جامعة بيرزيت
BIRZEIT UNIVERSITY

Homework 5

Bio pharmaceutics & Pharmacokinetics/PHAR434

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The data in Table 16-22 represent the average findings in antibiotic plasma samples taken from 10 humans (average weight 70 kg), tabulated in a 4-way crossover design.

A.Which of the four drug products in Table 16-22 would be preferred as a reference standard for the determination of relative bioavailability? Why?

B. From which oral drug product is the drug absorbed more rapidly?

C. What is the absolute bioavailability of the drug from the oral solution?

D. What is the relative bioavailability of the drug from the oral tablet compared to the reference standard?

E. From the data in Table 16-22, determine:

(i) Apparent *VD*

(ii) Elimination *t1/2*

(iii) First-order elimination rate constant *k*

(iv) Total body clearance

TABLE 16-22 Comparison of Plasma Concentrations of Antibiotic, as Related to Dosage Form and Time

	Plasma Concentration (μg/mL)			
Time after Dose (h)	IV Solution (2 mg/kg)	Oral Solution (10 mg/kg)	Oral Tablet (10 mg/kg)	Oral Capsule (10 mg/kg)
0.5	5.94	23.4	13.2	18.7
1.0	5.30	26.6	18.0	21.3
1.5	4.72	25.2	19.0	20.1
2.0	4.21	22.8	18.3	18.2
3.0	3.34	18.2	15.4	14.6
4.0	2.66	14.5	12.5	11.6
6.0	1.68	9.14	7.92	7.31
8.0	1.06	5.77	5.00	4.61
10.0	0.67	3.64	3.16	2.91
12.0	0.42	2.30	1.99	1.83
AUC $\left(\frac{\mu g}{mL} \times h\right)$	29.0	145.0	116.0	116.0

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Answers / H.W 5

A ① Reference standard should not have statistical difference between AUC for test and reference products, also the value of AUC and the form of drug (The Bioavailability) → **oral solution**

B ② **oral solution** of course ; because 1st its liquid, so it will absorb rapidly. and 2nd its AUC is the highest one.

C ③ Absolute Bioavailability => % Absorption = $\frac{D_{IV} * AUC_{oral}}{D_{oral} * AUC_{IV}} * 100\%$

(Here also explain why oral solution is the Ref)

For Q.A $= \frac{2 * 145}{10 * 29} * 100\% \Rightarrow$ **100 % or 1 (without %)**

D ④ Relative Bioavailability => % Relative B.A. = $\frac{D_{Ref} * AUC_{Test}}{D_{test} * AUC_{Ref}} * 100\%$

Ref = oral solution , Test = oral Tablet.

$= \frac{10 * 116}{10 * 145} * 100\% \Rightarrow$ **80 % or 0.8 (without %)**

E ⑤ First of all, we need to sketch a graph (I.V).

From graph I conclude that $C_p^\circ = 6.48$ µg/mL

(i) $VD = \frac{Dose_{(q)}}{C_{p^0}} \Rightarrow \frac{2\ mg/kg \times (1000\ mg/g)}{6.48\ mg/mL}$

$= 308.64 \approx 309$

$V_d = 309\ mL/kg$ → For 1 kg, the samples (10 humans and average weight 70 kg).

(ii) $t_{\frac{1}{2}}$ Elimination = Range (3.00 - 330 hr)

From graph I conclude that $t_{\frac{1}{2}} = 3.00$ hr

$t_{\frac{1}{2}}$ is constant = 3 hr

(iii) Rate constant $(K) = \frac{0.693}{t_{\frac{1}{2}}} \Rightarrow \frac{0.693}{3\ hr}$

$K = 0.231\ h^{-1}$

(iv) Total body clearance $(Cl_T) = K * V_D \Rightarrow 0.231 h^{-1} * 309\ mL/kg$

$= 71.379 \approx 71.4\ mL/kg.hr$

$Cl_T = 71.4\ mL/kg.hr$ → For 1 kg, the samples (10 humans and average weight = 70 kg)