (Drug-herb interaction was not directly studied. The ingestion of bilberry extract significantly decreased the incremental AUC for both glucose and insulin compared to placebo)	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient for signs of hypoglycaemia[c]
Black cohosh *(Cimicifuga racemosa)*	Chemotherapeutic agents (Docetaxel, doxorubicin, cisplatin)	May increase or decrease drug effect depending on chemotherapeutic agent	May increase cytotoxicity of docetaxel and doxorubicin or may decrease cytotoxicity of cisplatin	Level D *In vitro* study on mouse breast cancer cell line	Theoretical	Moderate - High	Avoid concomittant use
	CYP2D6 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity	Level B Human study	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	HMG-CoA reductase inhibitors (Statins) (Atorvastatin and simvastatin)	May increase drug effect and risk of elevated liver function	May have additive effect to drug	Level C Case reports	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Hepatotoxic drugs	May increase the risk of liver damage	May have an additive negative effect on the liver when taken with hepatotoxic drugs	Level C Case reports	Possible	High	Use with caution under supervision of a healthcare professional and monitor
	Organic anion-transporting polypeptide (OATP) substrates	May decrease drug effect	May decrease drug levels via inhibition of OATP function, thereby reducing drug absorption	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient. Significant interaction unlikely

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Boswellia *(Boswellia serrata)*	CYP450 enzyme substrates (CYP1A2, CYP2C9, CYP2C19, CYP2D6 and CYP3A4)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of these enzyme activities	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Immunosuppressants	May decrease drug effect	May have opposing effect to drug	Level D *In vitro* study	Theoretical	Moderate - High	Avoid concomitant use
	Multi-drug resistant protein (MRP)	May decrease drug effect	May decrease drug levels by inhibiting MRP2 function, thereby reducing drug absorption	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient. Significant interaction unlikely
	Organic anion-transporting polypeptide (OATP) substrates	May decrease drug effect	May decrease drug levels by inhibiting OATP function, thereby reducing drug absorption	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient. Significant interaction unlikely
	P-glycoprotein	May increase drug effect	Boswellia may inhibit P-gp pump efflux	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient. Significant interaction unlikely
Brahmi *(Bacopa monnieri)*	Acetylcholinesterase (AChE) inhibitors, anticholinergic drugs, cholinergic drugs	May increase effect of AChE inhibitor and cholinergic drugs. May decrease effectiveness of anticholinergic drugs	May increase acetylcholine levels due to inhibition of acetylcholinesterase	Level A Clinical trials	Likely	Moderate	Use with caution under supervision of a healthcare professional and monitor
	CYP450 enzyme substrates (CYP1A2, CYP2C19, CYP2C9, CYP3A4)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of these enzyme activities	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Thyroid hormone	May increase drug effect	May have an addictive effect to drug	Level D Animal study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hyperthyroidism[e]

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Bromelain	Amoxicillin	May increase drug effect	May increase levels of amoxicillin in tissue and blood by increasing the absorption and enhancing its penetration into tissues	Level A Clinical trials (160 mg bromelain appeared to increase intraoperative amoxicillin levels in tissue, serum and skin samples. The effect persisted 3 hours after surgery)	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Antacids	Drug effect on nutrient (May increase nutrient effect)	May increase retention of proteolytic effect of bromelain when in combination with antacids	Level D Animal and *in vitro* study (Oral bromelain retained substantial proteolytic activity throughout the gastrointestinal tract when in combination with antacids)	Theoretical	Low	No evidence from human studies to support clinical recommendations
	Anticoagulant and antiplatelet agents	May increase risk of bleeding	May have additive effect to drug	Level B Human study (Drug-herb interaction was not directly studied. Bromelain showed antiplatelet and anticoagulant effect)	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Cisplatin	May increase drug effect	Bromelain may increase apoptosis and autophagy	Level D *In vitro* study (Bromelain 25-50 mg/mL decreased IC50 value of cisplatin in malignant peritoneal mesothelioma cells)	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	CYP450 enzyme substrates (CYP2C9)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of these enzyme activities	Level D *In vitro* study	Possible	Variable *(depending on drug and disease state)*	Monitor patient. Significant interaction unlikely
	NSAIDs (Naproxen)	May increase drug side effects	Mechanism unclear	Level C Case report (Ecchymosis developed on forearms after taking naproxen with bromelain)	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Tetracycline antibiotics	Bromelain may increase blood and urine levels of these drugs	Bromelain may increase absorption and subsequent blood and urine levels of these drugs	Level B Human study	Possible	Moderate	Interaction may be minimised by separating the administration of medication and boswellia by at least 4 hours

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Calcium	Anticonvulsants	Drug effect on nutrient	Anticonvulsants may reduce intestinal absorption of calcium	Level B Human studies	Likely	Moderate	Assess nutrient status and supplement if necessary
	Antiretrovirals (Integrase inhibitors - dolutegravir, elvitegravir, raltegravir)	May decrease drug effect	Calcium may reduce blood levels of dolutegravir, elvitegravir and raltegravir through chelation	Level A Clinical trials	Possible	Moderate - High	Avoid concomitant use. If indicated, interaction may be minimised by taking 2 hours before or 6 hours after taking calcium
	Beta-blockers (Atenolol, sotalol)	May decrease drug effect	Calcium may decrease absorption of atenolol and sotalol	Level B Small human study. Calcium-rich food considered to be the major reason for reduced absorption	Possible	Moderate	Interaction may be minimised by separating dose of medication and calcium by at least 2 hours
	Bisphosphonates, tetracycline or quinolone antibiotics, thyroid hormones	May decrease drug effect	Calcium may decrease the absorption and efficacy of these drugs	Level A (Quinolones) Level B (Bisphosphonates) Level C (Tetracyclines, thyroid hormones)	Possible	Moderate	Interaction may be minimised by separating dose of medication and calcium by at least 2 hours
	Calcipotriol (Daivonex)	May increase the risk for hypercalcaemia	Theoretically, combining calcipotriol, a vitamin D analogue, with calcium supplements might increase the risk of hypercalcaemia	Level B Human study. Calcipotriol can be absorbed through the skin and affect systemic calcium homeostasis	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypercalcaemia[g]
	Calcium channel blockers (Verapamil, diltiazem)	May decrease drug effect	Calcium may decrease the hypotensive effect of verapamil	Level B Study in arrhythmic patients using IV calcium and case report	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Ceftriaxone (Cephalosporin antibiotic)	May increase drug side effect	IV calcium and IV ceftriaxone may result in precipitation of a ceftriaxone-calcium salt in the lungs and kidneys	Level C Case report	Possible	High	Avoid concomitant use
	Corticosteroids	Drug effect on nutrient	Corticosteroids may reduce intestinal absorption of calcium and increase renal calcium excretion, leading to hypocalcaemia	Level A Meta-analyses	Likely	Moderate - High	Assess nutrient status and supplement if necessary
	Iron	May decrease mineral absorption	Calcium may briefly interfere with iron absorption, but no long term effects are apparent	Level B Human studies	Possible	Low	Interaction may be minimised by taking iron at least 2 hours apart from calcium supplements or high-calcium foods

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Calcium *(cont)*	Lithium	May increase risk for hypercalcaemia	Long-term lithium use may lead to hyperparathyroidism and hypercalcaemia in a significant number of patients	Level B Human studies	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypercalcaemia[g]
	Proton pump inhibitors	Drug effect on nutrient	Proton pump inhbitors may reduce intestinal calcium absorption, leading to hypocalcaemia, especially with long-term use	Level B Human studies	Likely	Moderate	Assess nutrient status and supplement if necessary
	Thiazide diuretics	May increase drug side effect	Calcium may increase the risk of hypercalcaemia with these drugs	Level C Case reports	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Thyroid hormone (Levothyroxine)	May decrease drug effect	Calcium (carbonate, acetate, and citrate) may reduce the absorption and subsequent efficacy of levothyroxine	Level B/C Human study; case study	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypothyroidism[b]. Interaction may be minimised by separating dose of medication and calcium by at least 4 hours
Carnitine	Thyroid hormone	May decrease drug effect	L-carnitine blocks entry of thyroid hormone into the cell nucleus	Level B Human study	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypothyroidism[b]
	Warfarin	May increase drug effect	L-carnitine might increase the anticoagulant effects of warfarin	Level D Animal study	Possible	High	Use with caution under supervision of a healthcare professional and monitor
Celery *(Apium graveolens)*	Antidepressant and anxiolytic drugs	May increase drug effect	May have additive antidepressant and anti-anxiety effects	Level B Human study. The drug-nutrient interactions were not studied. Celery seed (1.34 g daily for 4 weeks) significantly improved Beck anxiety and depression inventories (BAI and BDI) in hypertensive patients	Possible	Low - Moderate	Monitor patient

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Celery *(Apium graveolens)* *(cont)*	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug	Level B Human study. The drug-nutrient interaction was not studied. Celery seed (1.34 g daily for 4 weeks) significantly reduced diastolic blood pressure, systolic blood pressure, arterial blood pressure and pulse pressure in hypertensive patients on medication	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypotension[d]
	CYP1A2 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity	Level D Animal and *in vitro* study	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Photosensitising drugs	May increase drug effect	May have additive effect to drug, increasing photosensitivity reactions	Level D *In vitro* studies	Theoretical	Low	Monitor patient. Significant interaction unlikely
	Thyroid hormone	May decrease drug effect	May decrease blood levels of drug	Level C Case reports	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypothyroidism[b]
	Venlaxafine	May increase drug effect	Celery may increase blood levels of venlafaxine by inhibition of CYP2D6	Level C Case reports	Possible	Moderate - High	Avoid concomitant use
Chaste tree	See **Vitex** (*Vitex agnus-castus*)			See **Vitex** (*Vitex agnus-castus*)			
Chondroitin sulfate	Warfarin	May increase drug effect	May have additive effect to drug. Chondroitin is a small component of a heparinoid and might have weak anticoagulant activity	Level C Case report	Possible	Moderate - High	Avoid concomitant use
Chromium	Antacids (Aluminium hydroxide and magnesium hydroxide)	Drug effect on nutrient (May decrease blood levels of nutrient)	May decrease absorption of chromium by forming insoluble complex when pH is raised in gastrointestinal tract by antacids	Level D Animal study (Chromium levels in blood were lower when in combination with antacids)	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Chromium *(cont)*	Hypoglycaemic drugs	Nutrient effect on drug (May increase drug effect but decrease associated side effects)	Multiple mechanisms proposed (addressing dietary intake, skeletal muscle fat oxidation, and insulin signalling) with studies ongoing	Level A Clinical trials (Evidence based on sulfonylureas. Combination of glipizide and chromium improved glycaemic control, increased insulin sensitivity and significantly attenuated body weight gain induced by glipizide)	Possible	Low	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
	Thyroid hormone (Levothyroxine)	May decrease drug effect	May decrease blood levels of drug by reducing absorption	Level B Human study (Chromium picolinate significantly decreased the AUC of serum thyroxine)	Possible	Moderate	Avoid concomitant use. If chromium is indicated, interaction may be minimised by separating the dose by 2 hours
	NSAIDs (Aspirin and indomethacin)	Drug effect on nutrient (May increase blood levels of nutrient)	May increase the absorption of chromium	Level D Animal studies (Chromium levels in blood, urine and tissues were higher when in combination with aspirin or indomethacin)	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
Co-enzyme Q10	Anticoagulant and antiplatelet agents	May increase or decrease drug effect	CoQ10 may have procoagulant or anticoagulant effect	Level A Conflicting data. Clinical trial found no interaction. Multiple case reports of changes to INR	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor for signs of bleeding
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug	Level A Meta-analyses in patients taking antihypertensive drugs	Likely	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypotension[d]
	Beta-blockers	Drug effect on nutrient (May decrease nutrient effect)	CoQ10 levels may be decreased by these drugs	Level D *In vitro* studies found beta blockers inhibited mitochondrial CoQ10 enzymes	Theoretical	Low	Assess nutrient status and supplement if indicated
	Chemotherapeutic agents (Anthracyclines such as daunorubicin, doxorubicin)	Nutrient effect on drug (May decreases drug side effect)	Despite the potential benefits of CoQ10 in preventing cardiotoxicity, it is unknown if CoQ10 diminishes the antineoplastic effect of doxorubicin therapy	Level A Clinical trial in leukaemia and lymphoma patients	Possible	Low	CoQ10 does not elicit its protective effect against doxorubicin-induced cardiotoxicity by reducing the drug levels in the blood or by inhibiting the formation of doxorubicinol

