Influence of an Herbal Formula *Guibi-tang* on Drug-Metabolizing Enzymes In Vitro and In Vivo
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**Purpose**
The aim of this study was to investigate the influence of traditional herbal formula *Guibi-tang* (GBT) on the activities of human microsomal cytochrome P450s (CYP450s) and UDP-glucuronosyltransferases (UGTs) as well as the mRNA expression of CYP450s in rats.

**Methods**
The activities of human major CYP450s (CYP1A2, CYP3A4, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP2E1) and UGTs (UGT1A1, UGT1A4, and UGT2B7) were assessed using *in vitro* fluorescence- and luminescence-based enzyme assays, respectively. The effects of GBT on the activities of CYP450s and UGTs were presented as IC<sub>50</sub> values. To confirm the level of mRNA expression in rat liver, GBT was orally administered to either male or female Sprague Dawley (SD) rats once daily at doses of 1000, 2000, or 5000 mg/kg/day for 13 weeks. The mRNA expression of CYP450s (CYP1A1, CYP1A2, CYP2B1/2, CYP2C11, CYP2E1, CYP3A1, CYP3A2, and CYP4A1) was analyzed in hepatic tissues by reverse transcription–polymerase chain reaction.

**Results**
GBT inhibited the activities of human CYP2C19 (IC<sub>50</sub> = 115.71 μg/mL) and CYP2E1 (IC<sub>50</sub> = 170.62 μg/mL), while exerted relatively weak inhibition on human CYP1A2 (IC<sub>50</sub> = 515.80 μg/mL), CYP3A4 (IC<sub>50</sub> = 209.31 μg/mL), and UGT1A1 (IC<sub>50</sub> = 869.86 μg/mL). GBT also negligibly inhibited the activities of human CYP2B6, CYP2C9, and CYP2D6, with IC<sub>50</sub> values in excess of 1000 μg/mL, and they exhibited no inhibition of the activities of human UGT1A4 and UGT2B7 at doses less than 1000 μg/mL. Repeated oral administration of GBT did not significantly influence the mRNA expression of hepatic CYP1A1, CYP1A2, CYP2B1/2, CYP2C11, CYP2E1, CYP3A1, CYP3A2, and CYP4A1 in male rats. By contrast, in female rats the mRNA expression of hepatic CYP1A2 and CYP2B1/2 was significantly increased by repeated GBT treatment.

**Conclusion**
Our findings indicate that caution is required in females when GBT is taken concomitantly with conventional drugs metabolized by CYP1A2, CYP2B1/2, CYP2C19, or CYP2E1. Our results provide information regarding the safety and effectiveness of GBT for clinical use.