



11TH EDITION

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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

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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
	<i>in vitro</i> 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	<i>in vitro</i> 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
Acetyl-L-Carnitine	Antidepressant drugs (Serotonergic drugs)	May increase drug effect	May increase the serotonergic effects of these drugs when taken together
	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
	Warfarin	May increase drug effect	May have additive effect to drug
Alpha Lipoic Acid	Anticoagulant and antiplatelet agents	May increase drug effect	May increase risk of bleeding when used alongside these drugs
	Anticonvulsants (Valproate)	May increase drug effect	May decrease the <i>in vitro</i> formation of VA-CoA in a concentration-dependent manner
	Chemotherapeutic agents	May increase or decrease drug effect	Antioxidants may decrease the activity of chemotherapy or make chemotherapy more effective
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect
	Thyroid hormone (Levothyroxine)	May decrease drug effect	Co-administration of levothyroxine with ALA may decrease conversion to active T3 form

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D <i>In vitro</i> study. No clinical studies in humans	Theoretical	Moderate	Significant interaction unlikely, however, monitor patient for signs of serotonin toxicity ^a
Level B Human study	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor the patient for signs of hypothyroidism ^b
Level D Animal study	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D Animal study. ALA was shown to significantly decrease the <i>in vitro</i> formation of VA-CoA in a concentration-dependent manner	Theoretical	Moderate	Monitor patient. Clinical significance is uncertain until human studies are conducted
Level D Animal study	Theoretical	Moderate - High	Avoid concomitant use
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
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
Andrographis <i>(Andrographis paniculata)</i>	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	Antihypertensive drugs	May increase drug effect	May increase the risk of hypotension when used with antihypertensive drugs
	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
	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
	Immunosuppressants	May decrease drug effect	May have opposing effect to drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal and <i>in vitro</i> study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level D Animal studies. Animal research suggests that andrographis has hypotensive effects	Possible	Moderate	Monitor patient for signs of hypotension ^d
Level D Animal studies	Possible	Low	If taking andrographis long-term, then monitor the effectiveness of the medication and consider alternative NSAIDs
Level D Animal and <i>in vitro</i> study	Theoretical	Variable (depending on drug and disease state)	Monitor patient
Level C Case report	Possible	Moderate - High	Avoid concomitant use

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Ashwagandha (<i>Withania somnifera</i>)	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect
	Benzodiazepines (Diazepam)	May increase drug effect	May have additive effect to drug due to GABAergic activity
	Chemotherapeutic agents (Doxorubicin, cyclophosphamide, epirubicin, fluorouracil)	Herb effect on drug (May improve chemotherapy-induced fatigue)	Unknown mechanism of the interaction
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect
	Psychotropic drugs (Olanzapine, typical antipsychotics, antidepressants, mood stabilisers, anti-anxiety, 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
	Thyroid hormone	May increase drug effect	May have additive drug effects

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal study	Possible	Moderate	Monitor patient for signs of hypotension ^d
Level D Animal study (Co-administration of extract of <i>Withania somnifera</i> (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
Level B Human study (<i>Withania somnifera</i> 6 g/d throughout 6 months chemotherapy in breast cancer patients)	Possible	Low	Use with caution under supervision of a healthcare professional and monitor
Level B Human study	Possible	High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia ^c
Level A Clinical trials (Adjunctive treatment with extract of <i>Withania somnifera</i> 1000 mg/d improved negative symptoms and stress in patients with recent exacerbation of schizophrenia. Another clinical trial showed extract of <i>Withania somnifera</i> 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
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
Astragalus (<i>Astragalus membranaceus</i>)	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect
	Chemotherapeutic agents (Cisplatin, vinorelbine, cyclophosphamide)	Herb effect on drug (May decrease drug side effect)	No direct interaction
	Diuretic drugs	May increase drug effect	May have additive diuretic effect
	Immunosuppressants	May decrease drug effect	Astragalus may have immunostimulant activity
	Lithium	May increase drug effect	Theoretically astragalus, through its diuretic action, might reduce excretion and increase levels of lithium
	Oestrogen	May increase or decrease drug effect	Astragalus may cause a phytoestrogenic effect
	P-glycoprotein	May increase drug effect	Astragalus may inhibit P-gp pump efflux
Beta-carotene	Orlistat and plant sterols	Drug effect on nutrient (May decrease nutrient effect)	Beta-carotene absorption may be decreased by these drugs
Bilberry (<i>Vaccinium myrtillus</i>)	Antibiotics (Doxycycline and cephalosporins)	Herb effect on drug (The combination may have an immunostimulatory effect)	May improve the viability of thymocytes
	Anticancer agent (Erlotinib)	May decrease drug effect	Bilberry anthocyanins may modulate the growth-inhibitory effect of erlotinib

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human study	Unlikely	Low	Monitor patient. Significant interaction is unlikely
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
Level B Human study	Possible	Low	Monitor patient. Significant interaction unlikely
Level D Animal and <i>in vitro</i> study	Theoretical	Moderate - High	Avoid concomitant use
Level D Animal study	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of lithium toxicity ^f
Level D <i>In vitro</i> study	Theoretical	Low-Moderate	Monitor patient. Significant interaction unlikely
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug and disease state)	Monitor patient. Significant interaction unlikely
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
Level D <i>In vitro</i> study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> 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
Bilberry (<i>Vaccinium myrtillus</i>) (cont)	Anticoagulant and antiplatelet agents	May increase risk of bleeding	May have additive effect to drug
	Antihypertensive drugs (ACE inhibitors)	May increase drug effect	May have additive effect to drug
	Hypoglycaemic drugs	May increase drug effect	May have additive effect to drug
Black cohosh (<i>Cimicifuga racemosa</i>)	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
	CYP2D6 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity
	HMG-CoA reductase inhibitors (Statins) (Atorvastatin and simvastatin)	May increase drug effect and risk of elevated liver function	May have additive effect to drug
	Hepatotoxic drugs	May increase the risk of liver damage	May have an additive negative effect on the liver when taken with hepatotoxic drugs
	Organic anion-transporting polypeptide (OATP) substrates	May decrease drug effect	May decrease drug levels via inhibition of OATP function, thereby reducing drug absorption

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
Level D <i>In vitro</i> 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
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 ^e
Level D <i>In vitro</i> study on mouse breast cancer cell line	Theoretical	Moderate - High	Avoid concomitant use
Level B Human study	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level C Case reports	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level C Case reports	Possible	High	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug and disease state)	Monitor patient. Significant interaction unlikely

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Boswellia (<i>Boswellia serrata</i>)	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
	Immunosuppressants	May decrease drug effect	May have opposing effect to drug
	Multi-drug resistant protein (MRP)	May decrease drug effect	May decrease drug levels by inhibiting MRP2 function, thereby reducing drug absorption
	Organic anion-transporting polypeptide (OATP) substrates	May decrease drug effect	May decrease drug levels by inhibiting OATP function, thereby reducing drug absorption
	P-glycoprotein	May increase drug effect	Boswellia may inhibit P-gp pump efflux

Brahmi (<i>Bacopa monnieri</i>)	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
	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
	Thyroid hormone	May increase drug effect	May have an additive effect to drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Moderate - High	Avoid concomitant use
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug and disease state)	Monitor patient. Significant interaction unlikely
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug and disease state)	Monitor patient. Significant interaction unlikely
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug and disease state)	Monitor patient. Significant interaction unlikely
Level A Clinical trials	Likely	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
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
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
	Antacids	Drug effect on nutrient (May increase nutrient effect)	May increase retention of proteolytic effect of bromelain when in combination with antacids
	Anticoagulant and antiplatelet agents	May increase risk of bleeding	May have additive effect to drug
	Cisplatin	May increase drug effect	Bromelain may increase apoptosis and autophagy
	CYP450 enzyme substrates (CYP2C9)	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of these enzyme activities
	NSAIDs (Naproxen)	May increase drug side effects	Mechanism unclear
	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

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
<p>Level A</p> <p>Clinical trials (160 mg bromelain appeared to increase intraoperative amoxicillin levels in tissue, serum and skin samples. The effect persisted 3 hours after surgery)</p>	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
<p>Level D</p> <p>Animal and <i>in vitro</i> study (Oral bromelain retained substantial proteolytic activity throughout the gastrointestinal tract when in combination with antacids)</p>	Theoretical	Low	No evidence from human studies to support clinical recommendations
<p>Level B</p> <p>Human study (Drug-herb interaction was not directly studied. Bromelain showed antiplatelet and anticoagulant effect)</p>	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
<p>Level D</p> <p><i>In vitro</i> study (Bromelain 25-50 mg/mL decreased IC50 value of cisplatin in malignant peritoneal mesothelioma cells)</p>	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
<p>Level D</p> <p><i>In vitro</i> study</p>	Possible	Variable (depending on drug and disease state)	Monitor patient. Significant interaction unlikely
<p>Level C</p> <p>Case report (Ecchymosis developed on forearms after taking naproxen with bromelain)</p>	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
<p>Level B</p> <p>Human study</p>	Possible	Moderate	Interaction may be minimised by separating the administration of medication and bromelain by at least 4 hours

