

PHAR 750: Biopharmaceutics/Pharmacokinetics  
 October 26, 2007 – Form 2

Name: Key-2  
 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 Questions 1–4, match the following points (1, 2, 3, 4) on the graphs to their respective equations below. TPA has a half-life of 5.2 minutes.

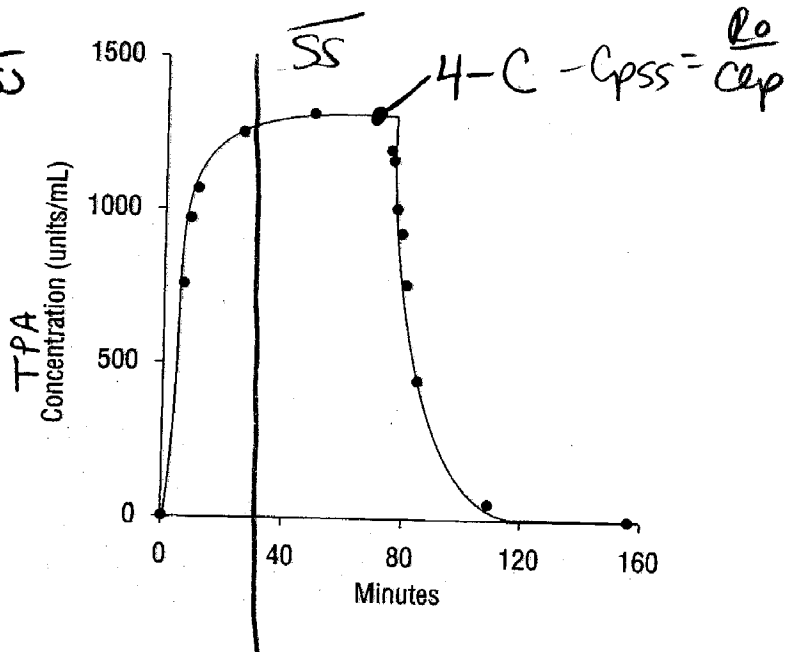
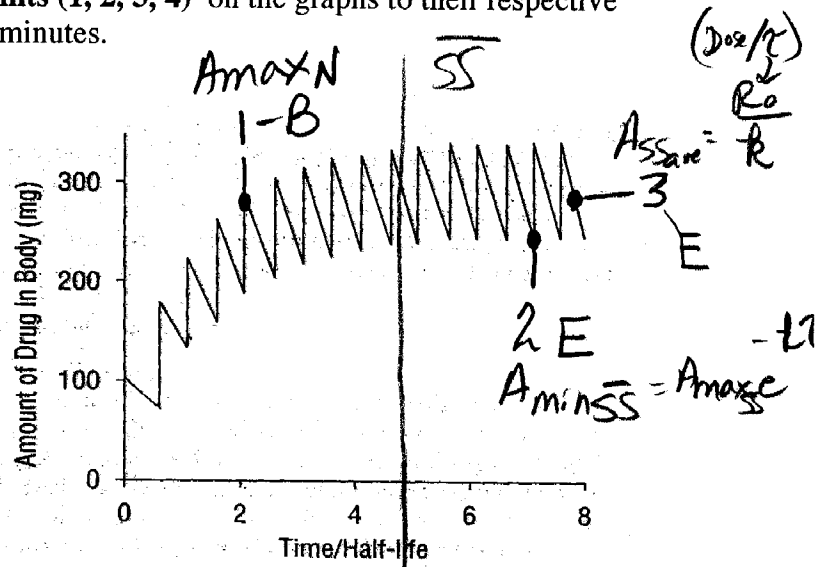
A.  $A = \frac{Dose \cdot F \cdot S}{(1 - e^{-k\tau})}$

B.  $A = Dose \cdot F \cdot S \left( \frac{1 - e^{-Nk\tau}}{1 - e^{-k\tau}} \right)$

C.  $C_p = \frac{R_0}{V_d k} = \frac{R_0}{Cl_p} = C_{p,ss}$

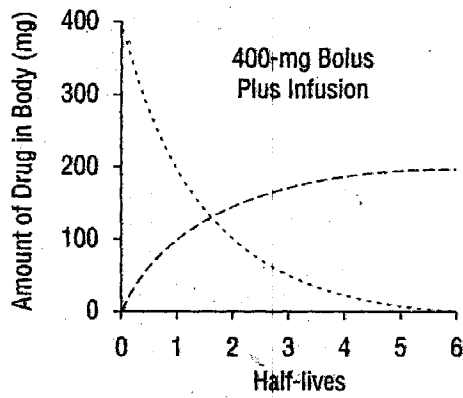
D.  $C_p = \frac{R_0}{Cl_p} \left( \frac{1 - e^{-kt_{inf}}}{1 - e^{-k\tau}} \right)$

