Complementary Medicine Interactions

PART 4

How do herbs, nutrients and food supplements interact with drugs for pain, fever, GI disturbance, or antibiotics and antiretrovirals? Lesley Braun and Prof Marc Cohen provide clinical guidance from their new publication.

Assumptions made when collating the information for this chart

- The clinical significance of many interactions is still unknown as controlled trials are lacking in most cases. In these instances, interactions are based on evidence of pharmacological activity and case reports and are largely speculative.
- All information refers to oral dose forms unless otherwise specified.
- Information listed here is correct at time of writing, however new research in the area is constantly being published.
- The interaction chart is provided as a guide only and should not replace the use of professional judgment.
- Information listed here is limited to 100 monographs in *Herbs & Natural Supplements – An Evidence-Based Guide* (©Elsevier Australia, 2004).

Using this guide in practice

- Commonly used prescription and over the counter medications are organised by therapeutic class and subclass and are listed alphabetically. Herbal and natural medicines are also listed alphabetically.
- Common names have been used when referring to herbs.
- Refer back to original monograph in *Herbs & Natural Supplements – An Evidence-Based Guide* (©Elsevier Australia, 2004) for more information about a particular substance.

Avoid	there may be insufficient information available to be able to advise using the two substances together, so avoid until more is known. The drug may have a narrow therapeutic index (NTI) and there is sufficient evidence to suggest the interaction may be clinically significant. Consider an alternative treatment that is unlikely to produce undesirable interaction effects.
Avoid long-term use unless under medical supervision	harmful effects of potential interaction can be avoided if doses are altered appropriately under medical supervision. Some of these interactions can be manipulated to the advantage of the patient. Changes to dose and regimen may be required for safe combined use.
Caution	the possibility exists of an interaction that may change effects clinically; be aware and monitor. It is prudent to tell patients to be aware and seek advice if they are concerned.
Observe	interaction may not be clinically significant at the usual recommended doses, however the clinician should be alert to the possibility of an interaction.
Beneficial interaction possible	prescribing the interacting substance may improve clinical outcomes, e.g. reducing drug requirements, complementing drug effects, reducing drug side-effects, counteracting nutritional deficiencies caused by drugs, alleviating drug withdrawal symptoms, enhancing patient well-being.

DRUG	COMPLEMENTARY MEDICINE	POTENTIAL OUTCOME	RECOMMENDATION	EVIDENCE/COMMENTS
Analgesia				
Narcotic analgesics				
Codeine	Adhatoda	Additive effects	Beneficial interaction possible	Theoretically will increase antitussive effects of drug
	Kava	Additive effects	Caution	Increased CNS depression effects theoretically possible
Morphine	Kava	Additive effects	Caution	Increased CNS depression effects theoretically possible
	L-tyrosine	Additive effects	Observe	L-tyrosine potentiates morphine-induced analgesia by 154% in mice – clinical significance unknown
	Withania	Reduced morphine tolerance/ dependance	Beneficial interaction possible	In animal studies, repeated administration of withania (100 mg/kg) inhibited morphine tolerance and dependence, so it is sometimes used in opiate withdrawal