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Co-enzyme Q10 *(cont)*	HMG-CoA reductase inhibitors (Statins)	Drug effect on nutrient (May decrease nutrient effect)	CoQ10 levels may be depleted by these drugs	Level A Several studies in hyperlipidaemic patients; statins decreased plasma CoQ10 levels (effect on tissue levels not established)	Likely	Low	Assess nutrient status and supplement if indicated
	HMG-CoA reductase inhibitors (Statins)	Nutrient effect on drug (May decrease drug side effect)	CoQ10 may decrease myalgia associated with statin use	Level A Conflicting data Clinical trials show conflicting results. Systematic review found inadequate evidence to recommend routine use with statins	Possible	Low	Inadequate evidence to support supplementation in all patients taking statins
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect	Level A Conflicting data from clinical trials	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
Coleus *(Coleus forskolii)*	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level D Animal studies	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug	Level B Human and animal studies using IV extracts. Relevance to oral doses unknown	Theoretical	Moderate - High	No significant adverse effect expected. Monitor patient for signs of hypotension[d]
	Calcium channel blockers (Verapamil, nifedipine, diltiazem)	May increase drug effect	May have additive coronary vasodilatory effects	Level B Human studies	Likely	High	Avoid concomitant use
	CYP450 enzyme substrates (CYP2C9, CYP3A4)	May increase or decrease drug effect	May increase or decrease substrate blood levels via induction or inhibition of these enzyme activities	Level D *In vitro* study, animal study	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient
	Nitrates (Glyceryl trinitrate, isosorbide)	May increase drug effect	Coleus increases blood flow. Taking coleus with medications that increase blood flow to the heart might increase their effects	Level B Human studies	Likely	High	Avoid concomitant use
Cordyceps *(Cordyceps sinensis)*	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level C/D Case study and *in vitro* and animal studies	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor for signs of bleeding. Discontinue cordyceps at least 2 weeks before elective surgical procedures

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Cordyceps *(Cordyceps sinensis)* *(cont)*	Immunosuppressants	May increase or decrease drug effect	Cordyceps exhibits both immunostimulant and immunosuppressive effects	Level B Human studies Level D *In vitro* and animal studies	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Cranberry *(Vaccinium macrocarpon)*	Anticoagulant and antiplatelet agents	May increase drug effect	May increase blood levels of drug	Level A Conflicting data. Clinical trials suggest no evidence of increasing drug affects with cranberry juice. Case reports exist. *In vitro* studies suggest cranberry effect on warfarin metabolism (CYP3A4 minor metaboliser)	Unlikely	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	CPY3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity	Level C Case report	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Organic anion-transporting polypeptide (OATP) substrates	May decrease drug effect	May decrease drug levels by inhibiting OATP function, thereby reducing drug absorption	Level D *In vitro* studies and *in vivo* animal studies	Theoretical	Moderate	Monitor patient. Significant interaction unlikely
	Tacrolimus	May decrease drug effect	May decrease blood levels of drug	Level C Case report	Possible	High	Avoid concomitant use
Dong quai *(Angelica sinensis)*	ACE inhibitors (Lisinopril)	May increase drug effect	May potentiate the effects of the drug and potentiate anaemia	Level D Animal study	Theoretical	Moderate	Monitor patient
	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level C Several case reports and animal studies	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Aspirin	May increase drug effect	May have additive effect to drug	Level A Clinical trials	Unlikely	High	Use with caution under supervision of a healthcare professional and monitor
	CYP450 enzyme substrates (CYP1A2, CYP2D6, CYP2C9, CYP2E1, CYP3A4)	May increase or decrease drug effect	Long term use may increase or decrease substrate blood levels via induction or inhibition of these enzyme activities	Level D *In vitro* studies	Theoretical	Moderate	Monitor patient

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Dong quai *(Angelica sinensis)* *(cont)*	Oestrogen	May decrease drug effect	May decrease effect of the drug by competing for oestrogen receptors	Level D *In vitro* studies	Theoretical	Moderate	Monitor patient
	Warfarin	May increase drug effect	May have additive effects to the drug and increase INR	Level C Case studies	Likely	High	Avoid concomitant use
Echinacea *(Echinacea angustifolia/ Echinacea purpurea)*	Chemotherapeutic agent (Etoposide)	May increase drug effect	May increase blood levels of drug via inhibition of CYP1A2, CYP2C19, CYP2C9, CYP3A4	Level C Case report involving concurrent use of etoposide, cisplatin, and echinacea. Patient developed profound thrombocytopenia	Possible	Moderate - High	Avoid concomitant use
	CYP1A2 and CYP2D6 substrates	May increase or decrease blood levels of drug via inhibition of these enzyme activities	May increase or decrease blood levels of drug via inhibition of these enzyme activities	Level B Human studies	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via induction of this enzyme activity	Level B Human studies	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Immunosuppressants	May increase drug side effect	May have opposing effect to drug	Level B Animal studies, *in vitro* and *in vivo* evidence of immunomodulatory effect. No case report evidence	Possible	Moderate - High	Avoid concomitant use
	P-glycoprotein	May increase drug effect	May inhibit P-glycoprotein activity, increasing drug effect in the body	Level D *In vitro* studies	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Evening primrose oil	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug with long term use (>4 mo) due to gamma-linolenic acid (GLA) in evening primrose oil	Level B/D Combined human study and animal study (used 3 g GLA per day)	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor. Avoid using high-dose GLA long-term
	Antiretrovirals (Lopinavir/Ritonavir)	May increase drug effect	May increase blood levels of drug	Level C Case report in patient using lopinavir/ritonavir with evening primrose experiencing an increase in blood levels of drugs	Possible	Moderate - High	Avoid concomitant use
	CYP450 substrates (CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A4)	May increase or decrease drug effect	May increase or decrease levels of these drugs by inhibiting these enzymes	Level D *In vitro* study	Possible	Low	Monitor patient. Significant interaction unlikely
	Lithium	May decrease drug effect	May decrease drug levels in the body	Level C Case study	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Phenothiazines	May increase drug side effect	May lower seizure threshold	Level B Conflicting data. Human study found no interaction. Case reports of seizures in schizophrenic patients exist	Unlikely	High	Use with caution under supervision of a healthcare professional and monitor
Fenugreek *(Trigonella foenum-graecum)*	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level C Case report in patients with arrhythmia using fenugreek capsule and warfarin	Possible	Moderate - High	Avoid concomitant use
	CYP2C9 and CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease levels of these drugs via inhibition of these enzyme activities	Level D Animal studies	Theoretical	Moderate	Monitor patient
	Hypoglycaemic drugs	May increase drug effect	May have additive effect to drug	Level A Human studies and meta-analyses confirm blood glucose-lowering effect in patients with type-2 diabetes	Likely	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Fenugreek *(Trigonella foenum-graecum)* *(cont)*	Metoprolol	May increase drug effect	May have additive effect to drug	Level D Animal study	Possible	Moderate	Monitor patient for signs of hypotension[d]
	SSRI drugs	May increase drug effect	May have additive effect to drug	Level C Case study	Possible	Moderate	Monitor patient for signs of serotonin toxicity[a]
Feverfew *(Tanacetum parthenium)*	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level B Conflicting data. *In vitro* and *in vivo* studies found feverfew inhibits platelet aggregation. Human study found no such effect	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	CYP450 enzyme substrates (CYP1A2, CYP2C8, CYP2C9, CYP2C19 and CYP3A4)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of these enzyme activities	Level D *In vitro* study found low inhibitory activity	Theoretical	Variable *(depending on drug and disease state)*	No significant adverse effect expected. Monitor patient.
Fish oil	Anticoagulant and antiplatelet agents	May increase drug effect depending on fish oil dose	High doses of fish oil (>3 g/d omega-3 fatty acids) may increase the risk of bleeding with these drugs	Level A Conflicting data. Multiple clinical trials have found no increase in risk of bleeding with antiplatelet or anticoagulant drugs, however there are some studies that suggest an interaction, particularly at higher doses	Possible (depending on fish oil dose)	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect depending on fish oil dose	Level A Meta-analyses in patients taking antihypertensive drugs	Likely	Moderate	Monitor for signs of hypotension[d] if patient is taking high dose fish oil
	Chemotherapeutic agents (Cisplatin, oxaliplatin, irinotecan)	May decrease drug effect	May cause compound resistance	Level C Case report	Possible	Moderate - High	Avoid concomitant use
	Glucocorticoid drugs (Dexamethasone)	May increase drug effect	May increase drug levels and contribute to drug-induced muscular atrophy	Level D Animal studies	Possible	Low	Monitor patient

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Fish oil *(cont)*	Imunosuppressants (Ciclosporin, sirolimus, tacrolimus)	May increase drug effect	May increase drug levels and adverse drug effects	Level B Human study (Patients were given 2.6 g marine omega-3 fatty acids daily for 4 weeks)	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Flaxseed oil	Anticoagulant and antiplatelet agents	May increase drug effect	High doses (30-40 g/d) of flaxseed oil may increase the risk of bleeding with these drugs	Level A Conflicting data. Human studies	Unlikely (possible with high doses)	Moderate - High	Interaction unlikely at normal doses. Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs	May increase drug effect. Dose dependent	May have additive hypotensive effect. Dose dependent	Level A Clinical trials	Likely	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patients on high-dose flaxseed oil for signs of hypotension[d]
	HMG-CoA reductase inhibitors (Statins)	May increase drug effect	May increase drug levels and adverse drug effects	Level A Retrospective study on ADRs	Possible	Moderate	Monitor patient
Folic acid	Co-trimoxazole, sulphazalazine, phenytoin, phenobarbital, primidone and methotrexate	Drug effect on nutrient (May decrease blood levels of nutrient)	May decrease folic acid levels	Level C Multiple case reports	Possible	Moderate - High	Assess and monitor nutrient status and supplement if indicated
	Fluorouracil and capecitabine	May increase drug side effect	Folic acid may increase the toxicity of fluorouracil and capecitabine	Level C Case reports	Possible	Moderate - High	Avoid concomitant use
	Methotrexate	May decrease drug effect	Folic acid may decrease the efficacy of methotrexate for children with lymphoblastic leukaemia Folic acid may decrease drug side effect in rheumatoid arthritis	Level A Clinical trials	Likely	Moderate - High	Follow your local medical association recommendations for concurrent use of folic acid and methotrexate
	Phenytoin	May decrease drug effect	Folic acid may decrease the efficacy of phenytoin	Level B Uncontrolled studies in epileptic patients	Likely	High	Use only under supervision of healthcare professional and monitor phenytoin blood concentration

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Garlic *(Allium sativum)*	Anticoagulant and antiplatelet agents	May increase drug effect depending on formulation and dose	May increase the risk of bleeding with these medications	Level A Conflicting data. Human studies show conflicting results. Interaction more likely at higher doses (>7 g). Case reports	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug. Dose dependent	Level A Clinical trials indicate antihypertensive activity with aged garlic extract (480-960 mg/d)	Likely	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypotension[d]
	Cholesterol-lowering drugs	May increase drug effect	May have additive effects to the drug	Level B Human studies. Research is mixed. Garlic significantly lowers TC but has a mild to moderate effect on LDL-C	Possible	Moderate	Monitor patient
	CYP2E1 substrates	May increase drug effect	May increase blood levels of substrates via inhibition of this enzyme activity	Level B *In vitro* and open studies using chlorzoxazone	Possible	Variable *(depending on drug and disease state)*	Monitor patient
	Hepatic CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of hepatic CYP3A4 enzyme activity	Level C Case report	Possible	Variable *(depending on drug and disease state)*	Monitor patient
	Hypoglycaemic agents	May increase drug effect	May have additive hypoglycaemic effect	Level B Human study	Possible	Moderate – High (depending on dose)	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
	Intestinal CYP3A4 substrates (Saquinavir)	May decrease drug effect	May decrease blood levels of drug via induction of intestinal CYP3A4 enzyme activity	Level B Human study	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Intestinal P-glycoprotein substrates	May decrease drug effect	May decrease blood levels of substrates via upregulation of intestinal ABCB1 or ABCC2 activity	Level B *In vitro* and human studies found garlic decreased levels of the protease inhibitors saquinavir and ritonavir	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Isoniazid	May decrease drug effect	May decrease drug effect possibly by inhibiting absorption, but mechanism not clear	Level D Animal studies	Possible	High	Monitor patient. Interaction may be minimised by separating dose of medication and garlic by at least 2 hours

