# St. John's Wort for the Treatment of Psychiatric Disorders

Jerome Sarris, MHSc, PhD[a,b,*]

**KEYWORDS**

• St. John's wort • *Hypericum perforatum* • Herbal medicine • Antidepressant • Depression • Anxiety • Psychopharmacology • Pharmacogenetics

**KEY POINTS**

- Evidence supports the use of St. John's wort (SJW) for the treatment of mild-to-moderate depression and somatization disorder, with tentative support in seasonal affective disorder (SAD).
- Evidence does not support the use of SJW for anxiety disorders, attention-deficit hyperactivity disorder (ADHD), or other psychiatric illnesses.
- Differences in the quality and safety of SJW extracts need to be addressed in recommending products to patients.
- Clinicians should be mindful of potential drug interactions if using products with higher (>1 mg) hyperforin and for coadministration with other psychotropic medications.

## OVERVIEW

The flowering tops of *Hypericum perforatum* (St. John's wort; SJW) have been used throughout millennia for a range of nervous system conditions, including depressed mood.[1] Dozens of clinical trials have consistently demonstrated the herbal medicine's efficacy in major depressive disorder (MDD). After two randomized controlled trials (RCTs) a decade ago revealed no greater efficacy than placebo,[2,3] clinician enthusiasm for SJW diminished. However, the findings of those studies were not due to a lack of antidepressant efficacy but, instead, reflect a pattern of increasing placebo

Disclosure Statement: No direct conflicts noted.
Dr Jerome Sarris is funded by an Australian National Health & Medical Research Council fellowship (NHMRC funding ID 628875), in a strategic partnership with The University of Melbourne and the Center for Human Psychopharmacology at Swinburne University of Technology.
[a] Department of Psychiatry, The Melbourne Clinic, The University of Melbourne, 2 Salisbury Street, Richmond, Victoria 3121, Australia; [b] Centre for Human Psychopharmacology, Swinburne University of Technology, Burwood Road, Hawthorn, Victoria 3122, Australia
* Department of Psychiatry, The Melbourne Clinic, The University of Melbourne, 2 Salisbury Street, Richmond, Victoria 3121, Australia.
*E-mail address:* jsarris@unimelb.edu.au

Psychiatr Clin N Am 36 (2013) 65–72
http://dx.doi.org/10.1016/j.psc.2013.01.004 **psych.theclinics.com**
0193-953X/13/$ – see front matter 

response and decreasing effect sizes, which also exists with conventional antidepressant studies for mild-to-moderate depression.[4,5] This phenomenon may be due to inappropriate recruitment, poor patient selection, inclusion of people with nonbiological depression, or ineligible participants motivated by financial incentives. Although an abundance of SJW MDD studies have been conducted and reviewed in other papers, there is less salient discussion on its clinical applications in other psychiatric disorders. This article outlines the current evidence of the efficacy of SJW in common psychiatric disorders, mechanisms of action, emerging pharmacogenetic data, and clinical and safety considerations.

## CLINICAL EVIDENCE

### *SJW for Depressive Disorders*

During the past two decades, more than 40 clinical trials of varying methodological quality have been conducted assessing the efficacy of SJW in treating depressed mood.

#### *Meta-analyses*

A meta-analysis of RCTs involving SJW for depression conducted by Linde and colleagues[6] revealed a relative risk (RR) of 1.48 (1.23, 1.77) from 18 combined studies for response to SJW versus placebo and an equivocal effect to selective serotonin reuptake inhibitors (SSRIs) of 1.00 (0.90, 1.15).

A meta-analysis conducted by Rahimi and colleagues[7] found a significant RR for response of 1.22 (1.03, 1.45) in favor of SJW over placebo, with a small weighted mean difference between treatments of 1.33 points (1.15, 1.51) on the Hamilton Depression Rating Scale (HAMD).

Comparison with SSRIs yielded a nonsignificant difference between treatments of 0.32 (−1.28, 0.64) for mean reduction of HAMD score from baseline.

#### *Long-term studies*

After 12 weeks of initial treatment in a double-blind RCT by Gastpar and colleagues,[8] subjects continued treatment for up to 24 weeks with either SJW (612 mg per day) or sertraline (50 mg per day). Results revealed that at week 12 both interventions were statistically equivalent; however, at week 24, in the follow-up phase, the mean HAMD score was 5.7 for SJW and 7.1 for sertraline. At the conclusion of the study, 84% of SJW and 81% of sertraline subjects were regarded as responders. It should, however, be noted that sertraline was prescribed at the lower end of the therapeutic range and a greater effect may have occurred at a higher dosage.

A longer term RCT by Kasper and colleagues[9] involving 426 responders (HAMD reduction of 50% or greater) to 6 weeks of SJW (WS 5570) found that, after continuation up to 26 weeks of SJW (900 mg per day) or matching placebo, SJW completers had a relapse rate of 18% (51/282) compared with 25.7% (37 of 144) for placebo. The mean relapse time for SJW was 14 days longer than placebo.

Not all studies are supportive of SJW for the treatment of MDD. The much publicized 2002 National Institute of Mental Health (NIMH)–funded "Hypericum Depression Trial Study Group"[2] (a 3-arm RCT; $n = 340$) revealed that, at the week 8 endpoint, on the primary outcome measure, neither SJW nor sertraline were significantly different from placebo in reducing HAMD scores. The HAMD total score reduction from baseline to week 8 was −8.68 for SJW versus −10.53 for sertraline and −9.20 for placebo, with no significant difference between groups. A recent analysis showed that, at conclusion of the follow-up part of the trial at week 26, HAMD scores for completers were: sertraline, 7.1; SJW, 6.6; and placebo, 5.7; with no significant difference between treatments.[10]