

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

## PHA 5127

### Final Exam Fall 2006

On my honor, I have neither given nor received unauthorized aid in doing this assignment.

---

Name

**Please transfer the answers onto the bubble sheet. The question number refers to the number on the bubble sheet. Please fill in all the information necessary to identify yourself. The proctors will also collect your exams.**

**Good LUCK.**

Total Questions      31 (5 points each)

Total Points            155 +2 bonus= 157

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

**Question 1:** Select the correct statement(s). The plasma drug concentration versus time curve for a two-compartment model is (5 points)

- 1            biexponential
- 2            monoexponential
- 3            based on zero order pharmacokinetic processes
- 4            based on first order pharmacokinetic processes

The correct statement(s) are (is):

- A:            1
- B:            2 and 3
- C:            1 and 4**
- D:            1 and 3
- E:            2 and 3

**Question 2:** We have defined several volumes of distribution when talking about a 2-compartment model (5 points).

The **correct** statement(s) are (is)

The volume of distribution in a 2 compartment model:

- 1            relates the amount of drug in the body to the plasma concentration.
- 2            is decreasing with time after drug administration, as the amount of the drug in the body is decreasing.
- 3            during the beta-phase does not depend clearance.
- 4            is changing because it takes time for the drug to enter and leave the peripheral compartment.
- 5            is changing from the time of administration up to the elimination phase, as the relative amount of drug in the peripheral compartment, (when compared to the amount in the central compartment), is changing.

- A:            (1, 2, 3, 4, 5)
- B:            (1, 2, 4, 5)
- C:            (1, 2, 5)
- D:            (1, 4, 5)**
- E:            (1, 4)

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

**Question 3-6:** The following applies to questions 3-6: A 60-kg patient is begun on a continuous intravenous infusion of theophylline at 36 mg/hr (based on theophylline, not aminophylline). Forty-eight hours after beginning of the infusion, the plasma concentration is 12 mg/L.

**Question 3:** If we assume that this concentration is at steady state, what is the theophylline volume of distribution? (5 points)

A: 0.25 L/kg

**B: Not enough information to provide answer.**

C: 30 L

D: 18 L/day

E: None of the above

A 60-kg patient is begun on a continuous intravenous infusion of theophylline at 36 mg/hr (based on theophylline, not aminophylline).

**Question 4:** If we assume that the volume of distribution is 30 L, and the clearance is 3.3 L/hr what is the half-life? Please perform calculations on paper, we will check. (5 points)

A: 1.7 hr

**B: 6.3 hr**

C: 13.3 hr

D: 22.1 hr

E: 45.3 hr

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

A 60-kg patient is begun on a continuous intravenous infusion of theophylline at 36 mg/hr (based on theophylline, not aminophylline).

**Question 5:** : If the volume of distribution is estimated to be 30 L, and the clearance is 3.3 L/hr, what would the plasma concentration be 3 days after beginning of the infusion? Remember: the infusion rate is 36 mg/hr (based on theophylline, not aminophylline) Please perform calculations, we might check. (5 points)

- A: 3.2  $\mu\text{g/mL}$
- B: 4.8  $\mu\text{g/mL}$
- C: 8.1  $\mu\text{g/mL}$
- D: 10.9  $\mu\text{g/mL}$**
- E: None of the above.

A 60-kg patient is begun on a continuous intravenous infusion of theophylline at 36 mg/hr (based on theophylline, not aminophylline).

**Question 6:** Assume that the volume of distribution is 30 L, and the clearance is 3.3 L/hr. If the infusion is continued for 4 days and then discontinued, what would the plasma concentration be 12 hours after the stop of the infusion? Please perform calculations, we might check. (5 points)

- A 1.2 mg/L
- B: 2.9 mg/L**
- C: 7.6 mg/L
- D: 8.1 mg/L
- E: None of the above

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

**Question 7:** Assume that the volume of distribution is estimated to be 30 L, and the clearance is 3.3 L/hr. What infusion rate would likely result in a steady state concentration of 24 mg/L. Please perform calculations, we will check. (5 points) **Round appropriately.**

- A: 10 mg/h
- B: 30 mg/h
- C: 40 mg/h
- D: 80 mg/h**
- E: None of the above.

