



CORNERSTONE MEDICAL CLINIC

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St. John's Wort

St. John's wort is an herbal extract now widely sold in health food stores and pharmacies for its effectiveness and safety in the treatment of depression. The herb is licensed in Germany for the treatment of anxiety, depression and insomnia. In the USA it is considered a dietary supplement and has not been evaluated by the FDA.

Ingredients - St. John's wort is a common name for the flowering plant *Hypericum perforatum* (1). It has many constituents with biological activity, including naphthodianthrones, flavonoids, phloroglucinols and xanthenes. Hypericum, a naphthodianthrone, is generally considered the active ingredient, and in Germany dosage of the herb is based on its hypericin content. The amount of hypericin varies widely in different parts of the plant, under different growth conditions and at different times of the year.

Pharmacology - Hypericum extract inhibits uptake of the neurotransmitters serotonin, norepinephrine and dopamine and binds to GABA receptors *in vitro*, but whether it crosses the blood-brain barrier is unknown. Some constituents of the plant inhibit monoamine oxidase (MAO), but their concentration in extracts appears to be low. With oral administration of an extract, serum concentrations of hypericin reach a peak in about five hours and a steady state in about four days. Whether it is metabolized and how it is excreted are unknown. The half-life of hypericin in plasma is about 25 hours (2).

Clinical Trials - A meta-analysis of 23 randomized trials in a total of 1757 outpatients with mild or moderate depression found hypericum extracts, after two to four weeks, superior to placebo and about as effective as standard antidepressants (3). However, in most of these studies the diagnosis of depression was not well established, the placebo rate response was lower than usually seen in such studies, the dosage of standard antidepressants was low, and the dosage of hypericin varied more than sixfold. One study lasted 12 weeks, three lasted eight weeks, one lasted only two weeks and the rest has a duration of four to six weeks.

Adverse Effects - No serious adverse effects have been reported with the use of St. John's wort. Some patients have complained of dry mouth, dizziness, constipation, other gastrointestinal symptoms and confusion. In trials, fewer than 2% of patients stopped taking the herb because of adverse effects. The plant has caused severe contact photosensitivity, grazing animals have had phototoxic reactions after eating it, and systemic photosensitivity has been reported in one patient taking an extract for depression (4).

Conclusion - Better, longer studies are needed to establish the effectiveness and safety of St. John's wort for treatment of depression. The active ingredient, the potency and the purity of the preparations sold in the USA are all unknown.

(1) R Upton, ed, *St. John's Wort*, Santa Cruz, CA: American Herbal Pharmacopoeia, July 1997

(2) B Staffeldt et al, *J Geriatric Psychiatry Neurol*, 7 suppl 1:S47, 1994

(3) K Linde et al, *BMJ*, 313:253, 1996

(4) S Golsch et al, *Hautarzt*, 48:249, 1997