

Perioperative Implications**Drug Interactions**

- Additive serotonergic effects and serotonin syndrome–like effects with antidepressants include SSRIs
- Due to serotonergic properties, the following should be avoided with SAME (in view of the risks of serotonin syndrome–like effects): dextromethorphan (Robitussin DM, other cough syrups), meperidine (Demerol), pentazocine (Talwin), tramadol (Ultram), sumatriptan (Imitrex), and other 5-HT_{1B/1D} receptor agonists.
- Additive side effects like hyperthermia, agitation, confusion, and coma when used with MAOIs.
- Other side effects may include dry mouth, nausea, gas, diarrhea, headache, anxiety, nervousness, restlessness, and insomnia.
- Large doses of SAME may cause mania (abn elevated mood). People with bipolar disorder (manic depression) should not take SAME because it may worsen manic episodes.
- Taking levodopa (L-DOPA) for Parkinson disease may lower the levels of SAME in the body. This contributes to depression and increases the side effects of levodopa.
- SAME decreases effectiveness of levodopa.
- SAME concentrations can be lowered in the presence of guanidinoacetate (also known as glycoyamine)

supplementation. Glycoyamine is a direct precursor of creatine, which is a popular nutritional supplement.

- SAME does not improve outcome or reduce the occurrence of adverse events for chronic liver diseases such as cholestasis and viral hepatitis.

Contraindications

- Pts taking MAO inhibitors or within 2 wk of their discontinuation
- Concurrent use with antidepressant drugs, including MAOIs, can lead to additive stimulatory effects. Agitation, tremor, insomnia, nervousness, irregular or accelerated heart rate are theoretical concerns.
- Parkinson disease with levodopa treatment.

Saw Palmetto

Joan Spiegel

Uses

- BPH
- Urinary tract inflammation (prostatitis)
- Underactive bladder
- Male- and female-pattern baldness
- Aphrodisiac
- Breast augmentation

Perioperative Risks

- No established interactions with anesthetic agents

Worry About

- Saw palmetto has been implicated in hepatitis, cholecystitis, bleeding diatheses, conduction defects, and erectile dysfunction. No studies confirm these effects.
- Unsubstantiated pharmacologic effects such as increasing the action of benzodiazepines

Overview

- Saw palmetto extract is an extract of the fruit of *Serenoa repens* from the American dwarf palm tree. Saw palmetto's active ingredients include fatty acids, plant sterols, and flavonoids.
- Saw palmetto has hormonal (estrogenic) effects as well as direct inhibitory effects on androgen receptors. There are also possible anti-inflammatory effects (from the berries of the plant).
- Saw palmetto has not been evaluated by the FDA.
- Saw palmetto is possibly ineffective for its intended use, the treatment of BPH.

Etiology

- Mechanism of action: Saw palmetto exhibits antiestrogenic and antiandrogenic effects by inhibiting the actions of 5-alpha reductase enzyme (thereby preventing the conversion of testosterone to dihydrotestosterone, a cause of BPH and baldness).

Possible Drug Interactions

- Any medication that alters male sex hormones should not be taken with saw palmetto. Examples include finasteride and flutamide.
- Drugs that affect coagulation should also not be consumed with saw palmetto; these include Coumadin and anti-inflammatory agents (clopidogrel, ibuprofen, aspirin)
- Because saw palmetto may have hormone-like effects, it may make oral contraceptives less effective, thus raising the risk of unplanned pregnancy.
- Tannins in saw palmetto may interfere with iron absorption.
- Tinctures may contain large amounts of alcohol and thus cause N/V when taken with metronidazole or disulfiram.

Assessment Points

System	Effect	Test
GI	Occasional upset, hepatitis, and cholecystitis (very rare)	LFTs
HEME	Bleeding, iron deficiency	None, iron studies, Hgb
GU	Improved urinary symptoms (conflicting data)	None
ENDO	Breast enlargement (unproved) Prevent hair involution due to dihydrotestosterone (unproved)	None

Key References: *Serenoa repens*, *Altern Med Rev* 3(3):227–229, 1998; Bent S, Kane C, Shinohara K, et al.: Saw palmetto for benign prostatic hyperplasia, *N Engl J Med* 354(6):557–566, 2006; Tacklind J, Macdonald R, Rutks I, et al.: *Serenoa repens* for benign prostatic hyperplasia, *Cochrane Database Syst Rev* 12:CD001423, 2012.

Perioperative Implications**Preoperative Concerns**

- Self-reporting of other herbal supplements

- Unknown effects in children; interference with birth control and in lactating mothers

Intraoperative Concerns

- None known

Postoperative Period

- Routine

St. John's Wort (*Hypericum perforatum*)

Theodore G. Cheek | Lee A. Fleisher

Uses

- More than 3% of presurgical pts report using St. John's wort.
- Taken mainly for depression, although pts may take it for a variety of reasons including anxiety, viral and bacterial infections, menstrual cramps, HIV, cancer, chest congestion, hemorrhoids, skin wounds, and burns.
- Efficacy in treating depression is controversial.
- Most integrative medical specialists will use every other alternative first because of drug interactions; this is at

best a third-line medication. Others such as S-adenosyl-L-methionine are equally or more effective and without undesirable drug interactions or other side effects.

Worry About

- Drug interactions: May prolong sedative effects of other drugs including anesthetics and sedatives. There are case reports of a severe hypertensive response to vasopressors such as ephedrine or phenylephrine in pts taking St. John's wort.

