PHA 5127 Dose Optimization I

Homework III (10 points)

Due on Friday, 09/25/2009

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

For a one compartment body model, K_e can be calculated as $\frac{C_0}{AUC_\infty}$

T F

Clearance and volume of distribution are independent

T F

A drug with a high volume of distribution always possesses a high clearance.

T F

If, for a given drug, $Q_H <<< f_u * CL_{int}$, the drug is considered to be a high extraction drug

T F

Metabolites are always less active than their parent compounds

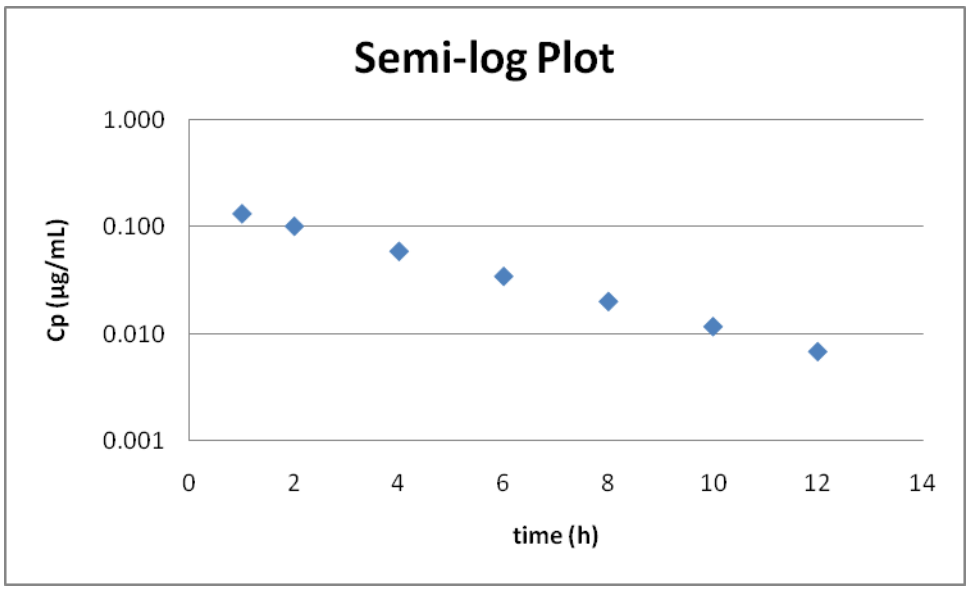
T F

Enzyme induction affects the hepatic clearance of low extraction drug

T F

2) **10 mg Dexamethasone were administered to 50-year old patient (70 kg) through an IV bolus injection. The following plasma concentrations (Cp) were measured. (Hint: A semi-log plot of the concentration vs. time profile will yield a straight line for a one-compartment body model) (3 points)**

time(h)	Cp (µg/mL]
1	0.133
2	0.101
4	0.059
6	0.034
8	0.020
10	0.012
12	0.007



time(h)	Cp (µg/mL]	ln Cp ( )
1	0.133	-2.01819
2	0.101	-2.28892
4	0.059	-2.83039
6	0.034	-3.37185
8	0.020	-3.91331
10	0.012	-4.45478
12	0.007	-4.99624

Determine k_e, C_0, VD, CL, AUC_∞, and C5 (plasma concentration at t = 5h) **(0.5 points each)**

3) Assume an intrinsic clearance of i) 80000 L/min and ii) 0.08 L/min. The plasma protein binding and liver blood flow are 50% and 80 L/min, respectively, for both situations. (4 points)

a) Calculate the hepatic clearance for both situations

I. High extraction drug

II. Low extraction drug

$$CL_H = \frac{Q_H * f_U * CL_{int}}{Q_H + f_U * CL_{int}} = \frac{80\frac{L}{min} * 0.5 * 80000\frac{L}{min}}{80\frac{L}{min} + 0.5 * 80000\frac{L}{min}} = 79.84\ \frac{L}{min} \approx Q_H = 80\frac{L}{min}$$

$$CL_H = \frac{Q_H * f_U * CL_{int}}{Q_H + f_U * CL_{int}} = \frac{80\frac{L}{min} * 0.5 * 0.08\frac{L}{min}}{80\frac{L}{min} + 0.5 * 0.08\frac{L}{min}} = 0.0399\ \frac{L}{min} \approx f_U * CL_{int}$$

$$= 0.04\frac{L}{min}$$

b) Calculate the hepatic clearance when the plasma protein binding is 1%.

$$CL_H = \frac{Q_H * f_U * CL_{int}}{Q_H + f_U * CL_{int}} = \frac{80\frac{L}{min} * 0.99 * 80000\frac{L}{min}}{80\frac{L}{min} + 0.99 * 80000\frac{L}{min}} = 79.92\ \frac{L}{min} \approx Q_H = 80\frac{L}{min}$$

$$CL_H = \frac{Q_H * f_U * CL_{int}}{Q_H + f_U * CL_{int}} = \frac{80\frac{L}{min} * 0.99 * 0.08\frac{L}{min}}{80\frac{L}{min} + 0.99 * 0.08\frac{L}{min}} = 0.0791\frac{L}{min} \approx f_U * CL_{int}$$

$$= 0.0792\frac{L}{min}$$