

PHA 5128

Homework 1

1. 1000 mg of a drug was given via intravenous bolus injection to two patients, one healthy subject and one suffering with cirrhosis. The following plasma concentrations were measured.

time (h)	Cp healthy (mg/L)	Cp cirrhosis (mg/L)
1	11.65	15.53
2	8.24	13.22
3	5.83	11.25
4	4.12	9.58
5	2.91	8.15
6	2.06	6.94
8	1.03	5.03

- Prepare a semilogarithmic plot of the concentration of the drug versus time. Determine the elimination rate constants and half-lives, with cirrhosis and without, of the drug
 - Using the trapezoidal rule determine if there is a difference in the area under the curve for both. Is there a difference?
 - Calculate the total clearance for both.
 - Calculate the volume of distribution for both.
2. A patient is admitted with an acute digoxin overdose. A serum level is measured at 10 ng/ml. Assuming a 48-hour half-life and no further drug absorption, how long does it take for the serum level to drop to the upper limit of the therapeutic range (2.0 ng/ml)?
3. A patient was given 1000 mg of vancomycin q 36 h over 30 min (i.v.) from 9:30 to 10:00 am. The following two serum levels were measured: 26.6 µg/ml at 11:00 am and 11.7 µg/ml at 10:00 am the following day. Calculate:
- The elimination rate constant k
 - The elimination half-life
 - The peak concentration at 10:00 am
 - The concentration at 9:30 pm the following day.
 - The volume of distribution
 - The clearance

4. How would doubling the protein binding of a high extraction drug affect the resulting unbound and total serum levels? What recommendation would you make for dose adjustment? Assume constant rate infusion and steady state.

5. C. J. a 68 kg male epileptic is to be started on an oral regimen of phenobarbital. The pharmacokinetic parameters for this patient are $V_d(0.65 \text{ L/kg})$, $Cl(0.004 \text{ L/kg/h})$ and $F(1.0)$. Design an oral dosage regimen of phenobarbital that will produce an average concentration of 20 mg/L (16, 32, 65 and 100 mg mg tablets are marketed) for this patient, be sure to maintain a plasma concentration within the therapeutic range ($15\text{-}40 \text{ mg/L}$). Assume the absorption of Phenobarbital is rapid and complete. (hint 1st calculate pk parameters, 2nd pick an appropriate τ , 3rd select a dose.)