Homework 2
PHA 5127 Fall 2005

Two failing pharmacy students were given 200mg IV bolus of the drug Studiehelp. The C_0 for patient A was 2.5mg/L and for patient B was 1.5mg/L. The clearance for both patients is 5L/h. The drug is 60% bound to plasma proteins. The drug follows a one-compartment body model, crosses membranes easily, distributes well into all tissues, and is solely eliminated by hepatic metabolism. Assume liver blood flow is 90L/h, tissue volume is 38L and plasma volume of 3L.

Questions:

1. Provide a quantitative explanation of why both patients have different initial plasma concentrations (consider distribution and binding properties).

2. Calculate the half-lives for each patient. At what point in time are their plasma concentrations the same?

3. Calculate the intrinsic hepatic clearance of the drug and the extraction ratio. Is this a high or low extraction drug?

4. The drug Passureclas is co-administered to patient A, which competes for plasma protein binding sites with Studiehelp (does not affect tissue protein binding), thereby increasing the free fraction in the plasma of Studiehelp two-fold. What is the new AUC and half-life of Studiehelp? Are they different from before?

5. Mark whether the following statements for a **high extraction drug** are True or False

T F The oral bioavailability(F) will be close to 1.
T F Clearance will increase significantly after induction of the relevant enzyme.
T F Increase in plasma protein binding will decrease the extraction ratio E.
T F The hepatocyte membranes do not represent a barrier.
T F If the hepatic blood flow is reduced, the clearance will be decreased.