Herbal Medicine and Perioperative Care — An Australian Perspective

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INTRODUCTION
In recent years, there has been a definite rise in the popularity and use of complementary and alternative medicines (CAM), including herbal medicines, in developed countries. A “herbal medicine” is defined as a plant-derived product used for medicinal or health purposes. Also known as nutraceuticals or natural remedies, they are perceived by many patients as being “natural” and therefore safe.

As anaesthetists, we cannot ignore the impact that these medicines have on anaesthetic practice. This includes the potential interaction that such products have either with a patient’s regular prescription medications or with anaesthetic drugs. Anaesthetic techniques (e.g. regional anaesthesia) may need to be reconsidered if patients have been taking herbal medicines.

HISTORY AND CULTURE
The earliest evidence of human use of plants for healing dates back to the Neanderthal period. In the 16th century, botanical gardens were created to grow medicinal plants for medical schools and herbal remedies flourished until the 17th century when more “scientific” pharmacological remedies came into favour. At that time, though, health care was commonly provided by women using home-made botanical remedies and purchasing similar products as “patent medicines”. Scientific methods became more advanced and preferred in the 19th century and the practice of botanical healing was dismissed as quackery. However, by the 1960s, with concerns over the iatrogenic effects of conventional medicine and desire for self-reliance, interest in “natural health” and the use of herbal products increased.

In 1985 the World Health Organisation estimated that up to 80% of the world’s population still relied on botanicals for their primary health needs. Many cultures espouse the use of botanicals in their traditional healing practices, such as Chinese medicine, Ayurveda (a holistic system originated in the Vedic civilization of India), Curanderismo (a Mexican-American healing tradition), or Kampo medicine in Japan. This widespread use is not restricted to developing countries; up to 30% of doctors in Germany and France use herbs in practice. In the pharmacopoeias of developed countries, 25% of drugs are substances first isolated from plants and a further 25% are modifications of chemicals first found in plants.
HERBAL PREPARATIONS
Herbs are available in many forms, depending on the type of plant and its use. They may include fresh, dried, chopped or whole herbs and can be steeped as teas (infusions) or simmered over low heat (decoctions). Other preparations include tinctures (fresh or dried herbs preserved in alcohol), vinegar extracts (acetextracts), syrups, glycerites (in vegetable glycerine) or miels (in honey). Freeze-dried or herbal powders also come in bulk, tablet, capsule, paste, or concentrate (4-6 times regular strength) forms. Other ways to administer herbs may be by suppositories, creams, gels, liniments, oils, compresses, steams, aromatics (oils) or baths.

WHO AND WHY DO PEOPLE USE HERBAL MEDICINES
Virtually all surveys on this subject agree on several characteristics associated with the typical user of herbal medicines. They are more likely to be female, 40-60 years old, better educated, have a higher income and be employed. The reasons for consumers turning to herbal medicine are complex and differ according to many factors. A patient with a life-threatening condition has different motivations for trying herbal medicines than a person who is essentially healthy but wants to invest in well-being or hopes to prevent future illness. Contrary to common belief, disappointment with orthodox medicine is not a prime reason for people to turn towards alternative medicines. Potential reasons for trying herbal medicines include: perceived effectiveness and safety, emphasis on holism and natural products, control over treatment, affluence, accessibility, rejection of science and technology, desperation and dissatisfaction with conventional pharmacological treatment.

