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Drug–Complementary Medicine Interactions PART 4

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Drug–Complementary Medicine Interactions PART 3

How do herbs, nutrients and food supplements interact with the contraceptive pill, hormonal treatments and drugs for metabolic disorders? **Lesley Braun** and **Prof Marc Cohen** provide clinical guidance from their updated 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 have a sound theoretical basis, although remain to be tested.
- All information refers to oral dose forms unless otherwise specified.

- Information is correct at time of writing, however new research in the area is constantly being published.
- The interaction table is provided as a guide only and should not replace the use of professional judgement. It has been developed to assist clinicians when advising patients.
- Information listed here is limited to 120 monographs in *Herbs & Natural Supplements – An Evidence-Based Guide* (© 2nd edn Elsevier, 2006).

Using this guide in practice

- Commonly used prescription and OTC 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* (© 2nd edn Elsevier, 2006) for more information about a particular substance.

Avoid	There may be insufficient information available to be able to advise using the two substances safely 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 an undesirable interaction.
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 and theoretical, 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.

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Drug	CM	Potential outcome	Recommendation	Evidence/Comments
CONTRACEPTIVE AGENTS				
Combined oral contraceptive agents				
Oral contraceptive pill	Chaste tree	Reduced herb effects	Observe	There has been speculation as to whether chaste tree is effective when OCPs are being taken. Several clinical studies conducted in women taking the OCP have confirmed that chaste tree still reduces symptoms of premenstrual syndrome
	Folate	Reduced folate levels	Beneficial interaction possible	Folate levels are reduced with long-term use. Increased intake may be required with long-term therapy
	Liquorice	Increased side-effects	Observe Caution with high-dose liquorice (>100 mg/day glycyrrhizin) or long-term use (> 2 weeks)	Increased risk of side-effects such as hypokalaemia, fluid retention and elevated blood pressure have been noted in case reports



Drug	CM	Potential outcome	Recommendation	Evidence/Comments
Oral contraceptive pill	St John's wort	Reduced drug effects	Caution — avoid use with low-dose OCP	Breakthrough bleeding has been reported in 12 cases, which may indicate decreased effectiveness. Caution related to hyperforin
	Vitamin A	Increased vitamin A levels	Observe	OCP increases serum vitamin A levels
	Vitamin B2 (riboflavin)	Reduced vitamin B2 levels	Beneficial interaction possible	OCP may increase demand for vitamin B2. Increased intake may be required with long-term therapy
	Vitamin B3 (niacin)	Reduced vitamin B3 levels	Beneficial interaction possible	Increased intake may be required with long-term therapy
	Vitamin B5 (pantothenic acid)	Reduced vitamin B5 levels	Beneficial interaction possible	Increased intake may be required with long-term therapy
	Vitamin B6 (pyridoxine)	Reduced vitamin B6 levels	Beneficial interaction possible	OCP may induce pyridoxine deficiency. Increased intake may be required with long-term therapy
	Vitamin B12	Reduced vitamin B12 levels	Observe for signs and symptoms of B12 deficiency Beneficial interaction possible	OCP users showed significantly lower concentrations of cobalamin than controls in a clinical study. Increased intake may be required with long-term therapy

ENDOCRINE AND METABOLIC DISORDERS

Adrenal steroid hormones

Corticosteroids	Calcium	Reduced side-effects	Beneficial interaction possible	Through inhibiting vitamin D-mediated calcium absorption, overall levels may be decreased. Increased calcium intake may be required with long-term therapy
	Chromium	Reduced side-effects	Beneficial interaction possible	Corticosteroids increase urinary losses of chromium, and chromium supplementation has been shown to aid in recovery from steroid-induced diabetes mellitus
	Licorice	Additive effects	Beneficial interaction possible but patients should be monitored closely for corticosteroid excess	Concurrent use of licorice preparations potentiates the effects of topical and oral corticosteroids (e.g. prednisolone) as glycyrrhizin inhibits the metabolism of prednisolone. Some practitioners use licorice to minimise requirements for, or to aid in withdrawal of, corticosteroid medications
	Vitamin C	Reduced vitamin C effects	Beneficial interaction possible	May increase requirement for vitamin C. Increased intake may be required with long-term therapy
	Vitamin D	Reduced vitamin D absorption	Beneficial interaction possible	Increased vitamin D intake may be required with long-term therapy
Betamethasone	Carnitine	Additive effects	Beneficial interaction possible	RCT has shown that a combination of low-dose betamethasone (2 mg/day) and L-carnitine (4 g/5 days) was more effective in preventing respiratory distress syndrome (7.3% vs 14.5%) and death (1.8% vs 7.3%) in preterm infants than high-dose betamethasone given alone (8 mg/2 days)

Agents affecting calcium and bone metabolism

Alendronate (e.g. Fosamax) and Etidronate (e.g. Didronel)	Calcium	Reduced drug absorption	Separate doses by ≥2 hours	Calcium may reduce drug absorption; however, adequate calcium is required for optimal drug effects
	Iron	Reduced drug absorption	Separate doses by ≥2 hours	
	Magnesium	Reduced drug absorption	Separate doses by ≥2 hours	Magnesium may reduce drug absorption; however, adequate magnesium is required for optimal drug effects
	Zinc	Reduced drug absorption	Separate doses by ≥2 hours	



