

St John's wort

What is St John's wort?

St John's wort (SJW) is a herbal remedy also known as hypericum. It is extracted from the flowers and leaves of the plant *Hypericum perforatum* and has been used over many centuries as a traditional medicine for wound healing and mental health problems. It remains popular with the public, bought over-the-counter from health food shops and chemists as a treatment for depression. However, it should strictly be considered a drug since it contains pharmacologically active agents, including hypericin. SJW's mechanism of action is unknown but it may inhibit the reuptake of serotonin and noradrenaline, inhibit monoamine oxidase, up-regulate serotonin receptors, and decrease serotonin receptor expression.^[1]

Whilst many clinically important drugs have their origins in herbal medicine, issues concerning safety (possible toxicity, drug interactions and teratogenicity) and efficacy have arisen with the use of herbal remedies in modern times. The regulatory framework for herbal remedies is different and less rigorous compared with that applied to pharmaceutical medicines. They may:

- Be unlicensed, where they are not industrially produced.
- Be registered under the Traditional Herbal Medicines Registration Scheme which requires specific standards of safety and quality. Much commercially available SJW falls under this category with a need only to prove traditional use rather than efficacy.
- Hold a product licence, which additionally requires evidence of efficacy.

See separate article [Complementary and Alternative Medicine](#) for further details. Problems also occur with variation in potency between brands and batches:

- Some of the proprietary preparations are standardised for hypericin, making them more consistent than products that are not standardised.
- It is likely that other ingredients (for example, flavonoids and flavonoid derivatives, xanthone derivatives, amentoflavone, biapigenin, volatile oil) in the preparation have some effect on depression and, whilst these are not standardised, potency may vary between batches.^[2]
- Different brands have different amounts of hypericin and other ingredients, so it is best to choose a standardised brand and to stick with the same brand.

There is some debate as to the correct dose - the usual recommended dose is about 900 mg a day of hypericum extract, but much higher doses have been used in trials.^[3]

The National Institute for Health and Care Excellence (NICE) guideline for Depression recommends that, although there is evidence that St John's wort may be of benefit in less severe depression, healthcare professionals should:^[1] ^[4]

- Advise people with depression of the different potencies of the preparations available and of the potential serious interactions of St John's wort with other drugs.
- Not prescribe or advise its use by people with depression because of uncertainty about appropriate doses, persistence of effect, variation in the nature of preparations and potential serious interactions with other drugs (including hormonal contraceptives, anticoagulants and anticonvulsants).

NICE also recommends that St John's wort should not be prescribed for the treatment of depression in children and young people.^[5]

Efficacy

SJW is usually recommended for low mood or mild depression. Its use in somatoform disorders has also been explored.^[6] Problems with clinical trials investigating the use of SJW in depression have included heterogeneity, short follow-up (often for only 4–8 weeks) and small numbers resulting in underpowering.^[7] Trials from German-speaking countries tend to report more positive results, possibly reflecting a cultural bias to its use. However, a number of reviews conclude it can be effective for major depression.^[8] ^[9] A 2008 Cochrane Review found SJW to be superior to placebo in patients with major depression and as effective as standard antidepressants but with better tolerability, and concluded that it was an effective treatment.^[10]

There is no evidence of benefit in attention deficit hyperactivity disorder (ADHD)^[11] or bipolar disorder.^[12] One randomised controlled trial failed to show evidence of benefit for SJW in irritable bowel syndrome.^[13]

Contra-indications

- SJW should be avoided in pregnancy or lactation, due to lack of high-quality, human-based studies demonstrating safety. Animal studies suggest that use during pregnancy does not affect cognitive development or cause long-term behavioural defects, but may cause lower birth weight. Early studies on women taking SJW who have unplanned pregnancy suggest no evidence of fetal harm.^[14] There is very limited evidence that use of SJW during lactation does not affect milk production but may cause colic, drowsiness or lethargy.^[15]
- It should not be used in [bipolar disorder](#) as it may be associated with mania.^[16]
- It should not be taken at the same time as other antidepressants, especially the selective serotonin reuptake inhibitors (SSRIs), venlafaxine and duloxetine, as there is risk of a serotonergic crisis.^[17]
- For the same reason it should not be used with the triptans including sumatriptan, naratriptan, rizatriptan and zolmitriptan

