Probing the inhibitory mechanism of Cyp3A4 metabolism of benzodiazepine drugs

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Benzodiazepines, such as flunitrazepam, are commonly used for treatment of insomnia and anxiety. However, their sedative effect makes abuse common in cases of drug-facilitated sexual assault. These situations often involve the compounds ethanol and caffeine, which may cause inhibitory effects on Cyp3A4 function. “The inhibitory strength of either caffeine and ethanol was weak, with a decrease in catalytic rate of less than 5% under physiological concentrations. Synergistic inhibition was observed between ethanol and caffeine, where the inhibitory strength decreased the rate of catalysis by up to 20%. In addition, acetaldehyde, a metabolite of ethanol oxidation, decreased the catalytic rate by up to ~80% under physiological concentrations. In combination with caffeine, the rate was further decreased to ~90% when physiological concentrations of these compounds were combined.” These effects may contribute to the increased sedative effects of benzodiazepines under conditions of misuse, where caffeine and ethanol are commonly present and open up a mechanism of possible inhibitory effects on Cyp3A4 that could occur in other situations.