### Overview

- β-sitosterol is one of the major plant sterols found in humans. Its chemical structure is similar to that of cholesterol with an ethyl group added at position 24.
- β-sitosterol is available in many nonprescription supplements and with dietary plant consumption.
- With a low absorption rate, it inhibits intestinal absorption of cholesterol by competing for limited space with cholesterol in mixed micelles and also accelerates the esterification rate of the lecithin cholesterol acyltransferase enzyme.
- In benign prostatic hyperplasia, it binds to prostatic tissue, inhibits prostaglandin synthesis in the prostate, and has anti-inflammatory activity.
- Enhances proliferative responses of T cells in vitro.
- Inhibits colon cancer growth in vitro.
- Alternative for pts seeking modest reductions in LDL-C (<15%): Higher doses (4 g/d) can lead to reductions in LDL-C up to 19.8%, equivalent to doubling the dose of statin in dyslipidemic pts.
- Reductions in triglycerides (6–9%) seen as well with 2 g/d doses of sterol.
- May alter CNS disease progression, especially disorders that are correlated with an altered cholesterol metabolism, such as AD, MS, and ALS-PDC.
- Some studies have shown anti-diabetic properties of β-sitosterol.

### Pharmacology/Usual Dose

- The reduction of dietary cholesterol available to the body may be due to inhibition of absorption in the intestine.
- Large amounts of dietary β-sitosterol may displace cholesterol during absorption and increase fecal excretion.
- Inhibition of 5-alpha reductase prevents the conversion of testosterone to dihydrotestosterone. This reduction of androgens may reduce prostatic hyperplasia in the same manner that finasteride (Proscar) does.
- For hypercholesterolemia, usual dosage is 800 mg–6 g before meals; for severe cases, can be up to 15 g.
- For benign prostatic hyperplasia and prostatitis, implement 60–130 mg tid.
- About 175–200 mg is consumed daily in typical diet.
- Contraindications include sitosterolemia, which is an inherited lipid storage disease with increased absorption of cholesterol and β-sitosterol from diet. Elevated liver β-sitosterol competitively inhibits cholesterol catabolism, which will lead to hypercholesterolemia.

### Assessment Points

| System | Effect | Assessment by Hx | PE | Test |
|---|---|---|---|---|
| CV | CAD | Angina MI | | ECG |
| RESP | Asthma | Wheezing | Wheezing | |

**Key References:** Wong NC: The beneficial effects of plant sterols on serum cholesterol, *Can J Cardiol* 17(6):715–721, 2001; Vanmierlo T, Bogie JF, Mailleux J, et al.: Plant sterols: friend or foe in CNS disorders? *Prog Lipid Res* 58:26–39, 2015.

### Perioperative Implications

- Obtain adequate Hx to determine indication since there may be significant comorbidity.
- No known periop implications.

### Anticipated Problems/Concerns

**Side Effects**

- May cause N/V, indigestion, gas, diarrhea, or constipation.
- Interactions: Ezetimibe (Zetia) may reduce absorption of β-sitosterol.
- Antihyperlipidemic drugs such as atorvastatin (Lipitor), cholestyramine, and gemfibrozil have additive effects in lowering cholesterol level.
- Pravastatin (Pravachol) can lower the blood level of β-sitosterol.
- Increased risk of deficiency of fat soluble vitamins. β-sitosterol may reduce absorption and blood level of α- and β-carotene and vitamin E.
- Erectile dysfunction and loss of libido have been reported in pts on β-sitosterol.

# Blue Cohosh *(Caulophyllum thalictroides)*

Christopher J. Cullom | Alan David Kaye

### Uses

- Commonly used by midwives as a uterine stimulant and for induction of labor. Major uses, therefore, include (1) inducing labor; (2) as an emmenagogue; (3) as an antispasmodic; and (4) as an abortifacient.
- Properties also include anti-inflammatory, antipyretic, diuretic, expectorant, vasoconstrictor, and smooth muscle relaxants.
- According to a national survey, 64% of midwives still use blue cohosh to induce labor and 7–45% of women use herbal medications during pregnancy.

