PHA 5128
Fall 2004
HW 4

1. The disposition kinetics of a drug after IV bolus injection is described by a one-compartment model. Assume the half life following therapeutic doses in humans is 4hr, therefore:

    a. What is its elimination rate constant?

ke=0.683/4=0.173/hr.

    b. How long does it take to eliminate 75% of the dose after injection of 5 mg.

exp(-ke*t)=0.25 t=-log(0.25)/0.173=8.01hr

    c. How long does it take to eliminate 75% of the dose after injection of 1 mg.

same as b. 8.01hr.

2. A patient with liver failure was given 70mg of a drug as an IV bolus injection. The plasma concentrations at 3 hours and 8 hours after injection were 1.31mg/L and 0.65mg/L respectively. The drug is eliminated by hepatic metabolism and renal excretion via glomerula filtration. The plasma protein binding for the drug is 50%.. What is the hepatic clearance and the volume of distribution of this drug in this patient? (Use 130ml/min for glomerula filtration rate).

k_e =-log(0.65/1.31)/5=0.14/hr
C_0 = 1.31*exp(0.14*3)=1.99 mg/L
Vd = Dose/C0=70/1.99=35.2L
Cl = ke*Vd=0.14*35.2=4.928L/hr
Cl_{ren} = GFR*fu=130*60*0.5/1000=3.9L/hr
Cl_{hep} = 4.928-3.9=1.028L/hr

3. A 22 year old male patient (80kg, 66inches) was given 2mg/kg of an aminoglycoside by IV bolus injection. The serum creatinine level of the patient is 1.5mg/dL. Assume that the clearance of this drug equals the creatinine clearance.

a. Calculate the creatinine clearance of this patient.

IBM= 50+2.3*(66-60)=63.8kg
CrCL=(140-22)*63.8/(72*1.5)=69.7mL/min

b. Blood samples were taken 1hour after the dose, and the plasma concentration was 7.5mg/L. How long will it take for the plasma level to reach 2mg/L?

ke= 0.0029*69.7+0.014=0.216/hr t=-log(2/7.5)/0.216=2.66hr

4. True or False:

a. If k_e decreases for a drug, its AUC(0-inf) will always increase.

false

b. Two drugs, given as an IV bolus injection, follow a one compartment body model. They do not show drug/drug interactions and their elimination rate constant were the same. Therefore their concentration-time profiles will be identical

false

c. A patient with liver failure (decrease liver blood flow) was given an IV bolus of drug X (high extraction drug). This drug follows a one compartment body model and is heavily metabolized in the liver. Compared with normal people, this patient would have a much smaller starting concentration and much longer half life for this drug.

false

d. A drug was given to patient A by IV bolus. The same dose was given to patient B also by iv bolus. Patient B shows a much higher plasma protein binding for the drug than patient A. If they have the same clearance for this drug, the AUC(0-inf) for both patients will be the same.

true