Your questions about complementary medicines answered: St John's wort

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This is the fifth article in a series providing evidence-based answers to common questions about complementary medicines from consumers and healthcare professionals.

What is St Johns wort?

Extracts of St John's wort (SJW) or *Hypericum perforatum*, a perennial herb with small yellow flowers, are widely available in pharmacies and health food stores. Historically, SJW has been used for a variety of conditions including abdominal pains, alcoholism, earaches and menopausal complaints. However, the most common reason for using SJW is depression and low mood. Patients will commonly be advised to take SJW when presenting to health food stores with symptoms of depression.[1] While high-quality, controlled studies found it to be effective for the treatment of mild-to-moderate depression,[2–4] it has not been included in mainstream treatment guidelines because of uncertainty about appropriate doses, persistence of effect, variation in the nature of preparations and potentially serious drug interactions.[5,6]

Who asks about SJW?

SJW was mentioned frequently in our medicines call centre databases.[1,7] There were 689 consumer queries (6.7% of all CM questions) and 367 healthcare professional queries (6.8%). The average SJW consumer caller was 47 years of age; 83% were women and most questions focused on interactions (54%), efficacy (17%) and adverse drug reactions (ADRs, 10%). Similarly, health professionals were predominantly concerned about interactions (67.3%), but much less so about ADRs (8.7%) and efficacy (2.2%).

Common consumer and health professional question

When swapping from SJW to a prescription antidepressant (or vice versa) what is the recommended washout period?

Constituents of SJW, hypericin and hyperforin, have antidepressant action and half-lives of 24–48 hours and 9 hours, respectively.[2] Studies in animals have shown that the antidepressant activity of SJW is complex and mediated through a combination of mechanisms including inhibition of serotonin, noradrenaline and dopamine synaptic reuptake, as well as via the neurotransmitters glutamate and gamma-aminobutyric acid (GABA).[2] Thus, SJW should not be taken with prescription antidepressants, to avoid the risk of serotonin toxicity (ie hyperreflexia, tremor, sweating, agitation, confusion, clonus and diarrhoea).[8] After stopping SJW, which should be withdrawn slowly,[9] a 1-week interval is recommended before starting a prescription antidepressant.[10]

When switching from a prescription antidepressant to SJW, the washout period is variable, depending on the metabolism of the drug.[8] However, most prescription antidepressants are cleared within 1 week of ceasing medication, so it is safe to commence SJW treatment after an interval of 1 week.[11] The exceptions are fluoxetine, phenelzine and tranylcypromine, which require a wait of up to 14 days.[8,11]

Common consumer question

Is it safe to take SJW with a prescription antidepressant?

It is not safe to take SJW with a prescription antidepressant.[7] SJW is effective for depression.[4] However, as its mechanism of action is similar to that of many common antidepressants that increase levels of serotonin and noradrenaline in the brain,[2] combined therapy can increase the risk of symptoms associated with serotonin toxicity (ie hyperreflexia, tremor, sweating, agitation, confusion, clonus and diarrhoea).[8]

Common health professional question

What is the effect of SJW on the oral contraceptive pill?

SJW should not be taken with the combined oral contraceptive (COC) pill as it can reduce the effectiveness of COCs and increases the risk of unintended pregnancy. SJW contains hypericin and hyperforin, extracts of which have been reported to induce the cytochrome P450 enzymes CYP1A2, CYP2C9 and CYP3A4, and increase intestinal P-glycoprotein expression.[12–14] These dose-related actions stimulate the liver to break down the oestrogen and progestogen constituents of the COC pill more rapidly, potentially making COCs less effective and increasing the chance of unintended pregnancy.[14–20] There have been several case reports of unplanned pregnancies when these medications have

been taken regularly and long term.[18–20] Clinical studies indicate that CYP3A activity returns gradually to the basal level approximately 1 week after cessation of SJW.[19]