E. None of the above.

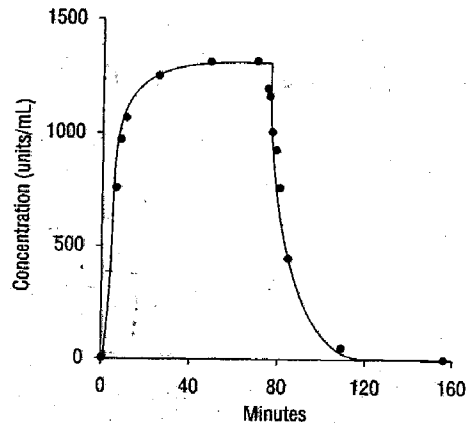


For Questions 5-7, please match the following graphs (A, B, C, D) or E for "None" to their respective equation below.

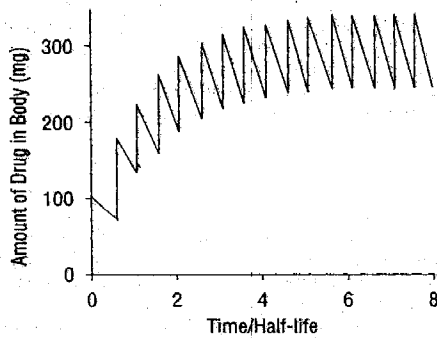
A



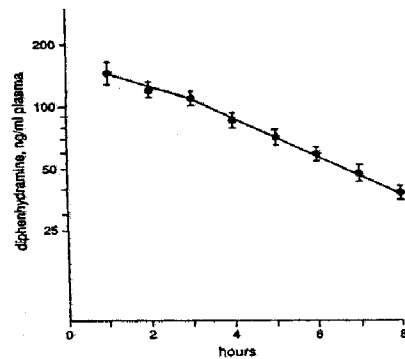
B



C



D



A 5.  $A = A^0 e^{-kt} + A_{ss}(1 - e^{-kt})$  Bolus + infusion

D 6.  $C_p = C_p^0 e^{-kt}$  - 1 comp

E 7.  $C_p = A e^{-\alpha t} + B e^{-\beta t}$  - 2 comp

For questions 8 and 11, use the information below:

Sumycin® (tetracycline) is primarily used as a broad spectrum antibiotic for infections. Sumycin® is available in 250 mg and 500 capsules and is usually administered every 12 hrs. Tetracycline has the following pharmacokinetic parameters:

$F = 0.77$ ,  $f_e = 0.58$ ,  $V_d = 105$  L, and  $k = 0.0654/\text{hr}$ . Assume one-compartment elimination kinetics and that absorption is instantaneous relative to its elimination.

$$t_{1/2} = 10.6 \text{ hr} \quad Cl_p = 6.867 \text{ L/hr} \quad (V_d \cdot k)$$

8. What is the renal clearance,  $Cl_r$ ?

- A. 2.88 L/hr  
 B. 3.98 L/hr  
 C. 6.86 L/hr  
 D. 60.9 L/hr  
 E. None of the above.

$$Cl_r = f_e Cl_p$$

$$\boxed{\frac{3.98 \text{ L}}{\text{hr}}} = (0.58)(6.867 \text{ L/hr})$$

9. What is the area under the curve (AUC) following an oral dose of 500 mg tetracycline?

- A. 42 mg\*hr/L  
 B. 56 mg\*hr/L  
 C. 72 mg\*hr/L  
 D. 5886 mg\*hr/L  
 E. None of the above.

$$\frac{500 \text{ mg} \cdot (0.77)}{6.867 \text{ L/hr}} = \frac{(D \cdot S \cdot F)}{Cl_p}$$

$$\boxed{AUC = \frac{56.06 \text{ mg} \cdot \text{hr}}{\text{L}}}$$

10. What fraction of the dose is remaining in the body after 3 half-lives?

- A. 0.75  
 B. 0.55  
 C. 0.25  
 D. 0.125  
 E. None of the above.