### Risk

- Ingestion of the leaf or seeds can lead to severe toxicity.
- Case reports document seizures, renal failure, and resp distress after use.
- Avoidance is advised in diabetic pts due to concern for hyperglycemia and potential inhibition of antiglycemic medications.
- Reports of perinatal stroke, aplastic anemia, chest pain (angina), hypertension, acute MI, CHF, shock, and multi-organ hypoxia in infants following maternal use from the first trimester to right before delivery.
- Should not be used by women with estrogen-sensitive conditions or cancers, and in pts with diarrhea.
- Also causes mucous membrane irritation, diarrhea, and cramping, and constricts coronary arteries.
- Possesses several components that can be teratogens, cytotoxic, or lethal to embryos and/or can cause birth defects and congenital malformations.

### Perioperative Risks

- Coronary artery vasoconstriction that can lead to myocardial ischemia
- Alteration in antiglycemic and antihypertensive drug levels
- Interaction with medications dependent on cytochrome P-450 enzymes

### Worry About

- Differentiate from black or white cohosh, which have other physiologic effects.
- Product safety and efficacy profiles differ among manufacturers.
- Usage in pregnancy due to concern of uterine stimulation, teratogenicity, and neonatal multisystemic complications.
- Usage in pts with diabetes, hypertension, or acute history of tobacco/nicotine use.

### Overview/Pharmacology

- Several alkaloids and saponins are considered responsible for the pharmacologic effects.
- Anagyrine, *N*-methylcytosine, and taspine are constituents identified likely to be teratogenic.
- *N*-methylcytosine acts similarly to nicotine, which can cause elevated BP, tachycardia, diaphoresis, abdominal pain, vomiting, fasciculations, and produce hyperglycemia in the developing fetus.
- Alkaloid components found to be cytochrome P-450 inhibitor based on in vitro studies, and thus may pose a risk of drug-drug interactions when taken with other medications dependent on CYP450 enzymes.
- Blue cohosh preliminarily appears to have estrogenic effects with enhancement of estradiol binding to estrogen receptors.

### Etiology

- Berberidaceae or Leonticaceae family.
- Listed in the US Pharmacopoeia 1882–1905 as a labor inducer.
- Typically the dried rhizome/root parts are used.

### Assessment Points

| System | Effect | Assessment by Hx | PE | Test |
|---|---|---|---|---|
| HEENT | Mucous membrane irritation | Complaints of oral irritation | Oral mucosa exam | |
| CV | Ischemia, Htn, tachycardia | Complaints of angina, dyspnea, or palpitations | Cardiac exam | ECG ± ECHO |
| GI | Increased GI motility, diarrhea, abdominal cramping | Changes in bowel movements (i.e., frequency, consistency), abdominal discomfort | Abdominal exam | |
| ENDO | Hyperglycemia | Fatigue, polydipsia, polyuria, vision changes, weight loss | Visual acuity exam | Blood glucose |
| OB/GYN | Uterine stimulation, estrogenic effects | Changes in contractions or menstruation | OB exam | Biophysical profile US, LH levels |

**Key References:** Finkel RS, Zarlengo KM: Blue cohosh and perinatal stroke, *N Engl J Med* 351(3):302–303, 2004; Rader JI, Pawar RS: Primary constituents of blue cohosh: quantification in dietary supplements and potential for toxicity, *Anal Bioanal Chem* 405(13):4409–4417, 2013.

### Perioperative Implications

**Preoperative Concerns**
- Reliable self-reporting of use by pts.
- Enhanced hyperglycemia in diabetics.
- Can be associated with coronary vasoconstriction.
- The ASA recommends holding all herbal products 2–3 wk prior to surgery since the half-life of most of these preparations are unknown, allowing for elimination out of the body.

**Monitoring**
- Use standard ASA monitors.
- Intraop blood glucose levels.

**Airway/Maintenance**
- No known effects

**Preinduction/Induction**
- Coronary vasoconstriction

**Adjuvant**
- May accentuate the response to vasopressors
- May attenuate effectiveness of antihypertensive medications
- Possible drug-drug interactions due to inhibitory effects on hepatic enzymes

