The perioperative implications of herbal medicines

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The use of Complementary and Alternative Medicine (CAM) is prevalent among individuals requiring surgery. CAM is a broad field encompassing a diverse group of medical and healthcare systems and products that aren’t part of conventional Western medicine. The types of CAM include mind and body medicine, manipulative and movement therapies, and natural products, such as herbal medicines. For more information about the different types of CAM, see the National Center for Complementary and Alternative Medicine’s website at http://nccam.nih.gov/health/whatiscam. This article examines one of the most common types of CAM: herbal medicines.

The growing use of herbal medicine has led to guidelines designed to inform healthcare providers and patients about potentially adverse consequences associated with herbal medicines and anesthesia.1,2 Organizations including the American Association of Nurse Anesthetists (AANA), American Society of Anesthesiologists (ASA), and American Society of Regional Anesthesia (ASRA) recommend caution when caring for patients taking herbal medicines, as they aren’t subjected to the same level of scrutiny and research requirements as prescription drugs or over-the-counter medications. The FDA addresses the misconception that, although these products are considered natural, they aren’t necessarily free from harm.3 In 2004, the FDA specifically recommended removing over-the-counter, Ephedra-containing products from the U.S. market. According to current ASRA recommendations, herbal medicines don’t interfere with the performance of neuraxial techniques.4 Mandatory discontinuation of herbal medicines, avoidance of regional techniques, and reversal of their effects on hemostasis preoperatively are considered unnecessary at this time.4 Despite these guidelines, current research is studying the effects of herbal medicines on physiologic processes and specific alterations of metabolic enzyme functions. The AANA continues to recommend that patients discontinue herbal medicines at least 1 to 2 weeks prior to surgery.3 The ASA hasn’t published a position statement on herbal medicines except to support the AANA’s recommendations. There are numerous herbal medicines that have potentially deleterious effects on patients, especially in the perioperative setting. Because their potency and purity depend on the manufacturer and distributor, significant variations in efficacy and adverse reactions may occur. The lack of standardization coupled with educational deficits among users and providers raises the risk of adverse physiologic reactions.5 Greater awareness and understanding among healthcare providers regarding these alternative remedies are necessary to provide optimal patient care.
Background
Current evidence has identified a knowledge deficit about herbal medicines among healthcare providers. A recent investigation demonstrated that only 23% of anesthesia providers were aware of the current recommendations to discontinue supplements up to 2 weeks prior to surgery. Additionally, providers scored only 21% when surveyed about the adverse reactions of common herbal medicines. Research has also identified that both physicians and nurses poorly document the use of herbal medicines among their patients. Ninety percent of healthcare providers failed to assess patient use of herbal medicines during the preoperative assessment. Over 85% of the participants requested further educational opportunities on herbal medicine uses and adverse reactions.

Regulation and quality control
The lack of evaluation and safety reporting processes for herbal medicines means there’s no standardization. This lack of organizational control leads to inconsistent potencies and pharmacologic activity. At this time, the only requirement for the manufacturers of these products is to send a copy of the product label to the FDA. A variety of contaminants, including toxic metals, have been found in herbal supplements. The lack of standardization makes it difficult for practitioners to advocate for patients and educate themselves on the adverse reactions and drug interactions of herbal medicines.

The use of herbal medicines is rising, and the consequences of drug-herb interactions are becoming more significant. Induction (increases regulation) and inhibition (decreases regulation) of hepatic enzymes (the cytochrome oxidase family known as the CYP 450 enzymes) are currently being investigated. Many herbal medicines share the same metabolic pathways and drug transporters as drugs used in the perioperative period, including the specific enzymes glucuronosyltransferases and P-glycoprotein. The implications of this information are striking. Not only must anesthesia providers consider the herbal medicines that patients are taking, they must also understand the interactions of these substances with other perioperative medications. With more research focusing on the induction or inhibition of CYP450 enzymes, anesthesia providers will have the knowledge to provide safer and more evidence-based care.

Clinically significant herbal medicines
The following is a brief overview of some of the more common and noteworthy herbal medicines that may be encountered in everyday practice. The generic name appears first, the Latin name is in italics, followed by other common names in parentheses.

Black Cohosh Actaea racemosa (black bugbane, black snakeroot, fairy candle)
Proposed effects:
- contains triterpene glycosides used to treat symptoms of menopause
- acts on estrogen and serotonin receptors.
Triterpene glycosides are organic plant toxins and are considered the active ingredient in Black Cohosh.
Implications:
- inhibition of the CYP450 3A4 enzymes:
  - Cytochrome P450 enzymes are a major source of drug metabolism. Inhibition may potentiate certain drugs that are metabolized by this pathway, including amiodarone, erythromycins, metoprolol, carvedilol, amiodipine, diltiazem, benzodiazepines, and warfarin.
- hepatotoxicity
- should be avoided during pregnancy and lactation.

Echinacea Echinacea angustifolia (American cone-flower, black sampson, comb flower)
Proposed effect:
- improved wound healing
- immune system enhancement
- arthritis therapy
Implications:
- inhibits CYP450 3A4 enzymes
- tachyphylaxis if use exceeds 8 weeks
- activates cell-mediated immunity causing allergic
reactions and reducing the actions of immunosuppressants\(^\text{14}\)
• potential for wound infection with long-term use\(^\text{6}\)
• hepatotoxicity when taken with other hepatotoxic drugs.\(^\text{6}\)

**Ephedra** *Ephedra sinica* (Ma huang)
Proposed effect:
• weight loss
• stimulatory effects that are similar to caffeine.
Implications:
• cardiovascular toxicity leading to dysrhythmias, hypertension, myocardial infarction, stroke, seizure, psychosis, and anxiety
• inhibition of antihypertensive, antiseizure, and benzodiazepine medications
• severe hypertension can be seen when used with Monoamine Oxidase Inhibitors (MAOIs)\(^\text{14}\)
• similar formulations exist, such as synephrine, which inhibits CYP450 3A4.\(^\text{12}\)

