PHA 5127 Homework 4

1. Drug X follows a one-compartment model after an IV bolus administration. The half-life of drug X is 0.693 hour, the volume distribution is 150 L and f_u is 0.5. There are multiple routes for the elimination of drug X. We know that filtration is the only factor involved in renal elimination (no re-absorption or secretion). Assume GFR is 130mL/min.
    a. Calculate the elimination rate constant k_e
    b. Calculate the total clearance
    c. Calculate the renal clearance and the renal elimination rate constant k_{eren}
    d. Calculate the non-renal clearance
    e. Besides renal elimination, is it possible that hepatic elimination is the only other route of elimination? Why?

2. Drug Y follows a one-compartment model after an IV bolus administration. 66 mg is given to a 70kg male patient by IV bolus. The concentrations at 0.5 and 3 hours are 0.236 μg/mL and 0.042 μg/mL, respectively.
    a. Calculate the elimination rate constant k_e
    b. Calculate C_0
    c. Calculate V_d
    d. Calculate the total clearance
    e. Calculate $AUC_{0-\infty}$
    f. If the drug is given twice daily (8 a.m. and 8 p.m.)), the concentration at noon of day 30 is 0.021μg/mL. What will be the concentration right before the second dose of that day (8 p.m.)?

3. How will the following parameters change (increase ↑, decrease ↓, no change ↔) for a low extraction drug which also undergoes renal elimination if f_u change from 0.2 to 0.8?
    a. V_d
    b. E_H (hepatic extraction ratio)
    c. F (oral bioavailability)
    d. CL_H (hepatic clearance)
    e. CLren
    f. CLtot
    g. $AUC_{0-\infty}$

Note: PLEASE circle your final answer for each question.