Name: _____

PHAR 7633 Fall 1999
Pharmacokinetics
OU HSC College of Pharmacy

Final Exam **16 December 1999**

Section ONE. Sketch a Graph or Diagram—Sketch the graphs or diagrams requested in the space provided. Make sure you carefully include any distinguishing characteristics. Assume that a linear one compartment model applies for each sketch **unless** otherwise specified. Don't forget to include labels and units for each axes of a graph. **8 x 3 = 24 points**

Q 1.1 A linear plot of Cp versus time for two drug products, A and B, given to the same subject. The extent of absorption is the same but product A has a faster absorption rate.

Q 1.1

Q 1.2 Draw a diagram showing the components of a two compartment pharmacokinetic model with two linear elimination kinetic pathways.

Q 1.2

Q 1.3 A semi-log plot of Cp versus time after an IV infusion of 4 hours, show Cp vs. t for 12 hours.

Q 1.3

Q 1.4 Linear plot of average drug concentration (at steady state) versus dose for a linear two compartment pharmacokinetic model. That is, a model with linear distribution and elimination.

Q 1.4

Q 1.5 Draw a diagram representing a one compartment pharmacokinetic model during an IV infusion with one saturable elimination pathway. Also, provide the differential equation for the plasma/central compartment.

Q 1.5

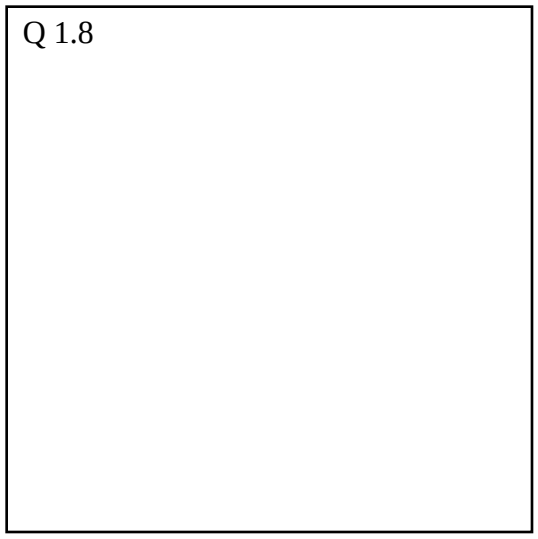
Q 1.6 Sketch a semi-log graph of plasma concentration versus time after a single I.V. bolus dose for a drug which follows one compartment pharmacokinetics and has one saturable elimination pathway. Include concentrations above and below the Km value.

Q 1.6

Q 1.7 Semi-log plot of Cp versus time after a PO dose for a drug with two compartment pharmacokinetics. In this case, the ratios between ka, α, and β are less than 5.

Q 1.7

Q 1.8 A Dettli plot for a drug with fe = 0.75.



<u>Section TWO</u>. True/False—Check the Correct Response. 8 x 2 = 16 points

Q 2.1 For a drug like phenytoin which exhibits Michaelis-Menten elimination kinetics, when Km is much lower than plasma concentrations elimination will appear to follow first order kinetics True ☐ False ☐

Q 2.2 For therapeutic drug monitoring to be necessary for a drug, one of the requirements that must be met is for that drug to have an established concentration versus effect relationship. True ☐ False ☐

Q 2.3 Metabolism is usually well developed in the neonate, thus dosage modification for many drugs, including caffeine and chloramphenicol, is unnecessary except for adjustment for body weight. True ☐ False ☐

Q 2.4 A second peak in the plasma concentration versus time curve after a single drug administration maybe due to enteriohepatic recycling. Especially if the peak appears shortly after a meal. True ☐ False ☐

Q 2.5 In protein binding determination, if the Scatchard plot is linear we can assume that only one type of binding site is responsible for the drug-protein binding. True ☐ False ☐

Q 2.6 The tight, lipid nature of the blood-brain barrier means that brain uptake of polar materials is usually quite limited or slow. True ☐ False ☐

Q 2.7 For a drug which undergoes saturable elimination the 'effective' pseudo-first order elimination rate constant will decrease as the concentration increases. True ☐ False ☐

Q 2.8 The parameter MRT has the units of $time^{-1}$. True ☐ False ☐

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<u>Section THREE</u> Calculations **20 + 18 + 22 = 60 points**

Show all your work for full credit. All material not deleted or crossed-out will be considered for grading.

Q 3.1 (20 points) A drug was given to a number of subjects by a single IV bolus dose (250 mg) and then as a single oral dose (500 mg), after a suitable wash-out period. The average data are presented below. **Complete** the tables and calculate MRT(IV), MRT(PO), MAT, the absolute bioavailability of the oral dosage form and V_{ss}.

Data after 250 mg IV Dose

Time (hr)	Concentration (mg/L)	ΔAUC	AUC	Time	Conc(iv)*t	ΔAUMC	AUMC
0	*6.78*	0.00	0.00	0	0.00	0.00	0.00
0.5	6.32			0.5	3.16	0.79	0.79
1	5.89	3.05		1			
2	5.12	5.51		2	10.24		
4	3.87			4	15.48	25.72	
6	2.92	6.79		6			
9	1.92	7.27		9	17.30	52.27	
∞				∞			

Data after 500 mg Oral Dose

Time	Concentration	ΔAUC	AUC	Time	Conc(po)*t	ΔAUMC	AUMC
0	0.00	0.00	0.00	0	0.00	0.00	0.00
0.5	9.20	2.30	2.30	0.5	4.60	1.15	1.15
1	10.53			1	10.53	3.78	4.93
2	9.63	10.08		2			
4	7.30	16.92		4			
6	5.51			6	33.08	62.26	
9	3.62	13.70		9	32.61		
∞		25.88		∞		417.73	

MRT(iv)		
MRT(po)		
MAT		
F		
V_{ss}		

Q 3.2 (18 points) A 56 year old woman (85 kg) is to be started on phenytoin once a day. She was initially given 300 mg/day for three weeks. A plasma concentration was collected and measured at 6.4 mg/L. The dose was increased to 400 mg/day and another sample was collected after a further three weeks. This time the concentration was 17.6 mg/L. Calculate the Vm and Km value for this patient and an exact daily dose to achieve a plasma concentration of 14 mg/L. The only available capsule sizes are 25, 50, 100, and 250 mg. Round the dose appropriately and calculate the expected plasma concentration.

Q 3.3 (22 points) A drug was given by I.V. bolus (dose 300 mg) and the following data were collected. Calculate A, B, α, β, k12, k21, kel, V_1 and V_{area}. Label and give units for the graph axes.

Data Collected after I.V. Bolus Dose

Time (hr)	Concentration (mg/L)		
0.25	12.4		
0.5	8.7		
0.75	6.7		
1	5.5		
1.5	4.2		
2	3.8		
3	2.5		
4	1.8		
6	0.90		
9	0.30		
12	0.10		

A		
B		
α		
β		
k12		
k21		
kel		
V_1		
V_{area}		