Name: _____

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PHA 5127

Final Exam
Fall 2001

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

_____

Name

Question/Points

1. _____ /12 pts
2. _____ /8 pts
3. _____ /12 pts
4. _____ /20 pts
5. _____ /27 pts
6. _____ /15 pts
7. _____ /20 pts
8. _____ /25 pts
9. _____ /15 pts
10. _____ /6 pts
11. _____ /5 Bonus pts

TOTAL _____/160 (out 165 possible)

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1.) Mark the following statements as True or False (12 points)

T F Decreasing dosing interval (τ) will cause steady-state to be reached faster.

T F Increasing plasma protein binding will decrease the volume of distribution.

T F The absorption rate constant (k_a) is always larger than the elimination rate constant (k_e).

T F Route of administration (e.g., i.v., i.m., p.o.) will affect the AUC (assume bioavailability is 100% for all routes).

T F The maximum value of renal clearance is greater than the maximum value of hepatic clearance.

T F Loading doses are mainly given for drugs with long half-lives.

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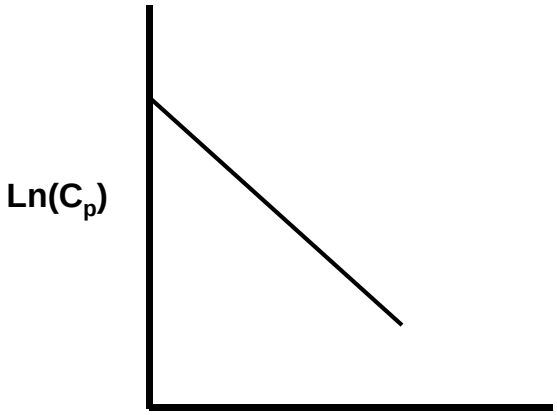
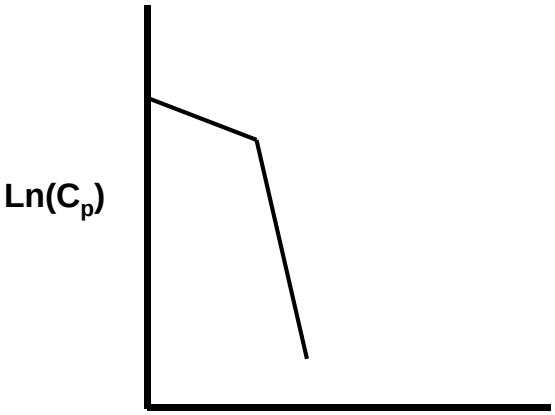
2.) Which graph(s) best depicts a two-compartment body model drug? (8 points)

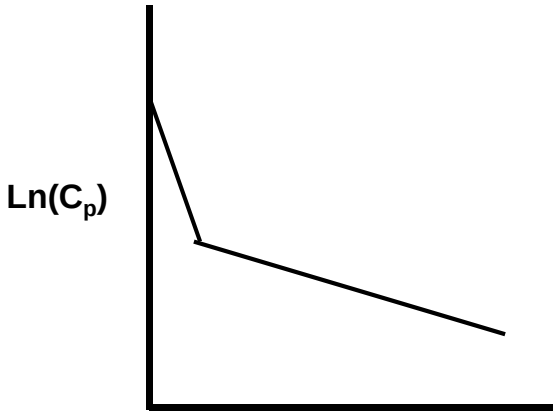
A



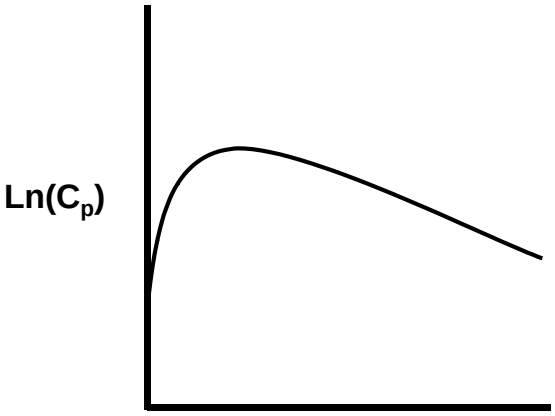
B



C



D



Answer(s): _____

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3.) With more people exercising, the question arises, does exercise alter the pharmacokinetics of drugs? Using the following information, answer the proceeding questions. (12 points)

Table 1 : Changes in blood flow during exercise according to intensity of exercise.