- SJW is a cytochrome P450 3A4 inducer.^[18] ^[19] This and other mechanisms underlie a large number of potentially significant drug interactions including:^[20] ^[21]
 - Hormonal contraceptives – SJW can reduce effectiveness of all methods of hormonal contraception, including implants, other than intrauterine contraceptive devices, for which there are currently no data.^[22] This can cause breakthrough bleeding and unwanted pregnancies.
 - Warfarin.
 - Cyclosporin.
 - Calcium-channel blockers – reduced plasma concentration of amlodipine, nifedipine and verapamil with concurrent use.
 - All anticonvulsants including carbamazepine, phenobarbital and phenytoin.
 - Simvastatin and atorvastatin
 - Methadone.
 - HIV treatments including indinavir, nelfinavir, ritonavir, saquinavir, efavirenz and nevirapine.
 - Digoxin.
 - Theophylline.
 - Anticoagulants – may reduce plasma concentration of dabigatran – avoid concurrent use.
 - Anti-cancer drugs. Anti-neoplastic agents such as imatinib, irinotecan and docetaxel may have reduced efficacy when used concurrently.^[23]

Patient interaction warnings are frequently inadequate on products for sale.^[24]

Initiation of treatment

Before a patient is started on a licensed antidepressant, they must see a doctor for a diagnosis. A prescription is issued and follow-up arranged. None of this is obligatory for SJW in the UK, as it can be bought freely, without consultation regarding diagnosis or safety advice. This is clearly unsatisfactory in the management of a serious and potentially fatal disease such as depression.

- Ideally patients should consult a doctor first, discuss treatment options and be followed up regardless of what treatment they elect to follow. Sometimes the use of complementary and alternative medicine (CAM) is perceived as a barrier to open communication between doctor and patient. Doctors should enquire about the current and intended use of herbal remedies and over-the-counter medication.
- When a patient plans to switch from a conventional antidepressant to SJW, a 'washout' period should be advised. This will vary depending on half-life of the drug being stopped. The patient should be warned about drug interactions, including antidepressants and oral contraceptives if appropriate.

Monitoring

- The depression should be monitored to assess progress. The patient should be seen after a week or two and then at intervals dictated by the doctor's clinical acumen and usual practice. As with other antidepressants, it may take 2 to 4 weeks to have effect.
- Where a patient is taking other drugs, particularly anticoagulants, careful monitoring is required on starting and stopping SJW. They must be counselled that different brands and strengths of SJW are likely to cause differences in the degree of interaction and therefore ideally they should stick to one particular preparation.

- Ask the patient about side-effects. Patients on conventional drugs are usually very ready to attribute physical signs and symptoms to an adverse drug reaction. With 'natural remedies' the opposite may be true. Cochrane reviews have found side-effects to SJW to be minor and uncommon, and that it is better tolerated than conventional antidepressants.^[10] The most commonly reported side-effects include:
 - Gastrointestinal symptoms such as nausea, vomiting or diarrhoea.
 - Allergic reactions.
 - Fatigue.
 - Dizziness.
 - Dry mouth.
 - Photosensitivity - this is uncommon and tends to be associated with high doses, but people taking it should increase their sun protection and avoid strong sunlight.
- The Medicines and Healthcare products Regulatory Agency (MHRA) encourages the reporting of adverse reactions to herbal medicines via the Yellow Card Scheme - patients are able to self-report or report via their pharmacist or doctor.
- Advise patients to discontinue the SJW where side-effects are intolerable or drug interactions unacceptable.
- Where the depression becomes worse/severe, advise the patient to stop the SJW and start an adequate dose of a drug of proven value in severe depression after a brief 'washout' period.

History

St John's wort is named after St John the Baptist, whose feast day on 24th June coincides with the plant's full bloom in Europe. Its five yellow petals resemble a halo, and its red sap symbolises the blood of the martyred saint. He was beheaded after criticising the morality of King Herod, the Jewish king. The name hypericum comes from the Greek, meaning 'greatest health'.

Further reading

- [St John's wort factsheet](#); MIND

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Authored by:	Peer Reviewed by: Dr Hayley Willacy, FRCGP	
Originally Published: 20/11/2023	Next review date: 17/01/2023	Document ID: doc_497

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