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Hypericum perforatum extracts as potential antidepressants

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Extracts of *Hypericum perforatum* have been used in the treatment of mild to moderate depression for years in Europe. More recently, these extracts have become available in the United States as dietary supplements and have been popularly used to improve mood. In support of this practice, data from several controlled clinical studies suggest that *Hypericum perforatum* is better than placebo and as effective as established antidepressant drugs. These data have, however, several limitations that should temper our enthusiasm and argue for more research before accepting *Hypericum perforatum* extracts into our pharmacopoeia of established antidepressants.

Out of 15 published placebo-controlled studies, the results of 9 studies showed a superiority of hypericum over placebo. Another 8 studies compared *Hypericum perforatum* with standard antidepressants (active control) and concluded that hypericum and standard antidepressants were equally effective. These studies, however, lacked the statistical power to identify significant differences between treatments and, in the absence of a placebo, it is not possible to infer the efficacy of the *Hypericum perforatum* extracts. Also, the doses of standard antidepressants were low, usually below the usual clinically useful therapeutic range. Moreover, the definition of depression adopted in these studies was variable and, in some cases, it is not clear if the subjects had a truly defined depressive disorder or just some symptoms of depression. In fact, only one placebo-controlled study utilized the DSM criteria for major depression and most studies used more general criteria of neurotic depression and adjustment disorder. Different *Hypericum perforatum* extracts were used in these studies. Because it is still unknown which are the pharmacologically active compounds in this herb that account for its effects on mood, the current standardization based on hypericin content may not be relevant.

To address some of the limitations listed above, the National Institute of Mental Health and the Office of Alternative and Complementary Medicine at the National Institutes of Health are sponsoring a large double-blind clinical trial of a well characterized *Hypericum perforatum* extract in adult patients with major depressive disorder. A total of 336 patients will be randomized to receive hypericum extract, a standard antidepressant of the group of the selective serotonin reuptake inhibitors, or a placebo. After an 8-week trial, responders will be blindly continued on study treatment for another 18 weeks. This trial is intended to provide a definitive answer to the question of the possible value of *Hypericum perforatum* extracts for patients suffering from depression.