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Ginger *(Zingiber officinale)*	Anticoagulant and antiplatelet agents	May increase drug effect	May increase the risk of bleeding with these medications	Level A Conflicting data. Clinical trials indicate normal doses ≤4 g/d are unlikely to cause platelet dysfunction. Human study with high dose ginger (10 g) and *in vitro* studies showed inhibition of platelet aggregation	Unlikely	Moderate - High	Do not use high doses (≥4 g/d) in patients with bleeding disorders or those taking antiocagulant medication. Use with caution under supervision of a healthcare professional and monitor
	Calcium channel blockers	May increase drug effect	May have additive hypotensive effects	Level D *In vitro* and animal studies	Theoretical	Moderate	Monitor patient for signs of hypotension[d]
	Ciclosporin	May decrease drug effect	May decrease blood level of drug	Level D Animal study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	CYP2C9 and CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease levels of these drugs via inhibition of these enzyme activities	Level D *In vitro* studies	Theoretical	Variable *(depending on drug or disease state)*	Monitor patient
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effects when taken in high doses	Level B/D Human studies and animal studies	Theoretical	Moderate	Monitor patient for signs of hypoglycaemia[c]
	Losartan	May increase drug effect	May increase drug level and have an additive effect to drug	Level D Animal study. Single dose only, continuous use not investigated	Possible	Moderate	Monitor patient
	Metronidazole	May increase drug effect	May increase absorption and plasma half life	Level D Animal study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	P-glycoprotein	May increase drug effect	May inhibit P-glycoprotein activity, increasing drug effect in the body	Level D *In vitro* studies	Theoretical	Variable *(depending on drug or disease state)*	Monitor patient
	Tacrolimus	May increase drug effect	May increase blood levels of drug via unknown mechanism	Level D Animal study	Theoretical	High	Avoid concomitant use

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Ginkgo *(Ginkgo biloba)*	Anticoagulant and antiplatelet agents	May increase drug effect	May increase the risk of bleeding with these medications	Level A Conflicting data. Clinical trials find ginkgo does not have a significant effect on platelet function and does not interact with warfarin, aspirin or clopidogrel. Case reports suggest an interaction is possible	Unlikely	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Anticonvulsants (Phenylbarbitone, sodium valproate, phenytoin)	May decrease drug effect	May increase risk of seizure	Level C Case reports	Possible	Moderate - High	Use only under supervision of healthcare professional and monitor phenytoin blood concentration
	Chlorpromazine and haloperidol	Herb effect on drug (May increase drug efficacy)	Ginkgo may add to the beneficial effect of haloperidol, chlorpromazine and olanzapine in the treatment of schizophrenia	Level A Meta-analysis and studies	Likely	Low	No significant adverse effect expected
	CYP450 enzyme substrates (CYP1A2, CYP2C9, CYP3A4)	May increase or decrease drug effect	May increase or decrease blood levels of drug via weak inhibition of these enzyme activities	Level D *In vitro* study	Theoretical	Variable *(depending on drug or disease state)*	Monitor patient
	CYP2C19 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via induction of this enzyme activity	Level B Conflicting data. Human studies found ginkgo decreased levels of omeprazole, but had no effect on voriconazole	Possible	Variable *(depending on drug and disease state)*	Monitor patient
	Efavirenz	May decrease drug effect	May increase blood levels of drug due to possible induction of CYP3A4 and P-glycoprotein	Level C Case report	Possible	Moderate - High	Avoid concomitant use
	Hypoglycaemic drugs	May increase or decrease drug effect	Ginkgo may increase or decrease blood glucose levels	Level B Conflicting data. Clinical trials and human studies found ginkgo had a variable effect on drug activity. Animal and *in vitro* studies suggest ginkgo may reduce insulin resistance	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Nifedipine	May increase drug effect	May increase blood level of drug	Level B Human studies	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Ginkgo *(Ginkgo biloba)* *(cont)*	Raltegravir	May increase drug effect	May increase blood level of drug	Level B Human studies	Possible	Moderate - High	Avoid concomitant use
	Sofosbuvir	May increase drug effect	May increase blood levels of the drug and drug effects by affecting P-glycoprotein activity	Level D Animal study	Possible	Moderate	Monitor patient
Ginseng (Korean) *(Panax ginseng)*	Amitriptyline	May increase drug effect	May have an effect on neurochemical system	Level C Case report	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Anticoagulant and antiplatelet agents	May increase or decrease drug effect	Possible CYP450 enzymes interaction and Vitamin K effect on ginseng	Level A Conflicting data. Clinical trial results suggest no interaction. Case studies exist and *in vitro* studies suggest possible interaction	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	CYP2D6 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity	Level A Clinical trials	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Digoxin	May interfere with the accuracy of a range of tests measuring serum digoxin	Korean ginseng may falsely elevate or decrease assays for blood digoxin levels	Level B *In vitro*, animal and human *ex vivo* studies	Possible	High	Avoid concomitant use
	Docetaxel	Herb effect on drug (May increase drug efficacy)	May enhance susceptibility of colon cancer cells to docetaxel	Level D *In vitro* study	Theoretical	Low	No evidence from human studies to support clinical recommendations

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Ginseng (Korean) *(Panax ginseng)* *(cont)*	Doxorubicin	Herb effect on drug (May decrease drug side effect)	May have a protective effect on doxorubicin induced toxicity	Level D Animal study	Theoretical	Low	No evidence from human studies to support clinical recommendations
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect	Level A Clinical trials in NIDDM patients and healthy subjects	Likely	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
	Imatinib	May increase drug side effect	May increase blood levels of drugs possibly due to inhibition of CYP3A4	Level C Case report	Possible	High	Avoid concomitant use
	Midazolam	May decrease drug effect	May decrease blood levels of drugs possibly due to induction of CYP3A4	Level A Clinical trials	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Monoamine oxidase inhibitors (MAOI) (Phenelzine)	May increase drug side effect	Korean ginseng may increase the side effect of phenelzine or other MAOIs	Level C Case reports (ginseng type not specified)	Unlikely	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Oestrogen	May increase or decrease drug effect	Korean ginseng may cause a phytoestrogenic effect	Level D *In vitro* study	Theoretical	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Ginseng (Siberian) *(Eleutherococcus senticosus)*	Anticoagulant and antiplatelet agents	May increase drug effect	Siberian ginseng may increase risk of bleeding with this medication	Level B *In vivo* study found anticoagulant activity for an isolated constituent. Human study in athletes adminstered a preparation of Siberian ginseng and andrographis found reduced coagulation	Possible	Moderate - High	Avoid concomitant use
	Chemotherapeutic agents	Nutrient effect on drug (May decrease drug side effect)	Siberian ginseng may increase tolerance for chemotherapy and improve immune response	Level A Human trials in women with breast and ovarian cancer undergoing chemotherapy treatment	Likely	Low	Use with caution under supervision of a healthcare professional and monitor
	CYP2A1, CYP2C9, CYP2D6, and CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of these enzyme activities	Level B Human study	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Digoxin	May interfere with the accuracy of a range of tests measuring serum digoxin	Siberian ginseng may falsely elevate or decrease assays for blood digoxin levels	Level B *In vitro*, animal and human *ex vivo* studies	Possible	High	Avoid concomitant use
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect to drug	Level A Clinical trials	Likely	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
	Monoamine oxidase inhibitors (MAOI) (Phenelzine)	May increase drug side effect	Siberian ginseng may increase side effect of phenelzine or other MAOIs	Level C Two case reports (ginseng type not specified)	Unlikely	Moderate	Use with caution under supervision of a healthcare professional and monitor
	P-glycoprotein substrates	May increase drug effect	May increase blood level of drug via inhibition of P-gp	Level D *In vitro* studies	Possible	Variable *(depending on the drug)*	Monitor patient
Glucosamine	Anticoagulant and antiplatelet agents	May increase drug effect	May increase the risk of bleeding with these medications	Level C Case reports	Possible	Moderate - High	Avoid concomitant use
	Hypoglycaemic drugs	May decrease drug effect	Glucosamine may affect blood glucose levels in people with diabetes	Level A Clinical trials indicate no interaction. Lower-level studies report changes to glucose and insulin levels	Unlikely	Moderate - High	Interaction unlikely, however use with caution under supervision of a healthcare practitioner. Monitor patient for signs of hypoglycaemia[c]

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Grape seed *(Vitis vinifera)*	Anticoagulant and antiplatelet agents	May increase risk of bleeding	May decrease platelet adhesion to fibrinogen	Level D *In vitro* studies	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs + vitamin C	May have opposing effect to drug	Unknown mechanism	Level A Meta-analyses in patients taking antihypertensive drugs	Possible	Moderate - High	Avoid combination of vitamin C and grape seed in hypertensive patients
	Cisplatin	Herb effect on drug (May reduce cisplatin induced oxidative/ nitrative stress)	Unclear mechanism. May suppress free radicals and rescue the down-regulated expression of testosterone synthesis induced by cisplatin	Level D Animal study (400 mg/kg of grape seed extract showed protective effects on the testicular toxicity induced by cisplatin (10 mg/kg) in rats)	Theoretical	Low	No evidence from human studies to support clinical recommendations
	CYP2D6 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity	Level B Human study (300 mg of grape seed did not significantly change metabolic rates of dextromethorphan (CYP2D6 substrate) in healthy volunteers) Level D *In vitro* study (100 mg of grape seed extract inhibited CYP2D6 activity)	Unlikely	Variable *(depending on drug and disease state)*	Monitor patient
	CYP450 enzyme substrates (CYP2C9, CYP2E1, Intestinal CYP3A4)	May increase or decrease drug effect	May increase or decrease blood levels of enzyme substrates via inhibition of these enzyme activities	Level D *In vitro* study (100 mg of grape seed extract inhibited CYP2C9 and intestinal CYP3A4 activity). *In vitro* and animal study (Wild grape seed procyanidins diminished CYP2E1 expression *in vitro* and downregulated the protein expression level of liver CYP2E1 in rats)	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Grape seed *(Vitis vinifera)* *(cont)*	Doxorubicin	Herb effect on drug (May attenuate doxorubicin-induced toxicity)	Unclear mechanism. May protect DNA from oxidative damage	Level D Animal study (100 mg/kg grape seed extract showed cardioprotective effect without affecting antitumor effects of 2 mg/kg doxorubicin)	Theoretical	Low	No evidence from human studies to support clinical recommendations
	Hepatic CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via induction of hepatic CYP3A4 enzyme activity	Level D Animal study (1 week treatment of grape seed extract (80 mg/kg) with the administration of intravenous midazolam (10 mg/kg) increased the effect of midazolam). Midazolam is bio-transformed to the active metabolite via hepatic CYP3A4 enzyme	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient
	Iron	Herb effect on nutrient	May decrease mineral absorption when administered together	Level D *In vitro* study	Theoretical	Moderate	Assess nutrient status and supplement if indicated. Interaction may be minimised by taking iron at least 2 hours apart from grape seed supplement
Green-lipped mussel	Anticoagulant and antiplatelet agents	May increase drug effect	May increase the risk of bleeding with these medications	Level B Conflicting data. Several case reports of raised INR. Small human study found no effect on platelet aggregation, prothrombin time, APTT, fibrinogen or factor VII	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Hawthorn *(Crataegus monogyna)*	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level C Case report	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug	Level A Clinical trials suggest hypotensive effect	Likely	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for hypotension[d]
	Nitrates	May increase drug effect	May have additive vasodilation effect	Level B Human studies	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Hawthorn *(Crataegus monogyna)* *(cont)*	Phosphodiesterase-5-Inhibitors	May increase drug effect	May have additive vasodilation effect	Level D Animal study	Theoretical	High	Use with caution under supervision of a healthcare professional and monitor
	QT prolonging drugs	May increase drug effect	May increase the risk for adverse cardiac effects when taken together	Level C Case study (in a single case study, a patient taking medications that can prolong the cardiac QT interval experienced a fatal drug interaction after ingesting hawthorn)	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
Holy Basil *(Ocimum tenuiflorum)*	Anticoagulant and antiplatelet agents	May increase drug effect	May inhibit platelet aggregation	Level D Animal study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect	Level A Clinical trial in NIDDM patients found holy basil may decrease blood glucose levels	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
	Phenobarbital	May increase drug effect	May potentiate phenobarbitone - induced sleeping time	Level D Animal study	Theoretical	High	Use with caution under supervision of a healthcare professional and monitor
Hops *(Humulus lupulus)*	CYP450 enzyme substrates (CYP1A1, CYP1A2, CYP1B1, CYP2C8, CYP2C9, CYP2C19, CYP3A4)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of these enzyme activities	Level D *In vitro* studies	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient
	Oestrogen	May decrease drug effect	May bind to oestrogen receptor site	Level D *In vitro* studies	Theoretical	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
	Paracetamol (Acetaminophen)	May increase drug effect	May increase analgesic effect by slowing drug clearance	Level D Animal study	Possible	Moderate	Monitor patient. Clinical significance is uncertain until human studies are conducted

