

PHA 5127 Dose Optimization I
Homework IV Solution
10 points

If you any questions about this homework assignment, do not hesitate to contact Benjamin Weber (benjaminweber@ufl.edu) or your respective facilitator.

Please provide all answers with their appropriate units and all graphs with appropriately labeled axes. 0.25 points will be deducted for each missing or inappropriate unit or axes label. Please provide all answers on separate sheets (does not apply to TRUE/FALSE questions).

Problem 1 (3.5 points)

A female patient (5'10" tall, 60kg, 40 years old) shows a serum creatinine level of 1.2 mg/dL.

- a) Use the Cockcroft-Gault-Equation to calculate her creatinine clearance.
- b) Drug A (highly lipophilic) shows a plasma protein binding and tissue protein binding of 40% and 50%, respectively. Drug A is eliminated by hepatic (30%) and renal processes (70%). Calculate the total systemic clearance of drug A (in L/h) when administered to the patient. Assume that the drug is neither actively secreted nor reabsorbed.
- c) Give the equation that can be used to calculate the plasma-concentration time profile for any given time t when 100mg of drug A are administered to the patient via IV bolus injection. Assume that the drug is immediately distributed throughout the body and that all elimination processes are first-order processes. (Linear pharmacokinetics)

Problem 2 (1 point)

What is the maximum renal clearance a drug can show? Explain briefly.

Problem 3 (1 point)

A patient receives a drug (lipophilic) as an IV bolus injection. Assume a one-compartment body model, linear pharmacokinetic and first-order elimination processes. The following characteristics about the drug are known.

$$CL = CL_{ren} = 50 \frac{L}{h}$$

$$Vd = 25L$$

$$f_u = 0.8$$

Which two of the following statements must necessarily be correct?

- The drug shows pronounced hepatic metabolism
- The tissue protein binding is larger than the plasma protein binding
- The drug is eliminated by active tubular secretion
- The drug is not passively reabsorbed from the tubulus
- The drug shows similar plasma binding characteristics as creatinine

Problem 4 (1.5 points)

The following equation describes the plasma concentration at any given time t for a one-compartment body model after IV bolus injection. Which (three) assumptions about the drug are necessary for this equation to be adequate?

$$C(t) = C_0 e^{-k_e t}$$

Problem 5 (3 points)

TRUE (T) or FALSE (F)

A drug that is neither a base nor an acid will most likely not show a renal clearance larger than 130 mL/min.

T F

A drug which is actively secreted cannot be passively reabsorbed.

T F

The pH of the urine does never affect the magnitude of renal reabsorption.

T F

A drug that is actively secreted must show a renal clearance larger than 130 mL/min.

T F

A drug that is fully reabsorbed is likely to show a tissue protein binding larger than 20%.

T F

The term “linear pharmacokinetics” does not imply that a plot of plasma concentration vs. time gives a straight line.

T F