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Goldenseal Drug Interactions

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Goldenseal is a popular herbal product containing the alkaloids berberine and hydrastine. It is used to treat infections of various types, inflammation, hypertension, and many other disorders. Evidence is accumulating that goldenseal may have some clinically important drug interactions.

Interactive Properties

Goldenseal appears to inhibit some cytochrome P450 (CYP) drug-metabolizing isozymes, CYP3A4, CYP2D6, and probably CYP2C9. Because CYP3A4 metabolizes more drugs than any other isozyme, there is a potential for numerous interactions with goldenseal. Available clinical evidence suggests that goldenseal does not inhibit CYP1A2 or CYP2E1, and the lack of an effect of goldenseal on digoxin pharmacokinetics suggests that it does not affect the transporter, P-glycoprotein (ABCB1).[1]

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CYP3A4 Inhibition

Pharmacokinetic studies of midazolam and cyclosporine in healthy subjects show that goldenseal inhibits CYP3A4.[2-4] Also, a randomized controlled study in 104 transplant patients on cyclosporine found that goldenseal (as berberine) produced substantial increases in cyclosporine levels.[5] Goldenseal would also be expected to interact with serolimus and tacrolimus, which are both CYP3A4 substrates.

Given the convincing evidence that goldenseal inhibits CYP3A4, it is likely that goldenseal inhibits the metabolism of other CYP3A4 substrates such as alfuzosin, calcium channel blockers, carbamazepine, colchicine, ergot alkaloids, phosphodiesterase inhibitors, ranolazine, vinca alkaloids, and selected members of other classes, such as benzodiazepines, statins, corticosteroids, opioid analgesics, antipsychotics, antiarrhythmics, antidiabetics, and protease inhibitors.

CYP2D6 Inhibition

Pharmacokinetic studies of debrisoquin and dextromethorphan (CYP2D6 substrates) in healthy subjects show that goldenseal inhibits CYP2D6.[2,3,6] Although far fewer drugs undergo metabolism by CYP2D6 compared with CYP3A4, one must still consider that reduced CYP2D6 activity can increase the risk of toxicity from certain members of drug classes, including antiarrhythmics, antipsychotics, and beta-blockers. Also, some drugs such as codeine and tamoxifen are administered as prodrugs, and CYP2D6 is required for their activation. Thus goldenseal would theoretically reduce the efficacy of such medications.

CYP2C9 Inhibition

In a randomized crossover study in 18 healthy subjects given a single dose of losartan 30 mg, berberine administration doubled the ratio of urinary losartan to its active metabolite.[2] The active metabolite of losartan is formed by the action of CYP2C9, so this study suggests that

berberine (or goldenseal) is a CYP2C9 inhibitor.

Although the effect of CYP2C9 inhibition on the efficacy of losartan is not clear, inhibitors of CYP2C9 are known to increase warfarin response, thus potentially increasing the bleeding risk if doses are not adjusted. Although the effect of goldenseal on CYP2C9 requires more study, one should assume that goldenseal can increase warfarin response until clinical studies of the combination are performed. Other CYP2C9 substrates that might interact with goldenseal include phenytoin as well as several oral antidiabetic agents.

Summary

Goldenseal is one of the few herbal products for which we have credible clinical information on its interactive properties. The most important of these properties is the ability of goldenseal to inhibit CYP3A4, because so many drugs are CYP3A4 substrates and some of these drugs have substantial toxicity.

The evidence for CYP2D6 inhibition by goldenseal is also substantial, although a limited number of drugs are CYP2D6 substrates. The ability of goldenseal to inhibit CYP2C9 is still under study, but if it proves to be real, one would expect adverse interactions with warfarin and other CYP2C9 substrates. ■

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