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Horsetail *(Equisetum arvense)*	Antiretrovirals (Lamivudine, zidovudine, emtricitabine, efavirenz, tenofovir)	May decrease drug effect	May decrease blood levels of drug by increasing renal excretion of drug due to its diuretic properties or via flavonoids and phenols in horsetail that could induce CYP450 enzyme activity	Level C Case reports (2 patients had detectable viral loads)	Possible	High	Avoid concomitant use
	CYP450 enzyme substrates (CYP1A2, CYP2D6)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of these enzyme activities	Level D *In vitro* study (Horsetail extract from 800 mg of horsetail)	Theoretical	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Diuretic drugs	May increase drug effect	Theoretically, taking various species of horsetail with diuretic drugs might increase potassium loss, as horsetail possesses diuretic properties	Level D Animal studies (a human study showed that taking horsetail for 4 days didn't affect potassium levels depsite it showing a siginficant diuretic effect. The effects of longer term use are unknown	Possible	Moderate	Monitor patient
Iodine	Amiodarone	May increase adverse effect on thyroid function	May increase blood levels of iodine	Level C Case reports	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Antithyroid drugs	May increase drug effect	Iodine may precipitate hypothyroidism	Level D *In vitro* studies	Theoretical	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypothyroidism[b]
	Lithium	May increase drug effect	Iodine at high doses may increase the hypothyroid activity of lithium carbonate	Level C Case reports and open study in patients taking lithium	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypothyroidism[b]
	Thyroid hormone	May increase drug effect	Iodine (at very high doses) may precipitate or exacerbate hyper or hypothyroidism	Level B Studies in euthyroid subjects - thyroid function inhibited	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Iron	Bisphosphonates	May decrease drug effect	May decrease the absorption of drug	Level B Human studies	Possible	Moderate	Avoid concomitant use. If iron is indicated, interaction may be minimised by taking 2 hours before or 6 hours after drug
	Captopril	May decrease drug effect	May decrease the absorption of drug	Level A Clinical trials	Possible	Moderate	Avoid concomitant use. If iron is indicated, interaction may be reduced by taking 4-6 hours before or 2 hours after drug

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Iron *(cont)*	Dolutegravir	May decrease drug effect	May decrease the absorption of drug	Level A Clinical trials	Likely	High	Avoid concomitant use. If iron is indicated, interaction may be minimised by taking 2 hours before or 6 hours after drug
	Methyldopa, levodopa, carbidopa and penicillamine	May decrease drug effect	May decrease the absorption of drug	Level B Studies in patients (carbidopa, levodopa, methyldopa) and healthy subjects (penicillamine)	Likely	High	Avoid concomitant use. If iron is indicated, interaction may be minimised by taking 2 hours before or 6 hours after drug
	Mycophenolate	May decrease drug effect	May decrease the absorption of drug	Level B Human studies	Possible	Moderate - High	Avoid concomitant use. If iron is indicated, interaction may be minimised by taking 2 hours before or 6 hours after drug
	Proton pump inhibitors (PPIs), H_2-receptor antagonists, bile acid sequestrants, antacids	Drug effect on nutrient	May decrease mineral absorption when administered together	Level C Case studies	Possible	Moderate	Assess nutrient status and supplement if indicated
	Tetracycline and quinolones	May decrease drug effect	May decrease the absorption of drug	Level B Human studies	Likely	High	Avoid concomitant use. If iron is indicated, interaction may be minimised by taking 2 hours before or 6 hours after drug
	Thyroid hormone	May decrease drug effect	May decrease the absorption of drug	Level B Human studies	Likely	Moderate	Avoid concomitant use. If iron is indicated, interaction may be minimised by taking 2 hours before or 6 hours after drug
Ivy leaf *(Hedera helix)*	CYP450 enzyme substrates (CYP2C19, CYP2C8, CYP2D6)	May increase drug effect	May increase drugs levels through inhibition of these enzymes	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient. Significant interaction unlikely

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Kava *(Piper methysticum)*	CNS depressants	May increase drug effect	May increase sedative effects of these drugs	Level A/B CNS depressant effects of kava have been confirmed in numerous RCTs	Likely	High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of sedation
	CYP450 substrates (CYP2C9, CYP2C19)	May increase drug effect	May increase blood levels of the drug through inhibition of these enzymes	Level D *In vitro* studies	Theoretical	Low	Monitor patient. Significant interaction unlikely
	CYP450 substrates (CYP1A2, CYP2E1)	May increase drug effect	May increase blood levels of the drug through inhibition of these enzymes	Level B Human studies	Possible	Low	Monitor patient
	Haloperidol/ Haloperidol + Lorazepam	May increase drug side effects	May increase risk of cardiovascular adverse effects and hypoxia	Level C Case studies (not known if effects were due to induction on CYP2D6 enzymes or additive effects of drugs)	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Paracetamol	May increase drug side effects	May increase severity of paracetamol-induced hepatotoxicity	Level D *In vitro* study	Theoretical	High	Monitor patient. Avoid concomitant use of kava with high doses of paracetamol
Kelp *(Fucus vesiculosus)*	Lithium	May increase or decrease drug effect	May increase or decrease blood level of drug	Level C Case reports	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Thyroid hormone	May increase or decrease drug effect	Taking kelp may precipitate or exacerbate hyper or hypothyroidism	Level A Clinical trial found T3 decreased and TSH increased. Case reports of hyperthyroidism and hypothyroidism	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Liquorice *(Glycyrrhiza glabra)*	Anticoagulant and antiplatelet agents	May increase or decrease drug effect	Additive effect to drug classes, however may induce CYP3A4 and CYP2C9 (metabolisers of warfarin) which may decrease blood levels of warfarin	Level A *In vitro* and *in vivo* studies and systematic review	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs	May have opposing effect to drug	May have hypertensive effect (at high doses 50-200 g/d)	Level B Open studies and case report	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Cisplatin	May decrease drug effect	May decrease blood level of drug	Level D Animal study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Corticosteroids (Prednisolone)	May increase drug effect	May increase blood levels of drug	Level B Open human studies	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition or induction of this enzyme activity	Level B Human studies	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	CYP450 enzyme substrates (CYP2C9, CYP2C19, CYP2B6, CYP2C8)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of these enzyme activities	Level D *In vitro* studies	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient
	Digoxin	May increase drug side effect	Liquorice may increase the risk of digoxin toxicity (possibly via hypokalaemia and/or inhibition of P-gp)	Level C Case report, *in vitro* study and animal study	Possible	High	Avoid concomitant use
	Methotrexate	May increase adverse drug effects	May increase liver enzyme and bilirubin levels when administered together	Level D Animal studies	Possible	Low	Use with caution under supervision of a healthcare professional and monitor
	Monoamine oxidase inhibitors (MAOIs)	May increase drug effect	May have additive effects to the drug	Level D *In vitro* study	Theoretical	Moderate	Monitor patient. Clinical significance is uncertain until human studies are conducted

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Liquorice *(Glycyrrhiza glabra)* *(cont)*	P-glycoprotein substrates	May decrease drug effect	May increase P-glycoprotein activity, decreasing drug effect in the body	Level D Animal study	Possible	Moderate	Monitor patient
	Potassium-depleting diuretics, laxatives	May increase drug side effect	Liquorice (at high doses - over 100 g/d) may increase the risk of electrolyte disturbances, especially hypokalaemia, with these medications	Level B Open human studies (dosage 100-200 g/d) and case reports	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Lutein	Cisplatin	Nutrient effect on drug (May prevent cisplatin-induced retinal damage)	May have antioxidant and anti-inflammatory effects	Level D Animal study (Co-administration of Lutein 0.5 mg/kg and cisplatin 5 mg/kg in rats)	Theoretical	Low	No evidence from human studies to support clinical recommendations
	CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity	Level D *In vitro* studies showed dose-dependent effects. (Lutein (5-100 mg/L) had inhibitory effects on CYP3A4. Lutein (2.8 mg/L) did not inhibit CYP3A4 activity)	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Doxorubicin	Nutrient effect on drug (May enhance cytotoxicity and reduce cancer resistance)	May have additive effect to drug on reactive oxygen species-mediated apoptosis. May reduce doxorubicin-induced inflammatory response via inhibition of NF-kB expression	Level D *In vitro* study study showed enhanced cytotoxic effect in breast cancer cells. Another *in vitro* and animal study showed that the combination of lutein and doxorubicin reduced sarcoma cell proliferation and tumour growth	Theoretical	Moderate - High	No evidence from human studies to support clinical recommendations
	Ethambutol + isoniazid	Nutrient effect on drug (May prevent isoniazid-induced toxic optic neuropathy)	May have antioxidant and anti-inflammatory effects	Level D Animal study (Co-administration of lutein 0.5 mg/kg, ethambutol 50 mg/kg and isoniazid 50 mg/kg in rats)	Possible	Low	No evidence from human studies to support clinical recommendations

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Lysine	5-HT4 agonist drugs (e.g. Prucalopride)	May decrease drug effect	Lysine acts as a partial 5-HT4 antagonist in the gut which may decrease 5-HT4 agonist drug activity	Level D Animal studies	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Calcium	Nutrient effect on nutrient	Lysine significantly increases intestinal absorption of calcium	Level B Human study	Possible	Moderate	Monitor patient. Avoid concomitant use with high-dose calcium
	Arginine	Nutrient effect on nutrient	High-dose arginine may reduce lysine levels	Level B Human study	Possible	Moderate	Avoid concomitant use with high-dose arginine
Magnesium	Aminoglycosides	May increase drug side effect such as muscle weakness	May have additive inhibitory effects on presynaptic acetylcholine release	Level C Case report	Possible	Moderate - High	Avoid concomitant use
	Amphotericin-B	Drug effect on nutrient (May decrease blood levels of nutrient)	Electrolyte disturbances, including low serum magnesium levels, may occur with this medication. This has been association with nephrotoxicity, and may necessitate stopping the drug and giving intravenous electrolyte replacement	Level B Human studies and case reports	Possible	Low	Assess nutrient status and supplement if indicated
	Antiarrythmic drugs	Nutrient effect on drug (May increase drug efficacy)	Magnesium may have additive antiarrythmic effect	Level A Clinical trial using high dose of magnium (3204 mg/d magnesium chloride)	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Anticoagulant and antiplatelet agents	May decrease drug effect	Magnesium may reduce the efficacy of warfarin	Level B *In vitro* study and human study based on IV route of administration	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs (Calcium channel blockers)	May increase drug effect	Magnesium may have additive hypotensive effect	Level A Meta-analysis	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypotension[d]

