

# Opioid routes of metabolism

**Drug Metabolite Inactive**    **Parent Drug** → **Active Metabolite**

## CYP3A4 (Phase I)

oxycodone, methadone,  
hydrocodone buprenorphine,  
tramadol, fentanyl

## 3A4 Inhibitors Increase risk of toxicity

clarithromycin,  
erythromycin, azole  
antifungals, PIs (HIV),  
verapamil, etc

## CYP2D6 (Phase I)

Codeine → morphine  
Hydrocodone → hydromorphone  
tramadol → M1  
oxycodone → oxymorphone

## 2D6 Inhibitors Decrease analgesic potential

Paroxetine, fluoxetine,  
bupropion, ritonavir,  
terbinafine, etc

## Glucuronidation (Phase II)

hydromorphone, oxymorphone  
morphine (M6G), codeine (C6G)

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