

Protective effects of goldenseal (*Hydrastis canadensis* L.) on acetaminophen-induced hepatotoxicity through inhibition of CYP2E1 in rats

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ABSTRACT

Background Goldenseal (*Hydrastis canadensis* L.) inhibits various cytochrome P450 (CYP) isoforms such as CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A in vitro. High doses of acetaminophen (APAP) generate the highly reactive intermediate, N-acetyl-p-benzoquinone imine (NAPQI), catalyzed mainly by CYP2E1. The aim of this study was to investigate the hepatoprotective effects of orally administrated goldenseal against APAP-induced acute liver failure (ALF) via inhibition of CYP2E1. **Materials and Methods** Male Wistar rats were treated orally with goldenseal (300 and 1000 mg/ kg) 2, 18, and 26 h before and 6 h after oral APAP (400 mg/kg) administration. Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities as well as serum APAP concentration were evaluated. **Results** Goldenseal extract inhibited CYP1A2, CYP2D6, CYP2E1, and CYP3A activity, and the inhibitory effect on CYP2E1 was the strongest (IC₅₀ 4.32 g/mL). Treatment with goldenseal (300 mg/kg) significantly attenuated the APAP-induced increase in serum AST and ALT, and the hepatoprotective effect of goldenseal was stronger than that of silymarin (200 mg/kg). Moreover, serum APAP concentration was increased by goldenseal treatment, presumably as a result of the inhibitory effect of goldenseal on the metabolism of APAP to NAPQI. **Conclusion** These results suggest that goldenseal ameliorates APAP-induced ALF and that this protection can likely be attributed to the inhibition of CYP2E1 activity, which generates the highly reactive intermediate of APAP.

KEYWORDS

Acetaminophen . acute liver failure . CYP2E1 . hepatoprotective effect . goldenseal

REFERENCES