ANAESTHETISTS KNOWLEDGE OF AND ATTITUDE TOWARDS HERBAL MEDICINES
Do physicians and, in particular anaesthetists actually know much about the significance of these herbal medicines? What is the point of patients reporting herbal medicine usage if we are not aware of the clinical importance of these preparations? In a study by Lennox, of the 28 anesthesiologists who participated by completing a ‘herbal medicine’ questionnaire containing 27 yes/no type responses, only 32% of the questions were answered correctly. Attitudes of physicians, in either being dismissive of herbal medicines or considering them as no more relevant than harmless placebos, do not foster knowledge or understanding. Two studies highlighted the low percentage of documentation of herbal medicine use on the anaesthetic chart, even after the patient had reported their usage. However, attitudes to herbal medicines are evolving. The Australian and New Zealand College of Anaesthetists, American Society of Anesthesiologists and the Australian Medical Association have all produced statements or papers on herbal medicines. The recent anaesthetic literature contains numerous articles on “anaesthesia and herbal medicines”. Multiple choice questions on herbal medicines even appeared in the College Part 2 Exams last year.

USAGE AND COST OF HERBAL MEDICINES
A 1993, a South Australian survey of 3004 subjects found that 12% had used herbal medicines in the previous year. Although current Australian expenditure on herbal remedies is unknown, $621 million is spent per year on CAM. In the US, recent data estimated that 49% of the adult population have used a herbal product during the
previous year, with 24% of the population regular users and US$5.1 billion spent on such remedies.\textsuperscript{18} The European market is valued at US$6 billion per year.\textsuperscript{5} A conservative estimate of US$10 per month is being spent on herbs per patient.\textsuperscript{20} Sales of herbal medicines are growing by 20% a year and are the largest growth area in retail pharmacy, far exceeding growth in the conventional drug category.\textsuperscript{3} Sales have moved from specialty stores to mainline shopping environs.\textsuperscript{21}

Numerous studies have investigated the use of herbal remedies by patients about to undergo surgery. In Australia, a 2002 study of 1102 patients (about to be published), revealed the prevalence rate for perioperative herbal usage to be 14.3%. Individual studies from Canada, England and Ireland have found a rate of 33.4%, 4.8% and 12.1% respectively.\textsuperscript{13, 12, 22} In seven recent studies from the USA, the prevalence of perioperative herbal usage lies between 9.7%-37.0%, with a mean of 25.6%.\textsuperscript{2, 11, 20, 23-26}

Failure to disclose patients’ use of herbal medications to the treating doctor is common. Explanations for this include patient-held beliefs that physicians are not knowledgeable about herbal medications or are prejudiced against them, patients not considering these substances to be medications and others’ fearing admitting to their physicians use of unconventional therapies.\textsuperscript{27} Importantly, failure of the doctor to specially ask the patient about their use of herbal medications discourages disclosure. A South Australian survey of 3,027 people in 2000, found that only 42.8% told their doctor of their use of alternative medicines.\textsuperscript{10} A survey of 325 patients attending a Sydney teaching hospital emergency department in 1994 revealed that 35.5% of users had informed their medical practitioner about any use of CAM.\textsuperscript{17} This low rate of disclosure is similarly reflected in the surgical population.\textsuperscript{1} In Crowe’s study, 83% of the surgical team were unaware that the patient took herbal medications.\textsuperscript{22} The rate of disclosure of herbal medications usage by patients to their anaesthetists is also low, being 30% and 43.6% in two US studies.\textsuperscript{20, 23} An Australian 2002 study, found that only 27.8% of preoperative patients informed the hospital’s doctors or other staff of their usage of herbal remedies, whereas 41.8% had told their family doctor.

REGULATION OF HERBAL MEDICINES IN AUSTRALIA

Australia has one of the more stringent regimes for regulation of alternative medications production and labelling.\textsuperscript{15} Products for medicinal use (prescription, scheduled proprietary medicines and all complementary medicines) must be placed on the Australian Register of Therapeutic Goods (ARTG), in one of two categories — ‘listed’ or “registered”.\textsuperscript{17, 28} Formulations can be “listed” for a small fee if they contain substances regarded by the Therapeutic Goods Administration (TGA) as being of low public health concern and comply with the TGA advertising code. This restricts wording of claims to “assist” rather than to “treat” and limits indications to minor self-limiting conditions.\textsuperscript{17} Manufacturers and sponsors are only required to “hold the evidence” for preparations for which minor therapeutic claims are being made. These claims are not routinely evaluated for a listable preparation.\textsuperscript{29} About 4,500 plant-based products are listed; these are given an “AUST L” number.\textsuperscript{17}

