Perioperative Implications of Herbal Medications

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LESSON OBJECTIVES
Upon completion of this lesson, the reader should be able to:

1. Explain the role of the Food and Drug Administration in the regulation of herbal medications.
2. Discuss the ASA recommendations for perioperative use of herbal medications.
3. Differentiate direct and indirect health effects associated with herbal remedies.
4. List common reasons why patients are reluctant to disclose herbal medication use.
5. Compare and contrast the effect of herbal medications on commonly used pharmaceuticals.
6. Discuss the perioperative implications of commonly used herbals.
7. Describe the anesthesia-specific implications of commonly used herbals.
8. Integrate herbal medications into medication reconciliation.
9. Identify common perioperative problems stemming from herbal medication use.
10. Explain the importance of quality medication reconciliation.

Current Reviews for Nurse Anesthetists® designates this lesson for 1 CE contact hour in clinical pharmacology/therapeutics.

Introduction
Plants have been used for medicinal purposes for thousands of years, with reports dating back to 3000 BC in the Chinese work Shennong Bencao Jing by Shennong. The isolation of morphine from Papaver somniferum (opium) in 1803 by the pharmacist Friedrich Wilhelm Adam Sertürner marked the beginning of the extraction process of active ingredients from plants for medicinal purposes. Since then other substances have been isolated, such as digitalis from purple foxglove, quinine and quinidine from Cinchona, and atropine from belladonna. Some of these substances are still found in anesthesia drug trays and medicine cabinets today.

The use of herbal medications and remedies is becoming increasingly widespread, likely driven by the notion that natural substances have fewer side effects than pharmaceuticals. Approximately 1 in 5 US adults takes herbal supplements, but the actual number is probably higher. Americans will spend approximately $21 billion on herbals and supplements in 2015, and if protein powders are included in the above calculations, the herbal and supplement market is as big as the entire organic food market. Such widespread use of herbal medications presents numerous perioperative risks for potential adverse drug-herb interactions.

Regulation of Herbal Medications
Herbal medicines are regulated as food supplements under the Dietary Supplement Health and Education Act (DSHEA) of 1994. As such, there are no quality assurance requirements for manufacturing and labeling. Claims on the labels about efficacy or use are loosely regulated by the DSHEA, which only requires the following disclaimer on package labeling: "This (statement about use of the product) has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure, or prevent any disease."
Under DSHEA, once the product is marketed the Food and Drug Administration (FDA) must prove the substance is unsafe before it can be withdrawn from the market. Due to resource limitations, the FDA only spot tests 1% of the 65,000 dietary supplements on the market. Consequently, herbal products are readily available and widely promoted, often with unsubstantiated claims of benefit and seldom with any mention of potential harm.

ASA Recommendation for Perioperative Use of Herbal Medications

The American Society of Anesthesiologists (ASA) recommends the discontinuation of all herbal medications and supplements at least two weeks in advance of scheduled surgery. Realizing that this is not always feasible with urgent and emergent surgical procedures, the ASA further recommends that anesthesia providers have knowledge of herbal medications and their potential perioperative interactions.

Perioperative Implications

It has been found that morbidity associated with herbal medicine may be more prevalent in the perioperative period because of an increased physiological susceptibility to adverse effects and multiple drug use. The reluctance of patients to report herbal medication use to their physicians further complicates the problem (Table 1). In one study, more than 70% of patients failed to disclose their use of herbal medications during routine perioperative assessment.

Direct Health Effects

Direct health risks associated with herbal remedies include recognized pharmacological effects, such as hypertension secondary to licorice or ephedra use, unexpected allergic and anaphylactic reactions, and the very real potential for untoward drug-herb interactions.

Indirect Health Effects

The use of herbal medications may result in suboptimal therapy with conventional medications by reducing plasma levels, counteracting therapeutic effects, or increasing toxicity. Conversely, conventional medications may increase the toxicity of the herbal medication. Patients may also decrease, delay or discontinue conventional medication therapy in favor of herbal medications, and may subsequently have a less favorable result.

Some imported herbal medications may contain toxic levels of heavy metals, such as mercury, lead, arsenic or other contaminants. Contaminants may be introduced during the growing and fertilizing stage or during processing. Potency is affected by growing conditions, altitude, storage, temperature, handling and preparation. There may be up to a 10,000-fold difference in potency based upon changes in these factors.

