**Homework # 2**
**(PHA 5127)**
**(Total 10 Points)**
**Fall 2006**

**Question 1 (2 Points each part):**
A teenager was admitted into hospital due to drug intoxication. Patient A is female with a body weight of 60kg. Clinicians decide to give her an IV bolus of Drug XY-134 to control the symptoms. XY-134 is administered at a dose of 0.25 mg/kg. After drug exposure, they found that drug concentration-time profile can be best described by one-compartmental linear model with the equation, $\{C = 0.33 \cdot e^{-0.116 \cdot t}$ (Unit: mg/L)$\}$, where C represents Drug XY-134 concentration at time t (hr).

A: Calculate dose that was given, drug XY-134 concentration at time zero, volume of distribution, half-life of Drug XY-134.

$$Dose: 60 \cdot 0.25 = 15(mg)$$

According to the equation: $C = 0.33 \cdot e^{-0.116 \cdot t}$, and equation for standard one-compartment model: $C = C_0 \cdot e^{-K_e \cdot t}$, then:

$$C_0 = 0.33(mg / L)$$

$$K_e = 0.116(1/hr)$$

$$t_{1/2} = \frac{\ln 2}{K_e} = 5.98(hr)$$

$$V_d = \frac{Dose}{C_0}$$

$$V_d = \frac{15}{0.33} = 45(L)$$ .

B: If the free fraction of Drug XY-134 in plasma is 0.3 in this patient, what is the free fraction of Drug XY-134 in tissues for the patient?

$$V_d = V_p + V_t \cdot \frac{f_u}{f_{ut}}$$

$$f_{ut} = f_u \cdot \frac{V_t}{(V_d - V_p)}$$

$$V_p = 3(L)$$

$$V_t = 38(L)$$

$$f_{ut} = f_u \cdot \frac{V_t}{(V_d - V_p)} = 0.3 \cdot \frac{38}{(45-3)} = 0.27$$

C: When the patient was in the hospital, a stroke reduced the blood flow to the brain. After the stroke, it took a longer time for the effect of the following injections of XY-134 to kick in. A less lipophilic drug acting also in the brain showed normal onset- of action. Explain?

Blood flow rate only affects distribution rate when drug distribution is perfusion limited. If Drug XY-134 is not highly lipophilic, this drug distribution is permeability limited, and change of blood flow rate will not affect Drug XY-134 distribution, then the onset of the drug induced effect is normal. (See slide 59 in Powerpoint-3:Distribution2)

**Question 2 (1 point each):**

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|---|---|---|
| T | F | The volume of distribution depends only on the degree of plasma binding. |
| T | F | Drugs are generally less well distributed to highly perfused tissues. |
| T | F | Ionized drug are hard to cross most membrane barriers. |
| T | F | Blood flow rate does not affect drug distribution rate at all. |

False
False
True
False