Registered products, which bear an “AUST R” number, contain herbs that either make substantial efficacy claims (e.g. disease prevention, modification or management) or those that the TGA specify as being of some health concern or are a restricted substance.\textsuperscript{17} Registered medicines are individually evaluated for safety, quality and efficacy before they are released onto the market.\textsuperscript{29} For registration, which is much more costly, appropriate documentation outlining clinical trial work must be submitted
to the Complementary Medicines Evaluation Committee (CMEC), which advises the TGA. Less than five CAM products have been evaluated in this way.¹⁷

Adverse drug reporting (ADR) is as essential for CAM products as it is for pharmaceuticals in providing post-marketing surveillance. Given the widespread use of CAM, the low number of (voluntary) adverse reports to Adverse Drug Reactions Advisory Committee (ADRAC) suggests that either CAM have a low risk of adverse effects or such effects are significantly under-reported.¹⁷ The latter is likely for the following reasons: the public perception that “natural” products are safe, the use of CAM is not routinely included in patients’ drug histories and that, until recently, ADRAC has not actively encouraged the reporting of adverse reactions by practitioners and consumers of alternative medicines.¹⁷

**EFFICACY AND SAFETY STUDIES**

Although herbal medicines have been used for hundreds of years, traditional use is a poor indication for either efficacy or safety.⁶ Randomised clinical trials (RCT), the accepted standard for testing efficacy, have had limited impact in regards to herbal medicines for several reasons. Since herbal remedies (i.e. plants) cannot be patented, and as they are unlikely to recoup the estimated US$350 million it costs to prove a new drug effective and safe, there is little motivation for manufacturers to conduct RCTs.³ Despite this, RCTs of medicinal products have been conducted but, more often than not, trials assessing a certain treatment for a given condition differ in their methodological details and findings.⁶ Therefore, the majority of literature on herbs is based on case reports, uncontrolled case series and studies on compounds that cannot be consistently reproduced.⁷

In 1978, the German Federal Health Agency established Commission E, which comprised an expert panel of physicians, pharmacists, toxicologists and industrial representatives. They were charged with the task of regulating and researching the safety and efficacy of herbal medicines. Until 1994, Commission E independently evaluated all available scientific data on herbs and published results in the form of monographs. These have been translated, reviewed and are widely used as reliable sources of information on herbs.³⁰

**ADVERSE EFFECTS OF HERBAL MEDICINES**

The uncritical acceptance of the mantra “natural=safe” by both the public and doctors has been a major problem. The media have also helped to perpetuate this myth.³¹ Natural plant products are perceived to be “healthier” than manufactured medicines.³ In one study, 92% of patients attending a Sydney emergency department felt that CAM agents were completely safe.³² In fact, there are adverse effects of herbal medications; these may be either intrinsic or extrinsic.

**Intrinsic Effects**

Intrinsic effects are those of the herb itself and are characterised as for pharmaceuticals, as type A (predictable, dose-dependent) and type B (unpredictable, idiosyncratic).¹⁷

**Extrinsic Effects**

Extrinsic effects are not related to the herb itself, but to problems in commercial manufacture or extemporaneous compounding.¹⁷
Misidentification: Plants can be named four different ways, the common English name, the translated name, the Latinised pharmaceutical name and the scientific name. For example the Chinese herb “dong quai” is also known as “dong guai”, “danggui”, “tang kuei”, “Angelica polymorpha” and “Radix angelica”.17

Lack of Standardisation: The therapeutic and toxic components of plants vary depending on the part of the plant used, stage of ripeness, geographical area where the plant is grown and storage conditions. In one study the biological activity of ginseng was examined in fifty commercial brands sold in 11 countries. In 44 of these products, the concentration of ginsenoside (the active component of ginseng) ranged from 1.9% to 9% w/w; six products contained no ginsenoside and one product contained large amounts of ephedrine.17