Tissue	Blood Flow (ml min^{-1})			
	Rest	Light Exercise	Moderate Exercise	Intense Exercise
Liver	1500	1100	600	300
Muscle	1000	4500	12500	22000
Kidney	1100	900	600	250

Based on Table 1, answer the following questions

A. **Circle the correct answer**. Intense exercise would change the **hepatic clearance** of a:

- High Extraction Drug
- Low Extraction Drug
- Both a High and Low Extraction Drug
- Exercise would have no effect.

B. **Fill in the blank**. Intense exercise would _____ the **extraction ratio** of a low extraction drug?

a) Increase b) Decrease c) Not Change

C. **Fill in the blank**. Intense exercise would _____ the **bioavailability** of a high extraction drug?

a) Increase b) Decrease c) Not Change

D. **Fill in the blank**. Intense exercise would _____ the onset of action of a lipophilic muscle relaxant.

a) Shorten b) Lengthen c) Not Change

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4.) Mr. D. Johnson from the University of Miami, needs to gain weight for his upcoming lead-role in “The Scorpion King”. His physician, Dr. Adam, puts Mr. Johnson (Rocky to his friends) on the **oral** anabolic steroid, Dianabol, 5 mg every 6 hours. Dianabol has the following pharmacokinetic parameters: V_D = 100 L, k_a = 1 h^{-1}, $t_{1/2}$ = 3 h, and bioavailability is 80%. Assume first order kinetics. (20 points)

A. What is the AUC for a single dosing interval at steady-state?

B. What is the average steady-state concentration?

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4 cont'd.) Mr. Johnson decides he doesn't like oral anabolic steroid due to their side effects. Dr. Adam prescribes the intramuscular steroid Deca-Durabolin which is administered once a day. The terminal half-life of this drug after intramuscular injection is much longer than if it was given as an iv. bolus.

C. Explain the differences in terminal half-life between the 2 routes of administration.

D. Can this explain the once a day dosing regiment?

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5.) A 26 year-old white male, AMP, is admitted to the emergency room with a ruptured appendix. Before surgery (even though AMP had no health insurance), you are asked to begin this patient on a new antibiotic. (Assume 1-compartment body model). (27 points)

Useful Information

- Drug is predominately eliminated by kidney
- AMP is 5'10", 70 kg and a creatinine clearance (CrCL) of 89 mL min^{-1}
- V_D=0.25 L kg^{-1}
- Population estimate of K_e = 0.00321*(CrCL in ml min^{-1})+0.014 (k_e is in h^{-1})
- Based on the Population estimate of K_e, AMP is start of the following dosing schedule
  - K_0 = 1000 mg h^{-1}
  - Dosing interval (τ) = 6 hours
  - Infusion time (T) = 1h
  - Desired steady state plasma range: 60 mg L^{-1} to 12 mg L^{-1}
- Blood samples are taken during the first dose to verify proper dosing schedule was calculated-:
  - Cp 1 hour after stop of infusion = 36.5 mg L^{-1}.
  - Cp 3 hour after stop of infusion = 20 mg L^{-1}.

A. Calculate the half-life for this drug in AMP. Do you think the dosing schedule needs to be readjusted for Adam based on his value and the expected population estimate?

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5 cont'd.)

B. Is the desired C_{MAX} at steady state (60 mg L^{-1}) being obtained in AMP?

C. Suppose (at steady state), the nurse starts the infusion an hour late. What will be the plasma levels when the infusion is started?

