

## Assessment Points

| System | Effect   | Test   |
|--------|--|--|
| CV     | Reduces VLDL, LDL, and triglyceride levels<br>Reduces matrix metalloproteinases and CRP involved in vascular remodeling<br>Increases adiponectin levels<br>Reduces eNOS regulatory factor<br>Increases expression of eNOS. | VLDL, LDL, HDL, triglycerides<br>Matrix metalloproteinases 2 and 9 and CRP<br>Adiponectin, LDL-C, HDL, triglycerides, leptin |
| HEPAT  | Rare hepatocellular damage and cholestasis   | AST, ALT   |
| MS     | Rare myopathy, myalgia, and rhabdomyolysis   | CPK  |
| ENDO   | Reduces pancreatic B-cell destruction and oxidative stress   | Pancreatic B-cell numbers  |

**Key References:** Becker DJ, Gordon RY, Halbert SC, et al.: Red yeast rice for dyslipidemia in statin-intolerant patients. A randomized trial, *Ann Intern Med* 150(12):830–839, 2009; Cicero AF, Derosa G, Parini A, et al.: Red yeast rice improves lipid pattern, high-sensitivity C-reactive protein, and vascular remodeling parameters in moderately hypercholesterolemic Italian subjects, *Nutr Res* 33(8):622–628, 2013.

## Perioperative Implications

### Preoperative Concerns

- Lovastatin has been designated as pregnancy category X by the FDA. Thus red yeast rice should be avoided in pregnancy and lactation.

### Preinduction/Induction

- Succinylcholine is contraindicated in myopathies associated with elevated serum CPK values.

## S-Adenosyl-L-Methionine

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### Uses

- As an antiaging, antidisease therapeutic agent.
- May protect against the hepatotoxic effect of certain drugs (e.g., alcohol, acetaminophen, phenobarbital, and steroids).
- Depression, mild to moderate and adolescent.
- Anxiety, PMS.
- Heart disease.
- Liver disease, cirrhosis, intrahepatic cholestasis, disorders of porphyrin, and bilirubin metabolism.
- Osteoarthritis, tendinitis, bursitis, chronic low back pain.
- Dementia, Alzheimer disease, Parkinson disease.
- MS, migraine, seizure, spinal cord injury.
- Chronic lead poisoning.
- Disorder of porphyrin and bilirubin metabolism.
- Chronic fatigue syndrome.
- Intellectual enhancement, ADHD.
- Postop SAME therapy can benefit residual liver function of pts with cirrhosis, especially pts suffering marked ischemia reperfusion injury.
- SAME supplementation restores hepatic antioxidant glutathione (GSH) deposits. Depleted glutathione is associated with alcoholism, acetaminophen toxicity, Alzheimer disease, Crohn disease, diabetes, heart disease, and stroke.

### Perioperative Risks

- N/V, flatulence, diarrhea, irregular or accelerated HR
- Anxiety

### Overview/Pharmacology

- SAME is produced endogenously by ATP activation of methionine, which is produced by the body from dietary protein.

- SAME is required in numerous transmethylation reactions involving nucleic acids, proteins, phospholipids, amines, and other neurotransmitters. The synthesis of SAME is linked with folate and cyanocobalamin metabolism; deficiencies of both these vitamins have been found to reduce SAME concentrations in the CNS.
- May improve methylation by different mechanisms in several neurologic and psychiatric disorders.
- Is well tolerated with oral use and free of serious side effects. The oral supplement was developed in the 1970s and has been touted as a multipurpose treatment ever since.
- Exogenously administered SAME has a low bioavailability due to rapid first-pass metabolism by the liver.
- Peak plasma concentration reached in 3–5 h.
- Half-life of 100 min.
- Excreted in urine and feces.
- Crosses the blood-brain barrier.
- Metabolized to homocysteine; remethylated to form methionine, which can form more SAME.
- Tosylate salt has 1% oral bioavailability.
- Butane disulfonate salt has 5% oral bioavailability.

### Mechanism of Action

- Contributes to the synthesis, activation, and metabolism of hormones, neurotransmitters, nucleic acid, proteins, phospholipids, and some drugs.
- SAME crosses the blood-brain barrier and is involved in transmethylation and folate and monoamine metabolism as well as in membrane function and neurotransmission.
- SAME plays a role in more than 100 biochemical reactions: increases levels of serotonin, dopamine, norepinephrine, phosphatides, and proteoglycans.

- Improves intrahepatic cholestasis. SAME supplementation seems to improve hepatic function and reverse imbalances of various enzymes. In liver disease, deficiencies of MAP often lead to reductions in cysteine and choline, which can lead to depletion of glutathione. SAME restores levels of glutathione, decreases inflammation, and increases methylation of DNA.
- Stimulates growth of articular cartilage.
- Relieves joint pain, possibly owing to analgesic or anti-inflammatory effects. May stimulate articular cartilage growth and repair as a result of chondrocyte proteoglycan synthesis. May antagonize TNF-alpha, which may be beneficial in arthritic pts.
- Antidepressant effect is probably due to increased serotonin turnover and elevated dopamine and norepinephrine levels or alterations in cellular membrane fluidity, which would facilitate signal transduction across membranes and increase the efficiency of receptor-effector coupling.
- In liver disease, restores depleted biochemical factors.
- In myelopathy of AIDS, replenishes depleted endogenous SAME.

### Usual Dose

- For depression, 400–1600 mg daily PO or 200–400 mg daily IV to speed onset of action of tricyclic antidepressants.
- Addition of betaine to SAME counteracts high levels of homocysteine; combination more effective than SAME alone for treatment of depression.
- For osteoarthritis, 200 mg 3 times PO or 400 mg IV.
- For alcoholic liver disease, cirrhosis, or intrahepatic cholestasis, 1200–1600 mg/d PO or 800 mg/d IV.
- For AIDS myelopathy, 800 mg/d IV for 14 d.
- For fibromyalgia, 800 mg/d PO.

## Assessment Points

| System | Effect         | Assessment by Hx | PE  |
|--------|----------------|------------------|-----|
| GI     | N/V, diarrhea  | GI complaints    | KUB |
| MS     | Osteoarthritis | Stiff joints     | ROM |

**Key References:** Guo T, Chang L, Xiao Y, et al.: S-adenosyl-L-methionine for the treatment of chronic liver disease: a systematic review and meta-analysis, *PLoS ONE* 10(3):e0122124, 2015; Su ZR, Cui ZL, Ma JL, et al.: Beneficial effects of S-adenosyl-L-methionine on post-hepatectomy residual liver function: a prospective, randomized, controlled clinical trial, *Hepatogastroenterology* 60(125):1136–1141, 2015.

**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<sub>1B/1D</sub> 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 glycyocamine)

supplementation. Glycyocamine 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)<br>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.