**Postoperative Period**
- Monitor CV status (i.e., BP, pulse) and blood glucose levels.

# Carnitine

Renyu Liu | Dajin Sun

### Uses
- Treatment of primary carnitine deficiency and deficiency secondary to complications of several inborn errors of metabolism, such as organic acidemia and fatty acid oxidation defects in children and adults, and acquired medical or iatrogenic conditions such as valproate and zidovudine treatment, cirrhosis, chronic renal failure on dialysis, etc.
- Treatment of valproic acid poisoning and/or overdosing and prevention of valproic acid–induced hepatotoxicity.
- Used for ADHD, erectile dysfunction and male infertility, cardiomyopathy, PVD, CHF, chronic cardiac dysrhythmias, senile dementia, metabolic nerve diseases, HIV infection, tuberculosis, myopathies, renal failure–induced anemia, neuropathy, and neuropathic pain, etc. However, additional studies are needed to confirm these potential benefits.
- Experimental data indicated that carnitine might have neuronal protective effects against hypoxia/ischemia and neuronal inflammation. Clinical applications of these finding are unknown.

### Perioperative Risks
- Periop risks are related to carnitine deficiency rather than carnitine itself.
- Hypoglycemia, lactic acidosis, and muscle weakness related to carnitine deficiencies and discontinuation of carnitine supplement.
- Case report indicates that pts with carnitine deficiencies may develop symptoms similar to those assoc with propofol infusion syndrome. Periop usage of carnitine as a metabolic supplement might be related to periop outcome.

### Worry About
- Individuals with L-carnitine deficiency should continue this medication as scheduled preop to avoid acute hypoglycemia, lactic acidosis, etc. IV carnitine or dextrose-containing solutions may be needed for fasting individuals with L-carnitine deficiencies.

### Overview/Pharmacology
- Carnitine (3-hydroxy-4-trimethylamino-butyric acid or β-hydroxy-gamma-N-trimethylamino-butyrate) is a quaternary ammonium compound biosynthesized from the amino acids lysine and methionine.
- Carnitine exists in two stereoisomers: L-carnitine, the biologically active form, and D-carnitine, the biologically inactive form, which may be harmful.
- About 75% of L-carnitine comes from the diet, particularly from red meat and dairy products. Endogenous synthesis combined with high tubular reabsorption is enough to prevent deficiency in healthy people. Thus carnitine deficiency is uncommon in healthy, well-nourished adults.
- Most of the body's carnitine is stored in skeletal muscle, but it is also found in other high-energy-demanding tissues such as those in the myocardium, liver, and adrenal glands. Carnitine is excreted in urine. Thus carnitine and its metabolite may accumulate in pts with renal failure.

### Pharmacokinetics
- Formula: $C_7H_{15}NO_3$
- Mol. mass: 161.199 g/mol
- Bioavailability: <10%
- Protein binding: None
- Metabolism: Slightly
- Half life: 15 h
- Excretion: Urine (>95%)

### Drug Class/Usual Dose
- Carnitine is available both as a prescription drug and as a food supplement.
- Pregnancy: Category B. Studies in bacteria have found no evidence of mutagenicity. No human data are available. Carnitine occurs naturally in human breast milk.
- Dosing: The usual supplementation dose is 100–300 mg/kg/d. For infants and children, recommended dosage is between 50–100 mg/kg per d in divided doses with a maximum of 3 g/d. IV L-carnitine is used for treatment of lactic acidosis and cardiomyopathy secondary to L-carnitine deficiency. The recommended dosage is a 50 mg/kg bolus injection over 2–3 min followed by an equivalent dosage over the next 24 h (divided every 3-4 h). Subsequent dosages would be based on responses.
- Overdosage: There have been no reports of toxicity from L-carnitine overdosage. Oral doses of 15 g/d have been well tolerated.

### Assessment Points

| System | Effect | Assessment by Hx | PE | Test |
|---|---|---|---|---|
| CNS | Seizures (rare) | Oral or IV L-carnitine.<br>Reliable description of a witnessed seizure | Seizure activity<br>Postseizure state<br>Signs of other injuries | Rule out other etiology |
| GI | N/V, diarrhea | Oral or IV L-carnitine; it is important to differentiate between overdose and deficiency | | Blood carnitine level, serum glucose, lactic acid |
| DERM | Body odor | Oral or intravenous L-carnitine | Odor | |

**Key References:** Odle J, Adams SH, Vockley J: Carnitine. *Adv Nutr* 5:289-290, 2014. Steiber A, Kerner J, Hoppel CL: Carnitine: a nutritional, biosynthetic, and functional perspective, *Mol Aspects Med* 25(5–6):455–473, 2004.