

Author(s): Aken Desai, Michael Mathis, 2008

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Drug Absorption and Distribution

Friday, January 18, 2008
10:00 AM

1. Define absorption and distribution.
 - a. Absorption: passage of drugs from site of administration to the blood
 - b. Distribution: delivery of drugs to tissue
2. Describe the mechanisms that are responsible for transport of drugs across membranes.
 - a. Diffusion: concentration gradient driven; unionized form
 - b. Filtration and bulk flow through pores
 - c. Endocytosis
 - d. Ion-pair
 - e. Facilitated diffusion or active transport
 - i. Carrier mediated
 - ii. Saturable
 - iii. Selective
 - iv. Competition
3. Define lipid-water partition coefficient.
 - a. Amount of drug in organic phase/amount of drug in aqueous phase
 - b. A high coefficient means high lipid solubility
 - c. No ideal solvent to mimic cell membrane
4. What functional groups alter the lipophilicity of drugs?
 - a. Non-polar groups: alkyls, aromatics, hexanes, ethers, ketones, esters, amides, halogens
 - b. Polar: O, nitrate, carboxylic acids, hydroxyls, sulfates, ammonium
5. Calculate the ionization of drugs with the use of the Henderson-Hasselbalch equation.
 - a. Acid: $\text{pH} - \text{pKa} = \log \left(\frac{[\text{ionized}]}{[\text{non-ionized}]} \right)$
 - b. Base: $\text{pH} - \text{pKa} = \log \left(\frac{[\text{non-ionized}]}{[\text{ionized}]} \right)$
6. Describe how the ionization and lipophilicity of drugs affect the absorption and distribution of drugs.
 - a. Non-ionization increases absorption and distribution (easier to cross blood-brain barrier)
 - b. Increased lipophilicity also increases absorption/distribution
7. Define "ion trapping"
 - a. Drugs get stuck in compartments due to a high proportion being ionized due to pH changes
 - b. Example is diazepam; $\text{pKa} = 3.3$ so in stomach is almost completely ionized and none enters plasma; acetaminophen is a weak acid so it is almost completely unionized in the stomach and crosses into plasma
8. Describe how drug-drug interactions occur through drug transporters.
 - a. Because drug transporters often handle multiple substrates there is competition for the transporter
 - b. St. John's Wort for example induces the P-glycoprotein transporters to send the drug back out into the intestinal lumen, so St. John's Wort results in decreased drug absorption; grapefruit juice inhibits the transporter so it increases absorption
9. Describe how binding to plasma proteins can affect distribution of a drug.
 - a. Alters free drug concentration; binds to drug and decreases amount available to tissues
 - b. Some drugs are almost completely bound at their therapeutic concentration
 - c. Must account for amount bound; so some drugs plasma concentrations rapidly jump once plasma protein is all used up