During growth and fertilization, the herb may be exposed to pesticides or molds and fungi. Following cultivation and harvesting, the active component is extracted by chemical means such as distillation, fractionation, or concentration, using extraction solvents such as ethanol, methanol, aromatic hydrocarbons, or olive oil. The solvent is then extracted leaving an isolated oil or powder. Some volume of final product is lost in the extraction process, and that volume may be made up with other substances, referred to as “undeclared pharmaceuticals,” such as mandrake (scopolamine) or snakeroot (reserpine) in some ginseng preparations. The isolated oil or powder is then complexed with various gelatins, dextran or other polysaccharides to form soft geltabs or powdered tablets.

Anesthetic Implications of Cytochrome P450

Cytochrome P450 (CYP450) is a host of enzymes found in the liver and small intestine that are responsible for the metabolism of drugs, endogenous substances such as steroids, herbal medications, and other toxins. Studies have found that well over 50% of commonly administered medications, including anesthetic medications, are metabolized by CYP450 or its associated isofoms. Many herbs have inducing or inhibiting effects on the various isofoms of CYP450. The implications of this are significant, especially if the patient does not disclose the use of herbal medications, and may result in altered metabolism of anesthetic agents or other

Table 1

Reasons for Failure of Disclosure

Patients may be reluctant to disclose the use of herbal medications for the following reasons:
- A belief that because such products are “natural,” therefore, they must be entirely safe
- Fear of how healthcare providers may respond to self-medication
- Fear that their physician may have biases against the use of herbal medications
- A belief that herbs are not considered a medication
crucial pharmaceuticals such as cardiac medications or immunosuppressants (Table 2).

Profiles of Commonly Used Herbal Medications

Many studies have been undertaken and are currently in progress investigating the potential interactions of herbal medications and anesthetic agents. Consequently, many properties of herbal medications (Tables 3 and 4) have been documented which are of significance to the anesthetist in the perioperative period.

Echinacea purpurea

Echinacea is considered a useful prophylactic and therapeutic agent in the treatment and prevention of viral, bacterial and fungal infections of the upper respiratory tract. Echinacea is believed to improve the immune system through modulation of cytokine signaling and stimulation of macrophages and natural killer cells. While the immunostimulatory properties of echinacea have been studied, very little information is available which addresses the use of echinacea in patients taking immunosuppressant medications, such as patients having received organ transplants. Case reports describe acute rejection of renal transplants with the initiation of echinacea. Therefore, the general consensus is that echinacea should be avoided in patients necessitating immunosuppression.

The immunostimulatory effects of echinacea may antagonize the immunosuppressive actions of corticosteroids and cyclosporine. Echinacea can cause inhibition of CYP450, and there are numerous reports of adverse drug reactions from toxicity of other medications metabolized by CYP450. The use of echinacea for greater than 8 weeks has been associated with an increased risk of poor wound healing and opportunistic infections, illustrating a short-term immunostimulatory effect with a long-term immunosuppressant effect. Chronic use of echinacea can result in hepatic insufficiency, which can then enhance the hepatotoxic effects of drugs such as amiodarone and methotrexate.

Perioperative morbidity is higher when patients use herbal medications.

Ephedra vulgaris

Ephedra was considered useful for promoting weight loss, increasing energy and for treating most respiratory tract infections. Its therapeutic actions likely result from its active metabolites, such as ephedrine, pseudoephedrine, methylephedrine and norepinephrine. Prolonged use of ephedra produces a catecholamine-depleted state, which may result in marked hemodynamic instability during anesthesia, and tachyphylaxis to other sympathomimetic drugs. Side effects are predictable and include palpitations, hypertension, tachycardia, hyperthermia, and seizures. Chronic use has been associated with cardiomyopathy, myocardial infarction, stroke, fatal arrhythmias in the presence of halothane, acute hepatitis, and psychosis. Concurrent use with MAOI inhibitors may result in severe hypertension, hyperthermia, or coma.

Over the course of two years, the FDA received over 1000 reports of adverse effects related to ephedra with 155 deaths, including that of Baltimore
Orioles pitcher Steve Bechler. Subsequently, the FDA banned the use of ephedra as a weight loss supplement in 2004. After a series of legal and congressional challenges, the FDA ban was upheld. This was the first such ban of an herbal supplement by the FDA. Ephedra has now become a drug of abuse, with street names of ‘Herbal Ecstasy’ and ‘Cloud 9,’ and remains easily obtainable from a multitude of websites. Entering ‘ephedra’ into a popular online retail site yields 609 ephedra-containing products available for purchase.