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Calcium	Anticonvulsants	Drug effect on nutrient	Anticonvulsants may reduce intestinal absorption of calcium
	Antiretrovirals (Integrase inhibitors - dolutegravir, elvitegravir, raltegravir)	May decrease drug effect	Calcium may reduce blood levels of dolutegravir, elvitegravir and raltegravir through chelation
	Beta-blockers (Atenolol, sotalol)	May decrease drug effect	Calcium may decrease absorption of atenolol and sotalol
	Bisphosphonates, tetracycline or quinolone antibiotics, thyroid hormones	May decrease drug effect	Calcium may decrease the absorption and efficacy of these drugs
	Calcipotriol (Daivonex)	May increase the risk for hypercalcaemia	Theoretically, combining calcipotriol, a vitamin D analogue, with calcium supplements might increase the risk of hypercalcaemia
	Calcium channel blockers (Verapamil, diltiazem)	May decrease drug effect	Calcium may decrease the hypotensive effect of verapamil
	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
	Corticosteroids	Drug effect on nutrient	Corticosteroids may reduce intestinal absorption of calcium and increase renal calcium excretion, leading to hypocalcaemia
	Iron	May decrease mineral absorption	Calcium may briefly interfere with iron absorption, but no long term effects are apparent

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human studies	Likely	Moderate	Assess nutrient status and supplement if necessary
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
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
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
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 ⁹
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
Level C Case report	Possible	High	Avoid concomitant use
Level A Meta-analyses	Likely	Moderate - High	Assess nutrient status and supplement if necessary
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
Calcium (<i>cont</i>)	Lithium	May increase risk for hypercalcaemia	Long-term lithium use may lead to hyperparathyroidism and hypercalcaemia in a significant number of patients
	Proton pump inhibitors	Drug effect on nutrient	Proton pump inhibitors may reduce intestinal calcium absorption, leading to hypocalcaemia, especially with long-term use
	Thiazide diuretics	May increase drug side effect	Calcium may increase the risk of hypercalcaemia with these drugs
	Thyroid hormone (Levothyroxine)	May decrease drug effect	Calcium (carbonate, acetate, and citrate) may reduce the absorption and subsequent efficacy of levothyroxine
Carnitine	Thyroid hormone	May decrease drug effect	L-carnitine blocks entry of thyroid hormone into the cell nucleus
	Warfarin	May increase drug effect	L-carnitine might increase the anticoagulant effects of warfarin
Celery (<i>Apium graveolens</i>)	Antidepressant and anxiolytic drugs	May increase drug effect	May have additive antidepressant and anti-anxiety effects

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human studies	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypercalcaemia ⁹
Level B Human studies	Likely	Moderate	Assess nutrient status and supplement if necessary
Level C Case reports	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
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
Level B Human study	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypothyroidism ^b
Level D Animal study	Possible	High	Use with caution under supervision of a healthcare professional and monitor
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
Celery (<i>Apium graveolens</i>) (cont)	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug
	CYP1A2 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity
	Photosensitising drugs	May increase drug effect	May have additive effect to drug, increasing photosensitivity reactions
	Thyroid hormone	May decrease drug effect	May decrease blood levels of drug
	Venlafaxine	May increase drug effect	Celery may increase blood levels of venlafaxine by inhibition of CYP2D6
Chaste tree	See <i>Vitex (Vitex agnus-castus)</i>		
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
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

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
Level D Animal and <i>in vitro</i> study	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies	Theoretical	Low	Monitor patient. Significant interaction unlikely
Level C Case reports	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypothyroidism ^b
Level C Case reports	Possible	Moderate - High	Avoid concomitant use
See <i>Vitex (Vitex agnus-castus)</i>			
Level C Case report	Possible	Moderate - High	Avoid concomitant use
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
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
	Thyroid hormone (Levothyroxine)	May decrease drug effect	May decrease blood levels of drug by reducing absorption
	NSAIDs (Aspirin and indomethacin)	Drug effect on nutrient (May increase blood levels of nutrient)	May increase the absorption of chromium

Co-enzyme Q10	Anticoagulant and antiplatelet agents	May increase or decrease drug effect	CoQ10 may have procoagulant or anticoagulant effect
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug
	Beta-blockers	Drug effect on nutrient (May decrease nutrient effect)	CoQ10 levels may be decreased by these drugs
	Chemotherapeutic agents (Anthracyclines such as daunorubicin, doxorubicin)	Nutrient effect on drug (May decrease drug side effect)	Despite the potential benefits of CoQ10 in preventing cardiotoxicity, it is unknown if CoQ10 diminishes the antineoplastic effect of doxorubicin therapy

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
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
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
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
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
Level D <i>In vitro</i> studies found beta blockers inhibited mitochondrial CoQ10 enzymes	Theoretical	Low	Assess nutrient status and supplement if indicated
Level A Clinical trial in leukaemia and lymphoma patients	Possible	Low	CoQ10 doesn't appear to affect blood levels of these chemotherapeutic agents, however use with caution under supervision of a healthcare professional

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Co-enzyme Q10 (<i>cont</i>)	HMG-CoA reductase inhibitors (Statins)	Drug effect on nutrient (May decrease nutrient effect)	CoQ10 levels may be depleted by these drugs
	HMG-CoA reductase inhibitors (Statins)	Nutrient effect on drug (May decrease drug side effect)	CoQ10 may decrease myalgia associated with statin use
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect
Coleus (<i>Coleus forskolii</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug
	Calcium channel blockers (Verapamil, nifedipine, diltiazem)	May increase drug effect	May have additive coronary vasodilatory effects
	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
	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
Cordyceps (<i>Cordyceps sinensis</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
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
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
Level D Animal studies	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
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
Level B Human studies	Likely	High	Avoid concomitant use
Level D <i>In vitro</i> study, animal study	Theoretical	Variable (depending on drug and disease state)	Monitor patient
Level B Human studies	Likely	High	Avoid concomitant use
Level C/D Case study and <i>in vitro</i> 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
Cordyceps (<i>Cordyceps sinensis</i>) (cont)	Immunosuppressants	May increase or decrease drug effect	Cordyceps exhibits both immunostimulant and immunosuppressive effects
Cranberry (<i>Vaccinium macrocarpon</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May increase blood levels of drug
	CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity
	Organic anion-transporting polypeptide (OATP) substrates	May decrease drug effect	May decrease drug levels by inhibiting OATP function, thereby reducing drug absorption
	Tacrolimus	May decrease drug effect	May decrease blood levels of drug
Dong quai (<i>Angelica sinensis</i>)	ACE inhibitors (Lisinopril)	May increase drug effect	May potentiate the effects of the drug and potentiate anaemia
	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	Aspirin	May increase drug effect	May have additive effect to drug
	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

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human studies Level D <i>In vitro</i> and animal studies	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level A Conflicting data. Clinical trials suggest no evidence of increasing drug effects with cranberry juice. Case reports exist. <i>In vitro</i> studies suggest cranberry effect on warfarin metabolism (CYP3A4 minor metaboliser)	Unlikely	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level C Case report	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies and <i>in vivo</i> animal studies	Theoretical	Moderate	Monitor patient. Significant interaction unlikely
Level C Case report	Possible	High	Avoid concomitant use
Level D Animal study	Theoretical	Moderate	Monitor patient
Level C Several case reports and animal studies	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level A Clinical trials	Unlikely	High	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies	Theoretical	Moderate	Monitor patient

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Dong quai (<i>Angelica sinensis</i>) (cont)	Oestrogen	May decrease drug effect	May decrease effect of the drug by competing for oestrogen receptors
	Warfarin	May increase drug effect	May have additive effects to the drug and increase INR
Echinacea (<i>Echinacea angustifolia</i> / <i>Echinacea purpurea</i>)	Chemotherapeutic agent (Etoposide)	May increase drug effect	May increase blood levels of drug via inhibition of CYP1A2, CYP2C19, CYP2C9, CYP3A4
	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
	CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via induction of this enzyme activity
	Immunosuppressants	May increase drug side effect	May have opposing effect to drug
	P-glycoprotein	May increase drug effect	May inhibit P-glycoprotein activity, increasing drug effect in the body

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D <i>In vitro</i> studies	Theoretical	Moderate	Monitor patient
Level C Case studies	Likely	High	Avoid concomitant use
Level C Case report involving concurrent use of etoposide, cisplatin, and echinacea. Patient developed profound thrombocytopenia	Possible	Moderate - High	Avoid concomitant use
Level B Human studies	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level B Human studies	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level B Animal studies, <i>in vitro</i> and <i>in vivo</i> evidence of immunomodulatory effect. No case report evidence	Possible	Moderate - High	Avoid concomitant use
Level D <i>In vitro</i> studies	Theoretical	Variable (depending on drug and disease state)	Monitor patient