**Feverfew** *Tanacetum parthenium* (altamisa, chrysanthemum parthenium, pyrethrum parthenium, and wild chamomile)
Proposed effect:
• treatment of migraine headaches
• attenuation arthritis pain.
Implications:
• inhibits platelet activity, bleeding risk.\(^\text{10}\)

**Garlic** *Allium sativum*
Proposed effects:
• antimicrobial
• immune system enhancement (used by HIV-positive patients)
• coronary artery disease prevention
• antihypertensive
• lipid lowering.\(^\text{10,11}\)
Implications:
• decreased platelet aggregation and potentiation of antiplatelet medications, including warfarin, heparin, aspirin, and NSAIDS.\(^\text{9}\)
• While garlic can effect coagulation for up to 7 days, ASRA isn’t formally recommending discontinuation of this herb prior to neuraxial anesthesia.\(^\text{4}\)

**Ginger** *Zingiber Officinalis*
Proposed effect:
• prevention of nausea and motion sickness\(^\text{9}\)
• anti-inflammatory.

**Ginkgo** *Ginkgo Biloba* (maidenhair tree)
Proposed effects:
• treatment of peripheral vascular disease
• improved symptoms of macular degeneration
• relief from vertigo
• dissipate cognitive dysfunctions (Alzheimer’s disease)
• antioxidant properties
• minimize erectile dysfunction
• memory and cognition enhancement.\(^\text{11}\)
Implications:
• inhibitor of platelet activating factor (PAF)\(^\text{15}\)
• perioperative bleeding.\(^\text{16}\)

**Ginseng** *Panax Ginseng* (Panax)
Proposed effects:
• BP management
• lipid lowering
• cognition enhancement
• lessen fatigue
• ulcer healing
• neuroprotection
• cancer prevention
• antioxidant properties
• immune system enhancement.\(^\text{17}\)
Implications:
• possible enhanced clearance of warfarin (research has yet to support this claim)
• increases the clearance of alcohol by 30% due to its induction of the CYP 2E1 enzyme
• hypertensive interactions with select MAOIs\(^\text{18}\)
• possible delay in gastric emptying (cause for concern with patients who are high risk for aspiration).\(^\text{10,12}\)

**Kava** *Piper methysticum* (Kava Kava)
Proposed effect:
• sedative and anxiolytic properties by enhancing Gamma aminobutyric acid (GABA)\(^\text{19}\)
• inhibitory neurotransmission.\(^\text{10}\)
Implications:
• potentiate the effects of both barbiturates and benzodiazepines
• liver failure.\(^\text{10}\)
St. John’s wort  *Hypericum perforatum* (Johnsroot, SJW)
Proposed effect:
• treat mild-to-moderate depression.\(^{19}\)
Implications:
• induces specific CYP 450 enzymes; potential to decrease duration of action
• interacts with over 30 commonly used medications including digoxin, erythromycin, ibuprofen, midazolam, nifedipine, omeprazole, oral contraceptives, phenytoin, verapamil, and warfarin.\(^{11,20}\)

Valerian  *Valeriana officinalis* (valerian root)
Proposed effects:
• lessen anxiety and nervous tension
• promote sleep
• smoking cessation
• ease congestion
• relieve muscle spasms
• treat or prevent cancer.
Implications:
• decreases sleep latency through enhancement of GABA neurotransmission
• potentiates the effects of barbiturates
• amplifies the effects of sedatives and anxiolytics.\(^{10}\)

The herbal medicines discussed above are among the most commonly seen in the perioperative setting. However, the list of herbal medicines and dietary supplements used by patients is growing. Ellagic acid (EA) is a product currently undergoing scrutiny. EA is a dietary supplement and polyphenol compound found in fruits, including strawberries, raspberries, and pomegranates; it’s also found in nuts, such as pecans and walnuts. Therapeutic uses include anti-inflammatory and antinociceptive properties, free radical scavenging, anticoagulation, and depressed tumor genesis, especially prostate cancer cells. The proposed anticoagulation has been attributed to the inhibition of the Hageman factor. Hageman factor, also known as Factor XII, is a plasma protein that contributes to clotting in the common pathway of the coagulation cascade. EA inhibits a number of cell-signaling pathways that are important to tumor growth. This inhibition is demonstrated in inflammatory signaling through tumor necrosis factor alpha-induced COX-2 expression as well as nitric oxide synthase inhibition.\(^{21,22}\) Animal research indicates that concurrent administration of EA and ketorolac (a nonopioid analgesic) may cause a significant decrease in platelet activity resulting in increased blood loss.\(^{21,22}\) Further research, namely human trials, is necessary to determine EA’s effects on COX-2 and additional contributions to pain management.

Summary
The best approach for the perioperative nurse in assessing and caring for patients is to begin with a thorough preoperative assessment to guide interventions and avoid potential adverse reactions (see *Summary of physiologic effects of herbal medicines*). The preoperative assessment should begin 2 weeks prior to surgery during the initial telephone or preoperative evaluation. Patients must be educated about the
importance of stopping all herbal medicines 2 weeks prior to surgery. This approach involves asking patients directly about their herbal medicine use, educating them about what herbal medicines are, and explaining why disclosure is a safety issue. On the day of surgery, perioperative nurses need to confirm that the patient has complied with the discontinuation instructions. In order to effectively educate patients, nurses must first possess a thorough understanding of herbal medicines and their potential impacts. Further research will assist all clinicians in anticipating drug and procedural interactions that may result from herbal medicine use.

REFERENCES


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