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Drug Absorption and Distribution

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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. Faciliated 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 lipophlicity 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 diazepem; 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