



DRUG INTERACTIONS WITH SMOKING

Many interactions between tobacco smoke and medications have been identified. Note that it is the tobacco smoke—not the nicotine—that causes these drug interactions. Tobacco smoke may interact with medications through pharmacokinetic or pharmacodynamic mechanisms. Pharmacokinetic interactions affect the absorption, distribution, metabolism, or elimination of other drugs, potentially causing an altered pharmacologic response. The majority of pharmacokinetic interactions are the result of induction of hepatic cytochrome P450 enzymes (primarily CYP1A2). Pharmacodynamic interactions alter the expected response or actions of other drugs. The amount of tobacco smoking needed to have an effect has not been established and the assumption is that any smoker is susceptible to the same degree of interaction. The most clinically significant interactions are depicted in the shaded rows.

DRUG/CLASS	MECHANISM OF INTERACTION AND EFFECTS
Pharmacokinetic Interactions	
Alprazolam (Xanax)	<ul style="list-style-type: none"> Plasma concentrations decreased up to 50% among tobacco smokers.
Caffeine	<ul style="list-style-type: none"> Increased metabolism (induction of CYP1A2); clearance increased by 56%. Caffeine levels may increase after cessation.
Chlorpromazine (Thorazine)	<ul style="list-style-type: none"> Decreased area under the curve (AUC) (36%) and serum concentrations (24%). Smokers may experience less sedation and hypotension and require higher dosages.
Clozapine (Clozaril)	<ul style="list-style-type: none"> Increased metabolism (induction of CYP1A2); plasma concentrations decreased 28%.
Flecainide (Tambocor)	<ul style="list-style-type: none"> Clearance increased by 61%; trough serum concentrations decreased by 25%. Smokers may require higher dosages.
Fluvoxamine (Luvox)	<ul style="list-style-type: none"> Increased metabolism (induction of CYP1A2); clearance increased by 24%; AUC decreased 31%; decreased plasma concentrations (32%). Dosage modifications not routinely recommended but smokers may require higher dosages.
Haloperidol (Haldol)	<ul style="list-style-type: none"> Clearance increased by 44%; serum concentrations decreased by 70%.
Heparin	<ul style="list-style-type: none"> Mechanism unknown but increased clearance and decreased half-life are observed. Smokers may require higher dosages.
Insulin	<ul style="list-style-type: none"> Insulin absorption may be decreased secondary to peripheral vasoconstriction; smoking may cause release of endogenous substances that antagonize the effects of insulin. Likely not clinically significant. Smokers may require higher dosages.
Mexiletine (Mexitil)	<ul style="list-style-type: none"> Clearance (via oxidation and glucuronidation) increased by 25%; half-life decreased by 36%.
Olanzapine (Zyprexa)	<ul style="list-style-type: none"> Increased metabolism (induction of CYP1A2); clearance increased by 98%; serum concentrations decreased by 12%. Dosage modifications not routinely recommended but smokers may require higher dosages.
Propranolol (Inderal)	<ul style="list-style-type: none"> Clearance (via side chain oxidation and glucuronidation) increased by 77%.
Tacrine (Cognex)	<ul style="list-style-type: none"> Increased metabolism (induction of CYP1A2); half-life decreased by 50%; serum concentrations threefold lower. Smokers may require higher dosages.
Theophylline (Theo Dur, etc.)	<ul style="list-style-type: none"> Increased metabolism (induction of CYP1A2); clearance increased by 58–100%; half-life decreased by 63%. Levels should be monitored if smoking is initiated, discontinued, or changed. Passive smoking (second-hand smoke) also increases the clearance. Maintenance doses are considerably higher in smokers.
Tricyclic antidepressants (e.g., imipramine, nortriptyline)	<ul style="list-style-type: none"> Possible interaction with tricyclic antidepressants in the direction of decreased blood levels, but the clinical importance is not established.
Pharmacodynamic Interactions	
Benzodiazepines (diazepam, chlordiazepoxide)	<ul style="list-style-type: none"> Decreased sedation and drowsiness. May be caused by central nervous system stimulation by nicotine.
Beta-blockers	<ul style="list-style-type: none"> Less effective antihypertensive and heart rate control effects. May be caused by nicotine-mediated sympathetic activation; smokers may require higher doses.
Opioids (propoxyphene, pentazocine)	<ul style="list-style-type: none"> Decreased analgesic effect; smoking may increase the metabolism of propoxyphene by 15–20% and pentazocine by 40%. Mechanism unknown. Smokers may require higher opioid doses for pain relief.
Oral contraceptives	<ul style="list-style-type: none"> Increased risk of cardiovascular adverse effects (e.g., stroke, myocardial infarction, thromboembolism) in women who smoke and use oral contraceptives. Risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women age 35 and older.

Adapted from Zevin S, Benowitz NL. Drug interactions with tobacco smoking. *Clin Pharmacokinet* 1999;36:425–438.