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
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
	Antiretrovirals (Lopinavir/Ritonavir)	May increase drug effect	May increase blood levels of drug
	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
	Lithium	May decrease drug effect	May decrease drug levels in the body
	Phenothiazines	May increase drug side effect	May lower seizure threshold
Fenugreek (<i>Trigonella foenum-graecum</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	CYP2C9 and CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease levels of these drugs via inhibition of these enzyme activities
	Hypoglycaemic drugs	May increase drug effect	May have additive effect to drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
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
Level D <i>In vitro</i> study	Possible	Low	Monitor patient. Significant interaction unlikely
Level C Case study	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
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
Level C Case report in patients with arrhythmia using fenugreek capsule and warfarin	Possible	Moderate - High	Avoid concomitant use
Level D Animal studies	Theoretical	Moderate	Monitor patient
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
Fenugreek (<i>Trigonella foenum-graecum</i>) (cont)	Metoprolol	May increase drug effect	May have additive effect to drug
	SSRI drugs	May increase drug effect	May have additive effect to drug
Feverfew (<i>Tanacetum parthenium</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	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
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
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect depending on fish oil dose
	Chemotherapeutic agents (Cisplatin, oxaliplatin, irinotecan)	May decrease drug effect	May cause compound resistance
	Glucocorticoid drugs (Dexamethasone)	May increase drug effect	May increase drug levels and contribute to drug-induced muscular atrophy

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal study	Possible	Moderate	Monitor patient for signs of hypotension ^d
Level C Case study	Possible	Moderate	Monitor patient for signs of serotonin toxicity ^a
Level B Conflicting data. <i>In vitro</i> and <i>in vivo</i> 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
Level D <i>In vitro</i> study found low inhibitory activity	Theoretical	Variable (depending on drug and disease state)	No significant adverse effect expected. Monitor patient.
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
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
Level C Case report	Possible	Moderate - High	Avoid concomitant use
Level D Animal studies	Possible	Low	Monitor patient

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Fish oil <i>(cont)</i>	Immunosuppressants (Ciclosporin, sirolimus, tacrolimus)	May increase drug effect	May increase drug levels and adverse drug effects
	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
Flaxseed oil	Antihypertensive drugs	May increase drug effect. Dose dependent	May have additive hypotensive effect. Dose dependent
	HMG-CoA reductase inhibitors (Statins)	May increase drug effect	May increase drug levels and adverse drug effects
	Co-trimoxazole, sulfasalazine, phenytoin, phenobarbital, primidone and methotrexate	Drug effect on nutrient (May decrease blood levels of nutrient)	May decrease folic acid levels
Folic acid	Fluorouracil and capecitabine	May increase drug side effect	Folic acid may increase the toxicity of fluorouracil and capecitabine
	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
	Phenytoin	May decrease drug effect	Folic acid may decrease the efficacy of phenytoin

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
Level A Conflicting data. Human studies	Unlikely <i>(possible with high doses)</i>	Moderate - High	Interaction unlikely at normal doses. Use with caution under supervision of a healthcare professional and monitor
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
Level A Retrospective study on ADRs	Possible	Moderate	Monitor patient
Level C Multiple case reports	Possible	Moderate - High	Assess and monitor nutrient status and supplement if indicated
Level C Case reports	Possible	Moderate - High	Avoid concomitant use
Level A Clinical trials	Likely	Moderate - High	Follow your local medical association recommendations for concurrent use of folic acid and methotrexate
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
Garlic <i>(Allium sativum)</i>	Anticoagulant and antiplatelet agents	May increase drug effect depending on formulation and dose	May increase the risk of bleeding with these medications
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug. Dose dependent
	Cholesterol-lowering drugs	May increase drug effect	May have additive effects to the drug
	CYP2E1 substrates	May increase drug effect	May increase blood levels of substrates via inhibition of this enzyme activity
	Hepatic CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of hepatic CYP3A4 enzyme activity
	Hypoglycaemic agents	May increase drug effect	May have additive hypoglycaemic effect
	Intestinal CYP3A4 substrates (Saquinavir)	May decrease drug effect	May decrease blood levels of drug via induction of intestinal CYP3A4 enzyme activity
	Intestinal P-glycoprotein substrates	May decrease drug effect	May decrease blood levels of substrates via upregulation of intestinal ABCB1 or ABCC2 activity
	Isoniazid	May decrease drug effect	May decrease drug effect possibly by inhibiting absorption, but mechanism not clear

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
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
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
Level B <i>In vitro</i> and open studies using chlorzoxazone	Possible	Variable (depending on drug and disease state)	Monitor patient
Level C Case report	Possible	Variable (depending on drug and disease state)	Monitor patient
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 ^e
Level B Human study	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level B <i>In vitro</i> 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
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
Ginger (<i>Zingiber officinale</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May increase the risk of bleeding with these medications
	Calcium channel blockers	May increase drug effect	May have additive hypotensive effects
	Ciclosporin	May decrease drug effect	May decrease blood level of drug
	CYP2C9 and CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease levels of these drugs via inhibition of these enzyme activities
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effects when taken in high doses
	Losartan	May increase drug effect	May increase drug level and have an additive effect to drug
	Metronidazole	May increase drug effect	May increase absorption and plasma half life
	P-glycoprotein	May increase drug effect	May inhibit P-glycoprotein activity, increasing drug effect in the body
	Tacrolimus	May increase drug effect	May increase blood levels of drug via unknown mechanism

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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 <i>in vitro</i> 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
Level D <i>In vitro</i> and animal studies	Theoretical	Moderate	Monitor patient for signs of hypotension ^d
Level D Animal study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies	Theoretical	Variable (depending on drug or disease state)	Monitor patient
Level B/D Human studies and animal studies	Theoretical	Moderate	Monitor patient for signs of hypoglycaemia ^e
Level D Animal study. Single dose only, continuous use not investigated	Possible	Moderate	Monitor patient
Level D Animal study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies	Theoretical	Variable (depending on drug or disease state)	Monitor patient
Level D Animal study	Theoretical	High	Avoid concomitant use

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Ginkgo (<i>Ginkgo biloba</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May increase the risk of bleeding with these medications
	Anticonvulsants (Phenylbarbitone, sodium valproate, phenytoin)	May decrease drug effect	May increase risk of seizure
	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
	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
	CYP2C19 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via induction of this enzyme activity
	Efavirenz	May decrease drug effect	May increase blood levels of drug due to possible induction of CYP3A4 and P-glycoprotein
	Hypoglycaemic drugs	May increase or decrease drug effect	Ginkgo may increase or decrease blood glucose levels
	Nifedipine	May increase drug effect	May increase blood level of drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
Level C Case reports	Possible	Moderate - High	Use only under supervision of healthcare professional and monitor phenytoin blood concentration
Level A Meta-analysis and studies	Likely	Low	No significant adverse effect expected
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug or disease state)	Monitor patient
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
Level C Case report	Possible	Moderate - High	Avoid concomitant use
Level B Conflicting data. Clinical trials and human studies found ginkgo had a variable effect on drug activity. Animal and <i>in vitro</i> studies suggest ginkgo may reduce insulin resistance	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
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
Ginkgo (<i>Ginkgo biloba</i>) (cont)	Raltegravir	May increase drug effect	May increase blood level of drug
	Sofosbuvir	May increase drug effect	May increase blood levels of the drug and drug effects by affecting P-glycoprotein activity
Ginseng (Korean) (<i>Panax ginseng</i>)	Amitriptyline	May increase drug effect	May have an effect on neurochemical system
	Anticoagulant and antiplatelet agents	May increase or decrease drug effect	Possible CYP450 enzymes interaction and Vitamin K effect on ginseng
	CYP2D6 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity
	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
	Docetaxel	Herb effect on drug (May increase drug efficacy)	May enhance susceptibility of colon cancer cells to docetaxel

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human studies	Possible	Moderate - High	Avoid concomitant use
Level D Animal study	Possible	Moderate	Monitor patient
Level C Case report	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level A Conflicting data. Clinical trial results suggest no interaction. Case studies exist and <i>in vitro</i> studies suggest possible interaction	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level A Clinical trials	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level B <i>In vitro</i> , animal and human <i>ex vivo</i> studies	Possible	High	Avoid concomitant use
Level D <i>In vitro</i> study	Theoretical	Low	No evidence from human studies to support clinical recommendations

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Ginseng (Korean) <i>(Panax ginseng)</i> <i>(cont)</i>	Doxorubicin	Herb effect on drug (May decrease drug side effect)	May have a protective effect on doxorubicin induced toxicity
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect
	Imatinib	May increase drug side effect	May increase blood levels of drugs possibly due to inhibition of CYP3A4
	Midazolam	May decrease drug effect	May decrease blood levels of drugs possibly due to induction of CYP3A4
	Monoamine oxidase inhibitors (MAOI) (Phenelzine)	May increase drug side effect	Korean ginseng may increase the side effect of phenelzine or other MAOIs
	Oestrogen	May increase or decrease drug effect	Korean ginseng may cause a phytoestrogenic effect