**Allium sativum (Garlic)**

Garlic is thought to have beneficial cardiovascular effects as well as beneficial effects in diabetes, infection and some cancers. These actions are believed to be due to the cysteine contained in garlic, which decreases thromboxane formation and alters arachidonic acid metabolism.

Garlic inhibits platelet aggregation in a dose-dependent fashion, although this has not been demonstrated consistently in volunteers. It can potentiate the antiplatelet effects of aspirin and non-
steroidal anti-inflammatory drugs (NSAIDs), as well as warfarin and heparin, resulting in an increased risk of intraoperative and postoperative bleeding. This effect may be irreversible. Garlic at normal dietary doses of 4.2 grams or less, or about 2 cloves, did not adversely affect platelet function.

An animal study also reported a depressant effect on cardiac chronotropy and ionotropy, thus suggesting a β-adrenergic antagonist action mediated by garlic. Garlic is rich in iodine content and inhibits uptake of iodine by the thyroid. While data suggest no effect on therapeutic levels of levothyroxine, garlic may otherwise have complex interactions on thyroid function.

Garlic has complex interactions with CYP450, causing inhibition of some isoenzymes while inducing others. This activity on CYP450 is dependent on the specific constituents of the garlic formulation being used.

Patients may be reluctant to disclose herbal use.

Ginkgo biloba

While ginkgo biloba has been used medicinally for 1000 years, recently ginkgo leaf extract has been utilized for a number of vascular conditions, and its antioxidant properties are thought to be neuroprotective by improving cerebral metabolism. Consequently, it is frequently used for the treatment of memory loss, dementia, and macular degeneration. Ginkgo may increase cholinergic transmission in the brain via inhibition of acetylcholinesterase, which could impact Alzheimer’s disease therapies. Some ginkgo extracts serve as free-radical scavengers that may serve to mitigate some of the neurologic damage of Alzheimer’s disease. The vascular effects of ginkgo are thought to be due to vasodilation secondary to stimulation of the endothelium-derived relaxing factor and prostacyclin release.

Ginkgo also decreases serum fibrinogen levels and extracts inhibit platelet aggregation. While ginkgo did not demonstrate significant effects on laboratory tests of platelet aggregation, PT, or PTT, numerous case reports of increased bleeding have been documented, including subdural hematoma, vitreous hemorrhage, subarachnoid bleeding, and hematoma formation following plastic surgery. Therefore, concomitant use of gingko biloba with aspirin, NSAIDs, warfarin and heparin is not recommended due to the increased potential for bleeding in these patients.

Other constituents of ginkgo inhibit the binding of platelet-activating factor (PAF) to its membrane receptor. Inhibition of PAF leads to bronchodilation and decreased airway hyperactivity. PAF inhibition may also improve cardiac contractility and coronary blood flow.

Ginkgo inhibits CYP450 and prolongs the effect of medications metabolized by this pathway. In addition, it has been recommended that ginkgo should be avoided in patients taking tricyclic antidepressant agents because it might potentiate the seizure threshold-lowering action of these drugs.

Curcumin longa (Turmeric)

Turmeric has been used since ancient times as both a food spice and medicinal agent. Curcumin, the yellow coloring principle in turmeric, is polyphenolic and the major active constituent. Curcumin possesses potent antioxidant and anti-inflammatory effects as well as thrombolytic and anticarcinogenic properties.

Studies in mice demonstrated a neuroprotective effect following cerebral ischemia. Additional studies noted that chronic dietary curcumin use lowered amyloid-β protein deposition, a finding that may have favorable implications in Alzheimer’s disease.

According to the National Institutes of Health, turmeric acts as a free radical scavenger and is also a potent inhibitor of CYP450 and can decrease the metabolism of many drugs used in the perioperative period (Table 5). Interference with antacid medications is a possible side effect of turmeric, and may result in increased stomach acid if taken with antacid drugs such as H-2 blockers or PPIs. Curcumin also has described immunosuppressant activity as an mTOR (mechanistic target of rapamycin) inhibitor.
Zingiber officinale (Ginger)

Ginger is commonly used by patients preoperatively for the prevention of nausea. Other common uses are listed in Table 6. A study comparing the effects of ginger versus metoclopramide found that there were statistically significant lower incidences of nausea in the group that received ginger.

