PHA 5127 Dose Optimization I

Homework IV (10 points)
Due on Friday, 10/02/2009

Do not forget the units of the results. 0.1 points will be deducted for each time an answer is provided without the appropriate unit.

1. A patient was given 200mg of a drug as an IV bolus injection. The plasma concentrations at 2 hours and 8 hours after injection were 2.68mg/L and 0.81mg/L respectively. The drug is eliminated by hepatic metabolism which is 5.32L/h, and also renal excretion via only glomerula filtration. (Use 130ml/min for glomerula filtration rate).
Determine C_0, Vd, Cl, Cl_{ren}(renal clearance) and plasma protein binding. (2.5 points, 0.5 each)

Ke = -(ln0.81-ln2.68)/(8-2)≈0.20 /hr
C_0 = 2.68mg/L * exp(0.2/hr*2hr) ≈4.00mg/L **(0.5 points)**

Vd = Dose/ C_0 =200mg/ 4.00mg/L=50L **(0.5 points)**

Cl = ke * Vd=0.2/hr*50L=10L/hr **(0.5 points)**

Cl_{ren}= Cl-Cl_{hep}=10L/h-5.32L/h=4.68L/h=4.68L/h*1000mL/L / 60min/h = 78mL/min **(0.5 points)**

Cl_{ren}=GFR*fu, fu= Cl_{ren}/GFR=78mL/min / 130mL/min = 0.6
So plasma protein binding is 40% **(0.5 points)**

2. Predict the half life of a 65 year old, 5'8'' tall, 80 kg male patient, who is on aminoglycoside treatment. The serum creatinine level was determined to be 1.5mg/dL. (Hint: use Cockcroft-Gault equation for creatinine clearance, and the equation Ke=0.00293*CrCl + 0.014 for aminoglycoside) (2.5 points)

IBW= 50kg + 2.3kg * 8 = 68.4 kg **(0.5 points)**
TBW = 80 kg < 120% IBW → not an obese patient, so use TBW **(0.5 points)**
CrCl= (140-age)*TBW/(72*serum creatinine)=(140-65)*80/(72*1.5)=55.556mL/min **(0.5 points)**
Ke=0.00293*CrCl + 0.014=0.177/hr **(0.5 points)**
$t_{1/2}$=0.693/0.177≈3.915hr **(0.5 points)**

3. **TRUE (T) or FALSE (F) (2 points, 0.5 each)**

The glomerula filtration rate (GFR) is the maximum value of renal clearance

T F

Fluid is filtered across the glomerulus through passive diffusion

T F

Both bound and unbound drug can be filtered.

T F

Highly ionized substances tend to remain in the urine.

T F

4. Please predict how the following parameters will change when the liver blood flow is increased in a patient

(1) when taking a high extraction drug (1.5 points, 0.5 each)

the extraction ratio (E)	same
the clearance (Cl)	increase
oral bioavailability (F)	increase

(2) when taking a low extraction drug (1.5 points, 0.5 each)

the extraction ratio (E)	decrease
the clearance (Cl)	same
oral bioavailability (F)	same