

PHAR 750: Biopharmaceutics/Pharmacokinetics Name: \_\_\_\_\_

October 26, 2004 - A

Total 100 points

Please choose the **BEST** answer of those provided. For numerical answers, choose “none of the above” if your answer is not within  $\pm 5\%$  of the correct answer. Place your answers on the scantron sheet provided.

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 **T<sub>max</sub>**, **C<sub>max</sub>** and **AUC**.

1.  $Cl_p$  is decreased,  $V_d$  unchanged, absorption kinetics are unchanged.
  - (a)  $T_{max}$  = decreased,  $C_{max}$  = decreased, AUC = decreased
  - (b)  $T_{max}$  = increased,  $C_{max}$  = unchanged, AUC = unchanged
  - (c)  $T_{max}$  = unchanged,  $C_{max}$  = increased, AUC = increased
  - (d)  $T_{max}$  = increased,  $C_{max}$  = increased, AUC = increased
  - (e) none of the above
  
2.  $F$  is increased,  $k_a$  unchanged, Dose unchanged, disposition kinetics ( $Cl_p$ ,  $V_d$ ,  $k$ ) unchanged.
  - (a)  $T_{max}$  = decreased,  $C_{max}$  = unchanged, AUC = unchanged
  - (b)  $T_{max}$  = decreased,  $C_{max}$  = decreased, AUC = decreased
  - (c)  $T_{max}$  = unchanged,  $C_{max}$  = increased, AUC = increased
  - (d)  $T_{max}$  = increased,  $C_{max}$  = increased, AUC = increased
  - (e) none of the above
  
3.  $V_d$  unchanged,  $Cl_p$  unchanged,  $F$  is unchanged,  $k_a$  decreased, Dose unchanged
  - (a)  $T_{max}$  = decreased,  $C_{max}$  = decreased, AUC = decreased
  - (b)  $T_{max}$  = increased,  $C_{max}$  = unchanged, AUC = decreased
  - (c)  $T_{max}$  = increased,  $C_{max}$  = increased, AUC = unchanged
  - (d)  $T_{max}$  = decreased,  $C_{max}$  = increased, AUC = increased
  - (e) none of the above
  
4. If the volume of distribution is less than 5 L, the drug is most likely to be distributed to the:
  - (a) Extracellular compartments
  - (b) Tissues
  - (c) Vascular compartment
  - (d) None of the above
  
5. Which of the following is true?
  - (a)  $\alpha$  is the absorption rate constant.
  - (b)  $\alpha$  is the terminal half-life of a two-compartment model.
  - (c)  $\alpha$  is the terminal elimination rate constant of a two-compartment model.
  - (d) Rate-limiting absorption kinetics occurs when the rate of elimination,  $k$ , is much greater than the rate of absorption,  $k_a$ .
  - (e) All of the above statements are false.

6. The elimination half-life for ciprofloxacin, Cipro, ( $F = 0.6$ ) is approximately 4 hours. What *amount* of this drug *will be eliminated* in 16 hours after an IV bolus dose of 750 mg?
- (a) 703 mg  
 (b) 422 mg  
 (c) 94 mg  
 (d) 47 mg  
 (e) 28 mg
7. *How long* will it take for 300 mg of ciprofloxacin to decompose by 30%?  $k = 0.173/\text{hr}$  (Assume first-order kinetics and constant temperature.)
- (a) 1.2 hr  
 (b) 2.1 hr  
 (c) 3.5 hr  
 (d) 520 hr  
 (e) None of the above
8. *How much* drug in question #6, *will be remaining* in a patient 8 hrs after a 250 mg oral ciprofloxacin dose.
- (a) 188 mg  
 (b) 113 mg  
 (c) 63 mg  
 (d) 38 mg  
 (e) None of the above

**Use the following information to answer question 9.**

Misoprostol (Cytotec, GD Searle) is a synthetic prostaglandin  $E_1$  analog. According to the manufacturer, the following information was obtained when a 200  $\mu\text{g}$  oral dose of misoprostol was taken with an antacid or high fat breakfast:

Condition	$C_{\text{max}}$ (pg/mL)	AUC (pg*hr/mL)	$T_{\text{max}}$ (min)
fasting	811	417	$14 \pm 8$
with antacid	689	349	$20 \pm 14$
with high fat breakfast	303	373	$64 \pm 79$

9. What is *relative bioavailability* of the antacid to the fasting conditions ( $F_a/F_i$ )?
- (a) 1.19  
 (b) 0.84  
 (c) 0.90  
 (d) not enough information is given.  
 (e) none of the above

For questions # 10 – 12, use the following information:

Lidocaine is effective in most patients when its plasma concentration exceeds  $1.5 \text{ mg/L}$  but results in unacceptable toxicity when the plasma concentration exceeds  $6 \text{ mg/L}$ . The equation that best describes the elimination kinetics of lidocaine following a  $150 \text{ mg}$  iv dose is:

$$C_p = 1.98 \mu\text{g/mL} e^{-(0.419/\text{hr}) \cdot t}$$

10. What is the elimination  $t_{1/2}$  for lidocaine in this patient?
  - (a) 1.65 hr
  - (b) 1.45 hr
  - (c) 0.32 hr
  - (d) 4.56 hr
  - (e) None of the above
11. The  $Cl_p$  for lidocaine in this patient is:
  - (a) 0.423 L/hr
  - (b) 15.87 L/hr
  - (c) 28.71 L/hr
  - (d) 31.75 L/hr
  - (e) None of the above
12. What is the *greatest i.v. bolus dose* that can be administered without producing toxicity?
  - (a) 190 mg
  - (b) 350 mg
  - (c) 450 mg
  - (d) 600 mg
  - (e) None of the above

Use the following information to answers questions 13 through 15.

Park and associates (1983) studied the pharmacokinetics of amrinone after a single i.v. bolus injection ( $75 \text{ mg}$ ) in 14 healthy adult male volunteers. The pharmacokinetics of this drug followed a two-compartment open model and the equation best describing amrinone kinetics in humans was:

$$C_p = 4.62 \mu\text{g/mL} e^{-(8.94/\text{hr}) \cdot t} + 0.64 \mu\text{g/mL} e^{-(0.19/\text{hr}) \cdot t}$$

13. Estimate the initial concentration following the iv bolus dose of amrinone.
  - (a)  $5.26 \mu\text{g/mL}$
  - (b)  $4.62 \mu\text{g/mL}$
  - (c)  $3.65 \mu\text{g/mL}$
  - (d)  $0.64 \mu\text{g/mL}$
  - (e) None of the above
14. Estimate the Area Under the Curve of amrinone.
  - (a)  $1.73 \mu\text{g hr/mL}$
  - (b)  $3.10 \mu\text{g hr/mL}$
  - (c)  $3.88 \mu\text{g hr/mL}$
  - (d)  $24.4 \mu\text{g hr/mL}$
  - (e) None of the above
15. What is the plasma level of amrinone 20 minutes after the i.v. dose?
  - (a)  $0.06 \mu\text{g/mL}$
  - (b)  $0.53 \mu\text{g/mL}$
  - (c)  $0.84 \mu\text{g/mL}$
  - (d)  $4.94 \mu\text{g/mL}$
  - (e) None of the above

For questions 16 and 20, please use the information below:

Noroxin® (norfloxacin) is primarily used for lower respiratory tract infections and urinary tract infections. Noroxin® is available in 400 -mg film-coated tablets and is usually administered every 12 hrs. Norfloxacin has the following pharmacokinetic parameters:

**F = 0.35, fe = 0.29, V<sub>d</sub> = 3.2 L/kg, and t<sub>1/2</sub> = 5 hrs.** Assume first-order absorption and elimination kinetics and that the absorption is instantaneous relative to the elimination.

16. A 62 kg female patient is given an I.V. infusion at an infusion rate, R<sub>o</sub>, of 40 mg/hr for 30 hrs for her urinary tract infection. At what time will steady state occur?
- 5 hrs
  - 10 hrs
  - 20 hrs
  - 25 hrs
  - None of the above
17. What is the EQUATION needed to determine the plasma concentration, C<sub>p</sub>, at 18 hrs for the patient in question #16?
- $C_p = C_p^0 e^{-kt}$
  - $C_p = C_{p_{ss}} [1 - e^{-kt}]$
  - $C_p = C_p^0 e^{-kt} + C_{p_{ss}} (1 - e^{-kt})$
  - $C_p = Ae^{-at} - Be^{-\beta t}$
  - None of the above
18. What is the plasma concentration, C<sub>p</sub>, at 18 hrs for the patient in question #16?
- 1.45 mg/L
  - 1.33 mg/L
  - 1.02 mg/L
  - 0.12 mg/L
  - None of the above
19. What is the plasma concentration, C<sub>p</sub>, at 34 hrs for the patient in question #16?
- 7.17 mg/L
  - 0.832 mg/L
  - 0.116 mg/L
  - 0.013 mg/L
  - None of the above
20. If the patient in question #16 *only received* an oral 800 mg loading dose of Noroxin® (no iv infusion), what will the plasma concentration of norfloxacin, C<sub>p</sub>, be at 13 hrs for the patient?
- 41.04 mg/L
  - 14.36 mg/L
  - 0.662 mg/L
  - 0.232 mg/L
  - None of the above