Contamination: During growth and storage, crude plant material can become contaminated by pesticide residues, microorganisms, aflatoxins, radioactive substances and heavy metals; lead, cadmium, mercury and arsenic have been reported as contaminants of some overseas herbal preparations.17

Substitution and Adulteration: In 2001, the TGA released a “Practitioner Alert” advising about the risk of Aristolochia fangchi, containing the nephrotoxic component aristolochic acid, instead of Stephania tetrandra in a commercial preparation of a slimming treatment. The condition known as “Chinese herb nephropathy” affected 100 women overseas, 30 of whom developed terminal renal failure.6, 17, 33

Incorrect Preparation/Dosage: A West Australian patient had a heart attack when he failed to follow a herbalist’s instructions.17

Inappropriate Labelling/Advertising: In the US, a 1999 study found that only 43% of dietary supplement products (including herbs) available for sale in stores, catalogues and on the Internet were correctly labelled as a “Supplement”.7 Some products labelled as ginseng actually also contained mandrake (scopolamine) or snake-root (reserpine) because of the high cost of pure ginseng.3

WITHDRAWAL OF HERBAL MEDICINES BEFORE SURGERY

Currently the American Society of Anesthesiologists advises patients to stop taking herbal medications at least 2 to 3 weeks before surgery to allow time for the herals to be cleared from the body. If the time span is shorter than two weeks, patients should be advised to bring the product in its original container to the hospital, so that the anaesthetist can see exactly what the patient is taking and what the ingredients are.21, 34 However, a review of the literature favours a more targeted approach. Pharmacokinetic data on selective active constituents indicate that some herbal medicines are eliminated quickly and may be discontinued closer to the time of surgery.27

MEDICINAL HERBAL USE IN AUSTRALIA

The ten most popular herbs used for medicinal purposes in descending order, from an Australian study, are: Garlic, Evening Primrose, Gingko, St. John’s Wort, Echinacea, Valerian, Horseradish, Ginseng, Cranberry and Aloe. The top five to eight herbs consistently reappear in similar studies conducted throughout the world.11, 12, 13, 20, 30, 35 Although there are a large number of different herbal medications available (over 1500 in the US), the top eight herbs account for more than 50% of single herb preparations sold.27

The possibility of drug interactions between herbal and orthodox medications is of
major concern. Twenty to 34% of herbal medicine users also report concurrent prescription or over-the-counter medication use.

Typical popular herbal treatments and their indications, adverse effects and possible interactions are listed in Appendix 1. Specific perioperative considerations are detailed in Appendix 2.

CONCLUSION

Herbal medicine is here to stay. For the benefit of the patient and the physician, it is important for the anaesthetist to inform themselves about the potential benefits, drug interactions and adverse effects of herbal medications. Although there is a vast array and confusing nomenclature of different medicinal herbs, familiarity with the common 15-20 herbs, which account for the great majority that are sold, is all that really is required. Additional information if necessary, can always be sourced from a reliable reference. The question “Do you take any herbal medications or other substances” should be a routine part of every anaesthetist’s pre-operative assessment.

APPENDIX 1: COMMON HERBAL TREATMENTS

Garlic (Allium sativum)

Indications:
Hypertension (moderate effect) Level 1 evidence
Hypercholesterolaemia (moderate effect) Level 1 evidence
Atherosclerosis (moderate effect) Level 4 evidence

Significant Adverse Effects:
Risk of spontaneous (including epidural haematoma) and post operative bleeding

Drug Interactions:
Increased INR levels in patients previously stabilised on warfarin
Avoid in combination with aspirin, NSAID because of enhanced antiplatelet activity

Cessation prior to Surgery:
At least 7 days before surgery

Evening Primrose (Oenothera biennis)