- Induces cytochrome P450 enzymes; promotes metabolism and decreased blood levels of warfarin, cyclosporine, digoxin, CCBs, and steroids; even renders birth control pills and menopausal drug therapies ineffective. Watch for unplanned and sometimes unwanted pregnancies due to this effect.)
- Serotonin-like syndrome (Htn, tachycardia, agitation, restlessness).
- Unpredictable effects due to lack of strict regulation.

Overview/Pharmacology

- Classified as a dietary supplement and not subject to FDA; pharmacologic activity can be unpredictable and highly variable in different preparations. Hypericum extract (0.3% hypericin) is marketed to be taken PO at 300 mg 3 times daily.
- Contains many complex chemicals, but hypericin and hyperforin are responsible for the antidepressant effects.

- Absorbed within 40 min of oral administration.
- Mainly metabolized by the liver and cleared by renal excretion; elimination half-time 43 h.

Mechanism of Action/Usual Dose

- May act as a nonspecific reuptake inhibitor of serotonin, norepinephrine, and dopamine.
- Appears to work differently from conventional antidepressants.

- MAO inhibition reported in early studies but not confirmed in follow-up studies.
- Usually taken as a capsule consisting of the plant extract; typical dosage is 300–500 mg of hypericum extract 3 times daily.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Photosensitivity			
CV	Rarely, Htn, tachycardia, and serotonin-like syndrome	Dosage taken; determine whether patient is also taking an SSRI	BP/HR	ECG
GI	Nausea			
DERM	Rarely, rash			
CNS	Restlessness, fatigue, antidepressant			

Key References: Skidmore-Roth L editor: *Mosby's handbook of herbs and natural supplements*, ed 3, St Louis, 2006, Mosby, pp 957–963; Abe A, Kaye AD, Gritsenko K, Urman RD, Kaye AM: Perioperative analgesia and the effects of dietary supplements, *Best Pract Res Clin Anaesthesiol* 28(2):183–189, 2014.

Perioperative Implications**Preoperative Concerns**

- Hx can include dose, duration, preparation taken, and reason for use.
- Best to discontinue at least 1 wk preop so as to clear the drug from the body.
- May see as much as a 50% decrease in effect of warfarin. Consider alternatives to warfarin.
- Can decrease digoxin levels, possibly by induction of a P-glycoprotein transporter.

- Serotonin-like syndrome, especially when combined with an SSRI, tricyclics, or MAO inhibitor.

Induction/Maintenance/Emergence

- May prolong anesthesia via potentiation of central effects of inhaled agents, sedatives, and opioids.

Anticipated Problems/Concerns

- Effects may be variable among different preparations owing to lack of standardization.

- Anticipate decreased effects of certain drugs such as warfarin, cyclosporine, beta-blockers, CCBs, steroids, and digoxin.
- May prolong the sedative effects of anesthetics.
- Watch for serotonin-like syndrome (Htn, tachycardia, agitation, restlessness).

Valerian (*Valeriana officinalis*)

Lee A. Fleisher

Uses

- Treatment of:
 - Insomnia (valerian is present in virtually all herbal sleep aids)
 - Anxiety
 - Depression
 - Htn
 - GI hyperactivity
 - Headaches
 - Muscle spasms
 - Benzodiazepine withdrawal

- Valerian may act synergistically with sedative anesthetics, leading to prolonged emergence.
- Valerian can potentiate medications such as barbiturates, benzodiazepines, opioids, antidepressants, and alcohol.

Overview

- Valerian is a native herb of temperate regions; its name is believed to be derived from the Latin word *valere*, meaning to be healthy or strong. It has been used for centuries as a sleep aid by Greeks, Romans, Chinese, American Indians, and Europeans.
- Prior to the introduction of barbiturates to the US National Formulary, valerian was indicated for treatment of unrest and nervous sleep disturbance. It has since been dropped from the US National Formulary.
- Valerian contains many constituents that work synergistically, including volatile oils, valepotriates, monoterpene alkaloids, and furanofuran lignans.
- Volatile oils: These oils give valerian a pungent odor due to the release of isovaleric acid. The sesquiterpene skeleton present on volatile oils such

as valerenic acid, valeranone, and kessyl glycol is a proposed primary source of pharmacologic effects. These components have been shown to act on the amygdaloid body in the brain and to inhibit breakdown of GABA, thus leading to sedation.

- Valepotriates: Have a furanopyranoid monoterpene skeleton, which can be found in glycosylated forms known as iridoids. The compounds have been shown in animal experiments to decrease spontaneous motility after oral administration.

Mechanism of Action/Usual Dose

- Produces dose-dependent sedation and hypnosis mediated mainly through the GABA_A receptor, the adenosine A₁ receptor, and, as recently noted, the 5-HT_{5a} receptor.
- Tablets: 300–400 mg PO 30 min–1 h prior to sleep.
- Tea: 1 cup of boiling water over 1–2 teaspoons (2–3 g) of the root and infused for 10–15 min. One may drink up to 2 cups daily.
- Tincture: 2–6 mL (½–1 teaspoon) up to 3 times daily.

Perioperative Risks

- Potential for valerian withdrawal exists if usage is stopped suddenly after chronic high-dose administration. This withdrawal can present as delirium, tachycardia, and diaphoresis.
- Chronic dosing with high-dose valerian has been linked with cardiac failure and emergence delirium.

Worry About

- No direct drug interactions are reported.