

Table 14. Phases of drug metabolism

Phase 1 drug metabolism = Functional conversion to polar metabolites in preparation for conjugation

- Mostly in endoplasmic reticulum of the liver
- -OH, -NH₂, -SH, -COOH
- Often results in inactive metabolite, although sometimes metabolite more active
- Prepares drug for Phase 2 metabolism
- Oxidation via cytochrome P450 enzymes (CYP450), etc.
- Reduction via NADPH, etc.
- Hydrolysis via esterases, etc. (Statins are usually administered in the active acid form as open chain structures; however, lovastatin and simvastatin are administered as closed chain lactone ester prodrugs which require esterases for conversion to active drug.)
- Pro-drugs require conversion to active metabolite to produce their therapeutic effect

Phase 2 drug metabolism = Enzymatic conjugation reaction in the intestine and liver to form (mostly) inactive polar metabolite that is excreted in urine or feces

- Mostly in the cellular cytosol (except glucuronidation enzyme, which is a microsomal enzyme)
- Conjugation with sugar, glucuronic acid, sulfate, acetate, amino acid, glutathione
- Glucuronidation via uridine diphosphate–glucuronosyltransferase (UDP) – may lead to lactonization (creation of an inactive, closed chain lactone cyclic ester)
- Sulphation via sulfotransferases
- Acetylation via acetyltransferases
- Glutathione conjugation via glutathione s-transferases
- Detoxification in preparation for excretion (e.g. water soluble for renal excretion)