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Magnesium *(cont)*	Bisphosphonates	May decrease drug effect	Bisphosphonates may form complexes with multivalent cations such as magnesium	Level A Clinical trials	Likely	Moderate	Use with caution under supervision of a healthcare professional and monitor. Interaction may be minimised by taking medication at least 2 hours before or after magnesium supplementation
	Digoxin, chlorpromazine, penicillamine, tetracycline, nitrofurantoin and quinolone antibiotics	May decrease drug effect	Magnesium may decrease the absorption and efficacy of these drugs	Level A (Tetracycline and quinolone antibiotics) Level B (Chlorpromazine) Level B (Penicillamine) Level D (Digoxin) Level D (Nitrofurantoin)	Possible	Low	Interaction may be minimised by separating the administration of medication and magnesium by at least 2 hours
	Gabapentin	May decrease drug effect	May decrease blood level of drug	Level B Human studies	Possible	Moderate - High	Avoid concomitant use
	HMG-CoA reductase inhibitors (Statins)	May decrease drug effect	May decrease drug levels in the body when administered together	Level B Human study. One human study showed that simultaneous dosing of rosuvastatin with a magnesium-containing antacid resulted in a decrease in rosuvastatin systemic exposure of approximately 50%	Likely	High	Use with caution under supervision of a healthcare professional and monitor. Interaction may be minimised by taking medication at least 2 hours before or after magnesium supplementation
	Hypoglycaemic drugs (Glibenclamide, glipizide)	May increase drug effect	May enhance drug absorption and systemic drug effects	Level B Human study	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor. Interaction may be minimised by taking medication at least 2 hours before or after magnesium supplementation
	Levodopa	May decrease drug effect	May decrease drug levels in the body and systemic effects of the drug	Level B/D Human study and animal study	Possible	High	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Magnesium *(cont)*	Loop and thiazide diuretics	Drug effect on nutrient (May decrease blood levels of nutrient)	Loop diuretics and, to a lesser extent, thiazide diuretics, interfere with magnesium reabsorption in the kidneys, which increase urinary losses and may reduce serum magnesium levels	Level B Multiple studies and case reports	Likely (with long term use)	Moderate	Assess nutrient status and supplement if indicated
	Proguanil	May decrease drug effect	Proguanil may form complexes with magnesium	Level B Human studies	Possible	High	Avoid concomitant use
	Proton pump inhibitors	Drug effect on nutrient (May decrease blood levels of nutrient)	Proton pump inhibitors may cause hypomagnesaemia if taken long-term (usually >1 year)	Level B Multiple case reports, case series, reviews	Likely (with long term use)	Moderate	Assess nutrient status and supplement if indicated
	Rocuronium	May increase drug effect	May have additive inhibitory effects on acetylcholine release	Level A Clinical trial using IV administration	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Methionine	Levodopa	May decrease drug effect	Methionine may decrease the efficacy of levodopa in Parkinson's disease	Level B Open study in patients with Parkinson's disease	Possible	Low	Use with caution under supervision of a healthcare professional and monitor
Milk thistle/St Mary's thistle *(Silybum marianum)*	Chemotherapeutic agents (Cisplatin, doxorubicin)	Herb effect on drug (May decrease drug side effect)	Milk thistle may have cardioprotective activity against doxorubicin and nephroprotective activity against cisplatin	Level A Clinical trials	Possible	Low	No significant adverse effect expected. Use with caution uder supervision of a health care professional and monitor
	CYP3A4 and CYP2C9 substrates	May increase or decrease drug effect	May increase or decrease blood levels of substrate via inhibition or induction of this enzyme activity	Level A Clinical trials	Unlikely	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Glucuronidated drugs	May increase blood levels of these drugs	May inhibit uridine diphosphoglucuronosyl transferase (UGT), could decrease the clearance and increase levels of these drugs	Level D Animal studies	Possible	Moderate	Monitor patient
	Hypoglycaemic drugs	May increase drug effect	May increase blood levels and clinical effects of these drugs	Level B Human studies	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Milk thistle/St Mary's thistle *(Silybum marianum)* *(cont)*	Ledipasvir/Sofosbuvir	May increase drug effect	May increase blood levels and clinical effects of these drugs	Level D Animal study	Possible	Moderate	Monitor patient
	Morphine	May increase or decrease drug effect	May affect blood levels of the drug and increase or decrease its effects	Level D Animal study	Theoretical	Moderate	Monitor patient
	P-glycoprotein substrates	May increase or decrease drug effect	May inhibit or induce P-gp activity	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Raloxifene	May increase drug effect	May increase blood levels of drug by inhibiting glucuronidation of drug	Level D *In vitro* study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Sirolimus	May increase drug effect	May decrease drug hepatic clearance	Level B Human studies	Possible	High	Avoid concomitant use
	Tamoxifen	May increase or decrease drug effect	May increase blood level of drug via inhibition of CYP2CP, CYP3A4 and P-gp activity	Level B Human studies	Possible	High	Avoid concomitant use depending on severity of disease state
Niacin (Vitamin B3)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level C Case study. Patient was taking 500 mg daily of a slow-release niacin	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor. Avoid concomitant use of high doses of niacin (> 100 mg daily) with these drugs
	Aspirin	Drug effect on nutrient (May increase or decrease niacin side effect)	May reduce the clearance of niacin by competing for glycine conjugation	Level B Human studies	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Bile-acid sequesterants	May increase drug side effect	Mechanism unknown	Level C Case reports	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Gemfibrozil	May increase drug side effect	May increase risk of myopathy	Level C Case reports	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Niacin (Vitamin B3) *(cont)*	HMG-CoA reductase inhibitors (Statins)	May increase drug side effect	High dose nicotinic acid (1500 mg/d) may increase the risk of rhabdomyolysis and myopathy with statins	Level C Case reports	Possible	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
	Thyroid hormone	May decrease drug effect	May decrease blood levels of drug	Level A Clinical trials	Possible	Moderate	Use with caution under super vision of a healthcare professional. Monitor patient for signs of hypothyroidism[b]
	Transdermal nicotine	Drug effect on nutrient (May increase nutrient side effect)	May have additive effect to nutrient	Level C Case reports	Possible	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
Nicotinamide	Anticonvulsant drugs (Carbamazepine)	May increase drug effect	May increase blood levels and clinical effects of these drugs	Level C Case studies	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Oats *(Avena sativa)*	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect	Level A Clinical trials find oats decrease blood pressure. In one trial, 73% of patients were able to stop or reduce their medication	Likely	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for hypotension[d]
	Atorvastatin	May increase drug effect	May reduce intestinal absorption of atorvastatin	Level D Animal study	Theoretical	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
Omega-3 (EPA + DHA)	Anticoagulant and antiplatelet agents	May increase drug effect depending on omega-3 EPA + DHA dose	High doses of EPA + DHA (>3 g/day omega-3 fatty acids) may increase the risk of bleeding with these drugs	Level A Conflicting data. Multiple clinical trials have found no increase in risk of bleeding with antiplatelet or anticoagulant drugs, however there are some studies that suggest an interaction, particularly at higher doses	Possible (depending on omega-3 dose)	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs	May increase drug effect	May have additive effect to drug	Level A Meta-analyses in patients with hypertension showed that 2-3 g daily of EPA+DHA significantly lowers systolic and diastolic blood pressure	Likely	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for hypotension[d], especially those taking high-dose omega-3 fatty acids

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
PABA (Para-aminobenzoic acid)	Intramuscular cortisone	May increase drug effect	May decrease metabolism of cortisone	Level B Human study	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Sulphonamides and sulphones (Dapsone)	May decrease drug effect	May inhibit antimicrobial activities of drug	Level B *In vitro* studies and human study	Possible	Moderate	Avoid concomitant use
Pau d'Arco *(Tabebuia avellanedae)*	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive anticoagulant effect (at very high doses)	Level B One uncontrolled study found very high dose of isolated constitutent prolonged prothrombin time	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
PEA (Palmitoyle-thanolamide)	Opioid medication (Tramadol)	May increase drug effect	May have a synergistic effect with the drug	Level D Animal studies	Possible	Moderate	Monitor patient. No evidence from human studies to support clinical recommendations
Pelargonium *(Pelargonium sidoides)*	Anticoagulant and antiplatelet agents	May increase drug effect	Pelargonium contains coumarin which may reduce platelet aggregation, additive effect to drug	Level D Animal study suggests interaction unlikely	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Immunosuppressants	May decrease drug effect	May have opposing effect to drug	Level D *In vitro* studies find pelargonium has immune modulatory activity	Theoretical	Moderate - High	Avoid concomitant use
Peppermint *(Mentha x piperita)*	Ciclosporin	May increase drug effect	May increase blood levels of drug	Level D Animal study	Theoretical	High	Avoid concomitant use
	CYP450 enzyme substrates (CYP3A4, CYP1A2, CYP2C9, CYP2C19)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of CYP1A2, CYP2C9 and CYP2C19 enzyme activities and induction of intestinal CYP3A4 enzyme activity	Level B Open study using felodipine, simvastatin (CYP3A4 substrates) Level D Animal study (CYP1A2, CYP2C9 and CYP2C19 substrates)	Possible	Variable *(depending on drug or disease state)*	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Phytosterols/ Plant sterols	Carotenoids	Nutrient effect on nutrient	May decrease blood level of carotenoids	Level A Meta-analysis	Possible	Moderate	Assess nutrient status and supplement if required
	Lipid-lowering agents (Statins and ezetimibe)	May increase drug effect	May have additive LDL-C lowering effect	Level A Clinical trials and systematic reviews	Likely	Low - Moderate	No significant adverse effect expected. Use with caution under supervision of a healthcare professional and monitor
Potassium	ACE inhibitors, angiotensin receptor blockers and potassium-sparing diuretics	May increase drug side effect	Potassium may increase the risk of hyperkalaemia	Level C Multiple case reports	Likely (dose dependant)	Moderate - High	Avoid concomitant use
	Trimethoprim-sulfamethoxazole (Bactrim)	May increase drug side effect	Potassium may increase the risk of hyperkalaemia	Level C Multiple case studies	Possible	High	Use with caution under supervision of a healthcare professional. Monitor patient for hyperkalaemia[h]
Probiotics	Antibiotics	Nutrient effect on drug (May decrease drug side effect)	May restore gut flora and reduce diarrhoea secondary to antibiotic therapy	Level A Multiple trials in adults and children taking antibiotics	Likely	Low	No significant adverse effects expected. Supplementation may be beneficial
Lactobacillus species including: *L. acidophilus, L. reuteri*	Fluconazole	Nutrient effect on drug (May increase drug efficacy)	Combination therapy may improve clinical outcome	Level A Clinical trial in women with vulvovaginal candidiasis	Likely	Low	No significant adverse effects expected. Supplementation may be beneficial
	Nitrazepam	Nutrient effect on drug	May reduce drug adverse effects, by reducing β-glucuronidase, nitroreductase, and azoreductase, when co-administered	Level B Human study	Possible	Low	No significant adverse effects expected. Supplementation may be beneficial
L. rhamnosus GR-1 & *L. reuteri* RC-14	Immunosuppressants	May predispose opportunistic infection	May predispose opportunistic infection due to immunosuppression	Level C Case report	Possible (depending on disease state)	Moderate - High	Avoid concomitant use in critically ill and immunocompromised patients
Saccharomyces boulardii	Antifungal agents	Drug effect on nutrient	May decrease the probiotic effectiveness of *Saccharomyces boulardii*	Level D *In vitro* studies	Theoretical	Low	Monitor patient

