

PHA 5127
Key to Homework #4
Fall, 2003.

Question 1:

Drug X follows a one-compartment body model after an IV bolus injection. After a patient was given 200 mg through IV bolus administration, the drug concentrations at 0.5 hour and 5 hour were measured as 2.3 ug/ml and 0.5 ug/ml, respectively. Please find out:

- 1.) What is the elimination rate constant K_e ?
- 2.) What is half-life of the drug?
- 3.) What is initial concentration of drug. C_0 ?
- 4.) Please find out V_d .
- 5.) Calculate $AUC_{0-\infty}$.
- 6.) What is the clearance value?

Answer:

- 1.) $K_e = (\ln C_1 - \ln C_2) / (t_2 - t_1) = (\ln 2.3 - \ln 0.5) / (5 - 0.5) = 0.3391 \text{ (hr.}^{-1}\text{)}$
- 2.) $T_{1/2} = 0.693 / 0.3391 = 2.04 \text{ (hr.)}$
- 3.) $C_0 = C_t * e^{K_e * t} = 2.3 * e^{0.3391 * 0.5} = 2.7250 \text{ (mg / L)}$
- 4.) $V_d = \text{Dose} / C_0 = 200 / 2.7250 = 73.3945 \text{ (L)}$
- 5.) $AUC_{0-\infty} = C_0 / K_e = 2.7250 / 0.3391 = 8.0360 \text{ (mg * hr / L)}$
- 6.) $CL = K_e * V_d = 0.3391 * 73.3945 = 24.8881 \text{ (L / hr.)}$

Question 2:

Drug Y follows one compartment body model after an IV bolus injection. The half-life of the drug is reported as 1.5 hour. The volume of distribution is 100 L and fraction unbound (f_u) is 0.5. Please answer the following questions.

- 1.) Please find out the rate of elimination.
- 2.) Calculate the total body clearance.
- 3.) In lab, researchers found out that in kidney, drug Y is only eliminated through glomerula filtration, (No reabsorption, no secretion), what is the renal clearance? (Assume GFR = 130 ml /min).
- 4.) Is the renal clearance only route for drug Y to eliminate?
- 5.) If you answer is no to question 4, Please find out what is the non-renal clearance.

Answer:

- 1.) $K_e = 0.693 / 1.5 = 0.462 \text{ (hr.}^{-1}\text{)}$
- 2.) $CL = K_e * V_d = 0.462 * 100 = 46.2 \text{ (L / hr.)}$
- 3.) $CL_{\text{renal}} = f_u * GFR = 0.5 * 130 = 65 \text{ (ml /min)} = 3.9 \text{ (L/hr.)}$
- 4.) No. Since $CL > CL_{\text{renal}}$.

5.) $CL_{\text{non-renal}} = CL - CL_{\text{renal}} = 46.2 - 3.9 = 42.3 \text{ (L / hr.)}$

Question 3:

Please find out if the following relationship is correct.

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| 1.) $CL_{\text{(hepatic)}} > CL_{\text{(total)}}$ | Answer: | F |
| 2.) Larger value of CL indicates larger value of Vd. | Answer: | F |
| 3.) $Ke_{\text{(renal)}} > Ke$ | Answer: | F |
| 4.) Larger value of Vd indicates that more drug is outside of the plasma. | Answer: | T |
| 5.) Ionized and hydrophilic drug is more likely to cross the biological membrane. | Answer: | F |