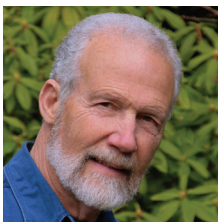


Oral Contraceptives and St John's Wort

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ASSESSING THE CLINICAL IMPORTANCE OF DRUG-DRUG INTERACTIONS involving herbal medications can be problematic. There is a general lack of high-quality studies, as shown by a recent systematic review of drug interactions of warfarin with herbal medicines. Just 9 randomized controlled trials were identified out of hundreds of published studies, and even these studies had some flaws.¹ In addition, it is often difficult to precisely assess the potency and content of herbal products. It is possible, for example, that one type of ginseng might interact with a particular drug while a different ginseng product might not.

For St John's wort, however, sorting out which drug interactions are real is somewhat more straightforward. First, St John's wort can be standardized based on hypericin content. Moreover, there is a substantial amount of evidence to show that St John's wort acts as an inducer of CYP3A4 and, to a lesser extent, CYP2C19 and CYP2C9. St John's wort also induces the transporter P-glycoprotein (*ABCB1*).² The induction of these enzymes and transporters could reduce the efficacy of a variety of other medications, including oral contraceptives. Cases of breakthrough bleeding and unintended pregnancy have been reported in women taking St John's wort with oral contraceptives, but it is difficult to assess such case reports because bleeding and pregnancy can occur whether or not the woman is taking interacting drugs.

A comprehensive evaluation of the evidence supporting the interaction of oral contraceptives and St John's wort has been published, and it provides new insights into this drug interaction.³ The study involved a search of PubMed and the Cochrane database, in which it identified 48 articles dealing with the interaction of St John's wort with oral contraceptives. Of these, just 4 studies compared the use of oral contraceptives alone with the combined use of St John's wort and oral contraceptives and met their rigorous inclusion criteria. The results suggest that the interaction is real and that pharmacist intervention is warranted.

In one study of 12 women using oral contraceptives (ethinyl estradiol 35 mcg, norethindrone 1 mg), the

subjects took the oral contraceptive alone for 1 month and then added St John's wort 300 mg 3 times a day (hypericin content 0.3%) for the next 2 months.⁴ During month 1, just 2 of the 12 women had breakthrough bleeding, but by the third month, more than half (7 of 12) did. Also, in the presence of St John's wort, ethinyl estradiol half-life was reduced to about half of its control values.

Another study of 16 women on ethinyl estradiol 20 mcg and norethindrone 1 mg compared 2 cycles with the oral contraceptive alone to 2 cycles with added St John's wort 300 mg 3 times a day (hypericin content 0.3%).⁵ With the addition of St John's wort, breakthrough bleeding increased from 19% to 50%, accompanied by modest reductions in ethinyl estradiol and norethindrone area under the curve. Also, during St John's wort administration, more women had follicles over 30 mm and more had probable ovulation.

Using a randomized crossover design, in a third study, 17 women taking ethinyl estradiol 20 mcg plus desogestrel 0.15 mg were studied for 1 month on the oral contraceptive alone, followed by 1 month of added St. John's wort 300 mg twice a day and then 1 month of added St. John's wort 300 mg 3 times a day (hypericin content 0.3%).⁶ With the oral contraceptive alone, 6 of the 17 women had breakthrough bleeding, but that increased to 13 women with St John's wort twice a day, and with St John's wort 3 times a day, most of the women (15 of 17) had breakthrough bleeding.

CONCLUSION

The evidence suggests that St John's wort taken with oral contraceptives is likely to increase the risk of unintended pregnancy in at least some women. The effect of St John's wort on implants or other types of hormonal contraceptives is not clear, but it would be prudent to assume that they may interact as well. Women on oral contraceptives should be advised of the potential interaction with St John's wort. Most would probably choose to avoid St John's wort, but if they feel it is necessary, they could be advised about nonhormonal contraceptive methods to replace oral contraceptives. ♦

FOR REFERENCES, GO TO PHARMACYTIMES.COM/ LINK/144.