PHA 5127 Homework 2

1. A 24 years old, 60kg, female patient was admitted into Shands hospital because of drug intoxication. The clinicians decided to give her drug A through i.v bolus at a dose of 10mg/kg to control the symptoms. The table below listed her plasma drug concentrations at 5 different time points. Suppose the drug follows a one compartment body model, with first-order elimination. (4pt)

Time (hr)	Cp (mg/L)
1	4.02
2	2.70
4	1.21
6	0.54
8	0.25

1.1 If the plasma protein binding of drug A in the patient is 60%, calculate the initial *free* plasma drug concentration and tissue binding. (V_p=3L, V_T=38L) (3pt)

1.2 If the tissue binding of this drug decreases by 10% (90% of the tissue binding calculated from question 1.1), predict the dose that should be administered to reach the same initial total drug concentration C_0. (1pt)

2. The table below listed some properties of five acidic drug molecules A, B, C, D, E, but some information is missing. Please complete the table by calculating the effective partition coefficient at pH=7.4 and give the rank order of the five drugs entering brain tissue. (2.5pt, 0.25 each)

Drug	Fraction unionized at pH=7.4	Partition coefficient of unionized form	Molecular weight (Dalton)	Effective Partition coefficient at pH=7.4	Rank order of entering brain tissue
A	0.51	3.5	360		
B	0.917	0.2	280		
C	0.079	1.0	475		
D	0.73	0.004	328		
E	0.84	0.38	490		

3. Match the following parameters with correct units (1pt, 0.25 each)

1. Concentration   a. mg*L/hr

2. Half-life   b. hr

3. AUC   c. hr^{-1}

4. k_e d. mg*hr/L

                                                         e. mg/L

4. True or False (2.5pt, 0.5 each)

T   F   For a drug that is unionized and lipophilic, the rate of drug uptake into lung tissue
            will be faster than the rate of the drug entering fat tissue.

T   F   Assume a drug that does not bind to plasma and extracellular proteins: If a drug is
            unable to cross membrane; V_d cannot be larger than the extracellular space.

T   F   Increase in plasma protein binding will increase the volume of distribution of a
            lipophilic, un-ionized drug (Assume $f_{u,T}$ stays constant).

T   F   The concentration gradient across tissue membranes is an important factor affecting
            the rate of drug uptake across these tissue membranes, when a drug has difficulty to
            cross the membrane (low permeability)

T   F   When the volume of distribution of a lipophilic drug in a 60kg female patient is 100L,
            it means this drug has a stronger tissue than plasma protein binding.