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal study	Theoretical	Low	No evidence from human studies to support clinical recommendations
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
Level C Case report	Possible	High	Avoid concomitant use
Level A Clinical trials	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level C Case reports (ginseng type not specified)	Unlikely	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Ginseng (Siberian) <i>(Eleutherococcus senticosus)</i>	Anticoagulant and antiplatelet agents	May increase drug effect	Siberian ginseng may increase risk of bleeding with these medications
	Chemotherapeutic agents	Nutrient effect on drug (May decrease drug side effect)	Siberian ginseng may increase tolerance for chemotherapy and improve immune response
	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
	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
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect to drug
	Monoamine oxidase inhibitors (MAOI) (Phenelzine)	May increase drug side effect	Siberian ginseng may increase side effect of phenelzine or other MAOIs
	P-glycoprotein substrates	May increase drug effect	May increase blood level of drug via inhibition of P-gp
Glucosamine	Anticoagulant and antiplatelet agents	May increase drug effect	May increase the risk of bleeding with these medications
	Hypoglycaemic drugs	May decrease drug effect	Glucosamine may affect blood glucose levels in people with diabetes

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B <i>In vivo</i> study found anticoagulant activity for an isolated constituent. Human study in athletes administered a preparation of Siberian ginseng and andrographis found reduced coagulation	Possible	Moderate - High	Avoid concomitant use
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
Level B Human study	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level B <i>In vitro</i> , animal and human <i>ex vivo</i> studies	Possible	High	Avoid concomitant use
Level A Clinical trials	Likely	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia ^c
Level C Two case reports (ginseng type not specified)	Unlikely	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies	Possible	Variable (depending on the drug)	Monitor patient
Level C Case reports	Possible	Moderate - High	Avoid concomitant use
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
Grape seed (<i>Vitis vinifera</i>)	Anticoagulant and antiplatelet agents	May increase risk of bleeding	May decrease platelet adhesion to fibrinogen
	Antihypertensive drugs + vitamin C	May have opposing effect to drug	Unknown mechanism
	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
	CYP2D6 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity
	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

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D <i>In vitro</i> studies	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level A Meta-analyses in patients taking antihypertensive drugs	Possible	Moderate - High	Avoid combination of vitamin C and grape seed in hypertensive patients
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
Level B Human study (300 mg of grape seed did not significantly change metabolic rates of dextromethorphan (CYP2D6 substrate) in healthy volunteers) Level D <i>In vitro</i> study (100 mg of grape seed extract inhibited CYP2D6 activity)	Unlikely	Variable (depending on drug and disease state)	Monitor patient
Level D <i>In vitro</i> study (100 mg of grape seed extract inhibited CYP2C9 and intestinal CYP3A4 activity). <i>In vitro</i> and animal study (Wild grape seed procyanidins diminished CYP2E1 expression <i>in vitro</i> 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
Grape seed (<i>Vitis vinifera</i>) (cont)	Doxorubicin	Herb effect on drug (May attenuate doxorubicin-induced toxicity)	Unclear mechanism. May protect DNA from oxidative damage
	Hepatic CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via induction of hepatic CYP3A4 enzyme activity
	Iron	Herb effect on nutrient	May decrease mineral absorption when administered together
Green-lipped mussel	Anticoagulant and antiplatelet agents	May increase drug effect	May increase the risk of bleeding with these medications
Hawthorn (<i>Crataegus monogyna</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug
	Nitrates	May increase drug effect	May have additive vasodilation effect

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
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
Level D <i>In vitro</i> 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
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
Level C Case report	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level A Clinical trials suggest hypotensive effect	Likely	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for hypotension ^d
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
Hawthorn (<i>Crataegus monogyna</i>) (cont)	Phosphodiesterase-5-Inhibitors	May increase drug effect	May have additive vasodilation effect
	QT prolonging drugs	May increase drug effect	May increase the risk for adverse cardiac effects when taken together
Holy Basil (<i>Ocimum tenuiflorum</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May inhibit platelet aggregation
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect
	Phenobarbital	May increase drug effect	May potentiate phenobarbitone - induced sleeping time
Hops (<i>Humulus lupulus</i>)	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
	Oestrogen	May decrease drug effect	May bind to oestrogen receptor site
	Paracetamol (Acetaminophen)	May increase drug effect	May increase analgesic effect by slowing drug clearance

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal study	Theoretical	High	Use with caution under supervision of a healthcare professional and monitor
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
Level D Animal study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
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
Level D Animal study	Theoretical	High	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies	Theoretical	Variable (depending on drug and disease state)	Monitor patient
Level D <i>In vitro</i> studies	Theoretical	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
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
Horsetail (<i>Equisetum arvense</i>)	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
	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
	Diuretic drugs	May increase drug effect	Theoretically, taking various species of horsetail with diuretic drugs might increase potassium loss, as horsetail possesses diuretic properties
Iodine	Amiodarone	May increase adverse effect on thyroid function	May increase blood levels of iodine
	Antithyroid drugs	May increase drug effect	Iodine may precipitate hypothyroidism
	Lithium	May increase drug effect	Iodine at high doses may increase the hypothyroid activity of lithium carbonate
	Thyroid hormone	May increase drug effect	Iodine (at very high doses) may precipitate or exacerbate hyper or hypothyroidism
Iron	Bisphosphonates	May decrease drug effect	May decrease the absorption of drug
	Captopril	May decrease drug effect	May decrease the absorption of drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level C Case reports (2 patients had detectable viral loads)	Possible	High	Avoid concomitant use
Level D <i>In vitro</i> 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
Level D Animal studies (a human study showed that taking horsetail for 4 days didn't affect potassium levels despite it showing a significant diuretic effect. The effects of longer term use are unknown)	Possible	Moderate	Monitor patient
Level C Case reports	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies	Theoretical	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypothyroidism ^b
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
Level B Studies in euthyroid subjects - thyroid function inhibited	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
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
Level A Clinical trials	Possible	Moderate	Avoid concomitant use. If iron is indicated, interaction may be minimised by taking 2 hours before or 4-6 hours after drug

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Iron (<i>cont</i>)	Dolutegravir	May decrease drug effect	May decrease the absorption of drug
	Methyldopa, levodopa, carbidopa and penicillamine	May decrease drug effect	May decrease the absorption of drug
	Mycophenolate	May decrease drug effect	May decrease the absorption of drug
	Proton pump inhibitors (PPIs), H ₂ -receptor antagonists, bile acid sequestrants, antacids	Drug effect on nutrient	May decrease mineral absorption when administered together
	Tetracycline and quinolones	May decrease drug effect	May decrease the absorption of drug
	Thyroid hormone	May decrease drug effect	May decrease the absorption of drug
Ivy leaf (<i>Hedera helix</i>)	CYP450 enzyme substrates (CYP2C19, CYP2C8, CYP2D6)	May increase drug effect	May increase drugs levels through inhibition of these enzymes

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
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
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
Level C Case studies	Possible	Moderate	Assess nutrient status and supplement if indicated
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
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
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug and disease state)	Monitor patient. Significant interaction unlikely

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Kava (<i>Piper methysticum</i>)	CNS depressants	May increase drug effect	May increase sedative effects of these drugs
	CYP450 substrates (CYP2C9, CYP2C19)	May increase drug effect	May increase blood levels of the drug through inhibition of these enzymes
	CYP450 substrates (CYP1A2, CYP2E1)	May increase drug effect	May increase blood levels of the drug through inhibition of these enzymes
	Haloperidol/ Haloperidol + Lorazepam	May increase drug side effects	May increase risk of cardiovascular adverse effects and hypoxia
	Paracetamol	May increase drug side effects	May increase severity of paracetamol-induced hepatotoxicity
Kelp (<i>Fucus vesiculosus</i>)	Lithium	May increase or decrease drug effect	May increase or decrease blood level of drug
	Thyroid hormone	May increase or decrease drug effect	Taking kelp may precipitate or exacerbate hyper or hypothyroidism

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
Level D <i>In vitro</i> studies	Theoretical	Low	Monitor patient. Significant interaction unlikely
Level B Human studies	Possible	Low	Monitor patient
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
Level D <i>In vitro</i> study	Theoretical	High	Monitor patient. Avoid concomitant use of kava with high doses of paracetamol
Level C Case reports	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
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
Liquorice (<i>Glycyrrhiza glabra</i>)	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
	Antihypertensive drugs	May have opposing effect to drug	May have hypertensive effect (at high doses 50-200 g/d)
	Cisplatin	May decrease drug effect	May decrease blood level of drug
	Corticosteroids (Prednisolone)	May increase drug effect	May increase blood levels of drug
	CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition or induction of this enzyme activity
	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
	Digoxin	May increase drug side effect	Liquorice may increase the risk of digoxin toxicity (possibly via hypokalaemia and/or inhibition of P-gp)
	Methotrexate	May increase adverse drug effects	May increase liver enzyme and bilirubin levels when administered together
	Monoamine oxidase inhibitors (MAOIs)	May increase drug effect	May have additive effects to the drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level A <i>In vitro</i> and <i>in vivo</i> studies and systematic review	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level B Open studies and case report	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level D Animal study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level B Open human studies	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level B Human studies	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies	Theoretical	Variable (depending on drug and disease state)	Monitor patient
Level C Case report, <i>in vitro</i> study and animal study	Possible	High	Avoid concomitant use
Level D Animal studies	Possible	Low	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Moderate	Monitor patient. Clinical significance is uncertain until human studies are conducted

