Drug-herb interaction potential: effects on cytochrome P450 and P-glycoprotein

In this guide

26. Freeman and Spelman (2008) conducted a literature review and found no verifiable reports of drug–herb interactions involving Echinacea products. They noted that herbal remedies derived from E. purpurea appear to have a low potential for cytochrome P450 (CYP450)-mediated interactions. The authors further estimated that, given the risk of adverse events (approximately 1 in 100,000), the annual consumption of Echinacea doses (around 10 million), and the fact that most use is short-term, products containing E. purpurea (roots and/or aerial parts) do not pose a significant risk to consumers. Nevertheless, they concluded that although current evidence does not support the need for specific precautions when Echinacea is co-administered with prescription

medications, a prudent clinical approach would be to monitor patients taking Echinacea concurrently with substrates of CYP3A4 or CYP1A2.

27. The in vitro studies identified as part of the literature search performed by the Secretariat suggest that Echinacea has the potential to inhibit CYP3A4 (Yale and Glurich, 2005; Modarai et al. 2010; Hellum et al. 2007; Husain et al., 2023), CYP1A2 (Yale and Glurich, 2005; Hellum et al. 2007), CYP2E1 (Raner et al. (2007) and P-glycoprotein (Husain et al., 2023; Hansen and Nilsen, 2009). Some of the in vitro studies reported a positive association between the total alkylamide content of the Echinacea preparation and its ability to inhibit CYP3A4 (Modarai et al. 2010) and CYP1A2 (Raner et al. 2007).

28. A clinical study on human volunteers by Gorski (2004) found that E. purpurea root extract (Nature’s Bounty) taken orally at 1,600 mg/day for 8 days was capable of causing significant changes in drug disposition by inhibiting CYP1A2 and intestinal CYP3A activity and by inducing hepatic CYP3A activity. This preparation contained greater than 1% phenols (caftaric acid, chlorogenic acid, echinacoside and chicoric acid). Gorski (2004) concluded that the modest change in the clearance of compounds metabolised by CYP1A2 is considered clinically significant as this can lead to increased toxicity of narrow therapeutic window drugs such as theophylline, which is a substrate for CYP1A2. The authors also speculated that other drugs metabolised by CYP1A2 such as cyclobenzaprine, tacrine, and clozapine can be affected by Echinacea coadministration.

29. Another human study with 12 healthy volunteers (6 men, 6 women) investigated the effects of E. purpurea (800 mg, twice daily) for 28 days on CYP1A2, CYP2D6, CYP2E1 and CYP3A4 phenotypes (Gurley et al., 2004). The composition of the Echinacea preparation was analysed using HPLC and it was determined that it contained 13.7 mg chicoric acid per capsule, providing a daily dose of 43.8 mg chicoric acid. No serious adverse events occurred during the course of the study; one subject experienced a mild rash while taking Echinacea. The administration of E. purpurea did not significantly change the activities of CYP3A4, CYP2E1, and CYP2D6 as estimated by comparing the phenotype ratios before and after treatment. Co-administration of E. purpurea caused an approximately 13% decrease in the ratio of paraxanthine/caffeine, suggesting that there was a possible inhibitory effect on CYP1A2 enzyme. However, the difference was not statistically significant and the authors did not think it was clinically relevant (Gurley et al., 2004).