Pharmacokinetics

Biotransformation/Metabolism

Learning Objectives & Knowledge Points

- Be able to list consequences of drug metabolism
- Be able to list sources of variation in metabolism
- Be able to discuss Phase I and Phase II reactions
- Be able to explain the effects of drug-drug interactions and food on CYP450 activity and the resultant effect on plasma drug levels
- Be able to explain the effects of pharmacogenetic variation on biotransformation activity and the resultant effect on plasma drug levels
- Be able to discuss the effects of ethnic prevalence of genetic variations in enzyme activity on plasma drug levels
- Be able to explain the role of alterations in drug inactivation in adverse drug reactions (ADRs)

Drug Biotransformation

- Drug biotransformation involves enzymes used for xenobiotics (i.e., foreign compounds such as drugs) & metabolism of endogenous compounds (e.g., steroid hormones, cholesterol, active Vitamin D congeners)
- Typically, drugs converted to more polar (i.e., more hydrophilic/ water soluble) metabolite(s)
- Variability in metabolism is the cause of a significant portion of the variability in biological activity of the drug
  - Pharmacogenetic variation as well as drug-drug & food drug interactions can affect drug biotransformation
- Biological Consequences of Drug Metabolism
  - Reduction in plasma drug levels
  - Change biological activity of the drug
  - Possible generation of toxic metabolites