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Liquorice (<i>Glycyrrhiza glabra</i>) (cont)	P-glycoprotein substrates	May decrease drug effect	May increase P-glycoprotein activity, decreasing drug effect in the body
	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
Lutein	Cisplatin	Nutrient effect on drug (May prevent cisplatin-induced retinal damage)	May have antioxidant and anti-inflammatory effects
	CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity
	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
	Ethambutol + isoniazid	Nutrient effect on drug (May prevent isoniazid-induced toxic optic neuropathy)	May have antioxidant and anti-inflammatory effects

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal study	Possible	Moderate	Monitor patient
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
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
Level D <i>In vitro</i> 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
Level D <i>In vitro</i> study study showed enhanced cytotoxic effect in breast cancer cells. Another <i>in vitro</i> 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
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
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
	Calcium	Nutrient effect on nutrient	Lysine significantly increases intestinal absorption of calcium
	Arginine	Nutrient effect on nutrient	High-dose arginine may reduce lysine levels
Magnesium	Aminoglycosides	May increase drug side effect such as muscle weakness	May have additive inhibitory effects on presynaptic acetylcholine release
	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
	Antiarrhythmic drugs	Nutrient effect on drug (May increase drug efficacy)	Magnesium may have additive antiarrhythmic effect
	Anticoagulant and antiplatelet agents	May decrease drug effect	Magnesium may reduce the efficacy of warfarin
	Antihypertensive drugs (Calcium channel blockers)	May increase drug effect	Magnesium may have additive hypotensive effect

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal studies	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level B Human study	Possible	Moderate	Monitor patient. Avoid concomitant use with high-dose calcium
Level B Human study	Possible	Moderate	Avoid concomitant use with high-dose arginine
Level C Case report	Possible	Moderate - High	Avoid concomitant use
Level B Human studies and case reports	Possible	Low	Assess nutrient status and supplement if indicated
Level A Clinical trial using high dose of magnesium (3204 mg/d magnesium chloride)	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level B <i>In vitro</i> study and human study based on IV route of administration	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
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
Magnesium <i>(cont)</i>	Bisphosphonates	May decrease drug effect	Bisphosphonates may form complexes with multivalent cations such as magnesium
	Digoxin, chlorpromazine, penicillamine, tetracycline, nitrofurantoin and quinolone antibiotics	May decrease drug effect	Magnesium may decrease the absorption and efficacy of these drugs
	Gabapentin	May decrease drug effect	May decrease blood level of drug
	HMG-CoA reductase inhibitors (Statins)	May decrease drug effect	May decrease drug levels in the body when administered together
	Hypoglycaemic drugs (Glibenclamide, glipizide)	May increase drug effect	May enhance drug absorption and systemic drug effects
	Levodopa	May decrease drug effect	May decrease drug levels in the body and systemic effects of the drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
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
Level B Human studies	Possible	Moderate - 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 4-6 hours after magnesium supplementation
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
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
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
Magnesium <i>(cont)</i>	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
	Proguanil	May decrease drug effect	Proguanil may form complexes with magnesium
	Proton pump inhibitors (PPIs)	Drug effect on nutrient (May decrease blood levels of nutrient)	Proton pump inhibitors may cause hypomagnesaemia if taken long-term (usually >1 year)
	Rocuronium	May increase drug effect	May have additive inhibitory effects on acetylcholine release
Methionine	Levodopa	May decrease drug effect	Methionine may decrease the efficacy of levodopa in Parkinson's disease
Milk thistle/St Mary's thistle <i>(Silybum marianum)</i>	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
	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
	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
	Hypoglycaemic drugs	May increase drug effect	May increase blood levels and clinical effects of these drugs

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Multiple studies and case reports	Likely <i>(with long term use)</i>	Moderate	Assess nutrient status and supplement if indicated
Level B Human studies	Possible	High	Interaction may be minimised by separating the administration of medication and magnesium by at least 2 hours
Level B Multiple case reports, case series, reviews	Likely <i>(with long term use)</i>	Moderate	Assess nutrient status and supplement if indicated
Level A Clinical trial using IV administration	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level B Open study in patients with Parkinson's disease	Possible	Low	Use with caution under supervision of a healthcare professional and monitor
Level A Clinical trials	Possible	Low	No significant adverse effect expected. Use with caution under supervision of a health care professional and monitor
Level A Clinical trials	Unlikely	Variable <i>(depending on drug and disease state)</i>	Use with caution under supervision of a healthcare professional and monitor
Level D Animal studies	Possible	Moderate	Monitor patient
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
Milk thistle/St Mary's thistle <i>(Silybum marianum)</i> <i>(cont)</i>	Ledipasvir/Sofosbuvir	May increase drug effect	May increase blood levels and clinical effects of these drugs
	Morphine	May increase or decrease drug effect	May affect blood levels of the drug and increase or decrease its effects
	P-glycoprotein substrates	May increase or decrease drug effect	May inhibit or induce P-gp activity
	Raloxifene	May increase drug effect	May increase blood levels of drug by inhibiting glucuronidation of drug
	Sirolimus	May increase drug effect	May decrease drug hepatic clearance
	Tamoxifen	May increase or decrease drug effect	May increase blood level of drug via inhibition of CYP2CP, CYP3A4 and P-gp activity
Niacin (Vitamin B3)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	Aspirin	Drug effect on nutrient (May increase or decrease niacin side effect)	May reduce the clearance of niacin by competing for glycine conjugation
	Bile acid sequestrants	May increase drug side effect	Mechanism unknown
	Gemfibrozil	May increase drug side effect	May increase risk of myopathy

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal study	Possible	Moderate	Monitor patient
Level D Animal study	Theoretical	Moderate	Monitor patient
Level D <i>In vitro</i> study	Theoretical	Variable <i>(depending on drug and disease state)</i>	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level B Human studies	Possible	High	Avoid concomitant use
Level B Human studies	Possible	High	Avoid concomitant use depending on severity of disease state
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
Level B Human studies	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level C Case reports	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
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
Niacin (Vitamin B3) <i>(cont)</i>	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
	Thyroid hormone	May decrease drug effect	May decrease blood levels of drug
	Transdermal nicotine	Drug effect on nutrient (May increase nutrient side effect)	May have additive effect to nutrient
Nicotinamide	Anticonvulsant drugs (Carbamazepine)	May increase drug effect	May increase blood levels and clinical effects of these drugs
Oats (Avena sativa)	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect
	Atorvastatin	May increase drug effect	May reduce intestinal absorption of atorvastatin
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
	Antihypertensive drugs	May increase drug effect	May have additive effect to drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level C Case reports	Possible	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
Level A Clinical trials	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypothyroidism ^b
Level C Case reports	Possible	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
Level C Case studies	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
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
Level D Animal study	Theoretical	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
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
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
PABA (Para-aminobenzoic acid)	Intramuscular cortisone	May increase drug effect	May decrease metabolism of cortisone
	Sulphonamides and sulphones (Dapsone)	May decrease drug effect	May inhibit antimicrobial activities of drug
Pau d'Arco (<i>Tabebuia avellanedae</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive anticoagulant effect (at very high doses)
PEA (Palmitoylethanolamide)	Opioid medication (Tramadol)	May increase drug effect	May have a synergistic effect with the drug
Pelargonium (<i>Pelargonium sidoides</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	Pelargonium contains coumarin which may reduce platelet aggregation, additive effect to drug
	Immunosuppressants	May decrease drug effect	May have opposing effect to drug
Peppermint (<i>Mentha x piperita</i>)	Ciclosporin	May increase drug effect	May increase blood levels of drug
	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

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human study	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level B <i>In vitro</i> studies and human study	Possible	Moderate	Avoid concomitant use
Level B One uncontrolled study found very high dose of isolated constituent prolonged prothrombin time	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level D Animal studies	Possible	Moderate	Monitor patient. No evidence from human studies to support clinical recommendations
Level D Animal study suggests interaction unlikely	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies find pelargonium has immune modulatory activity	Theoretical	Moderate - High	Avoid concomitant use
Level D Animal study	Theoretical	High	Avoid concomitant use
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
Phytosterols/ Plant sterols	Carotenoids	Nutrient effect on nutrient	May decrease blood level of carotenoids
	Lipid-lowering agents (Statins and ezetimibe)	May increase drug effect	May have additive LDL-C lowering effect
Potassium	ACE inhibitors, angiotensin receptor blockers and potassium-sparing diuretics	May increase drug side effect	Potassium may increase the risk of hyperkalaemia
	Trimethoprim-sulfamethoxazole (Bactrim)	May increase drug side effect	Potassium may increase the risk of hyperkalaemia
Probiotics	Antibiotics	Nutrient effect on drug (May decrease drug side effect)	May restore gut flora and reduce diarrhoea secondary to antibiotic therapy
<i>Lactobacillus</i> species including: <i>L. acidophilus</i> , <i>L. reuteri</i>	Fluconazole	Nutrient effect on drug (May increase drug efficacy)	Combination therapy may improve clinical outcome
	Nitrazepam	Nutrient effect on drug	May reduce drug adverse effects, by reducing β -glucuronidase, nitroreductase, and azoreductase, when co-administered
<i>L. rhamnosus</i> GR-1 & <i>L. reuteri</i> RC-14	Immunosuppressants	May predispose opportunistic infection	May predispose opportunistic infection due to immunosuppression
<i>Saccharomyces boulardii</i>	Antifungal agents	Drug effect on nutrient	May decrease the probiotic effectiveness of <i>Saccharomyces boulardii</i>

