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Pharmacokinetic interactions

Depression and anxiety disorders CHAPTER 3 Drug interactions with antidepressants Antidepressants are involved in a number of both pharmacokinetic and pharmacodynamic interactions. Pharmacokinetic interactions Pharmacokinetic interactions occur when one drug interferes with the absorption, distribution, metabolism or elimination of another drug. This may result in a subtherapeutic effect or toxicity. The largest group of pharmacokinetic interactions involves drugs that inhibit or induce hepatic CYP enzymes (Tables 3.11 and 3.12). Other enzyme systems include the flavin-containing monooxygenase (FMO) and the uridine diphosphate (UDP)--glucuronosyltransferases (UGT).1 While both these latter enzyme systems are involved in the metabolism of psychotropic drugs, the potential for drugs to inhibit or induce these enzyme systems has been less well studied. The clinical consequences of pharmacokinetic interactions in an individual patient can be difficult to predict. Some could be highly clinically significant; for example, when paroxetine (a potent CYP2D6 inhibitor) is taken with tamoxifen, metabolism to its active metabolite is reduced, possibly increasing the risk of breast cancer recurrence.2 The following factors affect outcome of interactions: the degree of enzyme inhibition or induction, the pharmacokinetic properties of the affected drug and other co-administered drugs, the relationship between plasma level and pharmacodynamic effect for the affected drug, and patient-specific factors such as genetic differences in metabolic enzymes variability3 in the role of primary and secondary metabolic pathways and the presence of comorbid physical illness.4 (Continued) Table 3.11 Summary of antidepressant effects on CYP enzymes.5–7 Antidepressant Substrate for Inhibits SSRIs Citalopram CYP2C19, CYP2D6, CYP3A4 CYP2D6 (weak) Escitalopram CYP2C19, CYP2D6, CYP3A4 CYP2D6 (weak) Fluoxetine CYP2D6, CYP3A4 CYP2D6 (moderate to potent), CYP2C9 (moderate), CYP3A4 (weak) Fluvoxamine CYP2D6; others possibly involved CYP1A2 (potent), CYP2C19 (potent), CYP3A4 (weak), CYP2C9 (weak) Paroxetine CYP2D6 CYP2D6 (potent) Sertraline CYP3A4, CYP2D6 (minor) and possibly other pathways CYP2D6 (weak) SNRIs Desvenlafaxine CYP3A4 CYP2D6 (weak) Duloxetine CYP1A2, CYP2D6 CYP2D6 (moderate) Levomilnacipran CYP3A4, CYP2C8, CYP2C19, CYP2D6 Venlafaxine CYP2D6, CYP3A4 CYP2D6 (weak)

Revision #1
Created 2026-01-04 20:15:39 UTC by Omar Ayman
Updated 2026-01-04 20:15:39 UTC by Omar Ayman