

ST. JOHN'S WORT Fact Sheet [G]

Bottom Line:

St. John's wort can be considered an option along with conventional antidepressants for short-term treatment of mild depression; however, be wary of its many drug interactions.

FDA Indications:

None.

Off-Label Uses:

Depression.

Dosage Forms:

Supplied over the counter most commonly as 100 mg, 300 mg, 450 mg tablets and capsules.

Dosage Guidance:

For mild to moderate depression, most clinical trials have used St. John's wort extract containing 0.3% hypericin and/or 3% hyperforin; most common dose is 300 mg TID. Doses of 1200 mg QD have also been used. Some studies have also used a 0.2% hypericin extract dosed at 250 mg BID. A St. John's wort extract standardized to 5% hyperforin and dosed at 300 mg TID has also been used.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: \$

Side Effects:

- Most common: Well tolerated at recommended doses. Insomnia (decrease dose or take in morning), vivid dreams, restlessness, anxiety, agitation, irritability, gastrointestinal discomfort, diarrhea, fatigue, dry mouth, dizziness, and headache reported. Sexual dysfunction may occur, but less often than with SSRIs.
- Serious but rare: Risk of severe phototoxic skin reactions and photosensitivity at high doses (2–4 g/day).

Mechanism, Pharmacokinetics, and Drug Interactions:

- Thought to exert antidepressant effects by modulating effects of monoamines, and may inhibit reuptake of these neurotransmitters.
- Metabolized primarily through the liver; $t_{1/2}$: 24–48 hours.
- Avoid concomitant use with serotonergic agents: Rare cases of serotonin syndrome reported. Potent inducer of many CYP450 enzymes (3A4, 2C9, 1A2) and P-glycoprotein transporter, which results in increased metabolism and reduced plasma concentrations of a large number of drugs. St. John's wort can decrease oral contraceptive levels by 13%–15%, resulting in bleeding or unplanned pregnancy; women should use an additional or nonhormonal form of birth control.

Clinical Pearls:

- Also known as *Hypericum perforatum*; active constituents (predominantly hypericin and hyperforin) are derived from the flowering buds.
- St. John's wort is more effective than placebo, likely as effective as low-dose tricyclic antidepressants and SSRIs in milder forms of depression; however, a study in *JAMA* found it no more effective than placebo or sertraline for moderate to severe depression.
- Avoid abrupt discontinuation due to the risk of withdrawal effects.

Fun Facts:

Although not indigenous to Australia and long considered a weed, St. John's wort is now grown as a cash crop, and Australia produces 20% of the world's supply. The use of St. John's wort dates back to the ancient Greeks; Hippocrates documented the medical use of St. John's wort flowers. St. John's wort is so named because it blooms near June 24th, which is the birthday of John the Baptist. "Wort" is an old English word for plant.