	TANTA UNIVERSITY Department of Clinical Pharmacy (2nd Year Pharmacy)			
	COURSE TITLE:	Final exam	Pharmacokinetics	COURSE CODE: 3168
DATE:	10/6/ 2021	TERM: Second	TOTAL ASSESSMENT MARKS: 150	TIME ALLOWED:2 h

- Each question worth 2 marks.
-Select only ONE best answer for each question.
-Transfer your selections properly to the answer sheet.
-Answer outside the answer sheet will not be marked.

Questions (1-10)

A single 300 mg dose of a drug was given by IV bolus administration and the plasma concentrations were determined. A plot of the plasma cone-time profile was linear on a semi log graph paper. The y-intercept of the plot was 50 mg/L and the slope of the line was -0.025 hr^{-1}. Calculate:

1- The elimination rate constant:
A- 0.058 hr^{-1} B- 0.012 hr^{-1} C- 0.036 hr^{-1} D- 0.025 hr^{-1}

2- The volume of distribution of this drug is:
A-10 L B- 6 L C- 30 L D- 2 L

3- The half-life of this drug is:
A- 6 hr B- 20 hr. C- 12 hr. D- 2 hr.

4- The AUC after administration of 300 mg IV is:
A- 517 mg.hr\L B- 129 mg.hr\L
C- 376 mg.hr\L D- 862 mg.hr\L

5- Total body clearance of this drug is:
A- 0.348 L\hr B- 0.51 L\hr C- 0.156 L\hr D- 0.825 L\hr

6- The plasma concentration of this drug 12 hours after drug administration is:
A- 12.5 mg\L B- 25 mg\L C- 37 mg\L D- 16 mg\L

7- The time required to achieve plasma concentration 15 mg\ml is:
A- 6 hr. B- 12 hr. C- 21 hr. D- 30 hr.

8- The slope of the plasma cone-time profile on semilog scale if a dose of 600 mg was given by iv bolus is:
A- -0.05 hr^{-1} B- -0.06 hr^{-1} C- -0.01 hr^{-1} D- -0.025 hr^{-1}

9- The initial plasma concentration if the dose of the drug was 600 mg iv bolus is:
A- 100 mg\L B- 25 mg\L C- 50 mg\L D- 75 mg\L

10- The AUC after administration of 600 mg IV is:
A- 517 mg.hr\L B- 1724 mg.hr\L
C- 376 mg.hr\L D- 862 mg.hr\L

11- In method of residuals, the slope of the residual line was -0.3 hr^{-1}, then the absorption rate constant is:

A- 0.69 hr^{-1} B- 1.38 hr^{-1} C- 0.87 hr^{-1} D- 1.16 hr^{-1}

12- The fraction of the intravenous bolus dose (Q) which is left after 5 half-lives have elapsed is:

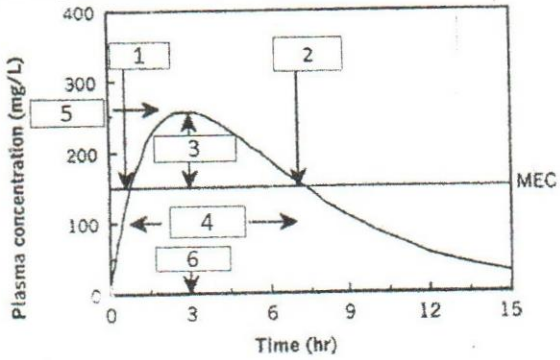
A- 1\2 B- 1\4 C- 1\8 D- 1\32

13- AUC of a certain drug in an individual is proportional to the administered doses.

A- True B- False

Question 14-19:

Regarding the following graph that was drawn after administration of single oral dose of a drug to a patient.:



14- Number 1 stands for:

A- Onset B- Offset C- Duration D- Intensity

15- Number 2 stands for:

A- Onset B- Offset C- Duration D- Intensity

16- Number 3 stands for:

A- Onset B- Offset C- Duration D- Intensity

17- Number 4 stands for:

A- Onset B- Offset C- Duration D- Intensity

18- Number 5 stands for:

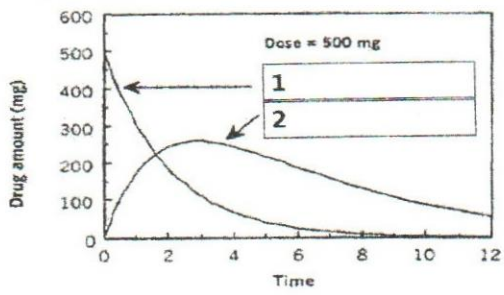
A- Cp_{max} B- Offset C- Duration D- T_{max}

19- Number 6 stands for:

A- Cp_{max} B- Offset C- Duration D- T_{max}

Question 20- 21:

Regarding the following graph that was drawn after administration of single oral dose of 500 mg of a drug to a patient.



