PHA 5127
Homework #5
Fall 2004

Question 1:

B.S. a 54 year old male patient is admitted to the hospital. He weighs 75 kg and is 5'5" high. He is going to receive a new investigational drug orally. We know from a previous study, that the absorption of the drug is so fast, that we can assume an I.V. bolus model. Furthermore we know that the drug has shown serious side effects if its maximum steady state concentration was over 60mg/l and was ineffective, when its minimum steady state concentration was lower than 35mg/l.
Propose a dosing regimen (state the dose, average concentration and dosing interval) that keeps the drug within the safe maximum and minimum steady state concentrations. How would you dose if you only had tablets of 500 mg?
(Vd=0.5 L/kg ; CL=CrCL; SeCr= 1.7 mg/100ml)

IBW= 50 + 2.3 * 5 =61.5 kg

Vd=0.5 L/kg * 75 kg = 37.5 L

CrCL=(140-age)*IBW / (72 *SrCl) = 43.2ml/min = 2.59 L/h → 2.6 L/h

CL=CrCL=2.6 L/h

Ke=Cl/Vd = 2.6 L/h / 37.5 L = 0.0693 /h

τ= ln(Cmax,desired / Cmin,desired) /ke = ln (60/35)/0.0693 = 7.7h → 8h

Dose = Cave * CL * τ = 47.5 * 2.6 * 8 = 988 mg → 1000 mg

Regimen: 2*500mg every 8 h.

2.6 points

Question 2:

A drug has the following parameters:
Dose : 200 mg, τ=6 h, CL=40L/h, Vd=35

How do the following parameters Cave, Cmin, Cmax, F change when you alter the parameters indicated in the columns: (indicate with ⇑,⇓,⇔) Assume IV bolus model.

	Double the dose	Decrease CL by 75%	Double the Vd	increase τ to 8h
Cmin	⇑	⇑	⇑	⇓
Cmax	⇑	⇑	⇓	⇓
Cave	⇑	⇑	⇔	⇓
F	⇔	⇓	⇓	⇑

0.15 each 2.4 total

Question 3:

Please answer the following questions with TRUE or FLASE :

At steady state the amount of drug that goes into the body is the same that is eliminated.
TRUE
It takes 5 half-lifes in order to reach 50% of the steady state.
FALSE It takes one-half life.
It takes 5 half-lifes to almost reach steady state.
TRUE
In order to reach steady state faster a loading dose can be administered.
TRUE
At steady state, the AUC during one dosing interval is equal to two times the AUC∞ of the first dose.
FALSE It is identical.

0.5 each 2.5 total

Question 4:

A 86 year old female patient (weight: 55kg) was administered a drug in the hospital. Unfortunately hurricane Charlie destroyed the records of the hospital. Since she has severe dementia, she does not remember the dose she was given, but she remembers taking the medicine twice a day . Her average steady state plasma concentration turned out to be 26 mg/l. (Hint: CL=CrCL; assume the IV bolus model can be used.) Can you help her? The red pills she claims she takes are available in 350 mg strength.

CL=CrCL= (140-age)*(weight/85) = 34.94 ml/min = 2.1 L/h

Dose = Cave * CL * τ = 26 * 2.1 * 12 = 655 mg → 700 mg

2*350 mg every 12 h

2.5