Ginger has been found to cause hyperglycemia. It has also been found to be a potent inhibitor of thromboxane synthetase and can prolong bleeding time. **Study reports indicated that some ginger compounds and derivatives are more potent antiplatelet agents than aspirin.** Large quantities of ginger may also cause cardiac arrhythmias, central nervous system depression, and potentiation of the effect of calcium channel blockers.

**Herbal preparations may contain toxic chemicals.**

Hypericum perforatum (St. John’s Wort)

St. John’s Wort is most commonly used for depression and related conditions such as anxiety, tiredness, loss of appetite and insomnia. Its postulated mechanism of action is that it exerts its effects by inhibiting serotonin, norepinephrine, γ-aminobutyrate (GABA), and dopamine reuptake by neurons. Additionally, irreversible monoamine oxidase (MAO) inhibition activity has been noted in vitro.

St. John’s Wort also induces the CYP450, which may lower the blood levels of other drugs that are metabolized by this system, including anesthetic agents, anxiolytics, and analgesics. The most affected enzyme appears to be CYP450-3A4. **Several cases of cardiac and renal transplant rejection have been reported in patients whose previously stable level of cyclosporine was lowered after initiation of St. John’s Wort.**

Concomitant use of St. John’s Wort is not recommended with monoamine oxidase inhibitors, beta-sympathomimetic amines, or selective serotonin reuptake inhibitors. One case report describes delayed emergence with St. John’s Wort when taken perioperatively.

<table>
<thead>
<tr>
<th>Table 7 Proposed Mechanisms of Action of Saw Palmetto</th>
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<tr>
<td>- Inhibition of estrogen receptors</td>
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<tr>
<td>- Prevention of conversion of testosterone to dihydrotestosterone</td>
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<tr>
<td>- Blocking of prolactin receptor signal transduction</td>
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<td>- Interference with fibroblast proliferation</td>
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<td>- Induction of apoptosis</td>
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<td>- Alpha-1 receptor antagonism</td>
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<td>- Anti-inflammatory effects</td>
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<th>Table 8 Proposed Mechanisms of Actions of Ginseng</th>
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<tr>
<td>- Augmentation of adrenal steroidogenesis</td>
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<tr>
<td>- Increased IgG and IgM production</td>
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<tr>
<td>- Increased interferon production</td>
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<tr>
<td>- Enhancement of cell-mediated immunity</td>
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<td>- Enhancement of natural killer cell activity</td>
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France has banned the use of St. John’s Wort products based on a report issued by the French Health Product Safety Agency warning of significant interactions between St. John’s Wort and conventional medications. Several other countries, including Japan, the United Kingdom, and Canada, now include drug-herb interaction warnings on St. John’s Wort products.

Many herbal medications adversely effect platelet aggregation.

Serenoa repens (Saw Palmetto)

Saw palmetto is widely used to treat benign prostatic hyperplasia. The principal active ingredients are sterols and free fatty acids. The mechanism of action is unclear, and many have been proposed (Table 7). Saw palmetto has been associated with excessive intraoperative bleeding attributed primarily to inhibition of cyclooxygenase and platelet dysfunction.

Although no detailed studies have been done with regard to the anesthetic interactions, caution should be used if the patient is using benzodiazepines because saw palmetto can alter the pharmacokinetics of these medications. Saw palmetto does not appear to influence CYP450, so its effect on benzodiazepines is by another mechanism.

Panax ginseng (Ginseng)

Ginseng is an expensive herb with purported benefits such as immunomodulation, hypoglycemia and antioxidant, mood enhancement and aphrodisiac effects. Its pharmacologic profile is incompletely understood because of the heterogeneous and sometimes opposing effects of its constituents. Proposed mechanisms of action are numerous (Table 8). The hypoglycemic effect is likely mediated via panaxans and ginsenosides.

Ginseng should be avoided in patients on anticoagulant medications such as warfarin, heparin, NSAIDs, and aspirin, as ginsenosides inhibit platelet aggregation in vitro and result in prolongation of PT and PTT. The platelet inhibitory effect is likely
irreversible, so ginseng should be discontinued at least 1 week in advance of surgery.

