

# Evidence Based Management of Complementary and Alternative Medicines in the Perioperative Period



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## Background

Approximately 70%<sup>1</sup> of Australians use complementary and alternative medicines (CAM). Many CAM may affect perioperative medication management and increase perioperative morbidity<sup>2</sup>, however there is a lack of consensus evidence based guidelines regarding the pharmacological effects and management of CAM in the perioperative period. Because of the assumption that these products are natural and this confers safety, their use by patients is often unreported.

## Aim

To review the evidence and determine when to cease eighteen commonly used CAM prior to surgery in adults to minimise perioperative adverse effects.

## Method

The PubMed and Cochrane Libraries, Natural Medicines database and UpToDate were searched for articles addressing the perioperative effects of CAM. Meta-analyses, randomised-controlled-trials, in-vivo studies, case series, case reports and pharmacokinetic studies were reviewed. Articles were assessed to determine the pharmacological effects of concern perioperatively and recommendations regarding when to cease CAM prior to surgery.

## Results

Table 1. CAM Perioperative effects of concern

CAM	Possible Perioperative Risks
Glucosamine +/- Chondroitin	Unstable glycaemia (theoretical risk), Increased bleeding risk, Drug Interactions (warfarin)
Garlic	Increased bleeding risk (irreversible dose dependent antiplatelet effect), Hypotension (marginal effect), Drug Interactions (antiplatelets, anticoagulants)
Ginkgo Biloba	Increased bleeding risk (case reports of spontaneous intracranial bleeding), Drug Interactions (antiplatelets, anticoagulants & ciclosporin)
Ginseng (American, Siberian, Panax)	Hypoglycaemia, Increased bleeding risk, Drug Interactions (antiplatelets & anticoagulants)
Echinacea	Decreased effectiveness of immunosuppressants, Drug Interactions (Inhibits CYP1A2 & induces hepatic & inhibits intestinal CYP3A4)
St Johns Wort (Hypericum perforatum)	Drug Interactions & long t <sub>1/2</sub> (induces CYP3A4 & CYP2C9 - antiplatelets & anticoagulants, immunosuppressants, risk of Serotonin Syndrome), may lower digoxin levels, Hypotension during anaesthesia, Prolonged anaesthesia & post-operative sedation
Saw Palmetto	Increased bleeding risk, Drug Interactions (antiplatelets & anticoagulants) (anecdotal 2 case reports)
Valerian	CNS depressant effects, Dependence, Drug Interactions (inhibits CYP3A4 ONLY at high doses >375mg daily)
Turmeric (Curcumin)	Increased bleeding risk (theoretical risk), Drug Interactions (Inhibits CYP3A4) antiplatelets & anticoagulants
Omega 3 Fatty Acids	No clinically significant increased bleeding risk, Potential Drug Interactions (antiplatelets) at high doses.
Arnica (herbal)	Increased bleeding risk, Drug Interactions (antiplatelets & anticoagulants) (theoretical risk)
Magnesium	Increased bleeding risk, Drug Interactions (antiplatelets & anticoagulants, aminoglycoside antibiotics, oral quinolone antibiotics, analgesics – adjuvant effect)
Vitamin C (Ascorbic acid)	High doses may precipitate haemolysis in those with G6PD deficiency, Kidney stones, GIT upset
Vitamin E	High Dose >400IU daily may Increase bleeding risk (dose-dependent), May inhibit wound healing, Drug Interactions (antiplatelets & anticoagulants, caution with chemotherapy as antioxidant-consult oncologist)
Pyridoxine (Vitamin B6)	May potentiate the effect of antihypertensives, Drug Interactions (phenobarbitone & phenytoin, avoid high doses; >100mg daily), High doses may cause pyridoxine neuropathy (usually reversible)
Olive Leaf Extract (Olea europaea)	May cause Hypoglycaemia (monitor BGL in patients with diabetes), May cause Hypotension (theoretical)
Zinc	Drug Interactions (oral quinolone & tetracycline antibiotics)

