

Homework 2
PHA 5127 Fall 2007 (Total 10 Points)

1. Mark whether the following statements are True or False. (0.5 points each)

- T F** a. Apparent volume of distribution (V_d) will never exceed the total body volume.
- T F** b. At equilibrium, the free drug concentrations in plasma and tissue will be identical.
- T F** c. Most drugs which are tightly bound to plasma protein tend to stay in the blood and thus have relatively low apparent volumes of distribution.
- T F** d. Drugs that are extensively distributed into specific tissue regions, such as chloroquine into the liver, tend to have quite small values for the apparent volume of distribution.
- T F** e. Disease state rarely affects the drug protein binding in the body.
- T F** f. Since $CL = k_e \cdot V_d$, so if the volume of distribution increases the clearance must increase.

2. Two patients (A and B) were given 200mg IV bolus of the drug D. The C_0 for patient A was 2.5mg/L and for patient B was 1.5mg/L. Assume: the drug follows a one-compartment body model; the drug is 60% bound to plasma proteins; both patients have typical tissue volume of 38L and plasma volume of 3L. Provide a quantitative explanation of why the two patients have different initial plasma concentrations (consider distribution and binding properties)? (3 points)

From the class, you should understand what factors determine the rate of distribution and be able to tell the difference between perfusion and permeability limited distribution. Please apply your knowledge of distribution to the following situations:

3. It is well documented that physicochemical properties can be correlated to many ADME (Absorption, Distribution, Metabolism and Elimination) properties, particularly in terms of distribution rate in our case. Drug A has pKa of 7.4 and partition coefficient of unionized form of 0.21. Drug B has pKa of 11.3 and partition coefficient of unionized form of 0.005. Both Drug A and Drug B are weak acid drugs. Please use their physicochemical properties to predict their distribution rates in high perfused tissues, i.e. which one distributes faster and why (hint: since the partition coefficients of both drugs are small, you can assume the distribution is limited by the permeability). (2 points)

4. 4OH-GTS21 is a water soluble active compound for Alzheimer's disease. However, to achieve fast and effective response, we have to deliver its lipophilic pro-drug GTS21 to patients (usually orally). Explain the reason of doing this. (2 points)