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Psyllium husk	Hypoglycaemic drugs	May increase drug effect	Psyllium may decrease post-prandial blood glucose levels	Level A Clinical trial	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
	Oral drugs and nutritional supplements	May decrease drug effect	Psyllium may decrease the absorption of oral drugs if doses are taken comcommitantly	Level B Human studies	Possible	Variable *(depending on drug and disease state)*	Interaction may be minimised by separating dose of medication and psyllium by at least 2 hours
Quercetin	Anticoagulant and antiplatelet agents	May increase drug effect	May increase blood level of drug by displacing warfarin from human serum albumin binding site and CYP2C9 inhibition	Level D *In vitro* study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs (Calcium channel blockers)	May increase drug effect	May have additive effect to drug	Level A Clinical trial found quercetin supplementation reduced systolic, diastolic and mean arterial pressure in stage 1 hypertensive subjects Level D *In vitro* study found increased bioavailability for diltiazem but mechanism is unknown	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypotension[d]
	CYP450 enzyme substrates (CYP1A1, CYP1A2, CYP2C8, CYP3A4, CYP2C9, CYP2D6)	May increase or decrease drug effect	May increase or decrease blood levels of enzyme substrates via inhibition of these enzyme activities	Level B Human, animal and *in vitro* studies	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Mitozantrone	May increase drug effect	May increase blood levels and adverse effects of the drug	Level D *In vitro* study	Theoretical	Moderate	Monitor patient
	Organic anion transporting polypeptide (OATP) substrates (OATP1B1)	May increase drug effect	Quercetin may inhibit OATP1B1-mediated transport	Level B Human studies	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Quercetin *(cont)*	P-glycoprotein substrates	May increase drug effect	Quercetin may inhibit P-gp pump efflux	Level B Human studies	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Sulfasalazine	May increase drug effect	May increase blood levels and adverse effects of the drug	Level D *In vitro* study	Theoretical	Moderate	Monitor patient
Red clover/ Isoflavones *(Trifolium pratense)*	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level D Animal study and *in vitro* study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	CYP450 enzyme substrates (CYP1A2, CYP2C9,CYP2C19, CYP3A4)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of these enzyme activities	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Daunorubicin	May increase drug side effect	May decrease drug metabolism due to decrease in glutathione cellular concentration	Level D *In vitro* study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Digoxin	May increase drug effect	May increase blood levels of drug via inhibition of P-gp expression	Level D *In vitro* study	Theoretical	Moderate - High	Avoid concomitant use
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect to drug	Level D *In vitro* study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor for signs of hypoglycaemia[c]
	Lipid-lowering drugs	May increase drug effect	May have additive lipid-lowering effect to drug	Level A Clinical trials	Possible	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
	Methotrexate	May increase drug side effect	Mechanism unknown	Level C Case report	Possible	Moderate - High	Avoid concomitant use
	Oestrogen	May increase or decrease drug effect	Red clover binds to oestrogen receptors and is capable of acting as both agonists and antagonists	Level D Animal study	Theoretical	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Red clover/ Isoflavones *(Trifolium pratense)* *(cont)*	Tamoxifen	May increase drug effect	Red clover may have oestrogenic activity and may theoretically interfere with tamoxifen efficacy	Level B Human studies	Possible	High	Avoid concomitant use
	Vinblastine	May increase drug effect	May increase blood levels of drug via inhibition of P-gp expression	Level D *In vitro* study	Theoretical	Moderate - High	Avoid concomitant use
Reishi mushroom *(Ganoderma lucidum)*	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level B/D Human study. Study showed an anticoagulant effect at a dose of 3 g daily. *In vitro* study	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs	May increase drug effect	May have additive effect to drug	Level B/D Human studies/animal studies (hypotensive activity has been shown in animal studies but clinical effects are still unclear)	Theoretical	Moderate	Monitor patient for signs of hypotension[d]
	Hypoglycaemic drugs	May increase drug effect	May have additive effect to drug	Level D Animal studies (studies show that reishi decreases blood sugar, but clinical studies have failed to confirm this)	Theoretical	Moderate	Monitor patient for signs of hypoglycaemia[c]
	Immunosuppressants	May increase drug side effect	May have opposing effect to drug	Level A/B Human clinical studies	Possible	High	Avoid concomitant use
	CYP450 substrates (CYP1A2, CYP2E1, CYP3A4)	May increase drug effect	May increase drug effect via inhibition of these enzyme activities	Level D Animal studies	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient
SAMe (S-adenosyl methionine)	Levodopa	May reduce drug effect	May methylate the drug, reducing its effectivess	Level D Animal study	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Serotonergic drugs	May increase drug effect	May increase the risk of serotonin syndrome when taken with these drugs	Level C Case studies (in contrast, a lower quality clinical study showed that combining SAMe with SSRI medication was effective and well-tolerated in patients with major depressive disorder)	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of serotonin toxicity[a]

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Saw palmetto *(Serenoa repens)*	5-alpha reductase inhibitors	May increase drug effect	May have additive effect to drug due to inhibitory effect on 5-alpha reductase	Level D *In vitro* study (Drug-herb interaction was not directly studied. Saw palmetto extract showed an inhibitory effect on 5-alpha reductase activity)	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Androgen (Testosterone and dihydrotestosterone)	May decrease drug effect	May have inhibtory effect on 5-alpha reductase	Level D *In vitro* study (Drug-herb interaction was not directly studied. Saw palmetto decreased the androgen-sensitive LNCaP human prostate cancer cell number in the presence of testosterone or dihydrotestosterone)	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level C Case report (Drug-herb interaction was not directly studied. Saw palmetto can lead to prolonged bleeding time)	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	CYP450 enzyme substrates (CYP1A2, CYP3A4, CYP2E1, CYP2D6)	May increase or decrease drug effect	May increase or decrease blood level of drugs via inhibition of these enzyme activities	Level B Human study (Study with 12 volunteers showed interaction with CYP1A2, CYP3A4, CYP2E1, CYP2D6 is unlikely) Level D *In vitro* study (Saw palmetto extract showed potent inhibition of CYP3A4, CYP2D6 and CYP2C9)	Unlikely	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Oestrogen	May decrease drug effect	May reduce the effect of oral contraceptive drugs through its antioestrogenic effects	Level B Human studies	Possible	High	Use with caution under supervision of a healthcare professional and monitor
	Oral contraceptive drugs	May decrease drug effect	May reduce the effect of oral contraceptive drugs through its antioestrogenic effects	Level B Human study	Possible	High	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Selenium	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level B Human study (study used 10 mcg/kg/day which exceeds the daily UL for adults)	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor. High-dosing of selenium is not recommended
	Barbiturate drugs (Phenobarbitol)	May increase drug effects	May prolong sedative effects of the drug	Level D Animal studies (studies used doses which far exceed the recommended UL in human adults)	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor. High-dosing of selenium is not recommended
	Corticosteroid drugs	Drug effect on nutrient	Selenium may be depleted by these drugs	Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
	Oral contraceptive drugs	Drug effect on nutrient	Selenium may be depleted by these drugs	Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
	Warfarin	May increase drug effect	May have additive effect to drug	Level D Animal studies (studies used doses which far exceed the recommended UL in human adults)	Possible	Moderate	Use with caution under supervision of a healthcare professional and increase INR monitoring frequency
Soy/Isoflavones *(Glycine max)*	Anticoagulant and antiplatelet agents	May decrease drug effect	Soy protein may decrease the anticoagulant effect of warfarin	Level B Human study and case report (Warfarin)	Possible	Moderate - High	Avoid concomitant use
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug	Level A Clinical trials	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypotension[d]
	Chemotherapeutic agents	May increase drug effect	Mechanism unknown	Level D *In vitro* study	Theoretical	Moderate - High	Avoid high doses (>7 g) prior to surgery. Use with caution under supervision of a healthcare professionaal and monitor
	CYP450 enzyme substrates (CYP2C9, CYP2E1, CYP3A4)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of CYP1A2 and CYP2E1 enzyme activities and induction of CYP2C9 and CYP3A4 enzyme activities	Level B Human studies (CYP2C9 and 3A4) Level D *In vitro* studies (CYP1A2) and animal study (CYP2E1)	Possible	Variable *(depending on drug or disease state)*	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Soy/isoflavones *(Glycine max)* *(cont)*	Diuretic drugs	May increase drug effect	May have additive diuretic effect to drug	Level D Animal study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Gemfibrozil	May increase drug side effect	May increase blood levels of drug	Level D Animal study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect to drug	Level A Clinical trials	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
	HMG-CoA reductase inhibitors (Atorvastatin, simvastatin)	May increase drug effect	May have additive effect to drug	Level A Clinical trials	Possible	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
	Monoamine oxidase inhibitors (MAOIs)	May increase drug effect	Tyramine in fermented soy products may cause additive blood pressure effect	Level D *In vitro* studies (fermented soy products contain tyramine)	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Organic anion-transporting polypeptides (OATPs)	May decrease drug effect	May reduce cellular uptake of drugs transported by OATP2B1	Level D *In vitro* study	Theoretical	Variable *(depending on drugs)*	Monitor patient
	P-glycoprotein substrates (Daunorubicin)	May increase drug effect	May increase blood level of drug via inhibition of P-gp	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Progesterone	May increase drug side effect	May have additive effect to drug	Level A Clinical trials	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Tamoxifen	May decrease drug effect	Soy may have estrogenic activity and may theoretically interfere with tamoxifen activity	Level D Animal study	Possible	Moderate - High	Avoid concomitant use
	Thyroid hormone	May decrease drug effect	Soy may decrease blood levels of drug	Level B Human study and case report	Possible	Moderate	Use with caution under super vision of a healthcare professional. Monitor patient for signs of hypothyroidism[b]

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
SPMs (Specialised pro-resolving mediators)	See **Omega-3 (EPA + DHA)**			See **Omega-3 (EPA + DHA)**			
St John's wort *(Hypericum perforatum)*	CYP450 enzyme substrates (CYP2C19, CYP3A4)	May increase or decrease drug effect	May increase or decrease blood levels of drug via induction of these enzyme activities	Level A Multiple studies with oral contraceptives, warfarin, protease inhibitors, reverse transcriptase inhibitors, simvastatin, atorvastatin, verapamil, irinotecan, imatinib, methadone, cyclosporin, tacrolimus, fexofenadine, nifedipine, midazolam, omeprazole, voriconazole	Likely	Variable *(depending on drug and disease state)*	Avoid or consult with healthcare professional before concomitant use
	CYP450 enzyme substrates (CYP2B6, CYP2C9, CYP2E1 and CYP1A2)	May increase or decrease drug effect	May increase or decrease blood levels of drug via induction of these enzyme activities	Level B Human study of the various CYP enzymes	Possible	Variable *(depending on drug and disease state)*	Avoid or consult with healthcare professional before concomitant use
	Digoxin	May decrease drug effect	St John's wort may decrease blood levels of this medication	Level A Clinical trials	Possible	Moderate	Avoid concomitant use
	Organic anion-transporting polypeptide (OATP) substrates	May decrease drug effect	Hyperforin may reduce cellular uptake of drugs transported by OATP2B1, when taken together	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient
	Pethidine and dextromethorphan	May increase drug side effect	May have additive serotonergic effect	Level D *In vitro* and animal studies	Theoretical	Moderate	Avoid concomitant use
	P-glycoprotein substrates	May decrease drug effect	St John's wort may decrease blood levels of these medications via induction of P-gp expression	Level A Clinical trials - interaction seen at doses over 2 g/d (dried herb)	Possible	Variable *(depending on drug and disease state)*	Avoid or consult with healthcare professional before concomitant use
	Photosensitising drugs	May increase drug side effect	Hypericin content of St John's wort may increase the possibility of photosensitivity reactions	Level C Case study of aminolevulinic acid. *In vitro* study	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of photosensitivity[i]

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
St John's wort *(Hypericum perforatum)* *(cont)*	Prescription antidepressants - tricyclics, SSRIs and SNRIs, MAOIs	May increase drug effect	St John's wort has additive serotonergic effects that can lead to serotonin toxicity when taking the respective antidepressants concomitantly	Level B Multiple case reports of serotonergic syndrome. Human study in patients taking amitriptyline. Case report of monoxidase activity	Likely	Moderate - High	Avoid concomitant use
	Triptans	May increase drug effect	May have additive serotonergic effect	Level C Case report	Possible	Moderate - High	Avoid concomitant use
Taurine	Antihypertensive drugs	May increase drug effect	May have additive effect to drug	Level A/B Meta-analysis and randomised controlled trials	Likely	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypotension[d]
Thyme *(Thymus vulgaris)*	Acetylcholinesterase (AChE) inhibitors and anticholinergics	May increase drug effect	May increase acetylcholine levels due to inhibition of acetylcholinesterase	Level D *In vitro* study	Theoretical	Moderate	Monitor patient for cholinergic effects
	Anticholinergics	May decrease drug effect	May decrease effectiveness of anticholinergic drugs	Level D *In vitro* study	Theoretical	Moderate	Monitor patient for anticholinergic effects
	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level D *In vitro* and animal studies	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	CYP450 substrates (CYP1A2, CYP34A)	May increase or decrease drug effect	May increase or decrease substrate blood levels by inhibition of these enzyme activities	Level D *In vitro* studies	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient
	Oestrogen	May decrease drug effect	May competitively inhibit drug activity	Level D *In vitro* study	Theoretical	Moderate	Monitor patient and assess the effectiveness of oestrogen therapy

