Drug interactions with St John's wort: mechanisms and clinical implications.

Mannel M.

Ad libitum Medical Services, Berlin, Germany. mannel@ad-libitum-medical.com

The purpose of this paper is to review preclinical and clinical evidence relating to drug interactions with preparations of the medicinal herb St John's wort (Hypericum perforatum). A systematic literature search was carried out in three electronic databases up to June 2004. Information about case reports classified as St John's wort drug interactions was retrieved from the WHO Collaborating Centre for International Drug Monitoring and from the UK Medicines and Healthcare products Regulatory Agency in June 2003. Against the background of proven efficacy in mild to moderate depressive disorders and an excellent tolerability profile in monotherapy, there is sufficient evidence from interaction studies and case reports to suggest that St John's wort may induce the cytochrome P450 (CYP) 3A4 enzyme system and the P-glycoprotein drug transporter in a clinically relevant manner, thereby reducing efficacy of co-medications. Drugs most prominently affected and contraindicated for concomitant use with St John's wort are metabolised via both CYP3A4 and P-glycoprotein pathways, including HIV protease inhibitors, HIV non-nucleoside reverse transcriptase inhibitors (only CYP3A4), the immunosuppressants ciclosporin and tacrolimus, and the antineoplastic agents irinotecan and imatinib mesylate. Efficacy of hormonal contraceptives may be impaired as reflected by case reports of irregular bleedings and unwanted pregnancies. Drugs with a narrow therapeutic index should be monitored more closely when St John's wort is added, discontinued or the dosage is changed. The St John's wort constituent hyperforin is probably responsible for CYP3A4 induction via activation of a nuclear steroid/pregnane and xenobiotic receptor (SXR/PXR) and hypericin may be assumed to be the P-glycoprotein inducing compound, although the available evidence is less convincing. Combinations of St John's wort with serotonergic agents and other antidepressants should be restricted to prescription-only, by experienced clinicians, due to potential central pharmacodynamic interactions. In conclusion, providing certain precautions and contraindications are followed, and adequate information is given to healthcare professionals and patients, the safe and effective use of quality-tested St John's wort products can be ensured.

PMID: 15350151 [PubMed - indexed for MEDLINE]

Related Links:
The emerging recognition of herb-drug interactions with a focus on St. John's wort (Hypericum perforatum). [Psychopharmacol Bull. 2001] PMID:12397870

Pharmacokinetic interactions of drugs with St John's wort. [J Psychopharmacol. 2004] PMID:15260917

St John's wort (Hypericum perforatum L.): a review of its chemistry, pharmacology and clinical properties. [J Pharm Pharmacol. 2001] PMID:11370698
St John's wort and depression: slight efficacy at best, many drug interactions. [Prescrire Int. 2004] PMID:15499702

Effect of St John's wort on imatinib mesylate pharmacokinetics. [Clin Pharmacol Ther. 2004] PMID:15470331