PHA 5127 Dose Optimization I

Homework II (10 points)

Due on Friday, 09/18/2009

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.

1. **A patient is to be started on one medication administered by IV bolus injection. Blood samples were taken at 1 and 5 hours following the first injection of drug in order to determine whether concentrations are in an appropriate range. The information about this study is as follows: (6 points)**

Dose (mg)	Cp at 1h (mg/L)	Cp at 5h (mg/L)
1000	**2.21**	**1.35**

a. Estimate the initial concentration C_0 and the volume of distribution (Vd)

ke= - slope=- [ln(1.35)-ln(2.21)]/(5-1)=0.123/h

$lnCp(t=1h)=lnC_0-ke*t$,

$ln2.21=lnC_0-0.123*1$, $C_0=e^{0.916}=2.5mg/L$ **(1 point)**

$Vd=Dose/C_0=1000mg/2.5mg/mL=400L$ **(1 point)**

b. The plasma protein binding of this drug in this patient is 10%. Please estimate the tissue binding of this drug. (**Vp=3L, V_T=38L**)

fu=1-10%=90%=0.9

$Vd=Vp+ V_T*(fu/fuT)=3L+38L*(0.9/fuT)=400L$

$fuT\approx0.086$ **(1 point)**

fbT = (1-0.086)=0.914=91.4% **(1 point)**

c. If the tissue binding of this drug decreases by 10%, predict the dose that should be administered to reach the same C_0

After the change, the tissue binding is 90% of old one.

fuT,new=1-91.4%*90%=17.7%

$Vd,new=Vp+ V_T*(fu/fuT,new)=3L+38L*(90\%/17.7\%)\approx196L$ **(1 point)**

Dose=Vd,new*2.5mg/mL=490mg **(1 point)**

2. **TRUE (T) or FALSE (F) (3 points, 0.5 each)**

The volume of distribution (Vd) of a given drug relates the dose with the free plasma concentration at time point zero (C_0)

T **F**

If a drug has volume of distribution of 150L, the tissue binding is more pronounced than plasma protein binding

T **F**

If a drug is unable to cross membranes, the volume of distribution cannot be larger than extracellular space.

T **F**

Increase in plasma protein binding will increase the volume of distribution of a lipophilic drug

T **F**

Lipophilic unionized drugs are likely to enter tissues relatively fast.

T **F**

Free plasma levels of drugs with high plasma protein binding (99%) are more prone to be affected by changes in plasma protein binding than drugs with low plasma protein (10 %) binding. (Assume that $f_{u,\ tissue} = 0.1$ and consider only effects of protein binding on Vd).

T **F**

4. Match the following parameters with correct units (1 point, 0.25 each)

1. Concentration e	a. mg*L/hr
2. Half-life b	b. hr
3. AUC d	c. /hr
4. K_e c	d. mg*hr/L
	e. mg/L