

Table 13. Drug Metabolism Basics

Bioavailability and Half-Life: Cannot predict bioavailability and half-life on just one pharmacokinetic parameter

Absorption: What proportion (percent) of an oral drug gets from the GI tract into the blood?

Distribution: Where does the drug go?

- Lipophilic = distributes through membranes with preference for adipose tissue and muscle (greater volume of distribution)
- Hydrophilic = remains mostly in blood compartment until the drug is eliminated
- An increase in the volume of distribution of a drug will generally increase its elimination half-life
- A decrease in volume of distribution with an increase in elimination clearance will generally decrease elimination half-life

Metabolism: How is the drug changed so it can be excreted?

- The quicker the metabolism, the shorter the half-life
- The liver is the major site for drug metabolism, but biotransformation can also occur by the kidney and intestine
- Conversion of lipophilic drugs to more polar metabolites by the liver may increase excretion in the bile and kidney, and thus may decrease half-life

Excretion: How does the drug leave the blood (e.g. urine)?

- The quicker the excretion, the shorter the half-life
- Polar, hydrophilic drugs may have increased excretion in the urine

Lipophilic drugs

More likely to be metabolized, creating metabolites that are likely more polar, and then more easily excreted.

- Phase 1 = Convert lipophilic molecules into more polar molecules (hydrolysis, oxidation, reduction)
- Phase 2 = Further convert lipophilic molecules into more polar molecules through conjugation with glucuronic acid, sulfuric acid, acetic acid, or amino acid.

If reabsorbed and recirculated, then this may increase half-life

- Increased tubular reabsorption
- Enterohepatic recirculation

Hydrophilic drugs

More likely to be excreted unchanged by the kidney.

Kidney:

- Decrease half-life = Increased glomerular filtration and/or tubular secretion
- Increase half-life = Increased protein binding may reduce glomerular filtration of drug