Problem 1

A female patient (6'0'' tall, 65.5 kg, 35 years old) shows a serum creatinine level of 1.1 mg/dL.

a) Use the Cockcroft-Gault-Equation to calculate her creatinine clearance and glomerular filtration rate (GFR).

\[ \text{IBW}_{\text{female}} = 45.5 \text{kg} + 2.3 \times 12 = 73.1 \text{kg} \]

\[ \text{TBW} = 65.5 \text{kg} < \text{IBW} = 73.1 \text{kg} \]

Thus, use TBW is Cockcroft-Gault-Equation.

\[ \text{CrCL}_{\text{female}} = 0.85 \times \frac{(140 - 35) \times 65.5}{72 \times 1.1} = 73.8 \text{ mL/min} = \text{GFR} \]

b) Why do we use the creatinine clearance to estimate the GFR?

- Mainly eliminated by renal processes
- Only glomerular filtration
  - No active tubular secretion
  - No tubular reabsorption
- No plasma protein binding

c) Drug A shows a plasma protein binding and tissue protein binding of 20% and 30%, respectively. Drug A is eliminated by hepatic (20%) and renal processes (80%). 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.

\[ \text{CL}_{\text{ren}} = 0.8 \times 73.8 \frac{\text{mL}}{\text{min}} = 59 \frac{\text{mL}}{\text{min}} = 3.54 \frac{\text{L}}{\text{h}} \]

\[ \text{CL}_{\text{Total}} = \frac{3.54 \frac{\text{L}}{\text{h}}}{0.8} = 4.43 \frac{\text{L}}{\text{h}} \]

d) Graph the plasma-concentration time profile for the first 48 hours when 200mg of drug A are administered to the patient via IV bolus injection. A blood sample taken at the time of injection showed a plasma concentration of 2mg/L. Assume that the drug is immediately distributed throughout the body and that all elimination processes are first-order processes.

\[ Vd = \frac{\text{Dose}}{C_0} = \frac{200 \text{mg}}{2 \frac{\text{mg}}{\text{L}}} = 100 \text{L} \]
Problem 2

Which properties does a drug need to have in order to demonstrate the following? Explain briefly.

a) Active tubular secretion
b) Glomerula secretion
c) Passive tubular reabsorption

**Active tubular secretion:** As active transporters are mainly anionic or cationic transporters, drugs which are actively secreted must be bases or acids.

**Glomerula filtration:** Drugs which are filtrated must fall below a certain molecular weight size. I.e. proteins are not filtrated in the glomerulus because of their large molecular weight.

**Passive tubular reabsorption:** Neutral lipophilic drugs are reabsorbed easily. Passive tubular reabsorption of bases or acids depends on the pH of the urine. Hydrophilic drugs tend not be reabsorbed extensively.

Problem 3

Sketch the relationship between the following PK metrics and Dose for linear and non-linear pharmacokinetics.

a) CL vs. Dose
b) Vd vs. Dose
c) AUC vs. Dose
d) Ke vs. Dose

\[ k_e = \frac{4.43 \frac{L}{h}}{100L} = 0.0443 \frac{1}{h} \]

\[ C(t) = 2 \frac{mg}{L} e^{-0.043 \frac{1}{h} t} \]