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)

\[ IBW_{female} = 45.5kg + 2.3 \times 10 = 68.5kg \]

\[ TBW = 60kg < IBW = 68.5kg \]

Thus, use TBW is Cockcroft-Gault-Equation.

\[ CrCL_{female} = 0.85 \times \frac{(140 - 40) \times 60}{72 \times 1.2} = 59 \text{ mL/min} \]

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. (1 point)

\[ CL_{ren} = 0.6 \times 59 \text{ mL/min} = 35.4 \text{ mL/min} = 2.12 \text{ L/h} \]

\[ CL_{Total} = \frac{2.12 \text{ L/h}}{0.7} = 3.03 \text{ L/h} \]

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)

\[ Vd = 3L + \frac{0.6}{0.5} \times 38L = 48.6L \]

\[ k_e = \frac{3.03 \text{ L}}{48.6L} = 0.062 \frac{1}{h} \]

\[ C(t) = \frac{100 \text{ mg}}{48.6 \text{ L}} e^{-0.062 \frac{1}{h} t} \]
Problem 2 (1 point)

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

\[ \frac{mL}{min} = 1100 \]

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.

\[ CL = CL_{ren} = 50 \frac{L}{h} \]
\[ Vd = 250L \]
\[ f_u = 0.8 \]

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?

\[ C(t) = C_0 e^{-k_t t} \]

- 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