**The following pertains to Questions 8-9**

A 60 kg patient is started on 80 mg of gentamycin given every 6 hr as 1-hr infusion.

**Question 8:** This patient is assumed to have an “average” volume of distribution (value of the population mean) of 0.25 L/kg and a normal half-life of 3 hr, what would be the peak plasma concentration after the first infusion (**one hour after the stop of the infusion**). Please provide calculations. (5 points). Round appropriately.

- A: 3.8 mg/L**
- B: 4.8 mg/L
- C: 5.1 mg/L
- D: 15.4 mg/L
- E: None of the above

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

A 60 kg patient is started on 80 mg of gentamycin given every 6 hr as 1-hr infusion.

**Question 9:** Based on above information, what is the fluctuation that you can expect?  
Please provide calculations. Round appropriately.(5 points)

A: 1

B: 2

**C: 3**

D: 4

E: None of the above

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

**Questions 10 -14** (5 points each)

The following questions 10-14 are related to parts of equations that are shown in the equation blocks A, B, C, D, E (see bottom of page).

**Question 10:** What form of administration is captured by the equation whose parts (blocks) are listed in A, B, D, E (C is not included for this question)? (5 points)

A: single iv bolus injection

B: multiple oral absorption

C: multiple bolus injections

**D: multiple short term infusions**

Identify the block that best fits the following statements. (SELECT FROM BLOCKS A-E shown below)

**Question 11:** A factor suitable to quantify how much a single short term infusion is away from the steady state level that would be observed if a patient receives the drug with the same  $k_0$  for an extended period of time.

**A**

**Question 12:** This block is necessary to allow calculation of the Trough concentration at steady state from  $C_{max}$  values, when given either as multiple short term infusions or multiple iv bolus injections

**E**

**Question 13:**  $C_{max}$  after the first dose when given as a short term infusion

**C**

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

**Question 14:** Degree of accumulation (at steady state) observed when drug is given either as multiple bolus injections or short term infusions.

**D**

A.  $(1 - e^{-k_e T})$

B.  $k_0/CL$

C.  $\frac{k_0}{CL} (1 - e^{-k_e T})$

D.  $\frac{1}{1 - e^{-k_e \tau}}$

E.  $e^{-k_e t'}$

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

**Question 15:**

The oral bioavailability of a lipophilic drug that is only eliminated through renal filtration (5 points)

- 1 will be high if it shows sufficient solubility
- 2 will depend on liver blood flow
- 3 will depend on plasma protein binding
- 4 might be low if it shows affinity to transporters in the GI tract that pump drug into the GI fluid.
- 5 will be affected by the GFR

Select the correct statement(s):

A: 1, 2, 3

B: 4, 5

C: 2, 3

D: 3, 4

**E 1, 4**

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

**Question 16-23:**

**Patient 1** and 2 received a drug as an **iv bolus injection**. Pharmacokinetic and physiological characteristics, such as dose, fraction of the drug unbound in plasma and tissue, intrinsic clearance, liver blood flow, and volume of plasma and volume of the tissue water in these patient are shown below.

**TABLE 1: INPUT PARAMETERS**

	Patient 1	Patient 2
<b>D [mg]</b>	40	40
<b>fu</b>	1	1
<b>fuT</b>	0.3	0.3
<b>CLi [L/h]</b>	30,000	30,000
<b>Q [L/h]</b>	<b>90</b>	<b>45</b>
<b>Vp [L]</b>	3	3
<b>VTW [L]</b>	38	38

The next table shows the resulting pharmacokinetic parameters in **Patient 1**.

Please circle in the free column of the Table 2 for each parameter whether the parameter (Peak concentration, Ke, V, CL, t<sub>1/2</sub>, E, F, AUC) will be about **the same (B)**, **will be larger (A)**, or **will be smaller (C)** than those estimates observed in **Patient 1**.

