Study Shows St. John's Wort Ineffective for Major Depression of Moderate Severity

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An extract of the herb St. John's wort was no more effective for treating major depression of moderate severity than placebo, according to research published in the April 10 issue of the Journal of the American Medical Association.¹ The randomized, double-blind trial compared the use of a standardized extract of St. John's wort (Hypericum perforatum) to a placebo for treating major depression of moderate severity. The multi-site trial, involving 340 participants, also compared the FDA-approved antidepressant drug sertraline (Zoloft®) to placebo as a way to measure how sensitive the trial was to detecting antidepressant effects.

“Many Americans use dietary supplements like St. John’s wort for depression without consulting a physician,” says principal investigator Jonathan R.T. Davidson, M.D., professor of psychiatry and director of the Anxiety and Traumatic Stress Program at Duke University Medical Center. “We felt there was a need to conduct a trial that could help us determine where St. John’s wort fits in the overall management of depression.”

The trial, funded jointly by the National Center for Complementary and Alternative Medicine (NCCAM), the National Institute of Mental Health (NIMH), and the Office of Dietary Supplements (ODS), all components of the National Institutes of Health, was launched in response to growing use of St. John’s wort in the United States and a need for more definitive data on its use for different types of depression. Although several smaller European studies have suggested that St. John’s wort is useful in treating mild to moderately severe depression, experts who reviewed those studies concluded that they had limitations and more rigorous trials were needed before firm conclusions could be drawn. Thus, NCCAM and its partners launched one of the first large-scale, multi-site clinical trials of St. John’s wort in the United States.

“Our commitment is to apply exacting scientific methods to studying popular complementary and alternative medicine practices and to publish the results of such studies in critical peer-reviewed journals, so that the public and practitioners can make the most informed decisions about them,” says Stephen E. Straus, M.D., NCCAM Director. “This study represents one of our first ‘downpayments’ on this commitment.”

“St. John’s wort is taken by many people for the relief of mild to moderate depression,” notes Paul M. Coates, Ph.D., Director of ODS. “It is important to assess the efficacy and safety of this and other commonly used dietary supplement ingredients.”

According to NIMH, major depression affects approximately 9.9 million American adults age 18 and older in a given year and is a leading cause of disability in the United States. A person experiencing a major depressive episode, according to the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), suffers from a depressed mood or loss of interest in normal activities that lasts most of the day nearly every day for at least 2 weeks; this mood can last longer if untreated. Other than depressed mood or loss of interest, symptoms include at least four of the following: significant weight loss or gain, sleep disturbances, agitation or unusual slowness, fatigue or loss of energy, feelings of worthlessness or guilt, lack of concentration, or recurrent thoughts of death or suicide.

“Major depression is a serious public health concern. Determining whether an herbal product, such as St. John’s wort, can work as a treatment is important,” said Richard K. Nakamura, Ph.D., Acting Director, NIMH. “We are always seeking treatment options to add to the list of proven medications and psychotherapies available to those suffering from depression.”

¹ For Immediate Release: St. John's Wort: No More Beneficial than Placebo for Moderate Depression.
Study participants’ initial diagnosis and severity of depression were confirmed using three primary measures: the DSM-IV depression criteria, the Hamilton Depression Scale (HAM-D), and the Global Assessment of Functioning Scale (GAF). Participants who met DSM-IV criteria for major depression, who had initial HAM-D scores of 20 or higher, and who had at least moderately severe major depression according to the GAF, were recruited from 12 academic or community psychiatric research clinics across the country. The study was conducted in two phases. The first 8-week phase, or acute phase, measured the number of people whose depression responded to treatment with St. John’s wort (from 900 mg to 1,500 mg per day), sertraline (50 mg to 100 mg per day), or placebo; this phase was the primary focus of the study. A second, or continuation, phase offered patients who had responded to their initial treatment another 18 weeks of therapy, which enabled researchers to gather data on longer-term use of the treatments. The preparation of St. John’s wort used in this study is one sold and produced in Europe and used in many earlier, smaller depression trials.

Two primary outcomes were measured during the first phase of the trial: improvements in the HAM-D scores, indicated by a reduction in score, and complete response to treatment, indicated by overall reduction in both the HAM-D score to normal levels and Clinical Global Impressions-Improvement Scale (CGI-I) score. The researchers found that HAM-D scores among patients taking St. John’s wort dropped about 8.7 points on average versus approximately 9.2 points for placebo and 10.5 points for sertraline. They also found that approximately 24 percent of patients taking St. John’s wort had full responses to treatment versus about 32 percent for placebo and 25 percent for sertraline. The differences in these rates of response were not large enough to be statistically significant. However, additional analyses of the data showed that those taking sertraline improved significantly more than those on placebo and on St. John’s wort on the CGI-I, a secondary measure of improvement. In spite of this finding, the overall response to sertraline on the primary measures was not superior to that of placebo, an outcome which is not uncommon in trials of approved antidepressants. In fact, this apparent lack of efficacy occurs in up to 35 percent of trials of antidepressants.

“Overall, we found that patients taking either St. John’s wort or placebo had similar rates of response according to scales commonly used for measuring depression,” says Dr. Davidson. “And, although sertraline produced no greater effect than placebo on the primary measures, it fared better than placebo on the Clinical Global Impressions-Improvement scale and produced results consistent with its known benefits.”

For additional information about this study, please consult “Questions and Answers: A Trial of St. John’s Wort (Hypericum perforatum) for the Treatment of Major Depression (q-and-a.htm).”

1 Hypericum Depression Trial Study Group. Effect of Hypericum perforatum (St. John’s wort) in major depressive disorder: a randomized, controlled trial. JAMA, 2002; 287:1807-1814. Full-text of the article is available on the JAMA website at www.jama.com (http://www.jama.com/).

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