Further resources

- http://www.australianprescriber.com/magazine/22/5/112/3
- http://www.nps.org.au/conditions/mental-health-conditions/mood-disorders/depression/for-individuals/medicines-for-depression-antidepressants/complementary-medicines-alternative-therapies-for-depression/st-johns-wort
- http://nccam.nih.gov/health/stjohnswort/ataglance.htm

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References

1. Glisson JK, Rogers HE, Abourashed EA, Ogletree R, Hufford CD, Khan I. Clinic at the health food store? Employee recommendations and product analysis. Pharmacotherapy 2003;23:64–72.
2. Natural Standard Professional Database. Available at www.naturaldatabase.com [Accessed 19 September 2013].
3. van der Watt G, Laugharne J, Janca A. Complementary and alternative medicine in the treatment of anxiety and depression. Curr Opin Psychiatry 2008;21:37–42.
4. Linde K, Berner MM, Kriston L. St John's wort for major depression. Cochrane Database Syst Rev 2008;CD000448.
5. National Institute for Health and Care Excellence. Nice clinical guideline 90. Depression in adults. Available at www.nice.org.uk/nicemedia/live/12329/45888/45888.pdf [Accessed 4 June 2014].
6. Therapeutic Guidelines. Available at: http://online.tg.org.au/complete/ [Accessed 4 June 2014].
7. Kreijkamp-Kaspers S, McGuire T, Bedford S, et al. Your questions about complementary medicines answered. Aust Fam Physician 2015;44:373–74.
8. Australian Medicines Handbook. Australian Medicines Handbook 2013. Available at: www.amh.net.au [Accessed 28 May 2014].
9. Dean AJ, Moses GM, Vernon JM. Suspected withdrawal syndrome after cessation of St John's wort. Ann Pharmacother 2003;37:150.
10. Imai H, Kotegawa T, Tsutsumi K, et al. The recovery time-course of cyp3a after induction by St John's wort administration. Br J Clin Pharmacol 2008;65:701–07.
11. Ogle NR, Akkerman SR. Guidance for the discontinuation or switching of antidepressant therapies in adults. J Pharm Pract 2013;26:389–96.
12. Durr D, Stieger B, Kullak-Ublick GA, et al. St John's wort induces intestinal p-glycoprotein/mdr1 and intestinal and hepatic cyp3a4. Clin Pharmacol Ther 2000;68:598–604.
13. Gurley BJ, Swain A, Hubbard MA, et al. Clinical assessment of CYP2D6-mediated herb-drug interactions in humans: Effects of milk thistle, black cohosh, goldenseal, kava kava, St John's wort, and Echinacea. Mol Nutr Food Res 2008;52:755–63.
14. Hall SD, Wang Z, Huang SM, et al. The interaction between St John's wort and an oral contraceptive. Clin Pharmacol Ther 2003;74:525–35.
15. Yue QY, Bergquist C, Gerden B. Safety of St John's wort (Hypericum perforatum). Lancet 2000;355:576–77.
16. Pfrunder A, Schiesser M, Gerber S, Haschke M, Bitzer J, Drewe J. Interaction of St John's wort with low-dose oral contraceptive therapy: a randomized controlled trial. Br J Clin Pharmacol 2003;56:683–90.
17. Schwarz UI, Büschel B, Kirch W. Unwanted pregnancy on self-medication with St John's wort despite hormonal contraception. Br J Clin Pharmacol 2003;55:112–13.
18. Mannel M. Drug interactions with St John's wort: Mechanisms and clinical implications. Drug Saf 2004;27:773–97.
19. Murphy PA, Kern SE, Stanczyk FZ, Westhoff CL. Interaction of St John's wort with oral contraceptives: Effects on the pharmacokinetics of norethindrone and ethinyl estradiol, ovarian activity and breakthrough bleeding. Contraception 2005;71:402–08.
20. Borrelli F, Izzo AA. Herb-drug interactions with St John's wort (hypericum perforatum): An update on clinical observations. AAPS J 2009;11:710–27.

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