Mark on the bubble sheet the appropriate A, B, C

**Table 2: OUTPUT PARAMETERS**

Question:		Patient 1	Patient 2
16 (5 points)	<b>Peak[μg/ml]</b>	<b>0.3</b>	Larger (A), <b>about the same (B)</b> , Smaller (C)
17 (5 points)	<b>Ke [1/h]</b>	<b>0.69</b>	Larger (A), about the same (B), <b>Smaller (C)</b>
18 (5 points)	<b>V [L]</b>	<b>130</b>	Larger (A), <b>about the same (B)</b> , Smaller (C)
19 (5 points)	<b>CL [L/h]</b>	<b>89.7</b>	Larger (A), about the same (B), <b>Smaller (C)</b>
20 (5 points)	<b>t1/2 [h]</b>	<b>1.0</b>	<b>Larger (A)</b> , about the same (B), Smaller (C)
21 (5 points)	<b>E</b>	<b>0.99</b>	Larger (A), <b>about the same (B)</b> , Smaller (C)
22 (5 points)	<b>F [%] for tablet</b>	<b>0.3</b>	Larger (A), about the same (B), <b>Smaller (C)</b>
23 (5 points)	<b>AUC [μg/ml*h]</b>	<b>0.446</b>	<b>Larger (A)</b> , about the same (B), Smaller (C)

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

**Question 24:**

Imagine a low extraction drug that **is given orally**. Two patients differ only in the degree of plasma protein binding for this drug. Patient 1 shows a higher plasma protein binding than Patient 2.

When given the same dose, the AUC of free drug for Patient 1 will be larger (a), smaller (b), about the same (c) as the AUC of free drug in Patient 2 or (d) not enough information provided. (5 points)

- A: smaller
- B: larger
- C: about the same**
- D: not enough information provided.

**Question 25:**

Imagine a high extraction drug that **is given orally**. Two patients differ only in the degree of plasma protein binding for this drug. Patient 1 shows a higher plasma protein binding than Patient 2.

When given the same dose, the AUC of free drug for patient 1 will be larger (a), smaller (b), about the same (c) as the AUC of free drug in Patient 2, or (d) not enough information provided.

- A: smaller
- B: larger
- C: about the same**
- D: not enough information provided.

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

**Question 26:**

Which of the following factors **might** significantly affect the renal clearance of an ionized acidic drug ( $pK_a = 1$ ) that has a molecular weight of 200 Dalton? (5 pts)

1. plasma protein binding
2. activity of cationic transporters in the tubuli.
3. urine flow
4. pH of urine
5. liver blood flow

**All answers were accepted**

**A: 1, 2, 3,**

**B: 1, 3,**

**C: 1, 3, 4, 5,**

**D: 1, 3, 5,**

**E: 1, 2**

Name: \_\_\_\_\_

UFID#: \_\_\_\_\_

Mark whether the following statements are true (A) or false (B).

**Question 27 (5 points)**

T (A) F (B) Loading doses are mainly given for drugs with large volume of distribution and/or low clearance

**Question 28 (5 points)**

T (A) F (B) Assume that the oral bioavailability of a drug is 100%. If the oral absorption of this drug is very fast, plasma time profiles after oral absorption and iv bolus injection will be very similar shortly after administration of the dose.

**Question 29 (5 points)**

T (A) F (B) Assume a drug with an oral bioavailability of 100% and a half-life after iv administration of 2 hours. When this drug is given as a sustained release formulation one can assume that the fluctuation will be the same as when the same dose is given as multiple iv bolus injections using the same tau.

**Question 30 (5 points)**

T (A) F (B) 200 mg given every 12 hours will result in the same *fluctuation* than 400 mg given once a day.

**Question 31 (5 points)**

T (A) F (B) 200 mg given every 12 hours will result in the same *AUC* than 400 mg given once a day.