Valeriana officinalis (Valerian)

Valerian is used as a sedative and anxiolytic. It produces dose-dependent sedation and hypnosis by modulation of GABA receptors, as demonstrated in animal studies. *Abrupt discontinuation may precipitate a benzodiazepine-like withdrawal syndrome, so tapering may be the more prudent strategy ahead of scheduled surgery.*

Based upon laboratory studies demonstrating a GABA-inhibitory effect, it would be expected that valerian would potentiate the effects of anesthetic agents. This has indeed been demonstrated in mice and animals anesthetized with isoflurane and a combination of midazolam and valerian. Mice so anesthetized took considerably longer to emerge from anesthesia than isoflurane plus either drug alone.

Piper methysticum (Kava)

Traditionally, kava was used to prepare a ceremonial drink in the South Pacific Islands. Its present day uses include the treatment of anxiety, stress, and insomnia. The active ingredients (kava-pyrones) have central muscle–relaxing properties and anticonvulsant activity. Kava can potentiate the effect of barbiturates and benzodiazepines and cause excessive sedation. Kava may also act through inhibition of sodium and calcium channels to cause direct decreases in systemic vascular resistance and blood pressure. Kava inhibits cyclooxygenase and thromboxane synthetase, both of which reduce platelet aggregation (Table 9).

**Garcinia cambogia**

Garcinia cambogia is a tropical fruit, the rind of which is used as a popular weight-loss supplement, and as an adjunct for the treatment of diabetes and hyperlipidemia. It is thought to inhibit fat production by blocking the enzyme citrate lyase, and to suppress the appetite by increasing levels of serotonin in the brain to decrease feelings of hunger. Additionally, it lowers blood glucose levels and has been found to improve cholesterol levels by lowering triglycerides and LDL cholesterol while increasing HDL cholesterol. Garcinia is reported to be an immunostimulant, but this has not been verified in the scientific literature.

The FDA issued a warning to discontinue the use of garcinia in 2009 due to reports of hepatotoxicity. There are multiple potential drug interactions of garcinia perioperatively (Table 10). Adverse reactions have also been described with garcinia and asthma and allergy medications. Based on a case report of normalization of INR after a patient began taking garcinia, it is likely that it induces CYP450 activity.

**Delayed emergence from anesthesia is possible with several herbal medications.**

**Summary and Conclusion**

*(Tables 11, 12 and 13)*

The American College of Medical Quality and The Joint Commission state that accurate medication reconciliation can be very influential in reducing adverse drug events and is therefore an integral component of patient safety. *Accurate medication reconciliation should include not only prescription medications, but nonprescription medications, herbals and supplements.* With the enormous upsurge in the number of patients

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### Table 9

**Potential Perioperative Complications with Kava**

- Prolonged sedation
- Perioperative hypotension
- Myocardial depression
- Delayed emergence
- Hepatotoxicity
- Platelet dysfunction

### Table 10

**Medication Interactions with Garcinia**

- Interference with antiarrhythmics
- Interference with nitrates
- Interference with calcium channel blockers
- Potentiation of cardiac glycosides
- Increased risk of hypokalemia
- Potentiation of oral hypoglycemic medications
- Potentiation of insulin effect
- Rhabdomyolysis with statins
- Increased metabolism of warfarin
- Risk of arrhythmia with succinylcholine

### Table 11

**Herbals with Known Perioperative Risk**

- Echinacea
- Ephedra
- Garlic
- Gingko
- Ginseng
- Kava
- St. John’s Wort
- Valerian
using herbal medications over the last 30 years and the lack of regulatory standards, patients may be unaware of the potential for drug-herb interactions. A detailed medication history that asks specifically about the use of herbal medications should be obtained at the perioperative anesthesia assessment. Failure to recognize the use of herbal medications can have dangerous adverse results.

Medication reconciliation should include herbal medications.

The vast majority of herbal medications have or enhance biological activity, and they must be considered active drugs. Accordingly, they should be regulated as such. Until such time as they are, it is incumbent upon the anesthetist to maintain a working familiarity with herbal substances and their myriad of potential perioperative adverse interactions.

References


### Table 13
Herbals Associated with Transplant Rejection
- Turmeric
- Echinacea
- Garlic
- Ginkgo
- Ginseng
- Kava
- St. John’s Wort

### Table 12
Delayed Emergence and Herbal Medications

Delayed emergence from anesthesia is possible with these herbal medications:
- Valerian
- Kava
- Ginger
- St. John’s Wort
- Saw Palmetto
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He lives with his wife and three sons in Hoover, Alabama.

