

St John's wort for depression

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There is growing, albeit not yet conclusive, evidence that St John's wort is effective for treating mild depression. Doctors should be aware of the clinically significant interactions that may occur.



PHOTOLIBRARY

What is St John's wort?

St John's wort is the name given to a medicinal extract of St John's wort (*Hypericum perforatum*), a herb that flowers around the time of St John's Day (24 June) in the northern hemisphere. The plant was introduced into Australia in the late nineteenth century; its rapid and widespread growth in rural areas has led to it being formally declared a noxious weed in many parts of this country.

Which patients are using it?

Approximately 5 to 6% of adults in the community are prescribed antidepressants for depression or anxiety. However, results of an Australian survey have shown that more than 2% of the population use complementary medication for this purpose – with St John's wort being the most common of these – and about 0.5% use both orthodox antidepressants and a complementary medication.¹ The common nature of usage for St John's wort is also

apparent from a survey of Australian psychiatrists, in which 80% reported having patients who had used it.² St John's wort tends to be mainly used by individuals with mild depression or anxiety. To some extent, this high rate of use for St John's wort and other complementary medications probably reflects the observation that about one-quarter of Australian adults believe antidepressants are harmful for a person who is depressed and suicidal.³

Use of St John's wort is increasing worldwide but particularly in Germany, where it was formally approved in the early 1980s for the treatment of 'psychogenic disturbances, depressive states, anxiety and nervous excitement'. In recent years, prescriptions of St John's wort in that country have substantially outnumbered those for SSRI antidepressants – this may reflect a cultural preference for herbal compounds as well as the German 'cap' on prescribing expenses for each medical practitioner.

How effective is it?

The evidence for the clinical efficacy of St John's wort in depression is controversial and contradictory. The most recent Cochrane review on the use of St John's wort, which was published in 2005, was a meta-analysis of 37 randomised double-blind trials of depressed subjects in which extracts of the plant were compared with either placebo or standard anti-

depressants.^{4,5} Marked variability in the results was observed. When the analysis was restricted to trials of patients with major depression, there was a significant but limited effect (response rate ratio, 1.15) in six larger trials but a larger effect (response rate ratio, 2.06) in six smaller trials, compared with placebo. When the analysis was not restricted to trials of patients with major depression, the response rate ratio was 1.71 in larger trials and 6.13 in smaller trials, compared with placebo. Comparisons against standard antidepressants indicated St John's wort, SSRIs and tricyclic antidepressants have similar efficacy. Overall, the larger (and usually better designed) trials suggest lesser efficacy than the smaller trials for St John's wort, and greater benefit for mild depression that does not fulfill criteria for major depression.

How safe is it?

The incidence of adverse effects due to St John's wort is low, with only 0.1 to 2.4% of patients being affected. The dropout rate due to these effects is only 0.1 to 0.9%,⁶ which is much lower than the dropout rates for standard antidepressants. It should be noted that there is a small risk of cutaneous photosensitisation.

How is it used?

Although commercial preparations of St John's wort are standardised by hypericin

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content, this compound is no longer considered to be the only specific active constituent. Current evidence suggests that any efficacy relates to the combination of active constituents. Most trials that have reported efficacy have used 300 mg of an extract standardised to contain 1 mg hypericin and a dosage frequency of three times daily. The 300 mg of an extract is equivalent to 1800 mg dried flowering herb from a 6:1 concentrate.

In Australia, many preparations of St John's wort have been approved under the Australian Regulatory Guidelines for Complementary Medications and listed on the Australian Register of Therapeutic Goods. These are available through pharmacies and health food outlets, but not via prescription by medical practitioners.

What about important precautions and interactions?

The major safety concern regarding use of St John's wort is potential interactions. The main pharmacodynamic interaction occurs with serotonergic antidepressants – particularly SSRIs – and there have been reports of the potentially lethal serotonin syndrome, which presents with restlessness, myoclonus, sweating, shivering, tremor and confusion.⁷

A number of pharmacokinetic interactions can occur, as St John's wort induces a number of the hepatic CYP450 metabolising enzymes (particularly CYP3A4). This has led to reduced levels of certain medications when prescribed for patients who are using St John's wort, in particular:⁸

- cyclosporin
- digoxin
- indinavir
- nevirapine
- SSRIs
- oral contraceptives
- theophylline
- warfarin.

In view of the potential for clinically significant interactions, clinicians should question patients who are taking any of

these medications about concurrent use of St John's wort.

Conclusions

There is growing, albeit not yet conclusive, evidence that St John's wort is effective for treating mild depression but not appropriate for severe depression. Clinicians need to be alert to the fact that a considerable proportion of their patients will be taking St John's wort. There is potential for the development of the serotonin syndrome with SSRI antidepressants and a loss of efficacy of oral contraceptives (with risk of pregnancy), immunosuppressants (with risk of graft rejection), oral anticoagulants (with risk of thrombosis) and HIV protease inhibitors. **MT**

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