Indications:
Premenstrual syndrome, menopause (No proven benefit) Level 1 evidence

Significant Adverse Effects:
None

Drug Interactions:
Potential to lower seizure threshold with anti-epileptic medications

Cessation prior to Surgery:
Probably not required

Gingko (Gingko biloba)
Indications:
Cognitive impairment (memory and concentration ability) in patients with Alzheimer’s disease and multi-infarct dementia Level 1 evidence\(^1, 36\)
Intermittent claudication Level 2 evidence\(^1, 31\)
Tinnitus (vascular origin) Level 2 evidence\(^31\)

Significant Adverse Effect:
Intracranial haemorrhage, postoperative bleeding (case reports)\(^1, 27, 31\)
Seizures — seen in children after excessive ingestion of seeds\(^31\)

Drug Interactions:
Concomitant use with aspirin, NSAID and anticoagulants not advised\(^36\)
May diminish the efficacy of anticonvulsants\(^36\)

Cessation prior to Surgery:
At least 2 days (probably safer 7 days) before surgery\(^27, 37\)

St John’s Wort (Hypericum perforatum)

Indications:
Mild to moderate depression Level 1 evidence\(^1, 36\)

Significant Adverse Effects:
Photosensitivity (high doses in fair skinned people)\(^36\)

Drug Interactions:
SSRI, TCA may precipitate the “serotonin syndrome”\(^1, 36\)
MAOI potentiates side effects\(^36\)
Induces hepatic enzymes — decrease level of cyclosporin, warfarin, theophylline, oral contraceptive pill, digoxin, antiretroviral agents, anticonvulsants\(^1, 27, 31\)

Cessation prior to Surgery:
Discontinue at least 5 days before surgery\(^27, 37\)

Echinacea (Echinacea species)

Indications:
To decrease the severity and duration of URTI Level 2 evidence\(^1, 31\)

Significant Adverse Effects:
Hepatitis, 3 cases reported to ADRAC\(^31\)
May cause an overactive immune response in patients with HIV, SLE, active TB, multiple sclerosis\(^1\)
Increased risk of allergic reactions (anaphylaxis, acute asthma) in patients with a history of asthma, atopy, allergic rhinitis\(^27, 38\)

Drug Interactions:
May interfere with immunosuppressant drugs (e.g. steroids)\(^1, 27\)
May potentiate hepatotoxicity in combination with anabolic steroids, amiodarone, methotrexate and ketoconazole\(^36\)
Cessation prior to Surgery:
Discontinue as far in advance as possible in patients with liver dysfunction\textsuperscript{27, 37}

\textbf{Valerian} (Valeriana officinalis)

\textit{Indications:}
Sedation, insomnia \hspace{1cm} Level 2 evidence\textsuperscript{1, 36}

\textit{Significant Adverse Effects:}
Withdrawal syndrome (similar to benzodiazepine)\textsuperscript{27}

\textit{Drug Interactions:}
Potentiates the sedative effects of barbiturates, benzodiazepines, anaesthetics\textsuperscript{27, 36}

\textit{Cessation prior to Surgery:}
If possible, taper dose weeks before surgery.\textsuperscript{27, 37} If not, continue medication during the perioperative period\textsuperscript{37}

\textbf{Horseradish} (Armoracia rusticana)

\textit{Indications:}
Cough, bronchitis \hspace{1cm} Level 3 evidence\textsuperscript{39}

\textit{Significant Adverse Effects:}
None\textsuperscript{39}

\textit{Drug Interactions:}
None known\textsuperscript{39}

\textit{Cessation prior to Surgery:}
Probably not required

\textbf{Ginseng} (Panax ginseng)

\textit{Indications:}
Treatment of Type 2 Diabetes (decrease glucose levels and weight loss, improved subjective ratings) \hspace{1cm} Level 2 evidence\textsuperscript{36}
To improve stamina, vigilance, well-being (No proven benefit) \hspace{1cm} Level 2 evidence\textsuperscript{31}