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level A Meta-analysis	Possible	Moderate	Assess nutrient status and supplement if required
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
Level C Multiple case reports	Likely (dose dependant)	Moderate - High	Avoid concomitant use
Level C Multiple case studies	Possible	High	Use with caution under supervision of a healthcare professional. Monitor patient for hyperkalaemia ^b
Level A Multiple trials in adults and children taking antibiotics	Likely	Low	No significant adverse effects expected. Supplementation may be beneficial
Level A Clinical trial in women with vulvovaginal candidiasis	Likely	Low	No significant adverse effects expected. Supplementation may be beneficial
Level B Human study	Possible	Low	No significant adverse effects expected. Supplementation may be beneficial
Level C Case report	Possible (depending on disease state)	Moderate - High	Avoid concomitant use in critically ill and immunocompromised patients
Level D <i>In vitro</i> studies	Theoretical	Low	Monitor patient

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Psyllium husk	Hypoglycaemic drugs	May increase drug effect	Psyllium may decrease post-prandial blood glucose levels
	Oral drugs and nutritional supplements	May decrease drug effect	Psyllium may decrease the absorption of oral drugs if doses are taken concomitantly

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
	Antihypertensive drugs (Calcium channel blockers)	May increase drug effect	May have additive effect to drug
	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
	Mitozantrone	May increase drug effect	May increase blood levels and adverse effects of the drug
	Organic anion transporting polypeptide (OATP) substrates (OATP1B1)	May increase drug effect	Quercetin may inhibit OATP1B1-mediated transport

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level A Clinical trial	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia ^c
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
Level D <i>In vitro</i> study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level A Clinical trial found quercetin supplementation reduced systolic, diastolic and mean arterial pressure in stage 1 hypertensive subjects Level D <i>In vitro</i> 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
Level B Human, animal and <i>in vitro</i> studies	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Moderate	Monitor patient
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
Quercetin (<i>cont</i>)	P-glycoprotein substrates	May increase drug effect	Quercetin may inhibit P-gp pump efflux
	Sulfasalazine	May increase drug effect	May increase blood levels and adverse effects of the drug
Red clover/ Isoflavones (<i>Trifolium pratense</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	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
	Daunorubicin	May increase drug side effect	May decrease drug metabolism due to decrease in glutathione cellular concentration
	Digoxin	May increase drug effect	May increase blood levels of drug via inhibition of P-gp expression
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect to drug
	Lipid-lowering drugs	May increase drug effect	May have additive lipid-lowering effect to drug
	Methotrexate	May increase drug side effect	Mechanism unknown
	Oestrogen	May increase or decrease drug effect	Red clover binds to oestrogen receptors and is capable of acting as both agonists and antagonists

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human studies	Possible	Variable (<i>depending on drug and disease state</i>)	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Moderate	Monitor patient
Level D Animal study and <i>in vitro</i> study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Variable (<i>depending on drug and disease state</i>)	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Moderate - High	Avoid concomitant use
Level D <i>In vitro</i> study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor for signs of hypoglycaemia ^c
Level A Clinical trials	Possible	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
Level C Case report	Possible	Moderate - High	Avoid concomitant use
Level D Animal study	Theoretical	Variable (<i>depending on drug and disease state</i>)	Use with caution under supervision of a healthcare professional and monitor

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Red clover/ Isoflavones (<i>Trifolium pratense</i>) (cont)	Tamoxifen	May increase drug effect	Red clover may have oestrogenic activity and may theoretically interfere with tamoxifen efficacy
	Vinblastine	May increase drug effect	May increase blood levels of drug via inhibition of P-gp expression
Reishi mushroom (<i>Ganoderma lucidum</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	Antihypertensive drugs	May increase drug effect	May have additive effect to drug
	Hypoglycaemic drugs	May increase drug effect	May have additive effect to drug
	Immunosuppressants	May increase drug side effect	May have opposing effect to drug
	CYP450 substrates (CYP1A2, CYP2E1, CYP3A4)	May increase drug effect	May increase drug effect via inhibition of these enzyme activities
SAMe (S-adenosyl methionine)	Levodopa	May reduce drug effect	May methylate the drug, reducing its effectiveness
	Serotonergic drugs	May increase drug effect	May increase the risk of serotonin syndrome when taken with these drugs

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human studies	Possible	High	Avoid concomitant use
Level D <i>In vitro</i> study	Theoretical	Moderate - High	Avoid concomitant use
Level B/D Human study. Study showed an anticoagulant effect at a dose of 3 g daily. <i>In vitro</i> study	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
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
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 ^e
Level A/B Human clinical studies	Possible	High	Avoid concomitant use
Level D Animal studies	Theoretical	Variable (depending on drug and disease state)	Monitor patient
Level D Animal study	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
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
Saw palmetto (<i>Serenoa repens</i>)	5-alpha reductase inhibitors	May increase drug effect	May have additive effect to drug due to inhibitory effect on 5-alpha reductase
	Androgens (Testosterone and dihydrotestosterone)	May decrease drug effect	May have inhibitory effect on 5-alpha reductase
	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	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
	Oestrogen	May decrease drug effect	May reduce the effect of oral contraceptive drugs through its antioestrogenic effects
	Oral contraceptive drugs	May decrease drug effect	May reduce the effect of oral contraceptive drugs through its antioestrogenic effects

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D <i>In vitro</i> 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
Level D <i>In vitro</i> 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
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
Level B Human study (Study with 12 volunteers showed interaction with CYP1A2, CYP3A4, CYP2E1, CYP2D6 is unlikely) Level D <i>In vitro</i> 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
Level B Human studies	Possible	High	Use with caution under supervision of a healthcare professional and monitor
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
Selenium	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	Barbiturate drugs (Phenobarbital)	May increase drug effects	May prolong sedative effects of the drug
	Corticosteroid drugs	Drug effect on nutrient	Selenium may be depleted by these drugs
	Oral contraceptive drugs	Drug effect on nutrient	Selenium may be depleted by these drugs
	Warfarin	May increase drug effect	May have additive effect to drug

Soy/Isoflavones (<i>Glycine max</i>)	Anticoagulant and antiplatelet agents	May decrease drug effect	Soy protein may decrease the anticoagulant effect of warfarin
	Antihypertensive drugs	May increase drug effect	May have additive hypotensive effect to drug
	Chemotherapeutic agents	May increase drug effect	Mechanism unknown
	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

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
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
Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
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
Level B Human study and case report (Warfarin)	Possible	Moderate - High	Avoid concomitant use
Level A Clinical trials	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypotension ^d
Level D <i>In vitro</i> study	Theoretical	Moderate - High	Avoid high doses (>7 g) prior to surgery. Use with caution under supervision of a healthcare professional and monitor
Level B Human studies (CYP2C9 and 3A4) Level D <i>In vitro</i> 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
Soy/isoflavones (<i>Glycine max</i>) (cont)	Diuretic drugs	May increase drug effect	May have additive diuretic effect to drug
	Gemfibrozil	May increase drug side effect	May increase blood levels of drug
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect to drug
	HMG-CoA reductase inhibitors (Atorvastatin, simvastatin)	May increase drug effect	May have additive effect to drug
	Monoamine oxidase inhibitors (MAOIs)	May increase drug effect	Tyramine in fermented soy products may cause additive blood pressure effect
	Organic anion-transporting polypeptides (OATPs)	May decrease drug effect	May reduce cellular uptake of drugs transported by OATP2B1
	P-glycoprotein substrates (Daunorubicin)	May increase drug effect	May increase blood level of drug via inhibition of P-gp
	Progesterone	May increase drug side effect	May have additive effect to drug
	Tamoxifen	May decrease drug effect	Soy may have estrogenic activity and may theoretically interfere with tamoxifen activity
	Thyroid hormone	May decrease drug effect	Soy may decrease blood levels of drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D Animal study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level A Clinical trials	Possible	Moderate - High	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypoglycaemia ^c
Level A Clinical trials	Possible	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies (fermented soy products contain tyramine)	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drugs)	Monitor patient
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level A Clinical trials	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D Animal study	Possible	Moderate - High	Avoid concomitant use
Level B Human study and case report	Possible	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
SPMs (Specialised pro-resolving mediators)	See Omega-3 (EPA + DHA)		
St John's wort (<i>Hypericum perforatum</i>)	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
	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
	Digoxin	May decrease drug effect	St John's wort may decrease blood levels of this medication
	Organic anion-transporting polypeptide (OATP) substrates	May decrease drug effect	Hyperforin may reduce cellular uptake of drugs transported by OATP2B1, when taken together
	Pethidine and dextromethorphan	May increase drug side effect	May have additive serotonergic effect
	P-glycoprotein substrates	May decrease drug effect	St John's wort may decrease blood levels of these medications via induction of P-gp expression
	Photosensitising drugs	May increase drug side effect	Hypericin content of St John's wort may increase the possibility of photosensitivity reactions

