

**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<sub>A</sub> receptor, the adenosine A<sub>1</sub> receptor, and, as recently noted, the 5-HT<sub>5a</sub> 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.

Assessment Points		
System	Effect	Test
CV	High-output cardiac failure Hypotension Arrhythmias Dilates coronary arteries	Rule out other causes of high-output cardiac failure: Sepsis, beriberi, cardiac shunt, or Paget disease ECG, ECHO
HEPAT	CYP4 4 inhibitor Hepatotoxicity	Baseline LFTs
CNS	Sedation Hypnosis Anticonvulsive effect Headache Restlessness Hallucinations Ataxia	Sleep studies: May improve sleep latency and slow-wave sleep EEG
GI	Nausea Intestinal irritability	Decrease dose or stop ingestion
MS	Muscle relaxation	

**Key References:** Ang-Lee MK, Moss J, Yuan CS: Herbal medicines and perioperative care, *J Am Med Assoc* 286(2):208–216, 2001; 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

- The valepotriate component of valerian may alkylate DNA, which could be potentially cytotoxic or carcinogenic. It has been recommended that valerian not be used in pregnancy or while breast feeding.
- Cessation of valerian consumption prior to surgical intervention should be decided on an individualized basis. If a 2- to 3-wk taper is not feasible, then pts should continue taking valerian. Benzodiazepines can be used to treat withdrawal symptoms should they develop.