SET I: (4 points)

Drug-X is mainly eliminated by liver and kidney. Renal elimination is only by glomerular filtration. C. M was given 70mg of this drug via IV bolus. Two plasma concentrations at 4 hours and 8 hours after dose were 3.22mg/L and 1.61mg/L, respectively. Calculate plasma protein binding of drug-X? (Use 125ml/min for glomerular filtration rate).

\[ k_e = -\log\left(\frac{1.61}{3.22}\right) / 4 = 0.173 \text{ hr}^{-1} \]

\[ t_{1/2} = \frac{0.693}{0.173} = 4 \text{ hr} \]

OR: 3.22mg/L \rightarrow 1.61mg/L \rightarrow \text{one half-life: 4 hr}

\[ C_0 = 3.22 \times \exp(0.173 \times 4) = 6.44 \text{ mg/L} \]

OR: 3.22mg/L \leftrightarrow 6.44mg/L \text{ one half-life: 4hr}

\[ V_d = \frac{\text{Dose}}{C_0} = \frac{70}{6.44} = 10.87L \]

\[ Cl = ke \times V_d = 0.173 \times 10.87 = 1.88L/hr \]

\[ Cl_{\text{fil}} = \text{GFR} \times fu = 125 \times 60 \times fu / 1000 = 1.88L/hr \rightarrow fu = 25\% \rightarrow fb = 75\% \]
SET II: (3 points)
True or False (0.5 point each)

T  F  1: Half-life of any drug is only dependent on the elimination rate constant, neither on clearance, nor on volume of distribution.  (F)

T  F  2: For linear pharmacokinetics, there is no any saturation process involved.  (T)

T  F  3: Total drug amount eliminated via urine is always less than the dose administrated.  (F)
\[ D > U \]

T  F  4: AUC$_\infty$ depends on both dose and volume of distribution.  (F)
\[ AUC_{\infty} = \frac{Dose}{CL} \]

T  F  5: In a linear one-compartmental model, initial drug concentration and half-life of drug can determine AUC$_\infty$ after IV bolus.  (T)
\[ AUC_{\infty} = \frac{C_0}{k_e} \]

T  F  6: Total clearance is always larger than hepatic clearance.  (F)
\[ CL_{tot} = CL_{ren} + CL_{bil} + CL_{met} \]
Drug-W, a novel aminoglycoside, has a clearance equal to creatinine clearance. In order to treat pneumonia, a female patient, 5’10”, 60 year old, 70 kg, received 200mg of Drug-W via IV bolus. The volume of distribution for Drug-W is 1.114L/kg*(TBW). Cp_{crea} in this patient is 0.588mg/dL. What is the drug concentration at 5hr after dose?

\[
Vd = 70kg \cdot 1.114L/kg = 78L
\]

\[
IBW = 45.5 kg + 2.3 kg for each inch over 5 ft in height
= 45.5 + 2.3 \cdot 11 = 70.8 kg \Rightarrow TBW < 1.2*IBW
\]

\[
CL_{crea}(female) = \frac{(140 - \text{age}) \cdot \text{weight}}{85 \cdot Cp_{crea}} = \frac{(140 - 60) \cdot 70}{85 \cdot 0.588} = 112 ml/min = CL_{Drug-W}
\]

\[
k_e = \frac{CL}{Vd} = 112 \cdot 60/1000/78 = 0.086/hr^{-1}
\]

\[
C(0) = \text{DOSE}/Vd = 200mg/78L = 2.56mg/L
\]

\[
Cp = C(0) \cdot e^{-ke*t} = 2.56 \cdot e^{-0.086 \cdot 5} = 1.66mg/L
\]