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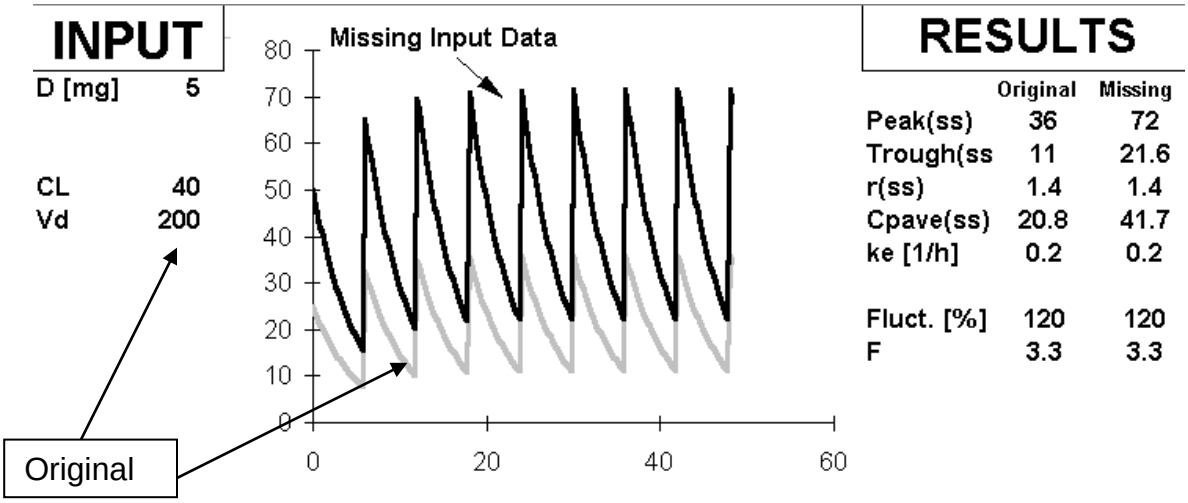
6.) The following concentration time profiles were observed after multiple i.v. bolus injections of a drug. The two curves differ in one of the input parameters (Dose, CL, Vd). (15 points)



Identify the input parameter that differs.

Explain your reasoning in one or two sentences.

What is the numeric value of this parameter?

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7.) Consider the following equation. (20 points)

$$Cp = \boxed{\frac{Dose}{Volume}} \bullet \boxed{\frac{1}{(1 - e^{-k_e \bullet \tau})}} \bullet \boxed{e^{-k_e \bullet \tau}}$$

a) What does this equation describe?

b) What do the blocked parts of the equation represent?

$$\frac{Dose}{Volume}$$

$$\frac{1}{(1 - e^{-k_e \bullet \tau})}$$

$$e^{-k_e \bullet \tau}$$

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8.) Due to the stress of finals, the entire 2PD class comes down with the flu and students are admitted to Shands Hospital. All the students are to be given an antiviral therapy by IV infusion (continuous constant rate infusion, not multiple short term infusions). The average **population $t_{1/2}$ is 2 h**, the **average V_D is 80 L**, and the effective plasma concentration is 15 mg L^{-1}. (25points)

A. Recommend an infusion rate in milligrams per hour to reach the steady state concentration of 15 mg L^{-1}.

B. Approximately how long will it take to reach this concentration?

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8 cont'd.) One student, J.R., does not seem to respond to therapy. Plasma protein binding for the drug is normally 20% (f_u=0.8) except in J.R. whose protein binding was 40% (f_u = 0.6). Tissue binding is similar to the rest of the class

C. (Circle best answer)

A possible reason why J.R. is not responding to therapy is:

A. The drug is a high extraction drug and lowering f_u will increase clearance and plasma levels will become sub-therapeutic
B. The drug is a low extraction drug and lowering f_u will increase clearance and plasma levels will become sub-therapeutic.
C. The drug is a high extraction drug. Clearance will not change but here is less free-drug caused by increased protein binding and it is free-drug that is active.
D. The drug is a high extraction drug. Clearance will be increased and the total and free drug levels will be decreased.

D. ***(Circle the best answer)***

The volume of distribution in JR is LARGER THAN / SMALLER THAN / THE SAME AS the rest of the class.

E. ***(Circle the best answer)***

To achieve the same **free** plasma steady-state concentrations, the daily dose in JR should be LARGER THAN / SMALLER THAN / THE SAME AS the rest of the class.

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9.) Fill in the blank with the most appropriate answer. (15 points)

A. _____ is the name of the mathematical technique used to separate and calculate the absorption rate constant (k_a) from a concentration-time profile.

B. Drugs that are unionized and _____ can cross membranes easily.

C. To increase the renal clearance of an acidic drug that is ionizable, you would want to _____ the pH of the urine.

D. Drugs like ethanol follow _____-order elimination because a constant amount of ethanol is eliminated in a given time.

E. In pharmacokinetics, _____, is a measure of the activity of hepatic enzymes.

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10.) What is the differential equation describing the change in drug concentration after an i.v. bolus administration for a one-compartment body model drug. (assume first order kinetics). (6 points)

11) Today (Dec 12th) is an extremely important day because (5 Bonus points)

A. It is the last day the 2PD class has finals
B. It is the eve of Frank Sinatra's birthday
C. Only 13 days till Christmas (or the third day of Hanukkah)
D. It is Dr. Hochhaus' and Adam's birthday (age 21 and 16, respectively).
E. All the above
F. None of the above