Pharmacokinetics: Biotransformation

The aim is to make the drug more soluble and to get rid of it one way or another.

FIRST PASS METABOLISM: combination of liver and intestinal wall enzymes
= responsible for much of this transformation.

Phase 1 reactions
- hydroxylation, oxidation, reduction, deamination... that's the general sound of these reactions.
- Making the drug more polar is the aim, usually by introducing or unmasking a polar group
  (-OH, or -NH2, or –SH)

The MEOS system is the key player:
- microsomal mixed function oxidase system
- these enzymes for into little “microsome” vesicles
- the most important of these enzymes is NADPH-cytochrome P450 reductase, and cytochrome P450
  450 because it binds carbon monoxide to absorb light at 450 nanometres wavelength
- Reactions performed by this enzyme require oxygen and NADPH
- Numerous P450 isoforms... too many to discuss.

INDUCTION
- Increases the rate of drug degradation and metabolite production
- Either increased production of P450 enzymes, or reduced degradation of them.

INHIBITION
- Inhibit P450 = reduce hepatic clearance of the drugs
- Some substances SUICIDALLY inhibit P450 (eg. spironolactone)

Phase 2 reactions
- Conjugation reactions
- typically, glucouronidation, sulfation, etc... adding a molecule like glucouronide, in order to improve the
  water solubility of the drug.