

PHA 5127 – Fall 2003
Homework # 5 - Answers

1. B.C., a 65-year-old, 55 kg, 6'1" tall male with a serum creatinine of 1.6mg/dL, is about to receive drug X orally (assume: absorption is so fast that we can use IV bolus model). Design a dosing regimen (calculate dosing interval, dose, average concentration) that will produce a steady-state peak concentration of 20mg/L and a steady-state trough concentration of 10mg/L. How would you give the drug if only tablets of 200mg are available? Show all calculations.

$$(Vd=0.7L/kg, CL=CrCL)$$

$$IBW = 50 + 2.3 \cdot 13 = 79.9 \approx 80kg$$

$$Vd = 0.7L/kg \cdot 55kg = 38.5L$$

$$CrCL = \frac{(140 - age) \cdot IBW}{72 \cdot SeCr} = \frac{(140 - 65) \cdot 80}{72 \cdot 1.6} = 52.1 mL/min \approx 3.13L/h$$

$$CL = CrCL = 3.13L/h$$

$$k_e = \frac{CL}{Vd} = \frac{3.13}{38.5} = 0.081h^{-1}$$

$$\tau = \frac{\ln\left(\frac{C_{max,desired}}{C_{min,desired}}\right)}{k_e} = \frac{\ln\left(\frac{20}{10}\right)}{0.081} = 8.6h \approx 8h$$

$$Dose = C_{ave} \cdot CL \cdot \tau = 15mg/L \cdot 3.13L/h \cdot 8h = 375.6mg \approx 400mg$$

2 x 200mg every 8 hours

2. A.S., a 43-year-old, 50kg female has received an oral dose of 500mg of theophylline for several weeks. Her steady-state plasma concentration was measured and turned out to be 12mg/L.

What is the fluctuation F in this patient?

(Assume that the absorption of this tablet is so fast that we can use IV bolus models for describing plasma levels.)

($V_d=0.5L/kg$, $CL=40mL/h/kg$)

$$V_d = 0.5L/kg \cdot 50 = 25L$$

$$CL = 0.04L/h/kg \cdot 50 = 2L/h$$

$$k_e = \frac{CL}{V_d} = \frac{2}{25} = 0.08h^{-1}$$

$$\tau = \frac{Dose}{C_{ave} \cdot CL} = \frac{500mg}{12mg/L \cdot 2L/h} = 20.8h \approx 24h$$

$$F = e^{k_e \cdot \tau} = e^{0.08 \cdot 24} = 6.82$$

3. 5mg of a drug are given as an IV bolus every 4 hours for several days. Mean pharmacokinetic parameter of this drug are

Pharmacokinetic parameter	
CL (L/h)	30
Vd (L)	75
$t_{1/2}$ (h)	1.73

For the following scenarios determine what will happen to the average steady-state concentration, the peak concentration and the fluctuation. Use arrows to mark if it increases, decreases or stays the same.

- The clearance drops to 15L/h.
- The volume of distribution increases to 100L.
- The dosing interval changes to 12 h.

	CL (L/h) decreases to 15 L/h	Vd (L) increases to 100 L	τ changes to 12 h
$C_{ss,ave}$ (mg/L)	↑	↔	↓
C_{max} (mg/L)	↑	↓	↓
F	↓	↓	↑