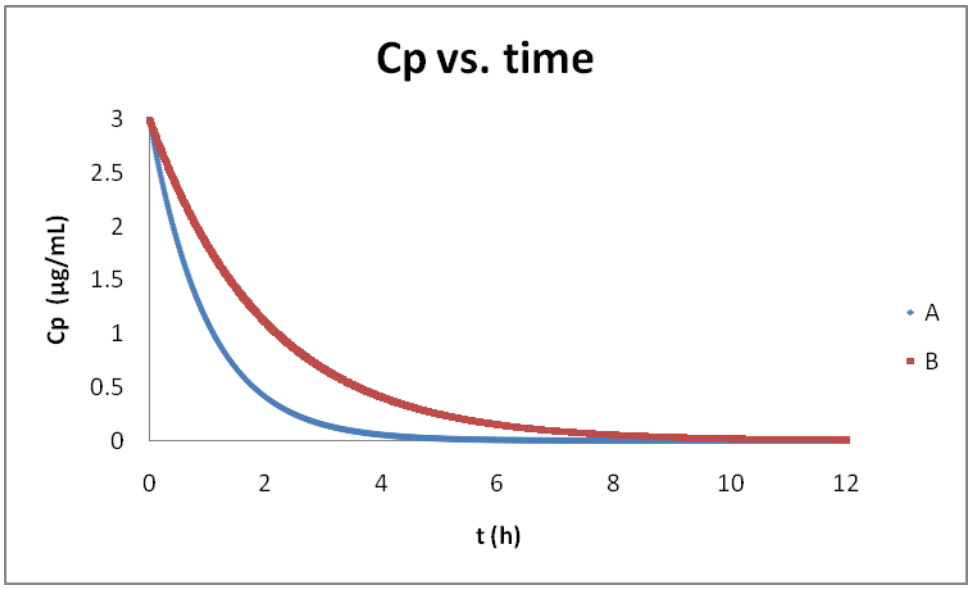
PHA 5127 Dose Optimization I

Homework V (10 points)

Due on Friday, 10/09/2009

Do not forget the units of the results. 0.1 points will be deducted for each time an answer is provided without the appropriate unit. If you do not show your work and your answer differs from the right solution, no points will be given. Assume that all elimination processes are first-order.

1. **The same dose (500 mg) of two distinct drugs was administered to two distinct patients via IV-bolus. The following plasma-concentration-time profiles were obtained. The plasma concentration at time point 0 is the same for both patients. Both drugs show a one-compartment body model behavior and only renal elimination. The drug that shows a lower plasma concentration at t = 4h is drug A. The drug that shows a higher plasma concentration at t = 4h is drug B.**



a. **TRUE (T) or FALSE (F) (2 points, 0.5 each)**

Both drugs have the same volume of distribution

T **F**

Both drugs have the same renal clearance

T **F**

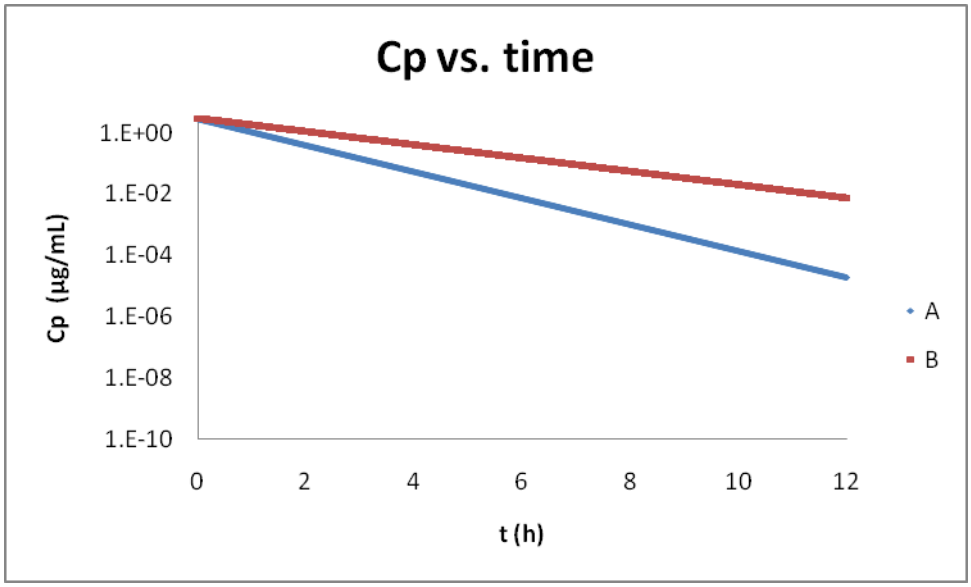
Protein binding in plasma must be more pronounced than in tissue for both drugs

