

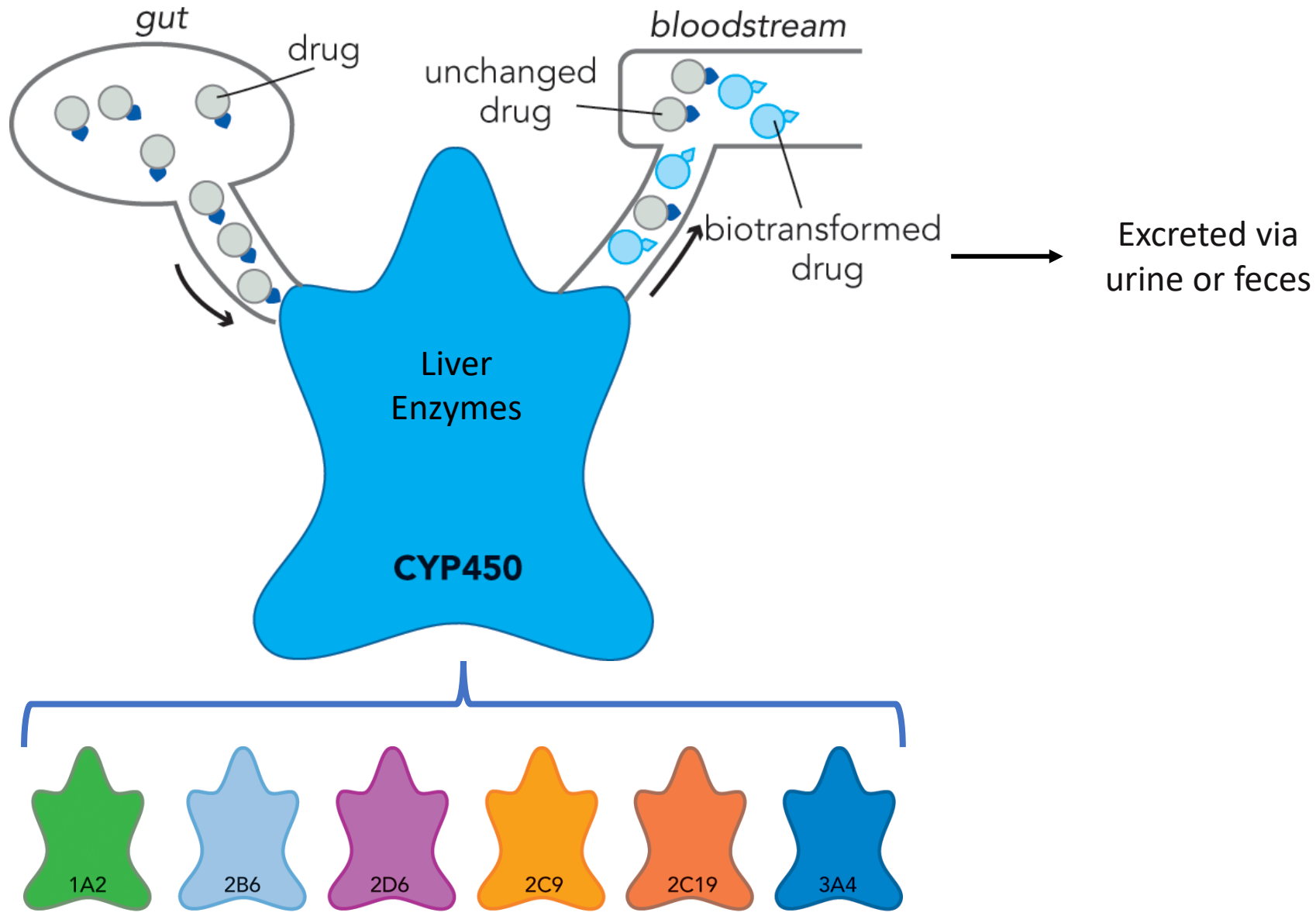
Clinically Significant CYP2D6 Drug-Drug Interactions

