

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

History

- St. John's wort is a weed with a yellow flower that blooms on the feast of John the Baptist. "Wort" is the Old English word for plant.
- Extracts have been used for centuries for insomnia and "nervous conditions".
- St. John's wort has been the most commonly prescribed anti-depressant in Germany.

Most studied use

Mild depression.

Summary of the evidence

- There is fair evidence that St. John's wort is safe and effective for mild depression.
- St. John's wort is not recommended for use in major depression: St. John's wort products may be less reliable than TCA's or SSRI's, and their efficacy in more serious depression is questionable.
- Serious drug interactions occur between St. John's wort and many other medications, making these other medications less effective.

Pharmacology

- St. John's wort contains > 10 substances (including hypericin and hyperforin) which bind neuroreceptors and inhibit the re-uptake of depression-related neurotransmitters.
- St. John's wort is a very potent inducer of cytochrome P450 (see interactions below).

Clinical studies

- For mild depression, almost all trials show better response rates to St. John's wort than to placebo. (Linde 2005, Gaster 2000)
- For more severe depression, two recent well-conducted trials have shown St. John's wort to be no more effective than placebo (Hypericum 2002, Shelton 2001), although in one of these trials the SSRI arm was also found to be no better than placebo. (Hypericum 2002)
- Several trials have shown no significant differences between St. John's wort and standard antidepressants (SSRI's or generally low dose of TCA's), but it is difficult to draw conclusions from these results given the small size of many of these trials and the variability in the results of antidepressant trials overall.

Adverse effects

- Rarely: nausea, rash, photosensitivity, sexual dysfunction.
- Rate of side effects is very similar to that of SSRI's.
- Overall, side effects are much less than for TCA's.

Contraindications/cautions

- Very serious herb/drug interactions (see below).
- Otherwise, generally considered safe. No significant adverse effects reported.

Important drug/herb interactions

- Induces cytochrome P450 (3A4). As such, other drugs metabolized by that pathway will be cleared faster, lowering their serum levels 30-80%, so that they become less effective.
 - Protease inhibitors and other antiretrovirals: HIV viral loads can sky rocket
 - Cyclosporine and other immunosuppressants: Organ transplant patients can suffer severe rejection, patients with auto-immune diseases / asthma can suffer flare ups.
 - Other drugs: Ca⁺⁺ channel blockers and statins may become less effective.
- Other potential interactions:
 - In combination with SSRI's, may cause serotonin syndrome (agitation, myoclonus).
 - Other case reports of interactions with: warfarin, digoxin, oral contraceptives.

Formulation and dosage

- 300 mg tid of extract standardized to 0.3% hypericin content.
- Most extracts are standardized by their hypericin content, although it now appears that hyperforin may play an even more important role in the efficacy of St. John's wort.

References

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3. Hypericum Depression Trial Study Group. Effect of *Hypericum perforatum* (St John's wort) in major depressive disorder: a randomized controlled trial. *JAMA*. 2002; 287:1807-14.
4. Shelton RC, et al. Effectiveness of St John's wort in major depression: a randomized controlled trial. *JAMA* 2001;285:1978-86.
5. Mannel M, Drug Interactions with St John's Wort: Mechanisms and Clinical Implications. *Drug Safety*. 2004; 27:773-797.
6. Markowitz JS. Effect of St John's Wort on Drug Metabolism by Induction of Cytochrome P450 3A4 Enzyme. *JAMA* 2003;290:1500-1504.