Drug	CM	Potential outcome	Recommendation	Evidence/Comments
Gonadal hormones				
Oestrogen	Hops	Additive effects	Observe	Theoretical interaction, based on mild oestrogenic effect of hops
	Red clover	Reduced drug effects	Observe	Theoretically, if taken in large quantities phytoestrogens may compete with synthetic oestrogens for receptor binding— clinical significance unknown
Oestrogen and progesterone	Calcium	Additive effects	Beneficial interaction possible	Possible beneficial interaction on bone mineralisation
	Liquorice	Increased side-effects	Observe Caution with high-dose liquorice or long-term use (>2 weeks)	OCP can increase sensitivity to glycyrrhizin side-effects such as hypertension, fluid retention, hypokalaemia
Testosterone	Liquorice	Altered testosterone effect	Observe Monitor testosterone levels	Contradictory evidence suggests possible effects on testosterone levels
Haemopoietic agents				
Erythropoietin	Ginseng — Korean	Enhanced drug effects	Beneficial interaction possible	The total saponin fraction has been shown to promote haemopoiesis — clinical significance for total herb unknown
		Enhanced drug effects	Beneficial interaction possible	
		Enhanced drug effects	Beneficial interaction possible	Animal studies indicate herb increases haematopoiesis — clinical significance unknown
Hypoglycaemic agents				
Hypoglycaemic agents (e.g. metformin). Adverse effects associated with increased hypoglycaemic effects include sweating, hunger, depression, tremor and headaches	Aloe vera	Additive effects	Observe	Oral aloe vera may have hypoglycaemic activity, so additive effects are theoretically possible
	Andrographis	Additive effects	Caution — blood glucose levels should be checked regularly Beneficial interaction possible under professional supervision	Andrographis has hypoglycaemic activity comparable to that of metformin <i>in vivo</i> , so additive effects are theoretically possible
	Bilberry	Additive effects	Observe	Animal study identified the constituent myrtillin as exerting hypoglycaemic actions — relevance for bilberry unclear
	Bitter melon	Additive effects	Caution Monitor drug requirements Possible beneficial effect under professional supervision	
	Chromium	Additive effects	Caution Monitor drug requirements Beneficial interaction possible under professional supervision	Clinical studies have shown that chromium has hypoglycaemic activity in some individuals
	Cinnamon	Additive effects	Observe— potentially beneficial interaction	Clinical studies have produced contradictory results
	Damiana	Additive effects	Observe	
	Fenugreek	Additive effects	Caution — blood glucose levels should be checked regularly Beneficial interaction possible under professional supervision	



Drug	CM	Potential outcome	Recommendation	Evidence/Comments
Hypoglycaemic agents	Ginseng — Siberian	Additive effects	Observe	Speculation is based on IV use in animal studies and has not been observed in humans with oral dose forms
	Green tea	Additive effects	Observe	Clinical significance unknown
	Myrrh	Additive effects	Caution — blood glucose levels should be checked regularly Beneficial interaction possible	Myrrh has been shown to increase glucose tolerance in both normal and diabetic rats — clinical significance unknown
	Olive leaf extract	Additive effects	Beneficial interaction possible— drug dose may need modification	
	Psyllium	Additive effects	Drug dose may need modification	
	Vitamin B3 (niacin)	Increased drug requirement	Caution Monitor drug effectiveness	Niacin may affect glycaemic control and increase fasting blood glucose levels, so medication doses may need to be reviewed
Metformin	Vitamin B12	Decreased vitamin B12 levels	Observe	Increased B12 intake may be required with long-term drug use

Thyroid hormones and antithyroid agents

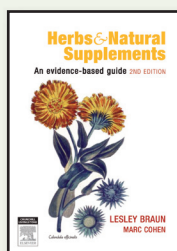
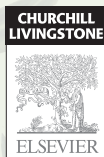
Levothyroxine (e.g. Oroxine)	Calcium	Reduced drug absorption	Separate doses by 2–4 hours	Calcium and thyroxine form an insoluble complex
	Celery	Decreased drug effect	Observe	One case report suggests that celery extract may reduce drug effects. Clinical significance unknown
	Horseradish	Increased drug requirement	Observe Monitor thyroid function. Dose may need to be adjusted	Isothiocyanates may inhibit thyroxine formation and be goitrogenic, although this has not been demonstrated clinically
	Iron	Decreased drug absorption	Separate doses by 2–4 hours	Iron supplements may decrease absorption of thyroid medication; however, iron deficiency may impair the body's ability to make thyroid hormones
	Magnesium	Reduced drug absorption	Separate doses by 2–4 hours	Magnesium and thyroxine form an insoluble complex together
	Tyrosine	Additive effects	Observe	Additive effects theoretically possible, as tyrosine is a precursor to thyroid hormones
	Withania	Additive effects	Observe	An in vivo study reported that daily administration of Withania somnifera root extract enhanced serum T4 concentration
	Zinc	Reduced drug absorption	Separate doses by 2–4 hours	Zinc and thyroxine form an insoluble complex together

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