Pharmacokinetic interactions

Pharmacokinetic drug—drug interactions

Example	ADME level	Mechanism
(Tetracyclines or quinolones) + multivalent cations (calcium, magnesium, or aluminum)	Absorption	Reduces absorption by forming complexes that cannot be absorbed
Itraconazole + antacids	Absorption	A weak base, it needs stomach acid to dissolve, so a higher pH reduces its absorption
Cyclosporine + St. John's wort	Absorption	St. John's wort increases the activity of P-glycoprotein* in intestinal cells, decreasing cyclosporine levels
Phenytoin + valproic acid	Distribution	Both drugs compete for binding sites on albumin
Rifampin + oral contraceptive pills	Metabolism	Rifampin induces cytochrome P450 (CYP450), decreasing estrogen levels
Warfarin + grapefruit juice	Metabolism	Grapefruit juice inhibits CYP450, increasing warfarin levels, which may cause bleeding
Penicillin + probenecid	Elimination	Increased penicillin levels, as probenecid competes with penicillin for transporters in the kidney

*P-glycoprotein is a transporter that pumps drugs out of cells — in the gut, back out of the intestinal cells, which lowers absorption.