$$\text{fraction remaining} = \left(\frac{1}{2}\right)^n$$

$$0.125 = \left(\frac{1}{2}\right)^3$$

11. What is  $C_p$  of tetracycline in a patient 6 hrs after a 0.5 gram oral dose of tetracycline?

- A. 2.48 mg/L  
 B. 3.22 mg/L  
 C. 260 mg/L  
 D. 338 mg/L  
 E. None of the above

$$C_p = \frac{(500 \text{ mg})(0.77)}{105 \text{ L}} e^{-\left(\frac{0.0654}{\text{hr}}\right)(6 \text{ hr})}$$

$$\boxed{C_{p6} = 2.48 \text{ mg/L}}$$

Indocin® (indomethacin) is an anti-inflammatory drug used for the treatment of rheumatoid arthritis. Indocin® is available in 25-mg, 50-mg immediate release capsule and as a 75-mg sustained release capsule. Indomethacin displays one-compartment model pharmacokinetics and has the following pharmacokinetic parameters:  $F = 0.98$ ,  $V_d = 0.29 \text{ L/kg}$ , and  $t_{1/2} = 2.4 \text{ hrs}$ . Assume that absorption is instantaneous relative to its elimination.

$k = 0.289/\text{hr}$

$V_d = \frac{0.29 \text{ L}}{\text{kg}} \cdot 75 \text{ kg} = 21.75 \text{ L}$       12 hrs to SS       $cl_p = 6.294/\text{hr}$

12. What is the accumulation ratio,  $R_{ac}$  in a 75 kg male patient who has been receiving 50 mg orally every 4 hrs for 3 days?

$\tau = 4 \text{ hr}$

$$R_o = \frac{1}{1 - e^{-(0.289/\text{hr})(4 \text{ hr})}} = \frac{1}{0.683} = 1.46$$

A. 3.18  
 B. 1.46  
 C. 1.00  
 D. Not enough information is given to determine  $R_{ac}$ .  
 E. None of the above

13. What is the "average concentration of indomethacin in the body,  $C_{p_{ave}}$ " in the above patient who has been receiving 50 mg orally every 4 hrs for 1 day? -24 hrs pt @ SS

$F = 0.98$        $\tau = 4 \text{ hr}$

$$C_{p_{ssave}} = \frac{D \cdot S \cdot F}{cl_p \tau} = \frac{(50 \text{ mg})(0.98)}{(6.294/\text{hr})(4 \text{ hrs})} = 1.95 \text{ mg/L}$$

A. 1.95 mg/L  
 B. 42.4 mg/L  
 C. 146 mg/L  
 D. The patient has not reached steady state; thus, the  $C_{p_{ave}}$  cannot be determined.  
 E. None of the above

Multiple dosing - oral

14. What will the patient's "minimum amount,  $A_{min}$ " in question #12 be following a 50-mg oral dose of Indocin® given every 6 hours for 7 days? @ SS  $\tau = 6 \text{ hr}$

$$A_{ssmin} = A_{ssmax} e^{-k\tau}$$

$$= \frac{D \cdot S \cdot F}{1 - e^{-k\tau}} e^{-k\tau}$$

$$= \frac{(50 \text{ mg})(0.98)}{1 - e^{-(\frac{0.289}{\text{hr}})(6 \text{ hr})}} e^{-\left(\frac{0.289}{\text{hr}}\right)(6 \text{ hr})}$$

$10.51 \text{ mg} = 59.51 \text{ mg}(0.1766)$

Please use the following information to answer questions 15 – 18.

Inocor® (amrinone) is a cardiac inotrope used for the short term management of severe congestive heart failure. Inocor® is available as a solution for i.v. administration for bolus doses or continuous infusions. Amrinone has the following first order pharmacokinetic parameters:

$fe = 0.25$ ,  $Cl_p = 13.2 \text{ L/hr}$ ,  $t_{1/2} = 4.4 \text{ hr}$ .  $k = \frac{0.1575}{\text{hr}}$   $t_{ss} = 22 \text{ hrs}$

15. At what TIME will steady state occur?

- A. 8.8 hrs
- B. 22 hrs ✓
- C. 5 half-lives ✓
- D. A and C
- E. B and C

16. What INFUSION RATE,  $R_o$ , is needed to maintain  $C_{p,ss}$  of  $300 \mu\text{g/L}$  for a 55 kg male?

- A. 3.96 mg/hr
- B. 47.25 mg/hr
- C. 3,960 mg/hr
- D. None of the above.

$$C_{p,ss} = \frac{R_o}{Cl_p} = \frac{300 \mu\text{g}}{\text{L}} = \frac{R_o}{13.2 \text{ L/hr}}$$

$$R_o = 3960 \mu\text{g/hr} = 3.96 \text{ mg/hr}$$

17. If the above patient in question #16 was given an I.V. infusion at an infusion rate,  $R_o$ , of  $15 \mu\text{g/min} \cdot \text{kg}$  for 48 hrs, what is the CONCENTRATION of amrinone,  $C_p$ , at 30 @  $ss$  hrs?

