Effect of *Hypericum perforatum* (St. John’s Wort) in Major Depressive Disorder: A Randomized Controlled Trial


Depression affects nearly 21 million American adults each year. In major depression, people experience symptoms that interfere with their ability to work, sleep, eat, concentrate, and take pleasure in activities they once enjoyed.

*Hypericum perforatum* (St. John’s wort) is a widely used herbal remedy for depression, sometimes used in an attempt to avoid adverse effects associated with prescription antidepressants. However, scientific evidence of efficacy is inconsistent. Dietary supplements like hypericum are often used without consulting a physician or learning about potential drug interactions. Research has shown that taking hypericum can limit the effectiveness of some prescription medicines.

We conducted a randomized trial on outpatients with well-defined major depression of moderate severity. The study was sponsored by the U.S. National Institutes of Health. We recruited 340 patients from 12 psychiatric clinics in the U.S. and randomly assigned them to a standardized extract of hypericum, placebo, or sertraline (an FDA-approved antidepressant medication) for 8 weeks. Two primary outcomes were measured: (1) improvement in the Hamilton Depression Scale (HAM-D) score and (2) complete response to treatment, indicated by both a reduction in the HAM-D score to normal levels and improvement on the Clinical Global Impression Improvement scale (CGI-I). The main hypothesis was that hypericum would be superior to placebo after 8 weeks of treatment.

Neither sertraline nor hypericum was significantly different from placebo on the primary outcomes. Sertraline was better than placebo on CGI-I. Although efficacy of sertraline was demonstrated on this secondary measure, hypericum had no efficacy on any measure. Sertraline and hypericum were associated with more adverse events, but no serious adverse events occurred.

According to available data, hypericum should not be substituted for standard clinical care of proven efficacy, including antidepressant medications and specific psychotherapies, for the treatment of major depression of moderate severity.