PHA 5127 Dose Optimization I
Homework IV Solution
10 points

Problem 1

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. **(1 point)**

$$\boldsymbol{IBW_{female} = 45.5kg + 2.3 * 10 = 68.5kg}$$

$$\boldsymbol{TBW = 60kg} < IBW = 68.5\boldsymbol{kg}$$

Thus, use TBW is Cockcroft-Gault-Equation.

$$\boldsymbol{CrCL_{female} = 0.85\frac{(140 - 40) * 60}{72 * 1.2} = 59\frac{mL}{min}}$$

a) 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. **(1 point)**

$$\boldsymbol{CL_{ren} = 0.6 * 59\frac{mL}{min} = 35.4\frac{mL}{min} = 2.12\frac{L}{h}}$$

$$\boldsymbol{CL_{Total} = \frac{2.12\frac{L}{h}}{0.7} = 3.03\frac{L}{h}}$$

b) 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) **(1.5 points)**

$$\boldsymbol{Vd = 3L + \frac{0.6}{0.5} * 38L = 48.6L}$$

$$\boldsymbol{k_e = \frac{3.03\frac{L}{h}}{48.6L} = 0.062\frac{1}{h}}$$

$$\boldsymbol{C(t) = \frac{100}{48.6}\frac{mg}{L}e^{-0.062\frac{1}{h}*t}}$$

Problem 2 (1 point)

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

$$\mathbf{1100}\frac{\boldsymbol{mL}}{\boldsymbol{min}}$$

Kidney blood flow

Problem 3 (1 point, only when both correct statements are chosen, zero points otherwise)

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 passive reabsorbed from the tubulus
- The drug shows similar plasma binding characteristics as creatinine

Problem 4 (1.5 points)

The following equations 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?

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

- **Linear pharmacokinetics**
- **First-order elimination processes**
- **Immediate distribution of drug throughout the body**

Problem 5 (3 points, 0.5 each)

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