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DRUG	COMPLEMENTARY MEDICINE	POTENTIAL OUTCOME	RECOMMENDATION	EVIDENCE/COMMENTS
Analgesia (continued)				
Simple analgesic and antipyretics				
Simple analgesic and antipyretics	Meadowsweet	Additive effects	Observe Beneficial interaction possible	Additive anti-inflammatory and analgesic effects theoretically possible
	Willowbark	Additive effects	Observe Beneficial interaction possible	Additive anti-inflammatory and analgesic effects theoretically possible
	Vitamin E	Additive effects	Beneficial interaction possible	Drug dosage may require modification. Vitamin E may enhance the pain modifying effects of drug
Aspirin * *see also antiplatelet drug interactions*, JCM *2004;3(5):73–4*	Grape-seed extract	Additive effects	Observe Beneficial interaction possible	Theoretically may enhance antiplatelet and anti-inflammatory activity of aspirin and may increase possibility of bleeding and bruising
	Meadowsweet	Increased bruising and bleeding	Observe, beneficial interaction possible	Theoretically may enhance anti-inflammatory and antiplatelet effects
	Policosanol	Increased bruising and bleeding	Observe	Doses >10 mg/day may further inhibit platelet aggregation
	Vitamin C	Decreased vitamin C effects	Beneficial interaction	Aspirin may interfere with both absorption and cellular uptake mechanisms for vitamin C, thereby increasing vitamin C requirements, as observed in animal and human studies. Increased vitamin C intake may be required with long-term therapy
	Willowbark	Increased bruising and bleeding	Observe Beneficial interaction possible Caution with high dose (>240 mg salicin daily	Theoretically may enhance anti-inflammatory and antiplatelet effects. Although a clinical study found that consumption of salicin 240 mg/day produced minimal effects on platelet aggregation, higher doses may have a significant effect
Paracetamol	Andrographis	Reduced side-effects	Beneficial interaction possible	Andrographis may exert hepatoprotective activity against liver damage induced by paracetamol
	Garlic	Reduced side-effects	Beneficial interaction possible	Garlic may exert hepatoprotective activity against liver damage induced by paracetamol
	SAMe	Reduced side-effects	Beneficial interaction possible	SAMe may exert hepatoprotective activity against liver damage induced by paracetamol
	Schisandra	Reduced side-effects	Beneficial interaction possible	Schisandra may exert hepatoprotective activity against liver damage induced by paracetamol
	Milk thistle	Reduced side-effects	Beneficial interaction possible	Milk thistle may exert hepatoprotective activity against liver damage induced by paracetamol
Gastrointestinal System				
Digestive supplements				
Pancreatin	Folate	Reduced folate absorption	Monitor for folate efficacy and folate status	

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DRUG	COMPLEMENTARY MEDICINE	POTENTIAL OUTCOME	RECOMMENDATION	EVIDENCE/COMMENTS
Gastrointestinal System (continued)				
Hyperacidity, reflux and ulcers				
Aluminium-based antacids	Vitamin C	Increased aluminium absorption	Separate doses by at least 2 hours	Vitamin C increases the amount of aluminium absorbed
antacids	Folate	Reduced folate absorption	Separate dose by 2–3 hours	
	Iron	Reduced iron absorption	Separate doses by at least 2 hours	
Anti-ulcer drugs				
sucralfate e.g., Carafate, Ulcyte	Vitamin E	Reduced vitamin absorption	Separate doses by at least 4 hours and monitor vitamin status	Increased vitamin intake may be required with long-term therapy
gastric-acid inhibitors Proton-pump inhibitors e.g. omeprazole; H_2-receptor antagonists e.g. ranitidine	Folate	Reduced folate absorption	Separate dose by 2–3 hours	
	Iron	Reduced drug and iron effect	Monitor for iron efficacy and iron status	Drug reduces gastric acidity and therefore iron absorption
	Vitamin B12	Reduced B12 absorption	Beneficial interaction possible — monitor B12 status	B12 supplementation may be required with long-term therapy
Helicobacter pylori triple-therapy treatment	Garlic	Additive effects	Interaction may be beneficial	Garlic inhibits growth of H. pylori in vitro and in vivo and two studies have shown a synergistic effect with omeprazole – clinical significance unknown
Laxatives				
	Aloe vera	Additive effects	Caution	Anthraquinones have significant laxative activity and may increase adverse effects
Infections and Infestations				
Antibiotics	Probiotics	Reduced side-effects Beneficial	interaction possible	Reduces GI and genitourinary side-effects. A meta-analysis of nine studies found that *Lactobacilli* and *Saccharomyces boulardii* successfully prevent antibiotic-induced diarrhoea. Increase intake with antibiotic therapy
	Vitamin B1 (thiamin)	Reduces endogenous vitamin production	Beneficial interaction possible	Increase dietary intake or consider supplementation with long-term therapy
	Vitamin B5 (pantothenic acid)	Reduces endogenous vitamin production	Beneficial interaction possible	Increase dietary intake or consider supplementation with long-term therapy
aminoglycosides e.g. gentamicin	Magnesium	Decreased magnesium absorption	Caution Monitor for signs and symptoms of magnesium deficiency	Aminoglycosides may deplete magnesium levels and result in neuromuscular weakness. Increased magnesium may be required with long-term therapy
quinolone antibiotics e.g. norfloxacin (e.g. Noroxin)	Dandelion	Reduced drug absorption	Caution. Separate doses by at least 2 hours	Reduced drug absorption observed in an experimental study