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
See Omega-3 (EPA + DHA)			
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
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
Level A Clinical trials	Possible	Moderate	Avoid concomitant use
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug and disease state)	Monitor patient
Level D <i>In vitro</i> and animal studies	Theoretical	Moderate	Avoid concomitant use
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
Level C Case study of aminolevulinic acid. <i>In vitro</i> study	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of photosensitivity ¹

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
St John's wort (<i>Hypericum perforatum</i>) (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
	Triptans	May increase drug effect	May have additive serotonergic effect
Taurine	Antihypertensive drugs	May increase drug effect	May have additive effect to drug
Thyme (<i>Thymus vulgaris</i>)	Acetylcholinesterase (AChE) inhibitors and anticholinergics	May increase drug effect	May increase acetylcholine levels due to inhibition of acetylcholinesterase
	Anticholinergics	May decrease drug effect	May decrease effectiveness of anticholinergic drugs
	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	CYP450 substrates (CYP1A2, CYP3A4)	May increase or decrease drug effect	May increase or decrease substrate blood levels by inhibition of these enzyme activities
	Oestrogen	May decrease drug effect	May competitively inhibit drug activity

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Multiple case reports of serotonergic syndrome. Human study in patients taking amitriptyline. Case report of monoamine oxidase activity	Likely	Moderate - High	Avoid concomitant use
Level C Case report	Possible	Moderate - High	Avoid concomitant use
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
Level D <i>In vitro</i> study	Theoretical	Moderate	Monitor patient for cholinergic effects
Level D <i>In vitro</i> study	Theoretical	Moderate	Monitor patient for anticholinergic effects
Level D <i>In vitro</i> and animal studies	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> studies	Theoretical	Variable (depending on drug and disease state)	Monitor patient
Level D <i>In vitro</i> study	Theoretical	Moderate	Monitor patient and assess the effectiveness of oestrogen therapy

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Tribulus (<i>Tribulus terrestris</i>)	Antihypertensive drugs (ACE inhibitors)	May increase drug effect	May have additive effect to drug
	Cisplatin	Herb effect on drug (May decrease renal side effects induced by cisplatin)	May decrease cisplatin accumulation in kidney via diuretic effect of tribulus
	Cyclophosphamide	Herb effect on drug (May improve reproductive damage induced by cyclophosphamide)	May have antioxidative effect
	Hypoglycaemic drugs	May increase drug effect	May have additive effect to drug
Turmeric (<i>Curcuma longa</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug (antiplatelet effect) at high doses (over 15 g/d)
	Antihypertensive drugs (Amlodipine)	May increase drug effect	May increase blood levels of drug
	Chemotherapeutic agents	May increase or decrease drug effect	Antioxidant effect of curcumin may inhibit apoptosis
	CYP1A1 substrates	May increase or decrease drug effect	May increase or decrease substrate blood levels via inhibition of this enzyme activity

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D <i>In vitro</i> 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
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
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
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
Level D <i>In vitro</i> studies find antiplatelet effect	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level D Animal studies	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of hypotension ^d
Level D Conflicting data <i>in vitro</i> study	Theoretical	Moderate - High	Avoid concomitant use
Level D <i>In vitro</i> 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
Turmeric (<i>Curcuma longa</i>) (cont)	CYP1A2 substrates	May increase or decrease drug effect	May increase or decrease substrate blood levels via inhibition of this enzyme activity
	CYP2A6 substrates	May increase or decrease drug effect	May increase or decrease substrate blood levels via induction of this enzyme activity
	CYP2D6 substrates	May increase or decrease drug effect	May increase or decrease substrate blood levels via induction of this enzyme activity
	CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease substrate blood levels via inhibition of this enzyme activity
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect
	Norfloxacin	May increase drug effect	May increase blood levels of drug
	Organic anion-transporting polypeptide (OATP) substrates	May increase drug effect	May increase drug absorption through inhibition of OATP proteins, when administered together
	P-glycoprotein substrates	May increase drug effect	May increase drug blood levels via inhibition of P-gp
	Paclitaxel	May increase drug effect	May increase drug blood levels due to increased bioavailability

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human studies	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level B Human studies	Possible	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
Level B/D <i>In vitro</i> study and a human study	Possible	Variable (depending on drug and disease state)	Monitor patient
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
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
Level D Animal study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> and animal studies	Theoretical	Variable (depending on drug and disease state)	Monitor patient
Level D Animal study	Theoretical	Variable (depending on drug and disease state)	Use with caution under supervision of a healthcare professional and monitor
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
Turmeric (<i>Curcuma longa</i>) (cont)	Sulfasalazine	May increase drug effect	May increase drug blood levels
Valerian (<i>Valeriana officinalis</i>)	Benzodiazepines (Lorazepam, alprazolam)	May increase inhibitory activity of drug and drug side effect	May have additive effect to drug by binding to the GABA receptors
	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
	Efavirenz	Herb effect on drug (May prevent efavirenz-induced neuropsychiatric adverse effects)	May act on GABA-A receptor and boost melatonin release
	UGT substrates (UGT1A1, UGT2B7) (Paracetamol, oestradiol, morphine)	May decrease excretion of drug	May have inhibitory effects on glucuronidation
Vitamin A	Orlistat and cholestyramine	Drug effect on nutrient (May decrease nutrient effect)	Vitamin A absorption may be decreased by orlistat

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human studies	Possible	Moderate - High	Avoid concomitant use
Level C Case report (Case of patient self-medicating with valerian and passionflower while on 2 mg lorazepam)	Possible	Moderate - High	Concomitant use can lead to increased drowsiness, dizziness and confusion. Avoid concomitant use.
Level A Clinical trial (1000 mg of valerian tablet daily did not significantly change CYP3A4 and CYP2D6 activities) Level D <i>In vitro</i> studies showed moderate to potent CYP3A4 inhibitory effects by valerian. Another <i>in vitro</i> 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
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
Level D <i>In vitro</i> 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
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
Vitamin A (cont)	Retinoids	May increase drug side effect	May have additive effect to drug
	Tetracycline	May increase risk of benign intracranial hypertension	May have additive effect to drug
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
Vitamin B3	See Niacin (Vitamin B3)		
Vitamin B6 (Pyridoxine, Pyridoxal 5 Phosphate)	Amiodarone	May increase drug side effects	May increase drug-induced photosensitivity
	Anticonvulsant drugs	Drug effect on nutrient	Vitamin B6 may be depleted by these drugs
	Antihypertensive drugs	May increase drug effect	May have additive effect to drug
	Anti-tubercular agents (Isoniazid)	Drug effect on nutrient	Vitamin B6 may be depleted by these drugs

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level A Systematic review	Likely	High	Avoid concomitant use
Level D Vitamin A and tetracycline are in the list of medications that may produce intracranial hypertension	Possible	High	Avoid concomitant use
Level B Human studies	Theoretical	Low	Supplementation may be beneficial
See Niacin (Vitamin B3)			
Level B Human studies	Possible	Moderate	Use with caution under supervision of a healthcare professional. Monitor patient for signs of photosensitivity ¹
Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
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
Level C Case studies	Possible	High	Assess nutrient status and supplement if indicated

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Vitamin B6 (Pyridoxine, Pyridoxal 5 Phosphate) (cont)	Chemotherapeutic agents (Cisplatin and altretamine)	May decrease drug effect	May reduce drug response time when administered together
	Oral contraceptives	Drug effect on nutrient	Vitamin B6 may be depleted by these drugs
	Penicillamine	Drug effect on nutrient	Vitamin B6 may be depleted by these drugs
	Phenobarbital	May decrease drug effect	May decrease blood levels and effects of the drug
	Phenytoin	May decrease drug effect	May decrease blood levels and effects of the drug

Vitamin B12	Carbamazepine	Drug effect on nutrient	Vitamin B12 may be depleted by this drug with long-term use
	Metformin	Drug effect on nutrient	Vitamin B12 may be depleted by this drug
	Oral contraceptives	Drug effect on nutrient	Vitamin B12 may be depleted by this drug
	Proton pump inhibitors, H ₂ -receptor antagonists	Drug effect on nutrient	Vitamin B12 may be depleted by this drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human observational study (study used 300 mg/m ² vitamin B6 daily for duration of the study. This is four-fold higher than the recommended daily UL)	Possible	Moderate	Monitor patient. Avoid concomitant high dosing of vitamin B6 with 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
Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
Level B Human study (one study showed that 200 mg daily of vitamin B6 resulted in a 45% reduction in phenobarbital 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
Level B Human study (study used 200 mg daily of vitamin B6 which is four-fold higher than recommended daily UL)	Possible	High	Avoid concomitant high dosing (≥200 mg/day) of vitamin B6 with this drug
Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
Level B Human study	Likely	Moderate	Assess nutrient status and supplement if indicated
Level B Human study	Possible	Moderate	Assess nutrient status and supplement if indicated
Level B Human study	Likely	Moderate	Assess nutrient status and supplement if indicated

