PHA 5124 Homework 3 solution

1. The renal clearances, the fractions unbound in plasma and the molecular weights of four drugs in a 70 kg subject are as follows:

	Cl_{ren} (mL/min)	fu	MW
X	20	0.5	500
Y	0.10	0.5	200
Z	20	0.1	800
Example	50	0.9	100

Check (with √) the factor(s) that you think MUST be involved in the renal handling of each of these drugs and give brief reasons for your choice. (GFR is 130 mL/min and urine flow is 1.5mL/min.)

	Filtration	Secretion	Reabsorption
X	√ MW<20000		√ 20<130*0.5=65
Y	√ MW<20000		√ 0.1<130*0.5=65
Z	√ MW<20000	√ 20>130*0.1=13	
Example	√ MW<20000		√ 50<130*0.9=117

Bonus question: Which drug has active reabsorption? **Y since 0.1<1.5*0.5=0.75.**

2. Tacainide is a week base with pKa=9.0. Its unionized form is non-polar. It has a volume distribution of 25L, $t_{1/2}$ of 1 hour and fraction unbound (fu) of 0.1. The renal clearance accounts for 14% of the total clearance.
   a. Calculate the renal clearance.
   b. Is secretion or reabsorption definitely involved in the renal clearance of Tacainide? Why?
   c. If we know that reabsorption is involved, how will the renal clearance change if pH of urine changes from 7.5 to 4.5? Why?

Answers:

a. $K_e=0.693/t_{1/2}=0.693h^{-1}$

$CL_{tot}=K_e*V_d=0.693*25=17.3$ L/hr

$CL_{ren}=CL_{tot}*0.14=17.325*0.14=2.4$ L/hr

b. Secretion is definitely involved because

$CL_{ren}=2.4$ L/hr=40 mL/min>fu*GFR=0.1*130=13mL/min.

c. The renal clearance of Tacainide will increase if pH of urine changes from 7.5 to 4.5 because at pH 4.5 more Tacainide will be of ionized form and not be able to be reabsorbed (only the non-polar unionized form can be reabsorbed).

3. A 30 year-old white male patient needs to take gentamicin (aminoglycosides) for the treatment of gram-negative pneumonia infection. The body weight of this patient is 70kg. The volume distribution of gentamicin is 16.5 L.
    a. Calculate the Creatinine Clearance (CrCL) for this patient
    b. Calculate the elimination rate constant (k_e)
    c. Calculate the total clearance (CL_T)
    d. Calculate the non-renal clearance (CLnonren) (Hint: intercept ke)
    e. Calculate the renal clearance (CLren)

Answers:

a. CrCL=(140-age)*weight/70=(140-30)*70/70=110 mL/min

b. k_e=0.00293*CrCL+0.014=0.00293*110+0.014=0.3363 hr^{-1}

c. $CL_T=k_e*V_d$=0.3363*16.5=5.55 L

d. $k_{enonren}$=0.014 hr^{-1} and $CL_{nonren}=k_{enonren}*V_d$=0.014*16.5=0.231 L/hr

e. $CL_{ren}=CL_T-CL_{nonren}$=5.55-0.231=5.319 L/hr