Tips for your Clinical Practice: Key Points

- A marketed herbal supplement can only be withdrawn if the FDA can prove it is injurious. Only 1% of these products are spot tested. Many of these supplements increase or decrease the activity of CYP450.
- Herbal medications can result in reduced efficacy of other medications by reducing their plasma levels or increasing their toxicity.
- While useful in treatment and prevention of infections of the upper respiratory tract, echinacea, should be avoided in immunosuppressed patients.
- Ephedra is used to promote weight loss, but it has many deleterious side effects including palpitations, hypertension, myocardial infarction, hyperthermia, and seizures.
- Garlic has beneficial cardiovascular effects but, by inhibiting platelet aggregation, can potentiate the antplatelet effects of aspirin and NSAIDs.
- Patients with neurologic problems can derive benefit from ginkgo biloba, but this herb also decreases fibrinogen and inhibits platelet aggregation. Like garlic, it should not be used with aspirin and NSAIDs.
- Tumeric increases bleeding time. It may increase cardiac arrhythmias, and produce CNS depression.
- Concomitant use of St. John’s Wort with MOAIs, beta-adrenergic drugs, or selective serotonin reuptake inhibitors is discouraged.

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DESIGNATION OF SPECIFIC CONTENT AREAS:

Current Reviews for Nurse Anesthetists (CRNA) is designed to meet the standards and criteria of the American Association of Nurse Anesthetists (AANA) for the prior-approved continuing medical education activity, Provider-Directed Independent Study, also known as home study. CRNA is an approved program provider.

CRNA has designated the lessons which meet specific content areas such as pharmacology, HIV/AIDS, etc. However, only the Board of Nursing of an individual State is the final authority in the determination of whether or not these lessons meet the State’s licensure requirements.
POST-STUDY QUESTIONS

1. Concerning the regulation of herbal medications:
   - □ A. The FDA is responsible for assuring the quality and uniform potency of all herbal medications.
   - □ B. Herbal manufacturers must meet strict quality assurance requirements.
   - □ C. Approximately 1% of the herbal medications on the market are subject to spot testing.
   - □ D. Herbal medications are regulated as Schedule IV controlled substances by the DEA.

2. ASA recommendations for the perioperative use of herbal medications state that:
   - □ A. Herbal medications can be continued on the day of surgery.
   - □ B. Herbal medications should be discontinued at least two weeks prior to scheduled surgery.
   - □ C. Herbal medications pose no perioperative risk.
   - □ D. Herbal medications are not in widespread use.

3. Patients may be reluctant to disclose their use of herbal medications due to:
   - □ A. A belief that because herbal products are natural they probably are not entirely safe.
   - □ B. Fear of how healthcare providers may respond to self-medication.
   - □ C. The strict federal regulation of herbals as medications.
   - □ D. Concerns that healthcare providers would recommend expensive herbs.

4. An INDIRECT health risk associated with the use of herbal medications is:
   - □ A. Recognized pharmacologic effects.
   - □ B. Toxicity due to contaminants.
   - □ C. Anaphylaxis.
   - □ D. Drug-herb interactions.

5. An herbal medication with MAO inhibitor effects is:
   - □ A. St. John’s Wort.
   - □ B. Saw Palmetto.
   - □ C. Echinacea.
   - □ D. Ginseng.

6. Delayed emergence from general anesthesia may be seen with:
   - □ A. Valerian.
   - □ B. Ginseng.
   - □ C. Ginkgo.
   - □ D. Ephedra.

7. Platelet aggregation is inhibited by:
   - □ A. St. John’s Wort.
   - □ B. Ephedra.
   - □ C. Garcinia.
   - □ D. Garlic.

8. A perioperative complication associated with Kava is:
   - □ A. Bleeding.
   - □ B. Hypertension.
   - □ C. Seizures.
   - □ D. Bronchospasm.

9. Hypoglycemia may be seen with:
   - □ A. Ginseng.
   - □ B. Ginger.
   - □ C. Saw Palmetto.
   - □ D. Echinacea.

10. Greater than 50% of commonly administered medications are metabolized by:
    - □ A. Pseudocholinesterase.
    - □ B. Monoamine oxidase.
    - □ C. Cytochrome P450.
    - □ D. HMG-CoA reductase.

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