

Potential drug interactions with smoking and quitting

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Many drug interactions have been reported with cigarette smoking.¹⁻⁴ Smoking induces drug metabolizing enzymes (primarily CYP1A2) in the liver. As a result, smokers have higher clearance of certain drugs and require higher doses to achieve clinical response. Conversely, when smokers quit smoking, their induced enzyme levels revert to normal. This may result in toxic drug levels in these patients whose drug doses were established while smoking.

Some potential drug interactions associated with cigarette smoking and quitting are depicted below. Although available information was based on case reports and small studies, clinicians should be aware of such potentials and monitor their patients closely for drug efficacy and toxicity.

Drug	Reported effects of smoking	Possible strategies after smoking cessation*
caffeine ^{1,3}	<ul style="list-style-type: none"> ↑ clearance (by 56%) 	<ul style="list-style-type: none"> Assess total caffeine intake from all sources; ↓ intake by half; monitor for caffeine toxicity (e.g., irritability & insomnia)
clozapine ^{5,6}	<ul style="list-style-type: none"> ↓ plasma concentrations (by 18%) 	<ul style="list-style-type: none"> Monitor for clozapine toxicity; ↓ dose (by a factor of ~ 1.5) may be required
flecainide ^{1,4}	<ul style="list-style-type: none"> ↑ clearance (by 61%), ↓ trough serum concentrations (by 25%); ↑ dose requirements (by 17%) 	<ul style="list-style-type: none"> May need to ↓ dose, but no specific recommendation available. Monitor for clinical response
fluvoxamine ^{1,4,7}	<ul style="list-style-type: none"> ↑ clearance (by 24%), ↓ AUC (by 31%), ↓ C_{max} (by 32%), ↓ C_{SS} (by 12-39%) 	<ul style="list-style-type: none"> Dosage adjustment not routinely recommended; close monitoring for adverse events
insulin ^{1,3,4} (subcutaneous)	<ul style="list-style-type: none"> ↑ insulin requirement possible due to nicotine-induced insulin resistance & vasoconstriction (i.e., ↓ absorption) 	<ul style="list-style-type: none"> Close monitoring of blood glucose, especially for patients prone to hypoglycemia or when tight glucose control is needed
mexiletine ^{1,4,8}	<ul style="list-style-type: none"> ↑ oral clearance (by 25%); ↓ t_{1/2} (by 36%) 	<ul style="list-style-type: none"> May need to ↓ dose, but no specific recommendation available. Monitor for clinical response. Use caution with older adults
olanzapine ^{1,3,5}	<ul style="list-style-type: none"> ↑ clearance (by 98%), ↓ plasma levels (by 12%) 	<ul style="list-style-type: none"> May need to ↓ dose, but no specific recommendation available. Monitor for excessive adverse effects
propranolol ^{1,4}	<ul style="list-style-type: none"> ↑ clearance (by 77%) 	<ul style="list-style-type: none"> Blood levels may ↑ but clinical implication is unclear due to wide dosage range; closely monitor for adverse events
theophylline ^{1,4}	<ul style="list-style-type: none"> ↑ clearance (by 58-100%); ↓ t_{1/2} (by 63%); ↑ volume of distribution (by 31%) 	<ul style="list-style-type: none"> Monitor levels and adjust dose accordingly; ↓ dose (by 25-33%) may be needed to maintain therapeutic drug levels
warfarin ^{1,4}	<ul style="list-style-type: none"> INR prolongation has been reported 	<ul style="list-style-type: none"> Closely monitor INRs; ↓ dose (by 14-23%) may be needed

* The relationship between the amount of cigarette smoking and the extent of drug interaction is unclear. The information in the table is based on current available literature and should not replace sound clinical judgments. Dosages should be individualized to achieve optimal therapeutic response with minimal toxicities. **Abbreviations:** **AUC** area under concentration-time curve; **C_{max}** peak concentrations; **C_{SS}** steady-state concentrations; **t_{1/2}** half-life

References

- Zevin S, Benowitz NL. Drug interactions with tobacco smoking. An update. *Clin Pharmacokinet* 1999;36:425-38.
- Kroon LA. Drug interactions and smoking: raising awareness for acute and critical care providers. *Crit Care Nurs Clin North Am* 2006;18:53,62, xii.
- Kroon LA. Drug interactions with smoking. *Am J Health Syst Pharm* 2007;64:1917-21.
- Schaffer SD, Yoon S, Zadezensky I. A review of smoking cessation: potentially risky effects on prescribed medications. *J Clin Nurs* 2009;18:1533-40.
- de Leon J. Psychopharmacology. Atypical antipsychotic dosing: the effect of smoking and caffeine. *Psychiatr Serv* 2004;55:491-3.
- Haring C, Meise U, Humpel C, et al. Dose-related plasma levels of clozapine: influence of smoking behaviour, sex and age. *Psychopharmacology (Berl)* 1989;99 Suppl.:S38-S40
- Spigset O, Carlborg L, Hedenmalm K, Dahlqvist R. Effects of cigarette smoking on fluvoxamine pharmacokinetics in humans. *Clin Pharmacol Ther* 1995;58:399-403.
- Grech-Belanger O, Gilbert M, Turgeon J, LeBlanc PP. Effect of cigarette smoking on mexiletine kinetics. *Clin Pharmacol Ther* 1989;37:638-43.