\textit{Significant Adverse Effects:}
Hypoglycaemia in fasting patients, Steven Johnson syndrome, increased risk of bleeding, nervousness, insomnia\textsuperscript{27, 36}

\textit{Drug Interactions:}
Increased bleeding risk with aspirin, NSAID, anticoagulants\textsuperscript{36}
Increased risk of headaches, tremulousness, mania with phenelzine\textsuperscript{36}

\textit{Cessation prior to Surgery:}
At least 7 days before surgery\textsuperscript{27, 37}
Cranberry (Vaccinium macrocarpon)

**Indications:**
Treatment and prevention of urinary tract infections Level 3 evidence^{40,41}

**Significant Adverse Effects:**
None

**Drug Interactions:**
Increased absorption of Vitamin B12 in patients taking omeprazole^{41}

**Cessation prior to Surgery:**
Probably not required

Aloe (Aloe vera)

**Indications:**
Psoriasis Level 3 evidence^{42}
Wound healing (No proven benefit) Level 3 evidence^{42, 43}
Constipation Level 4 evidence^{42}

**Significant Adverse Effects:**
Topical/Oral — hypersensitivity reactions, dermatitis^{42, 43}
Oral — hypokalaemia^{42}

**Drug Interactions:**
May potentiate hypoglycaemia in combination with glibenclamide^{45}

**Cessation prior to Surgery:**
Probably not required

APPENDIX 2: PERIOPERATIVE IMPLICATIONS OF HERBAL MEDICINES

**Adverse Cardiovascular System Effects**

*Ginseng:* has been noted to cause tachycardia and hypertension during anaesthesia^{1, 4}

*Ephedra (Ma-Huang):* associated with numerous reports of cerebral bleeds, CVA, panic attacks, palpitations, arrhythmia, chest pain and myocardial infarction^{1, 4, 15, 33}

**Adverse Coagulation Effects**

Ginger, Garlic, Gingko, Ginseng, and Feverfew: all possess antiplatelet activity and there have been reports of unanticipated excessive surgical bleeding with them^{1, 7, 8, 15}

Theoretical increase risk of epidural haematoma following neuraxial blockade, although no reported cases so far^{1}

*Dong quai:* contains coumarin, has caused increased INR level and widespread bleeding^{44, 45}

**Renal/Hepatic/Electrolyte Disturbance Effects**

*Liquorice:* due to its mineralocorticoid effect it may exacerbate renal insufficiency and has caused hypertension, hypokalaemia, sodium retention and oedema^{5, 7}

*Goldenseal:* is an aquaretic (not a diuretic), thus it may decrease the potential benefits of anti-hypertensive medications^{4}

*Echinacea:* may be hepatotoxic with chronic usage^{4}
Adverse Immunological Effects

*Echinacea:* (long term use >8 weeks) could cause immunosuppression which may result in poor wound healing and increased infection risk\(^1\)

**Prolongation of Anaesthesia**

*Kava:* potentiates barbiturate and benzodiazepine effect, resulting in prolonged sedation\(^1\)

*Valerian:* via its effect upon the GABA neurotransmitter, potentiates the sedative effects of both barbiturates and benzodiazepines\(^1,4\)

**APPENDIX 3: DEFINITIONS/KEY TERMS**

**Complementary and Alternative Medicines (CAM):** a term used to describe non orthodox (i.e. neither prescription nor “over the counter” regulated medications) consisting of herbs, dietary supplements, vitamins and homeopathic medicines

**Dietary Supplement:** a product not represented as a conventional food or as a sole meal item that increases the total dietary intake. They may contain parts, entire molecules or concentrated forms of vitamins, minerals, proteins or enzymes\(^46\)

**Herbs:** plant-derived product used for medicinal or health purposes

**Nutraceuticals:** herbal medicines and other supplements

**REFERENCES**