30- Product A is rapidly absorbed than product B.
A- True B- False

31- Product B has no pharmacological effect.
A- True B- False

32- Product A will produce toxicity.
A- True B- False

Question 33-36

The average half-life of a antiasthmatic drug in normal adults is 3 hr, and its average TBC is 0.75 L/hr. The drug was infused intravenously at a constant rate of 75 mg/kg-hr until steady state was reached.

33- What is the average volume of distribution of the drug is:
A- 3.2 L B- 4.7 L C- 1.8 L D- 0.76 L

34- The steady-state plasma concentration is achieved after:
A- 25 hr. B- 15 hr. C- 10 hr. D- 30 hr.

35- The steady-state plasma concentration achieved after drug infusion at a constant rate of 75 mg/kg-hr is:
A- 200 mg\L B- 500 mg\L C- 100 mg\L D- 350 mg\L

36- If the we need to achieve the steady state immediately calculated in previous question, what would be the IV loading dose?
A- 100 mg B- 500 mg C- 240 mg D- 320 mg

Questions 37-38:

The half-life of a new anti-infective agent in patients with normal renal function is 4hr. Eighty percent of the administered dose is eliminated by the kidneys. The average dose inpatients with normal renal function is 500 mg daily. The average volume of distribution is 13 liters.

37- Estimate the half-life in a patient who has a creatinine clearance of 25 ml/min (normal= 100 ml/min).
A- 10 hr. B- 15 hr. C- 20 hr. D- 30 hr.

38- What dose should you use in patients with creatinine clearance of 25 ml/min:
A- 50 mg B- 200 mg C- 440 mg D- 320 mg

(For questions 39-47) An antibiotic follows a one-compartment kinetic model is administered as 300 mg IV injection every 8 hr. The patient elimination rate constant is 0.15 hr^{-1} and volume of distribution is 45 L, calculate:

39. Total body clearance (TBC)
A) 6.75 L/hr. B) 299.7 L/hr. C) 207.94 L/hr. D) 1.00 L/hr.

20- Curve 1 refers to:

A- The change in the drug amount in the body after a single oral dose of a drug

B- The change in the drug amount in GIT after a single oral dose of a drug

21- Curve 2 refers to:

A- The change in the drug amount in the body after a single oral dose of a drug

B- The change in the drug amount in GIT after a single oral dose of a drug

---

22- Lag time is:

A- The time required to achieve the maximum concentration after single oral dose.

B- The time required after drug administration to reach the MEC

C- The delay time before starting drug absorption.

Questions 23-28:

A single oral dose of 500 mg of a drug (100% bioavailable) was given to a patient. The equation that describes the plasma concentration time profile is:

$Cp = 96 (e^{-0.15\ t} - e^{-1.8\ t})$

for the drug in this patient. Assuming that the concentration is in mg/L and the first-order rate constants are in hr^{-1} .

Calculate:

23- T_{max}:

A- 1.5 hr. B- 3 hr. C- 6 hr. D- 4 hr.

24- Cpmax:

A- 100 mg\L B- 70 mg\L C- 50 mg\L D-35 mg\L

25- $t_{1/2}$:

A- 1.5 hr. B- 3.2 hr. C- 4.6 hr. D- 5.4 hr.

26- Vd :

A-15 L B- 9.2 L C- 3.5 L D- 5.7 L

27- TBC:

A- 0.855 L\hr B- 0.51 L\hr

C- 1.5 L\hr D- 0.425 L\hr

28- AUC after administration of a single oral 500 mg of the drug:

A- 917 mg.hr\L B- 585 mg.hr\L

C- 376 mg.hr\L D- 862 mg.hr\L

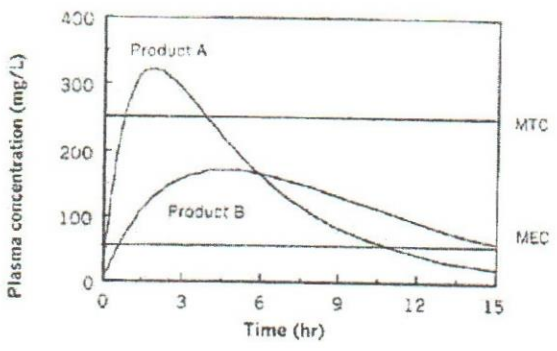
29- ..... means that the drug in two or more similar dosage forms reaches the systemic circulation at the same rate with same relative extent.

A- Bioequivalence B- Absolute bioavailability

C- Relative bioavailability

Questions 30-32:

Regarding the following graph:



40. Average concentration at steady state ($Cp_{(av)ss}$)
A) 10.00 mg/L. B) 5.56 mg/L. C) 0.13 mg/L. D) 0.18 mg/L.

41. Average concentration ($Cp_{(av)}$) at 6 hr after the last injection
A) 0.13 mg/L. B) 0.001 mg/L. C) 1.80 mg/L. D) 2.26 mg/L.

