1. A. What happens to the bioavailability of a high extraction drug when the following parameters are increased: $F_u$, $Q_H$, $Cl_{int}$

As $F_u$ and $Cl_{int}$ increase the bioavailability decreases. As $Q_H$ increases the bioavailability increases. $F=Q_H/(F_u*Cl_{int})$

B. Explain why changes in the above parameters do not change the bioavailability of a low extraction drug?

With a low extraction drug we know that a large amount of drug gets into the body and avoids first pass metabolism, meaning the extraction ratio is very small. This means that the bioavailability is about 1 ($F=1-E$, $F\sim 1$). By changing the small extraction ratio there is not much effect on bioavailability. Changing $F$ from 99% from 98% is insignificant.

2. A patient with liver failure was given 70mg of a drug as an IV bolus injection. The plasma concentrations at 3 hours and 8 hours after injection were 1.31mg/L and 0.65mg/L respectively. The drug is eliminated by hepatic metabolism and renal excretion via glomerula filtration. The plasma protein binding for the drug is 60%... What are the hepatic clearance and the volume of distribution of this drug in this patient? (Use 130ml/min for glomerula filtration rate).

$k_e = -\ln(0.65/1.31)/(8-3)=0.14/hr$

$C_0 = 1.31*\exp(0.14*3)=1.99 \text{ mg/L}$

$V_d = \text{Dose}/C_0=70/1.99=35.2L$

$Cl = k_e*V_d=0.14*35.2=4.93L/hr$

$Cl_{ren} = GFR*f_u=130*60*0.4/1000=3.12L/hr$

$Cl_{hep} = 4.93-3.12=1.81L/hr$

3. Mark True or False

T F highly ionized substances tend to remain in the urine

T F tubular reabsorption can only be an active transport process

T F fluid is filtered across the glomerulus through passive diffusion

4. For the following situations, indicate whether the drug is filtered, reabsorbed or actively secreted: Assume GFR is 130 mL min$^{-1}$, urine flow is 1.5 ml min$^{-1}$

A drug with $f_u = 0.1$ and a $Cl_{REN} = 20 \text{ mL min}^{-1}$ is Actively secreted
A drug with $f_u = 0.40$ and a $\text{Cl}_{\text{REN}} = 52 \text{ mL min}^{-1}$ is Filtered
A drug with $f_u = 0.30$ and a $\text{Cl}_{\text{REN}} = 0.45 \text{ mL min}^{-1}$ is Fully reabsorbed