

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).

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

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  $130 \text{ mL min}^{-1}$ , urine flow is  $1.5 \text{ mL min}^{-1}$

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