

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, $Q_H \ll f_u * CL_{int}$, 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 |

Determine k_e , C_0 , VD , CL , AUC_∞ , and C_5 (plasma concentration at $t = 5h$)

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