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Vitamin C	Aluminium-containing antacids	May increase drug side effect (especially in renal failure patients)	Vitamin C chelates aluminium and may increase aluminium absorption
	Antihypertensive drugs + Grape seed	May have opposing effect to drug	Unknown mechanism of the interaction
	Calcium channel blockers (Nifedipine)	Drug effect on nutrient (May decrease nutrient effect)	Calcium channel blockers may inhibit uptake of vitamin C by intestinal cells
	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
	Desferrioxamine	May have opposing effect to drug	Vitamin C may cause transient deterioration of cardiac function with desferrioxamine
	Oestrogen	May increase drug effect	May increase blood levels of drug
	Paracetamol	May increase drug effect	High doses of vitamin C (>3 g) may decrease the elimination rate of paracetamol
	Protease inhibitors (Indinavir)	May decrease drug effect	May decrease blood levels of drug
	Thyroid hormone	Nutrient effect on drug	Vitamin C increases oral absorption of thyroid hormone
	Warfarin	May decrease drug effect	Vitamin C in high doses (>10 g/day) may cause diarrhoea and possibly reduce warfarin absorption

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Case reports and human study	Possible	Moderate - High	Avoid concomitant use
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
Level D <i>In vitro</i> study	Theoretical	Moderate - High	Assess nutrient status and supplement if indicated
Level D <i>In vitro</i> study	Theoretical	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level C Case reports	Possible	High	Avoid concomitant use
Level B Human studies	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level B Human studies	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level B Open study	Possible	Moderate - High	Avoid concomitant use
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
Level C Case study	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor. The recommendation for patients on warfarin is to avoid high-dose vitamin C (>10 g/day)

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Vitamin D3	Aluminium	May increase drug effect	May increase drug absorption
	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
	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
	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
	Atorvastatin	Nutrient effect on drug	May decrease blood level of drugs via induction of CYP3A4
	Bile acid sequestrants (Cholestyramine)	Drug effect on nutrient	Vitamin D absorption may be decreased by cholestyramine
	Budesonide (oral)	Nutrient effect on drug (May increase drug efficacy)	Combination therapy may improve clinical outcome
	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
	Chemotherapeutic agents	Drug effect on nutrient (May decrease nutrient effect)	Mechanism unknown

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal study	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level A Clinical trials	Possible	Low	No significant adverse effect expected. Assess nutrient status and supplement if indicated
Level B Lower quality human studies	Possible	Moderate	Assess calcium and vitamin D status and supplement if indicated
Level A Clinical trials	Possible	Low	No significant adverse effect expected in humans. Assess nutrient status and supplement if indicated
Level B Human studies	Possible	Low - Moderate	Use with caution under supervision of a healthcare professional and monitor
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
Level A Clinical trials	Possible	Low	No significant adverse effect expected in humans. Use with caution under supervision of a healthcare professional and monitor
Level C Case report	Possible	Moderate - High	Avoid concomitant use
Level B Human studies	Possible	Moderate - High	Assess nutrient status and supplement if indicated

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
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
	CYP3A4 substrates	May decrease or increase drug effect	May decrease or increase blood levels of drug via inhibition or induction of these enzyme activities
	Digoxin	May increase drug side effect	May increase drug effect via inhibition of P-gp
	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
	Orlistat	Drug effect on nutrient (May decrease nutrient effect)	Vitamin D absorption may be decreased by orlistat
	Sirolimus	May decrease drug effect	May increase the metabolism of sirolimus
	Thiazide diuretics	May increase drug side effect	Vitamin D3 may increase the risk of hypercalcaemia if taken with calcium supplements and/or thiazide diuretics
Vitamin E	Anticoagulant and antiplatelet agents	May increase drug effect	Vitamin E may increase risk of bleeding
	Chemotherapeutic agents	May decrease drug effect	Antioxidant effects may reduce activity of drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level B Human studies	Possible	Moderate	Assess nutrient status and supplement if indicated
Level B/D Lower quality human studies and <i>in vitro</i> studies	Possible	Variable (depending on drug)	Monitor patient
Level B Human study suggests no significant interaction	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
Level B Human studies	Possible	Moderate - High	Assess nutrient status and supplement if indicated
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
Level B Human studies	Theoretical	High	Avoid concomitant use
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
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
Level D <i>In vitro</i> study	Theoretical	Moderate - High	Avoid concomitant use

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Vitamin E <i>(cont)</i>	Cisplatin	Nutrient effect on drug (May decrease drug side effect)	Vitamin E may decrease the incidence and severity of neurotoxicity caused by cisplatin
	CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via induction of this enzyme activity
	Nitrates (Nitroglycerine)	Nutrient effect on drug (May decrease drug side effect)	Vitamin E may prevent nitrate tolerance when given concurrently with transdermal nitroglycerin
	Orlistat	Drug effect on nutrient (May decrease nutrient effect)	Vitamin E absorption may be decreased by orlistat
	Selumetinib	May increase drug side effect	May have additive anticoagulant effect
	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

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
	Hypoglycaemic drugs	May increase drug effect	May have additive hypoglycaemic effect

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level A Clinical trials in patients taking vitamin E and cisplatin	Likely	Low	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> study	Theoretical	Variable <i>(depending on drug and disease state)</i>	Use with caution under supervision of a healthcare professional and monitor
Level A Clinical trial	Possible	Low	Use with caution under supervision of a healthcare professional and monitor
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
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
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
Level A Clinical trials and meta-analyses	Likely	Moderate - High	Avoid concomitant use
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 ^a

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Vitamin K (<i>cont</i>)	Orlistat	Drug effect on nutrient	Vitamin K absorption may be decreased by orlistat
Vitex (<i>Vitex agnus-castus</i>)	CYP2C19 and CYP3A4 substrates	May increase or decrease drug effect	May increase or decrease blood levels of drug via inhibition of this enzyme activity
	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
	Oestrogen, contraceptive drugs	May increase or decrease drug effect	Via hormone modulating activity
White willow (<i>Salix alba</i>)	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
	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug as white willow contains salicin, a plant salicylate
	CYP450 substrates (CYP2C19, CYP1A2, CYP3A4)	May increase or decrease drug effect	May increase or decrease blood levels of drug through inhibition of these enzymes

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
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
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug)	Monitor patient. Clinical relevance has yet to be determined
Level D <i>In vitro</i> study (Drug-herb interaction was not directly studied)	Theoretical	Moderate	Use with caution under supervision of a healthcare professional and monitor
Level D <i>In vitro</i> 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
Level C Case report	Possible	Moderate	Use with caution under supervision of a healthcare professional and monitor
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
Level D <i>In vitro</i> study	Theoretical	Variable (depending on drug)	Monitor patient. Clinical relevance has yet to be determined

INGREDIENT	DRUG	NATURE OF INTERACTION	MECHANISM OF INTERACTION
Withania (<i>Withania coagulans</i>)	Hypoglycaemic drugs (Glipizide)	May increase drug effect	May have additive effect to drug
Withania (<i>Withania somnifera</i>)	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
	Cefalexin	May decrease drug effect	Zinc may decrease absorption of drug by chelating with drug
	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
	Integrase inhibitors	May decrease drug effect	May decrease blood level of drug by chelating with drug
	Penicillamine	May decrease drug effect	Zinc may decrease the activity of penicillamine
	Tetracycline or quinolone antibiotics (not doxycycline)	May decrease drug effect	Zinc may decrease the absorption and blood levels of these drugs
	Thrombopoietin receptor agonists (Eltrombopag)	May decrease drug effect	May bind to the drug decreasing its absorption

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal study (Co-administration of extract of <i>Withania coagulans</i> 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
See Ashwangandha			
Level A Clinical trials	Possible	Low	Assess nutrient status and supplement if indicated
Level B Human study	Possible	High	Interaction may be minimised by separating dose of zinc at least 3 hours after taking cefalexin
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
Level A Systematic review	Likely	High	Avoid concomitant use
Level A Clinical trial	Possible	Moderate	Interaction may be minimised by separating dose of medication and zinc by at least 2 hours
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
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
Ziziphus (<i>Ziziphus jujuba</i> <i>var. spinosa</i>)	Anticoagulant and antiplatelet agents	May increase drug effect	May have additive effect to drug
	CNS Depressant/sedative drugs	May increase drug effect	May have additive sedative effects when taken with CNS depressants
	CYP450 enzyme substrates (CYP1A2)	May decrease drug effect	May decrease blood levels and effects of these drugs by induction of these enzyme activities
	Hypoglycaemic drugs	May increase drug effect	May have additive effect to drug

EVIDENCE	LIKELIHOOD OF INTERACTION	SEVERITY OF OUTCOME	RECOMMENDATION
Level D Animal and <i>in vitro</i> study	Possible	Moderate - High	Use with caution under supervision of a healthcare professional and monitor
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
Level D Animal studies	Possible	Moderate	Monitor patient. Clinical relevance has yet to be determined
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

Complementary medicine interactions guide

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.

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