Canterbury District Health Board
Te Poari Hauora ō Waitaha

Clinical Pharmacology Bulletin

Department of Clinical Pharmacology, Christchurch Hospital, Private Bag 4710, Christchurch
Medicines Information Service **Phone**: 80900 **Fax**: 80902
Medicines Utilisation Review **Phone**: 86596 **Fax**: 81003
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Interactions between herbal products and conventional medicines

Herbal products are commonly used by many patients alongside conventional medicines. The aim of this bulletin is to describe potential interactions with five popular products; **St John's wort, ginkgo, garlic, echinacea** and **fish oil**.

Pharmacokinetic interactions (see table below):

Enzyme inducers: (increase metabolism of enzyme substrates potentially reducing efficacy of conventional medication)

- St John's wort is a moderate inducer of CYP3A and 2C19 and may also induce other CYP enzymes. Potency of induction varies between products with different hyperforin content.
- Garlic is a weak inducer of CYP3A.
- Ginkgo is a weak inducer of CYP2C19, 2C9 and 3A (NB: inhibition of 3A has also been reported).

Enzyme inhibitors: (decrease metabolism of enzyme substrates resulting in raised concentrations of conventional medication, sometimes leading to toxicity)

- Echinacea is a weak inhibitor of CYP1A2.

Drug transporters:

- St John's wort is a moderate inducer of the efflux transporter protein P-glycoprotein (P-gp).

Pharmacodynamic interactions (see table below):

Antiplatelet effects: Many herbs including ginkgo, garlic and fish oil, are reported to have antiplatelet effects that may be additive with antiplatelet medications e.g. aspirin, clopidogrel. However, in most cases clinically significant effects have not been shown. Monitor for increased bruising and bleeding.

Serotonergic effects: Additive serotonergic adverse effects may occur when St John's wort is taken in conjunction with other serotonergic medicines e.g. antidepressants, some analgesics (e.g. tramadol) and anti-migraine agents (e.g. sumatriptan). Signs of serotonin toxicity include confusion, delirium, agitation, restlessness, sweating and tachycardia.

Photosensitising effects: St John's wort is associated with photosensitivity, which can be additive with other photosensitising agents e.g. tetracyclines and cytotoxic drugs.

Antagonistic effects: the immunostimulant effects of echinacea could theoretically antagonise the effects of immunosuppressant agents e.g. tacrolimus.

Important herb-drug interactions

The outcome of an herb-drug interaction can be harmful if the interaction causes increased toxicity of the drug or reduced efficacy. Concurrent use of any narrow therapeutic index drug with herbal products requires caution and appropriate monitoring. For example, all patients on an anticoagulant should be monitored (e.g. INR for warfarin) within a week of starting or stopping any herbal product.

Herb-drug interactions with selected narrow therapeutic index drugs

	St John's wort	Ginkgo	Fish oil	Garlic
Anticoagulants warfarin	Induction of metabolism (CYP2C8/9), may ↓ INR.	Additive bleeding effects. May ↑ INR. Caution in older people.	Dose dependent, may ↑ INR. (>3 g per day)	Additive bleeding effects. Conflicting data, may ↑ INR.
dabigatran	Induction of P-gp, may ↓exposure			
rivaroxaban	Induction of metabolism (CYP3A), may ↓ INR.			
Immunosuppressants CYP3A substrates e.g. ciclosporin, tacrolimus everolimus, sirolimus	Induction of metabolism (CYP3A), ↓efficacy likely. Induction of P-gp, may ↓ exposure. Risk of transplant rejection.	Unlikely to be clinically significant.	No known interactions	No known interactions
HIV protease inhibitors CYP3A substrates e.g. indinavir, nelfinavir, nevirapine, ritonavir, saquinavir	Induction of metabolism (CYP3A), may ↓efficacy Induction of P-gp, may ↓ exposure Risk of HIV treatment failure.	Unlikely to be clinically significant.	No known interactions	Unlikely to be clinically significant.
Anticonvulsants carbamazepine	Induction of metabolism (CYP3A), unlikely to↓ [carbamazepine]	A neurotoxin (in the leaves and seeds) may cause seizures.	No known interactions	No known interactions
phenytoin (2C8/9 and 2C19 substrate)	Induction of metabolism (CYP2C8/9 and 2C19), may ↓[phenytoin].			
Antiarrhythmics calcium channel blockers (CCBs) amiodarone digoxin	Induction of metabolism (CYP3A), may ↓ efficacy CCBs and amiodarone. Induction of P-gp, may ↓ [digoxin], unlikely to be significant	Possible inhibition of metabolism (CYP3A), may ↑ efficacy of CCBs e.g. nifedipine and amiodarone	No known interactions	No known interactions

Abbreviations: ↓ decrease, ↑ increase, [x] concentration of x, INR International Normalised Ratio
Note: this is not an exhaustive list of important herb-drug interactions.

Herbal products can vary widely in their composition, potency and contaminants; therefore, interactions can be difficult to predict and quantify. The risk of herb-drug interactions may be especially severe for the elderly, frail, or those taking multiple medicines for chronic diseases. Consider reporting all adverse herb-drug interactions to CARM. Spontaneous reporting is a practical way to identify herb-drug safety information.

The information contained within this bulletin is provided on the understanding that although it may be used to assist in your final clinical decision, the Clinical Pharmacology Department at Christchurch Hospital does not accept any responsibility for such decisions.