

Case Study 4
PHA 5127
Fall 2006

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).

$$\begin{aligned}k_e &= -\ln(0.65/1.31)/(8-3) = 0.14/\text{hr} \\C_0 &= 1.31 * \exp(0.14 * 3) = 1.99 \text{ mg/L} \\V_d &= \text{Dose}/C_0 = 70/1.99 = 35.2\text{L} \\Cl &= k_e * V_d = 0.14 * 35.2 = 4.93\text{L/hr} \\Cl_{ren} &= GFR * f_u = 130 * 60 * 0.4 / 1000 = 3.12\text{L/hr} \\Cl_{hep} &= 4.93 - 3.12 = 1.81\text{L/hr}\end{aligned}$$

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 $Cl_{REN} = 52 \text{ mL min}^{-1}$ is Filtered

A drug with $f_u = 0.30$ and a $Cl_{REN} = 0.45 \text{ mL min}^{-1}$ is Fully reabsorbed