## Results

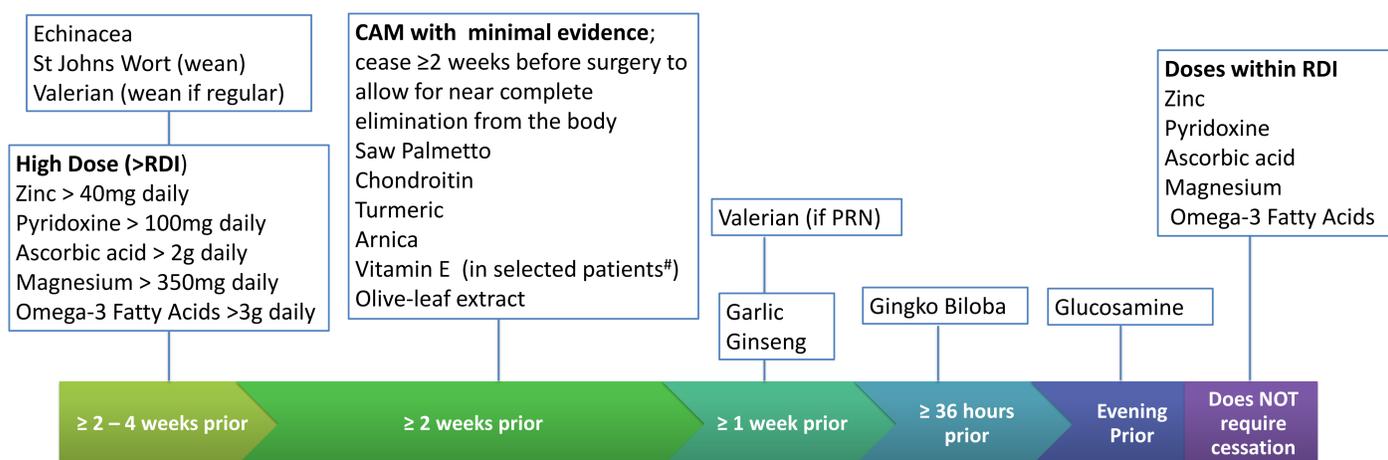


Figure 1. Timeline - When to cease CAM prior to Surgery

\*RDI = Recommended daily intake  
# See discussion

## Conclusion

CAM use potentially increases perioperative risk due to pharmacological effects and drug interactions. Further prospective and observational studies are required as CAM are used frequently and the current quality of evidence to guide recommendations is low. Until the perioperative safety of CAM is established, the benefit of cessation ≥2 weeks preoperatively outweighs the risks of continuing them<sup>7,8</sup>. Familiarity with CAM and their potential effects has become necessary, to avert complications in the perioperative period. Pharmacists should ask the patient directly about CAM in the preoperative assessment.

## Discussion

The quality of evidence and strength of recommendations regarding perioperative effects of most CAM reviewed were Grade 1C based on the UpToDate GRADE grading system. This is a strong recommendation applicable to most patients, but some of the evidence base supporting the recommendation is of low quality (much is from in-vitro, animal or pharmacokinetic studies, case reports, or randomised controlled trials with serious flaws), and any estimate of effect is uncertain. CAM considered to increase perioperative risk are those with effects on coagulation, blood pressure, glycaemia, electrolytes, sedation, wound healing and those with potential interactions; see Table 1. Timing of cessation is recommended as per Figure 1. CAM of particular concern include Valerian; which should be weaned over ≥2 to 4 weeks due to dependence with regular dosing and benzodiazepine-like withdrawal; and Echinacea and St John's Wort which should be ceased/ weaned respectively ideally ≥2 to 4 weeks prior to surgery. This is due to enzyme induction leading to potential drug interactions, very relevant for patients awaiting organ transplantation. Zinc, Pyridoxine, Ascorbic acid, Magnesium and Omega-3 Fatty Acids don't require cessation, unless high doses are taken, and then the doses should be reduced to RDI or discontinued ≥2 weeks before surgery. Vitamin E should be discontinued ≥2 weeks before surgery in selected patients: those on > 400 IU daily<sup>3</sup>; those having an angioplasty<sup>4</sup> or who need a strong collagen-mediated wound closure<sup>5</sup>; those undergoing tendon repairs (withhold until healing complete), and those who require antiplatelet/ anticoagulant agents. Many guidelines recommend ceasing dietary supplements 2 weeks before surgery, although it may be safe to continue vitamins and minerals up to the day of surgery provided they are not in combination with other CAM, and doses are within the RDI<sup>6</sup>. For CAM with minimal evidence, cessation is recommended ≥2 weeks before surgery to allow for near complete elimination.

## References and Contact

- Xue CC, Complementary and alternative medicine use in Australia: a national population-based survey, *J Altern Complement Med*. 2007 Jul-Aug; 13(6):643-50
  - Kaye AD, Clarke RC, Sabar R, et al. Herbal medicines: current trends in anesthesiology practice - a hospital survey. *J Clin Anesth* 2000; 12:468
  - Broughton G, Crosby MA, Coleman J, Rohrich RJ. Use of herbal supplements and vitamins in plastic surgery: a practical review. *Plast Reconstr Surg*. 2007 Mar; 119(3): 48e-66e.
  - Tardif JC. Probulcol and multivitamins in the prevention of restenosis after coronary angioplasty. *N Engl J Med* 1997;337:365-372.
  - Brown, S. et al. Oral nutritional supplementation accelerates skin wound healing: a randomized, placebo-controlled, double-arm, crossover study. *Plast.Reconstr.Surg*. 114:237, 2004
  - Wong, WW, Gabriel A, Maxwell GP, Gupta SC. Bleeding risks of herbal, homeopathic, and dietary supplements: a hidden nightmare for plastic surgeons? *Aesthet Surg J*. 2012 Mar; 32(3): 332-46.
  - Muluk V, Cohn SL, Whinney C, et al. Perioperative medication management, UpToDate. Waltham, MA: UpToDate Inc. <http://www.uptodate.com> Accessed on 27 March 2017.
  - Frost EA. Herbal medicines and interactions with anesthetic agents. *Middle East J Anaesthesiol*. 2006 Jun;18(5): 851-78.
  - Ang-Lee M, Moss J, Yuan chun-Su. Herbal Medicines and Perioperative care. *JAMA* 2001; 286: 208-16.
  - Heller J, Gabbay JS, Ghadjar K, Jourabchi M, O'Hara C, et al. Top-10 list of herbal and supplemental medicines used by cosmetic patients: what the plastic surgeon needs to know. *Plast Reconstr Surg*. 2006. 117(2): 436-47.
  - Katrine Munk Begtrup, Andreas Engel Krag, Anne-Mette Hvas, No impact of fish oil supplements on bleeding risk: a systematic review. *Dan Med J* 2017; 64(5): A5366
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