- A. 0.063 mg/L
- B. 3.75 mg/L
- C. 62.5 mg/L
- D. 315 mg/L
- E. None of the above

$$C_{p,30} = C_{p,ss} = \frac{R_o}{Cl_p} = \frac{15 \mu\text{g} \cdot (55 \text{ kg}) \cdot (60 \text{ min/hr})}{13.2 \text{ L/hr}}$$

$$= \frac{49500 \mu\text{g/hr}}{13.2 \text{ L/hr}} = 3750 \mu\text{g/L} = 3.75 \text{ mg/L}$$

18. What is the AMOUNT of amrinone, A, at 12 hours if the patient in question #16 is given an I.V. loading dose of 200 mg at same time an i.v. infusion begins at a  $R_o$  of 38 mg/hr?

- A. 235 mg
- B. 205 mg
- C. 67 mg
- D. 2.80 mg
- E. None of the above.

→ NOT at SS

I.V. Bolus = 200mg

I.V. infusion = 38 mg/hr →  $R_o/k$

$$A_{12} = A^0 e^{-k(12\text{hr})} + A_{ss} (1 - e^{-k(12\text{hr})})$$

$$= 200 \text{ mg} e^{-(0.1575/\text{hr})(12\text{hr})} + \frac{38 \text{ mg/hr}}{0.1575/\text{hr}} (1 - e^{-(0.1575/\text{hr})(12\text{hr})})$$

$$235 \text{ mg} = 30.214 \text{ mg} + 204.82 \text{ mg}$$

Tenormin® (atenolol) is a cardiac beta-blocker used for hypertension and chest pain. Tenormin® is available in 25-mg, 50-mg, and 100-mg tablets. Atenolol has the following first order pharmacokinetic parameters:  $f_e = 0.56$ ,  $Cl_p = 7.2 \text{ L/hr}$ ,  $t_{1/2} = 6.1 \text{ hr}$ .

$$k = 0.114/\text{hr}$$

$$t_{1/2} = 30.5 \text{ hrs to SS}$$

19. What is the  $C_p$  of atenolol, at 14 hrs in a patient that is receiving multiple i.v. infusions of 75 mg atenolol over 30 minutes every 6 hours?

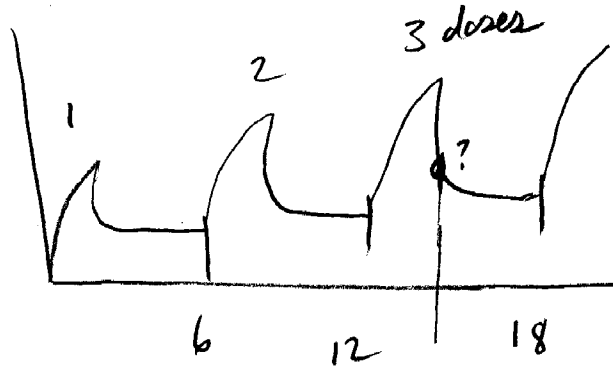
- A. 1.02 mg/L
- B. 1.38 mg/L
- C. 1.62 mg/L
- D. 2.03 mg/L
- E. None of the above.

$$R_0 = \frac{75 \text{ mg}}{0.5 \text{ hr}} = 150 \text{ mg/hr}$$

$\tau = 6 \text{ hr}$

$F = 1$

$N = 3$



$$-kt' \quad t' = 14 \text{ hr} - 12 \text{ hr} = 2 \text{ hr}$$

$$C_{p14} = C_{p\text{max}} e^{-kt'}$$

$$= \frac{R_0}{Cl_p} \left[ \frac{(1 - e^{-kt_{inf}})(1 - e^{-Nk\tau})}{1 - e^{-k\tau}} \right] e^{-kt'}$$

$$= \frac{150 \text{ mg/hr}}{7.2 \text{ L/hr}} \left[ \frac{(1 - e^{-(0.114/\text{hr})(0.5 \text{ hr})})(1 - e^{-3(0.114/\text{hr})(6 \text{ hr})})}{1 - e^{-(0.114/\text{hr})(6 \text{ hr})}} \right] e^{-(0.114/\text{hr})(2 \text{ hr})}$$

$$= \frac{20.833 \text{ mg}}{\text{L}} \left( \frac{(0.055406)(0.871522)}{0.49541} \right) (0.79612)$$

$$= \frac{20.833 \text{ mg}}{\text{L}} (0.09747) (0.79612)$$

$$C_{p14} = 1.62 \text{ mg/L}$$