Table 27-11: Metabolic Pathways of Frequently Abused Drugs Potentially Affected by HIV-1 Protease Inhibitors

Drug	Metabolic Pathway (P450 Isoenzyme)
Opiates	
Methadone, alfentanyl, fentanyl	Cytochrome P450 (CYP3A4)
Meperidine	Cytochrome P450 (CYP3A4?)
Codeine, hydrocodone, oxycodone	Cytochrome P450 (CYP2D6)
Heroin, morphine, hydromorphone	Glucoronidation?
Propoxyphene (Darvon)	Cytochrome P450 (CYP2D6)
Benzodiazepines	
Diazepam (Valium)	Cytochrome P450 (CYP3A4, CYP2C19)
Alprazolam, clorazepate, estazolam, flurazepam, midazolam, triazolam	Cytochrome P450 (CYP3A4)
Other drugs prone to abuse	
Marijuana, dronabinol, zolpidem	Cytochrome P450 (CYP3A4)
Sildenafil (Viagra)*	Cytochrome P450 (CYP3A4)
Cocaine**	Hydrolysis by plasma cholinesterase

* AUC of slidenafil (Viagra) is increased twofold to elevenfold in the presence of all protease inhibitors; patients should not exceed 25mg in a 48-hour period.

** Cocaine increases the speed at which HIV-1 virus replicates and so worsens overall prognosis by abolishing gains made by antiretroviral therapy. Metabolism of cocaine should not be affected by protease inhibitors.

Source: Adapted from Harrington RD, Woodward JA, Hooton TM, Horn JR. Life-threatening interactions between HIV-1 protease inhibitors and the illicit drugs MDMA and y-hydroxybutarate. *Arch Intern Med* 139:2221-4, 1999.