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Tribulus *(Tribulus terrestris)*	Antihypertensive drugs (ACE inhibitors)	May increase drug effect	May have additive effect to drug	Level D *In vitro* and animal studies (Drug-herb interaction was not directly studied. 10 mg/kg of lyophilised aqueous extract of tribulus fruit decreased ACE activity in rats)	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypotension[d]
	Cisplatin	Herb effect on drug (May decrease renal side effects induced by cisplatin)	May decrease cisplatin accumulation in kidney via diuretic effect of tribulus	Level D Animal study (Tribulus fruit extract at dose 100, 300 and 500 mg/kg body weight provided protection against the cisplatin induced renal toxicity in mice)	Theoretical	Low	No evidence from human studies to support clinical recommendations
	Cyclophosphamide	Herb effect on drug (May improve reproductive damage induced by cyclophosphamide)	May have antioxidative effect	Level D Animal study (Tribulus dry extract ameliorated the damage induced by cyclophosphamide in mice testes)	Theoretical	Low	No evidence from human studies to support clinical recommendations
	Hypoglycaemic drugs	May increase drug effect	May have additive effect to drug	Level A Clinical trials (Drug-herb interaction was not directly studied. Tribulus showed a significant blood glucose-lowering effect in diabetic women compared to placebo)	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
Turmeric *(Curcuma longa)*	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug (antiplatelet effect) at high doses (over 15 g/d)	Level D *In vitro* studies find antiplatelet effect	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Antihypertensive drugs (Amlodipine)	May increase drug effect	May increase blood levels of drug	Level D Animal studies	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypotension[d]
	Chemotherapeutic agents	May increase or decrease drug effect	Antioxidant effect of curcumin may inhibit apoptosis	Level D Conflicting data *in vitro* study	Theoretical	Moderate - High	Avoid concomitant use
	CYP1A1 substrates	May increase or decrease drug effect	May increase or decrease substrate blood levels via inhibition of this enzyme activity	Level D *In vitro* and animal studies	Theoretical	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Turmeric *(Curcuma longa)* *(cont)*	CYP1A2 substrates	May increase or decrease drug effect	May increase or decrease substrate blood levels via inhibition of this enzyme activity	Level B Human studies	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	CYP2A6 substrates	May increase or decrease drug effect	May increase or decrease substrate blood levels via induction of this enzyme activity	Level B Human studies	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	CYP2D6 substrates	May increase or decrease drug effect	May increase or decrease substrate blood levels via induction of this enzyme activity	Level B/D *In vitro* study and a human study	Possible	Variable *(depending on drug and disease state)*	Monitor patient
	CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease substrate blood levels via inhibition of this enzyme activity	Level C Case report on tacrolimus	Possible	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect	Level B Human study (for glibenclamide)	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
	Norfloxacin	May increase drug effect	May increase blood levels of drug	Level D Animal study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Organic anion-transporting polypeptide (OATP) substrates	May increase drug effect	May increase drug absorption through inhibition of OATP proteins, when administered together	Level D *In vitro* and animal studies	Theoretical	Variable *(depending on drug and disease state)*	Monitor patient
	P-glycoprotein substrates	May increase drug effect	May increase drug blood levels via inhibition of P-gp	Level D Animal study	Theoretical	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Paclitaxel	May increase drug effect	May increase drug blood levels due to increased bioavailability	Level D Animal study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Turmeric *(Curcuma longa)* *(cont)*	Sulfasalazine	May increase drug effect	May increase drug blood levels	Level B Human studies	Possible	Moderate - High	Avoid concomitant use
Valerian *(Valeriana officinalis)*	Benzodiazepines (Lorazepam, alprazolam)	May increase inhibitory activitiy of drug and drug side effect	May have additive effect to drug by binding to the GABA receptors	Level C Case report (Case of patient self-medicating with valerian and passionflower while on 2 mg lorazepam)	Possible	Moderate - High	Avoid concomitant use
	CYP450 enzyme substrates (CYP3A4, CYP2D6)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition or induction of these enzyme activities	Level A Clinical trial (1000 mg of valerian tablet daily did not significantly change CYP3A4 and CYP2D6 activities) Level D *In vitro* studies showed moderate to potent CYP3A4 inhibitory effects by valerian. Another *in vitro* study showed an induction of CYP3A4 and CYP2D6 activities by valerian	Unlikely	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Efavirenz	Herb effect on drug (May prevent efavirenz-induced neuropsychiatric adverse effects)	May act on GABA-A receptor and boost melatonin release	Level A Clinical trial (4 weeks treatment of valerian 530 mg at night 1 hour before sleep improved neuropsychiatric adverse effects of efavirenz such as anxiety and insomnia)	Possible	Low	Use with caution under supervision of a healthcare professional and monitor
	UGT substrates (UGT1A1, UGT2B7) (Paracetamol, oestradiol, morphine)	May decrease excretion of drug	May have inhibitory effects on glucuronidation	Level D *In vitro* study (Inhibitory effects of valerian on the glucuronidation of paracetamol, oestradiol and morphine)	Theoretical	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
Vitamin A	Orlistat and cholestyramine	Drug effect on nutrient (May decrease nutrient effect)	Vitamin A absorption may be decreased by orlistat	Level A Clinical trials	Likely	Low	Assess nutrient status and supplement if indicated. Interaction may be minimised by separating dose of medication and vitamin A by at least 2 hours

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Vitamin A *(cont)*	Retinoids	May increase drug side effect	May have additive effect to drug	Level A Systematic review	Likely	High	Avoid concomitant use
	Tetracycline	May increase risk of benign intracranial hypertension	May have additive effect to drug	Level D Vitamin A and tetracycline are in the list of medications that may produce intracranial hypertension	Possible	High	Avoid concomitant use
Vitamin B2	Migraine drugs	Nutrient effect on drug (May increase drug effect)	Vitamin B2 found to have migraine preventive activity. No additive effect with antimigraine drugs investigated	Level B Human studies	Theoretical	Low	Supplementation may be beneficial
Vitamin B3	See **Niacin (Vitamin B3)**			See **Niacin (Vitamin B3)**			
Vitamin B6 (Pyridoxine, Pyridoxal 5 Phosphate)	Amiodarone	May increase drug side effects	May increase drug-induced photosensitivity	Level B Human studies	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of photosensitivity[i]
	Anticonvulsant drugs	Drug effect on nutrient	Vitamin B6 may be depleted by these drugs	Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
	Antihypertensive drugs	May increase drug effect	May have additive effect to drug	Level B Human study (one study showed that vitamin B6 supplementation at a dose of 5 mg/kg/day, significantly reduces systolic and diastolic BP in patients with essential hypertension. This equates to a dose of 200 mg/day)	Possible	Moderate	Monitor patient for signs of hypotension[d]. Avoid concomitant high dosing of vitamin B6 with these drugs
	Anti-tubercular agents (Isoniazid)	Drug effect on nutrient	Vitamin B6 may be depleted by these drugs	Level C Case studies	Possible	High	Monitor patient. Interaction likely to occur at high doses (≥200 mg/day) of vitamin B6

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Vitamin B6 (Pyridoxine, Pyridoxal 5 Phosphate) *(cont)*	Chemotherapeutic agents (Cisplatin and altretamine)	May decrease drug effect	May reduce drug response time when adminstered together	Level B Human observational study (study used 300 mg/m2 vitamin B6 daily for duration of the study. This is four-fold higher that the recommended daily UL)	Possible	Moderate	Monitor patient. Avoid concomitant high dosing of vitamin B6 with these drugs
	Oral contraceptives	Drug effect on nutrient	Vitamin B6 may be depleted by these drugs	Level A Clinical trials and population-based studies show conflicting results, however the recommendation is to maintain vitamin B6 levels	Possible	Low	Assess nutrient status and supplement if indicated
	Penicillamine	Drug effect on nutrient	Vitamin B6 may be depleted by these drugs	Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
	Phenobarbital	May decrease drug effect	May decrease blood levels and effects of the drug	Level B Human study (one study showed that 200 mg daily of vitamin B6 resulted in a 45% reduction in phenobarbitol blood levels. This is four-fold higher than the recommended daily UL	Possible	High	Avoid concomitant high dosing (≥200 mg/day) of vitamin B6 with this drug
	Phenytoin	May decrease drug effect	May decrease blood levels and effects of the drug	Level B Human study (study used 200 mg daily of vitamin B6 which is four-folder higher than recommended daily UL)	Possible	High	Avoid concomitant high dosing (≥200 mg/day) of vitamin B6 with this drug
Vitamin B12	Carbamazepine	Drug effect on nutrient	Vitamin B12 may be depleted by this drug with long-term use	Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
	Metformin	Drug effect on nutrient	Vitamin B12 may be depleted by this drug	Level B Human study	Likely	Moderate	Assess nutrient status and supplement if indicated
	Oral contraceptives	Drug effect on nutrient	Vitamin B12 may be depleted by this drug	Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
	Proton pump inhibitors, H_2-receptor antagonists	Drug effect on nutrient	Vitamin B12 may be depleted by this drug	Level B Human study	Likely	Moderate	Assess nutrient status and supplement if indicated

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Vitamin C	Aluminium-containing antacids	May increase drug side effect (especially in renal failure patients)	Vitamin C chelates aluminium and may increase aluminium absorption	Level B Case reports and human study	Possible	Moderate - High	Avoid concomitant use
	Antihypertensive drugs + Grape seed	May have opposing effect to drug	Unknown mechanism of the interaction	Level A Clinical trial (6 weeks treatment with both vitamin C 500 mg and grape seed polyphenol 1000 mg daily increased blood pressure in hypertensive patients)	Possible	Moderate - High	Avoid combination of vitamin C and grape seed in hypertensive patients
	Calcium channel blockers (Nifedipine)	Drug effect on nutrient (May decrease nutrient effect)	Calcium channel blockers may inhibit uptake of vitamin C by intestinal cells	Level D *In vitro* study	Theoretical	Moderate - High	Assess nutrient status and supplement if indicated
	Chemotherapeutic agents	May increase or decrease drug effect	Antioxidants like vitamin C may reduce the activity of chemotherapeutic drugs or may make chemotherapy more effective by reducing oxidative stress	Level D *In vitro* study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Desferrioxamine	May have opposing effect to drug	Vitamin C may cause transient deterioration of cardiac function with desferrioxamine	Level C Case reports	Possible	High	Avoid concomitant use
	Oestrogen	May increase drug effect	May increase blood levels of drug	Level B Human studies	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Paracetamol	May increase drug effect	High doses of vitamin C (>3 g) may decrease the elimination rate of paracetamol	Level B Human studies	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Protease inhibitors (Indinavir)	May decrease drug effect	May decrease blood levels of drug	Level B Open study	Possible	Moderate - High	Avoid concomitant use
	Thyroid hormone	Nutrient effect on drug	Vitamin C increases oral absorption of thyroid hormone	Level B Human studies (two studies showed that taking thyroid hormone with vitamin C 500-1000 mg improves thyroid hormone absorption)	Likely	Low	Advise patients to take levothyroxine and vitamin C supplements at least 4 hours apart
	Warfarin	May decrease drug effect	Vitamin C in high doses (>10 g/day) may cause diarrhoea and possibly reduce warfarin absorption	Level C Case study	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor. The recommendation for patients on wafarin is to avoid high-dose vitamin C (>10 g/day)

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Vitamin D3	Aluminium	May increase drug effect	May increase drug absorption	Level D Animal study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Anticonvulsants	Nutrient effect on drug (May decrease drug side effect)	Vitamin D3 improves bone mineral density and decreases the risk of bone-related side effects	Level A Clinical trials	Possible	Low	No significant adverse effect expected. Assess nutrient status and supplement if indicated
	Anticonvulsants (Carbamazepine, phenobarbital and phenytoin)	Drug effect on nutrient	Long-term use of these drugs (>6 months) may trigger the catabolism of vitamin D, thereby negatively affecting the absorption of calcium	Level B Lower quality human studies	Possible	Moderate	Assess calcium and vitamin D status and supplement if indicated
	Antiretrovirals (Efavirenz, emtricitabine and tenofovir)	Nutrient effect on drug (May decrease drug side effect)	Vitamin D3 decreases the risk of bone mineral density loss with the initiation of antiviral agents	Level A Clinical trials	Possible	Low	No significant adverse effect expected in humans. Assess nutrient status and supplement if indicated
	Atorvastatin	Nutrient effect on drug	May decrease blood level of drugs via induction of CYP3A4	Level B Human studies	Possible	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
	Bile acid sequesterants (Cholestyramine)	Drug effect on nutrient	Vitamin D absorption may be decreased by cholestyramine	Level A Conflicting data. One RCT found a significant reduction in vitamin D in the group taking cholestyramine. However, three other studies on the same class of medications reported the opposite findings	Possible	Low	Assess nutrient status and supplement if indicated. Interaction may be minimised by separating dose of medication and vitamin D by at least 2 hours
	Budesonide (oral)	Nutrient effect on drug (May increase drug efficacy)	Combination therapy may improve clinical outcome	Level A Clinical trials	Possible	Low	No significant adverse effect expected in humans. Use with caution under supervision of a healthcare professional and monitor
	Calcium channel blockers (Diltiazem and verapamil)	May decrease drug effect (Dose dependent)	May have opposing effect to drug. Decrease drug effect by causing hypercalcaemia with high doses of vitamin D3	Level C Case report	Possible	Moderate - High	Avoid concomitant use
	Chemotherapeutic agents	Drug effect on nutrient (May decrease nutrient effect)	Mechanism unknown	Level B Human studies	Possible	Moderate - High	Assess nutrient status and supplement if indicated