T **F**

Free plasma concentrations at time point zero must be the same for both drugs

T **F**

b. Sketch a semi-logarithmic plasma-concentration-time-profile for both drugs. **(1 point)**

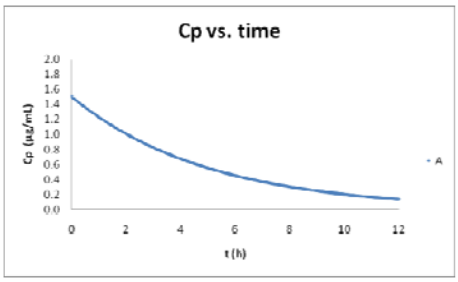


c. Indicate CLEARLY which profile belongs to drug A and which to drug B and EXPLAIN your decision briefly. **(2 points)**

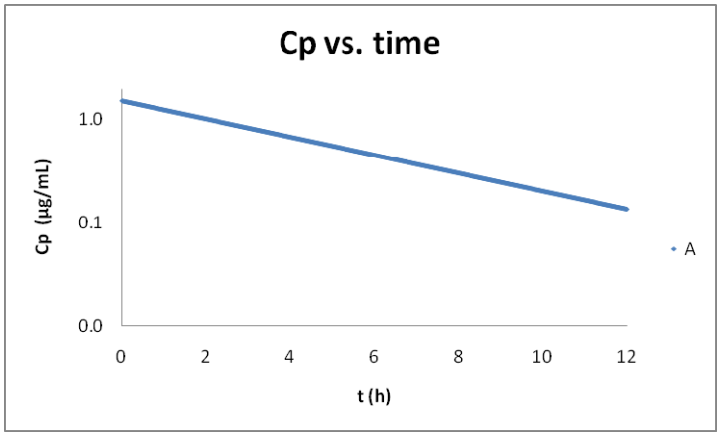
Same dose was administered for both drugs. Both drugs show the same C_0. Hence, both drugs must have the same VD. Since the plasma-concentration-time profiles are not the same, the clearance of the two drugs must be different. The plasma concentrations of drug B are higher than of drug A. Hence, the half-life of drug B is greater or k_e is smaller. Thus, the slope of drug A must be steeper than the one of drug B. Both straight lines must have the same starting point.

2. **150 mg drug A was administered to a patient (75 kg, 45-years old, male) via IV-bolus. The volume of distribution and the renal clearance of drug A are 100 L and 20 L/h, respectively. The oral bioavailability of the drug is 1%. Assume that the drug shows a one-compartment body model behavior and only renal elimination.**

a. Graph the plasma concentration-time profile from 0 – 12 h. (You can either use a software package for the plot or graph paper. If you decide to use graph paper, the plot must be accurate.) **(2 points)**



b. Graph a semi-logarithmic plasma concentration-time profile from 0 – 12 h. (You can either use a software package for the plot or graph paper. If you decide to use graph paper, the plot must be accurate. If you decide to use graph paper, it might be easier to perform a logarithmic transformation of the plasma concentration first and then plot it on a normal scale.) **(1 points)**



3. **TRUE (T) or FALSE (F)** **(2 points, 1 each)**

Linear pharmacokinetics assume that the plasma concentration vs. time profile is a straight line

T **F**

Linear pharmacokinetics assume that a semi-logarithmic plot of the plasma concentration vs. time profile is a straight line

T **F**