

PHAR 750 Quiz IV - B

PHAR 750: Biopharmaceutics/Pharmacokinetics
November 15, 2007

Name: KEY-B
Total 25 points

Circle your final answers. Use the following information to answer questions 1 – 3 (3 pts each).

For a single extravascular dose of a drug that exhibits monoexponential disposition and first order absorption, how do the following changes in absorption or disposition kinetics affect C_{max} , T_{max} and AUC.

$$Cl_p = V_d \cdot k$$

1. Cl_p is unchanged, V_d unchanged, F unchanged, Dose increased, and k_a unchanged.

$$AUC = \frac{D \cdot F}{Cl_p} = \boxed{\uparrow AUC \quad C_{max} = \uparrow, \quad T_{max} \text{ (no change)}}$$

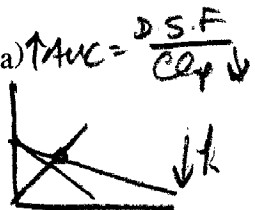
2. F is decreased, k_a unchanged, Dose unchanged, disposition kinetics (Cl_p , V_d , k) unchanged.

$$\boxed{T_{max} \text{ (no change), } \downarrow C_{max}, \downarrow AUC}$$

3. Cl_p is decreased, V_d unchanged, Dose unchanged, absorption kinetics (F , Dose, k_a) unchanged.

$$\boxed{\uparrow AUC, \uparrow C_{max}, \uparrow T_{max}}$$

$$\downarrow Cl_p = V_d \cdot k \downarrow$$



4. Which of the following parameters was not discussed in lecture as being used to calculate hepatic clearance? (3 points)
- A. Hepatic blood flow
 - B. Fraction of drug unbound in the plasma
 - C. Fraction of drug bound in the plasma
 - D. Intrinsic clearance
 - E. All of the above were discussed in lecture as being used to calculate hepatic clearance.

5. Disease states a patient may have may have a significant affect on: (2 points)

- A. Hepatic blood flow
- B. Hepatic clearance
- C. Plasma protein binding
- D. A and B
- E. A, B, and C

6. If an oral dose of a drug with a high extraction ratio ($E > 0.8$) is 100% absorbed, what fraction of the dose is able to reach systemic circulation? (2 points)

- A. < 0.2
- B. > 0.8
- C. 0.8
- D. 0.2
- E. None of the above

Use the information below for questions 7 and 8. Show ALL work and include proper units.

GD is a 50 year old female who will be started on digoxin for rate control in atrial fibrillation. She weighs 52 kg, is 5'4" tall, with a serum creatinine of 1.1 mg/dL.

Digoxin PK: $V_{(normal)} = 6.7 \text{ L/kg}$, $V_{(renal failure)} = 4.7 \text{ L/kg}$.

Dosage forms available are 0.5 mg, 0.25 mg, and 0.125 mg tablets ($F = 0.8$).

7. Calculate an oral loading dose to target a serum concentration of 0.9 ng/mL and recommend a dosing regimen. (4 points)

$$LD = \frac{C_{ss} V_d}{F} = \frac{(0.9 \mu\text{g/L})(6.7 \text{ L/kg} \cdot 52 \text{ kg})}{0.8} = \boxed{391.95 \mu\text{g}} \text{ or } \boxed{0.392 \text{ mg}}$$

$\frac{52 \text{ kg}}{54.7 \text{ kg}} = 0.95$ use ABW

Give 0.25 mg STAT, then 0.125 mg/dose $\times 2$ doses @ 4-6 hr intervals.

8. Calculate the digoxin clearance. (5 points).

$$IBW = 45.5 + 2.3(4) = 54.72 \text{ kg} \quad \text{ABW} < IBW \text{ for CrCl}$$

$$CrCl = \frac{(140 - 50)(52 \text{ kg})}{72(1.1 \text{ mg/dL})} \cdot 0.85 = \underline{50.23 \text{ mL/min}}$$

$$Cl_{dig} = 1.303(50.23 \text{ mL/min}) + 40 \text{ mL/min}$$

$$Cl_{dig} = 105.45 \text{ mL/min}$$

OR

$$\left(\frac{105.45 \text{ mL}}{\text{min}} \right) \left(\frac{60 \text{ min}}{1 \text{ hr}} \right) \left(\frac{\text{L}}{1000 \text{ mL}} \right) = \boxed{6.327 \text{ L/hr}}$$