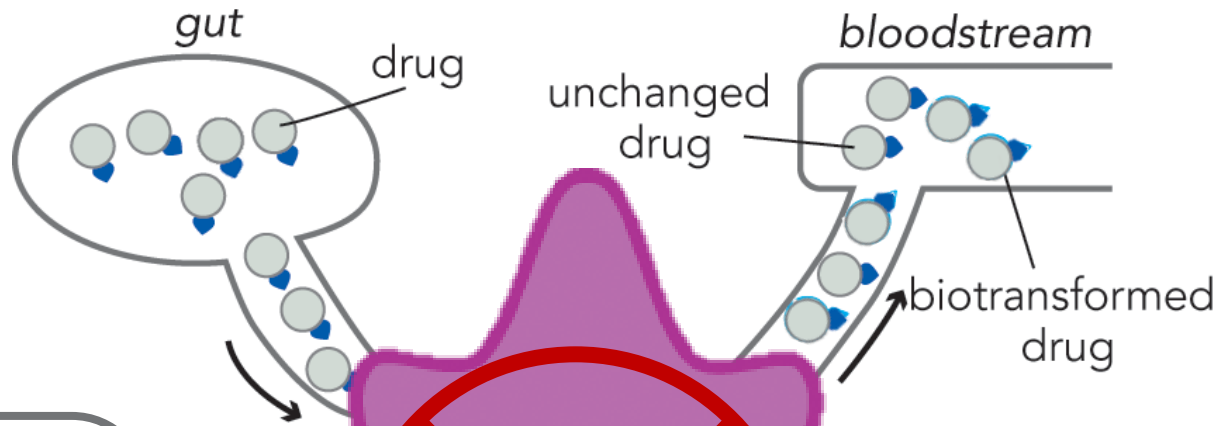
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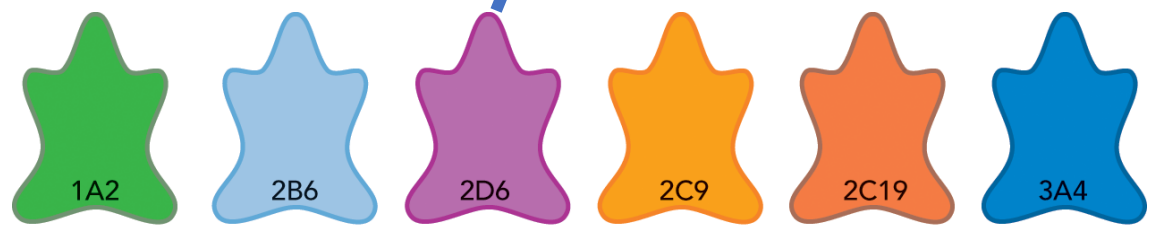
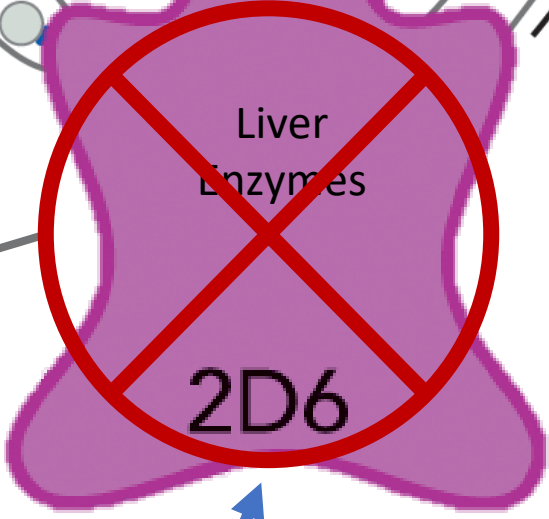
Clinical Psychiatric Pharmacist





Strong CYP2D6 Inhibitors

- Fluoxetine
- Paroxetine
- Bupropion



Patient 1 – 11-year-old female

- Mixed amphetamine salts + fluoxetine (strong CYP2D6 inhibitor)
 - Amphetamine is metabolized by CYP2D6 enzyme
 - Strong 2D6 inhibitors increase amphetamine concentrations
 - AUC increased by 22 to 89%
 - Increased risk of serotonin syndrome/serotonin toxicity (SS/ST)
 - Start amphetamine at lower doses and monitor frequently

SS/ST – hyperreflexia, clonus, hyperthermia, diaphoresis, tremor, autonomic instability, mental status changes

Patient 2 – 17-year-old female

- Aripiprazole + fluoxetine (strong CYP2D6 inhibitor)
 - Aripiprazole is metabolized by CYP2D6 and CYP3A4 enzymes
 - Strong CYP2D6 inhibitors increase aripiprazole concentrations
 - AUC increased by 112 to 140%
 - Cmax increased by 39%
 - Increased risk of neuroleptic malignant syndrome (NMS) and extrapyramidal symptoms (EPS)
 - Reduce aripiprazole dose by 50%

NMS – mental status changes, lead-pipe muscle rigidity, autonomic instability

EPS – dystonia, akathisia, parkinsonian symptoms

Patient 3 – 16-year-old male

- Atomoxetine + bupropion (strong CYP2D6 inhibitor)
 - Atomoxetine is metabolized by CYP2D6 enzyme
 - Strong 2D6 inhibitors increase atomoxetine concentrations
 - AUC increased 6- to 8-fold
 - Cmax increased by 3- to 4-fold
 - Weight \leq 70 kg:
 - Reduce atomoxetine dose of 0.5 mg/kg/day
 - Only increase to 1.2 mg/kg/day if symptoms fail to improve after 4 weeks and initial dose is well tolerated
 - Weight $>$ 70 kg:
 - Reduce dose to 40 mg/day
 - Only increase to 80 mg/day if symptoms fail to improve after 4 weeks and tolerating

Resources

1. UpToDate/Lexicomp - Purchase/subscription required 

2. Micromedex - Purchase/subscription required 

3. Drug Interactions Flockhart Table™

- <https://drug-interactions.medicine.iu.edu/MainTable.aspx>



4. CYP450 Drug Interactions Table for Psychiatric Medications

Metabolism and CYP450 Drug Interactions for Psychiatric Medications: Bolded enzyme system means definitely important. Others are minor.

Medications used in depression

Drug	How Metabolized	Induces	Inhibits
Bupropion	2B6	None	2D6
Citalopram	2C19, 2D6, 3A4	None	1A2, 2B6, 2C19, 2D6