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DRUG	COMPLEMENTARY MEDICINE	POTENTIAL OUTCOME	RECOMMENDATION	EVIDENCE/COMMENTS
Infections and Infestations (continued)				
	Calcium	Reduced drug absorption	Caution – separate antibiotic dose by at least 2 hours before or 4 hours after oral calcium	
	Iron	Reduced drug absorption	Separate antibiotic dose by at least 2 hours before or 4–6 hr after oral iron	
	Magnesium	Reduced drug absorption	Separate antibiotic dose by at least 2 hours before or 4 hours after oral magnesium	
	Zinc	Reduced drug and zinc absorption	Caution Separate doses by at least 2 hours	Complex formation between zinc and quinolones results in reduced absorption of both substances, with potential reduction in efficacy
tetracycline antibiotics e.g. minocycline (e.g. Minomycin), doxycycline	Calcium	Reduced drug and calcium absorption	Caution Separate dose by at least 2 hours	Tetracyclines form insoluble complexes with calcium, thereby reducing its absorption
	Iron	Reduced drug and iron absorption	Caution – separate doses by at least 4 hours	Tetracyclines form insoluble complexes with iron, thereby reducing its absorption
	Magnesium	Reduced drug and magnesium absorption	Caution Separate doses by at least 2 hours	Tetracyclines form insoluble complexes with iron, thereby reducing its absorption
	Vitamin B12	Reduced drug absorption	Caution Separate doses by at least 2 hours	B complexes containing B12 may significantly reduce the bioavailability of tetracycline hydrochloride
	Zinc	Reduced drug and zinc absorption	Caution Separate dose by at least 2 hours	Complex formation between zinc and tetracycline results in reduced absorption of both substances, with potential reduction in efficacy
Other antibiotics and anti-infectives (trimethoprim e.g. Triprim)	Folate	Reduced folate levels	Caution Monitor folate status with long-term or high-dose therapy	Increased folate intake may be required with long-term or high-dose therapy
Antimalarials				
pyrimethamine e.g. Daraprim	Folate	Reduced folate effects	Beneficial interaction possible with folinic acid	Impaired folate utilisation occurs with drug use
chloroquine e.g. Chlorquin	Vitamin E	Reduced drug effects	Observe	According to *in-vitro* research, vitamin E inhibits drug uptake in human cultured fibroblasts. Clinical significance unknown
Antituberculotics and antileprotics				
Cycloserine and isoniazid	Vitamin B6 (pyridoxine)	Reduced B6 levels	Beneficial interaction possible under supervision	Drug may induce pyridoxine deficiency. Increased intake may be required with long-term therapy
Isoniazid	Vitamin B3 (niacin)	Reduced B3 levels	Beneficial interaction possible under supervision	Prolonged isoniazid therapy (the drug replaces niacinamide in NAD) may induce pellagra. Increased intake may be required with long-term therapy

Complementary Medicine Interactions – PART 4 continued

DRUG	COMPLEMENTARY MEDICINE	POTENTIAL OUTCOME	RECOMMENDATION	EVIDENCE/COMMENTS
Infections and Infestations (continued)				
Antituberculotics and antileprotics (continued)				
	Vitamin E	Reduced vitamin absorption	Caution – separate doses by at least 4 hours and monitor vitamin status	Increased vitamin intake may be required with long-term therapy
Rifampicin	Vitamin D	Reduced vitamin D levels	Beneficial interaction possible	Increase vitamin D intake with long-term therapy
Antiviral agents				
HIV drugs e.g. zidovudine (AZT/HAART, e.g. Retrovir) *HIV non-nucleoside transcriptase inhibitors, HIV protease inhibitors*	Carnitine	Reduced carnitine levels	Beneficial interaction possible	*In-vitro* studies indicate prevention of muscle damage due to carnitine depletion — clinical significance unclear. Increased intake may be required with long-term therapy
	Echinacea	Reduced drug effects	Caution – use under practitioner supervision	Contra-indicated by German Commission E based on theoretical considerations
	Grapefruit juice	Increased drug exposure	Observe	Not considered clinically relevant
	Milk thistle	Altered drug clearance	Observe	*In-vitro* evidence of potential inhibition of the CYP3A4 and UGT1A substrates metabolism
	St John's wort	Reduced drug effects	Avoid	St John's wort increases drug metabolism, thereby reducing drug serum levels
Amprenavir	Vitamin E	Blood coagulation defect	Caution	Monitor for vitamin K deficiency and coagulation problems
Saquinivir	Garlic	Reduced drug effects	Avoid	A clinical study found garlic reduced serum levels of saquinivir and thus drug efficacy