PHA 5127
Key to case study #5
Fall, 2003.

Case # 1:

Drug A has a half-life of 1.5-hour with an apparent volume of distribution of 10L.The usual therapeutic range of this drug is 5 mg/L to 15 mg/L. Please answer the following questions. (Assume you want to design a dosing regimen for multiple IV bolus to maintain the serum drug concentration between 5 and 15 mg/L)

1.) What is Ke and CL?
2.) Please find out the fluctuation factor.
3.) What will be the dosing interval you want to suggest?
4.) Please find out what is the proper dose.

Answer:

1.) Ke = 0.693 / 1.5 =0.462 ($hr.^{-1}$) , CL = Ke * Vd = 0.462 * 10 = 4.62 (L /hr.)
2.) F = Cpssmax / Cpssmin = 15 / 5 =3. **Please note**: F here means fluctuation factor, not the bioavailability.
3.) τ = ln F / Ke = ln 3 / 0.462 =2.4 (hr.)
4.) D = Cmax * Vd * (1-$e^{-Ke*\tau}$) = 15 * 10*(1-$e^{-0.462*2.4}$) = 100 (mg)

Case # 2:

A patient received drug X with the dose of 200mg every 8 hours. After reaching steady state, a peak level of 20 mg/L was measured. And 4 hours later after peak, the concentration was reported as 10 mg/ L. Please find out.

1.) The Ke of drug X.
2.) Find the volume of distribution.
3.) Calculate the average concentration.
4.) Find out the trough concentration.

Answer:

1.) Ke = (ln C1-ln C2)/(t2-t1) = (ln 20- ln10) / (4-0) = 0.1733 (hr^{-1})
2.) C(peak) = C_0 / (1-$e^{-ke*\tau}$) = D /(V_d*(1-$e^{-ke*\tau}$)), Plug in numbers, we can get,
20 = 200 / (Vd * (1-$e^{-0.1733*8}$)) ,
Then by solving the equation, we obtain: Vd=13.3 (L).

3.) $\overline{C_{pss}}$ = D / (CL* τ) = D / (Ke * Vd * τ) = 200 / (0.1733 * 13.3 * 8) = 10.85 (mg/L)
Note the average concentration is **NOT** = 0.5*(Css(peak) + Css (trough))
4.) Trough concentration:
Css (trough) = Css (peak) * $e^{(-Ke*\tau)}$ = 20 * $e^{(-0.1733*8)}$ = 5.00 (mg/L)

Case #3 : Simulation study

Practice for the simulation on One Compartment Model Multiple IV Bolus Injection
(**http://www.cop.ufl.edu/cgi-bin/hh9.exe**)

Change the Dose, Clearance, Volume of distribution, and see what the curve looks like.