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: pH-pKa = log ([ionized]/[non-ionized])
   b. Base: pH-pKa = log ([non-ionized]/[ionized])

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; 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

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