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Vitamin D3 *(cont)*	Cimetidine	Drug effect on nutrient (May decrease nutrient effect)	Cimetidine inhibits an enzyme involved in conversion of vitamin D to its active form in the liver and affect vitamin D metabolism in men	Level B Human studies	Possible	Moderate	Assess nutrient status and supplement if indicated
	CYP3A4 substrates	May decrease or increase drug effect	May decrease or increase blood levels of drug via inhibition or induction of these enzyme activities	Level B/D Lower quality human studies and *in vitro* studies	Possible	Variable *(depending on drug)*	Monitor patient
	Digoxin	May increase drug side effect	May increase drug effect via inhibition of P-gp	Level B Human study suggests no significant interaction	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Heparin and low-molecular-weight heparin (LMWH)	Drug effect on nutrient (May decrease nutrient effect)	Heparin and LMWH decrease the metabolism of vitamin D to its active form	Level B Human studies	Possible	Moderate - High	Assess nutrient status and supplement if indicated
	Orlistat	Drug effect on nutrient (May decrease nutrient effect)	Vitamin D absorption may be decreased by orlistat	Level A Clinical trials	Likely	Low	Assess nutrient status and supplement if indicated. Interaction may be minimised by separating dose of medication and vitamin D by at least 2 hours
	Sirolimus	May decrease drug effect	May increase the metabolism of sirolimus	Level B Human studies	Theoretical	High	Avoid concomitant use
	Thiazide diuretics	May increase drug side effect	Vitamin D3 may increase the risk of hypercalcaemia if taken with calcium supplements and/or thiazide diuretics	Level A Multiple case reports. Clinical trial in hypoparathyroid patients taking vitamin D and thiazide diuretics	Likely	Moderate	Use with caution under supervision of a healthcare professional and monitor
Vitamin E	Anticoagulant and antiplatelet agents	May increase drug effect	Vitamin E may increase risk of bleeding	Level A Conflicting data. Clinical studies have found no interaction with warfarin or aspirin, or inhibition of platelet aggregation. Case reports of interaction with warfarin and reduced clotting exist	Unlikely	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	Chemotherapeutic agents	May decrease drug effect	Antioxidant effects may reduce activity of drug	Level D *In vitro* study	Theoretical	Moderate - High	Avoid concomitant use

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Vitamin E *(cont)*	Cisplatin	Nutrient effect on drug (May decrease drug side effect)	Vitamin E may decrease the incidence and severity of neurotoxicity caused by cisplatin	Level A Clinical trials in patients taking vitamin E and cisplatin	Likely	Low	Use with caution under supervision of a healthcare professional and monitor
	CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via induction of this enzyme activity	Level D *In vitro* study	Theoretical	Variable *(depending on drug and disease state)*	Use with caution under supervision of a healthcare professional and monitor
	Nitrates (Nitroglycerine)	Nutrient effect on drug (May decrease drug side effect)	Vitamin E may prevent nitrate tolerance when given concurrently with transdermal nitroglycerin	Level A Clinical trial	Possible	Low	Use with caution under supervision of a healthcare professional and monitor
	Orlistat	Drug effect on nutrient (May decrease nutrient effect)	Vitamin E absorption may be decreased by orlistat	Level A Clinical trial	Likely	Low	Assess nutrient status and supplement if indicated. Interaction may be minimised by separating dose of medication and vitamin E by at least 2 hours
	Selumetinib	May increase drug side effect	May have additive anticoagulant effect	Level C Case studies based on anticoagulant effects of high-dose vitamin E	Possible	High	Use with caution under supervision of a healthcare professional and monitor
	Warfarin	May increase drug effect	The use of more than 400 IU/day of vitamin E with warfarin might increase INR and the risk of bleeding	Level B Human study (study used high-dose vitamin E supplementation 1000 IU/day for 12 weeks)	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Vitamin K	Anticoagulant and antiplatelet agents	May decrease drug effect	Vitamin K may decrease activity of warfarin and other coumarin (oral) anticoagulants. Avoid changes in vitamin K intake whilst taking these drugs	Level A Clinical trials and meta-analyses	Likely	Moderate - High	Avoid concomitant use
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect	Level D Human study that suggests higher intake of vitamin K1 is associated with increased insulin sensitivity and reduced postprandial glucose levels in adults but no direct study between vitamin K and hypoglycaemic drugs	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Vitamin K *(cont)*	Orlistat	Drug effect on nutrient	Vitamin K absorption may be decreased by orlistat	Recommendation from manufacturer	Possible	Low	Assess nutrient status and supplement if indicated. Interaction may be minimised by separating dose of medication and vitamin K by at least 2 hours
Vitex *(Vitex agnus-castus)*	CYP2C19 and CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity	Level D *In vitro* study	Theoretical	Variable *(depending on drug)*	Monitor patient. Clinical relevance has yet to be determined
	Dopamine receptor antagonist and agonist	May increase or decrease drug effect	Binding to dopamine-2 receptor and suppresses prolactin release due to dopamine agonistic effects of vitex	Level D *In vitro* study (Drug-herb interaction was not directly studied)	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Oestrogen, contraceptive drugs	May increase or decrease drug effect	Via hormone modulating activity	Level D *In vitro* and animal studies (Drug-herb interaction was not directly studied. Vitex may exhibit oestrogen receptor binding effects and induce progesterone receptor expression)	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
White willow *(Salix alba)*	Acetazolamide	May increase drug side effect	May have additive adverse effect to drug as white willow contains salicin, a plant salicylate which may increase unbound plasma level of acetazolamide	Level C Case report	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug as white willow contains salicin, a plant salicylate	Level B Cohort study reported increased self-reported bleeding when taken with warfarin. Clinical trial using herb alone found a mild antiplatelet effect	Possible	Moderate - High	Avoid concomitant use
	CYP450 substrates (CYP2C19, CYP1A2, CYP3A4)	May increase or decrease drug effect	May increase or decrease blood levels of drug through inhibition of these enzymes	Level D *In vitro* study	Theoretical	Variable *(depending on drug)*	Monitor patient. Clinical relevance has yet to be determined

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Withania *(Withania coagulans)*	Hypoglycaemic drugs (Glipizide)	May increase drug effect	May have additive effect to drug	Level D Animal study (Co-administration of extract of *Withania coagulans* Dunal dried fruit (1000 mg/kg) and glipizide (1 mg/kg or 2.5 mg/kg) for 4 weeks in rats)	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]
Withania *(Withania somnifera)*	See **Ashwangandha**			See **Ashwangandha**			
Zinc	ACE inhibitors, angiotensin receptor blockers, thiazide diuretics	Drug effect on nutrient (May decrease nutrient effect)	Urinary zinc excretion may be increased with long-term use of these drugs	Level A Clinical trials	Possible	Low	Assess nutrient status and supplement if indicated
	Cefalexin	May decrease drug effect	Zinc may decrease absorption of drug by chelating with drug	Level B Human study	Possible	High	Interaction may be minimised by separating dose of zinc at least 3 hours after taking cefalexin
	Hypoglycaemic drugs	Nutrient effect on drug (May increase drug efficacy)	Low zinc status is common in diabetic patients. Zinc supplementation and normalisation of zinc levels has been shown to improve glycaemic control	Level A Clinical trials	Possible	Low	Assess nutrient status and supplement if indicated. Monitor blood glucose level and alter drug dose if required under the supervision of a healthcare professional
	Integrase inhibitors	May decrease drug effect	May decrease blood level of drug by chelating with drug	Level A Systematic review	Likely	High	Avoid concomitant use
	Penicillamine	May decrease drug effect	Zinc may decrease the activity of penacillamine	Level A Clinical trial	Possible	Moderate	Interaction may be minimised by separating dose of medication and zinc by at least 2 hours
	Tetracycline or quinolone antibiotics (not doxycycline)	May decrease drug effect	Zinc may decrease the absorption and blood levels of these drugs	Level B Multiple studies	Possible	Moderate	Interaction may be minimised by taking tetracycline at least 2 hours before, or 4-6 hours after zinc supplementation
	Thrombopoietin receptor agonists (Eltrombopag)	May decrease drug effect	May bind to the drug decreasing its absorption	Level A/B Human clinical studies	Possible	High	Monitor patient. Interaction may be minimised by taking medication at least 4 hours before or after zinc supplementation

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION	EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Ziziphus *(Ziziphus jujuba var. spinosa)*	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug	Level D Animal and *in vitro* study	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
	CNS Depressant/ sedative drugs	May increase drug effect	May have additive sedative effects when taken with CNS depressants	Level A/B Meta-analysis (in which small RCTs were included); small RCTs	Possible	High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of sedation
	CYP450 enzyme substrates (CYP1A2)	May decrease drug effect	May decrease blood levels and effects of these drugs by induction of these enzyme activities	Level D Animal studies	Possible	Moderate	Monitor patient. Clinical relevance has yet to be determined
	Hypoglycaemic drugs	May increase drug effect	May have additive effect to drug	Level D Animal studies (There are conflicting results in clinical trials regarding the impact of ziziphus supplementation on fasting blood glucose levels in diabetic patients)	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia[c]

Appendix: Key to condition signs and symptoms

a Signs of serotonin toxicity include tremor, incoordination, mental state changes, shivering, sweating, fever, and diarrhoea.

b Signs of hypothyroidism include fatigue, cold intolerance, weight gain, constipation, dry skin, myalgia, and menstrual irregularities.

c Signs of hypoglycaemia include a sensation of hunger, sweating, dizziness, tiredness (fatigue), blurred vision, trembling or shaking, sudden pallor, rapid pulse, or palpitations.

d Signs of hypotension include dizziness, light-headedness, fainting, blurred vision, palpitations, confusion, nausea, and general weakness.

e Signs of hyperthyroidism include heat intolerance, tremor, palpitations, anxiety, weight loss despite a normal or increased appetite, increased frequency of bowel movements, and shortness of breath

f Signs of lithium toxicity include extreme thirst and frequent urination, nausea, and vomiting.

g Signs of hypercalcaemia include polyuria, polydipsia, dehydration, anorexia, nausea, muscle weakness, and changes in sensorium.

h Signs of hyperkalaemia include muscle fatigue, weakness, paralysis, arrhythmia, and nausea.

i Signs of photosensitivity include a rash or sunburn, with or without redness, scaling, itching, and sometimes blisters and spots that resemble hives.

INDEX

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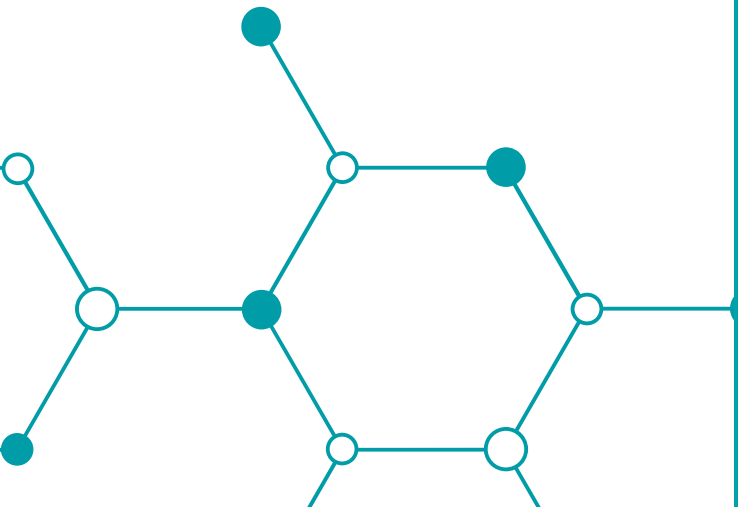

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