42. Average concentration ($Cp_{(av)}$) 5 hr after the beginning of the injections
A) 0.18 mg/L. B) 2.93 mg/L. C) 1.10 mg/L. D) 6.70 mg/L.

43. Maximum concentration at steady state ($Cp_{(max)ss}$)
A) 9.54 mg/L. B) 6.67 mg/L. C) 17.20 mg/L. D) 8.67 mg/L.

44. Minimum concentration at steady state ($Cp_{(min)ss}$)
A) 5.20 mg/L. B) 6.67 mg/L. C) 2.87 mg/L. D) 0.01 mg/L.

45. Area under the curve ($AUC_{(0-\infty)ss}$)
A) 63.6 mg.hr./L. B) 172 mg.hr./L. C) 44.4 mg.hr./L. D) 12.4 mg.hr./L.

46. Area under the curve ($AUC_{(0-Tau)ss}$)
A) 120 mg.hr./L. B) 63.6 mg.hr./L. C) 44.4 mg.hr./L. D) 23.8 mg.hr./L.

47. Loading dose
A) 300 mg. B) 172 mg. C) 374 mg. D) 429 mg.

(For questions 48-57) After administration of a single IV bolus dose of 120 mg of a drug to a healthy volunteer, the pharmacokinetics of this drug followed a two-compartment model. The following parameters were obtained: $A = 5.5$ mg/L, $B = 0.78$ mg/L, $\alpha = 6.2\ hr^{-1}$, $\beta = 0.32\ hr^{-1}$, $K_{10} = 1.89\ hr^{-1}$, $K_{12} = 3.58\ hr^{-1}$ and $K_{21} = 1.05\ hr^{-1}$, Calculate:

48. Plasma concentration at time zero (Cp_0)
A) 7.35 mg/L. B) 3.03 mg/L. C) 6.28 mg/L. D) 4.72 mg/L.

49. Plasma concentration after 1 hr from drug administration
A) 1.01 mg/L. B) 0.57 mg/L. C) 1.25 mg/L. D) 1.05 mg/L.

50. The slope of the terminal part of the concentration-time curve (at the pseudo equilibrium)
A) 1.89 hr^{-1}. B) 0.78 hr^{-1}. C) 0.34 hr^{-1}. D) 1.79 hr^{-1}.

51. Volume of distribution (Vd_c)
A) 19.11 L. B) 10.26 L. C) 14.3 L. D) 18.40 L.

52. Volume of distribution (Vd_β)
A) 101.6 L. B) 100.1 L. C) 112.8 L. D) 14.19 L.

53. Volume of distribution (Vd_{ss})
A) 11.96 L. B) 84.25 L. C) 37.10 L. D) 88.40 L.

54. Alpha half-life ($\alpha_{1/2}$)
A) 0.13 hr^{-1}. B) 0.08 hr^{-1}. C) 0.89 hr^{-1}. D) 0.11 hr^{-1}.

55. Beta half-life ($\beta_{1/2}$)
A) 1.27 hr^{-1}. B) 2.17 hr^{-1}. C) 3.65 hr^{-1}. D) 0.89 hr^{-1}.

56. Area under the curve (AUC)
A) 1.54 mg.hr/L. B) 3.89 mg.hr/L. C) 3.32 mg.hr/L. D) 26.43 mg.hr/L.

57. Total body clearance (TBC)
A) 36.09 L/hr. B) 4.54 L/hr. C) 78.05 L/hr. D) 19.30 L/hr.

(For questions 58-63) Patient received a single 1000 mg IV dose of an antibiotic (QAZ) follows a one-compartment kinetic model that is only eliminated by renal excretion. Urine and plasma samples were collected, and the following results were obtained:

Interval (hr)	Urine volume (mL)	Urine conc (µg/mL)	Plasma Concentration (Cp_{tmid}) (µg/mL)
0-1	39.41	1.24	not determined
1-2	41.18	0.59	not determined
2-4	58.82	0.29	0.4 ug/ml at time 3hr
4-8	147.06	0.03	very low

58. Calculate the average renal excretion rate of the drug during the first urine collection interval (0-1 hr)
A) 24.46 µg/hr. B) 31.90 µg/hr. C) 48.69 µg/hr. D) 69.31 µg/hr.

59. Calculate the average renal excretion rate of the drug during the third urine collection interval (2-4 hr)
A) 17.06 µg/hr. B) 8.53 µg/hr. C) 24.46 µg/hr. D) 200.00 µg/hr.

60. Calculate the renal clearance of this drug in this patient
A) 200.00 L/hr. B) 3.46 L/hr. C) 43.25 L/hr. D) 21.32 L/hr.

61. The urine was collected in a patient over 24-hr period to determine the creatinine clearance. The total volume of urine collected was 1500 mL and the creatinine concentration in urine was 0.95 mg/ml. If the serum creatinine determined in this patient was 0.9 mg/dL
A) 1.10 L/hr. B) 65.97 L/hr. C) 6597.22 L/hr. D) 109.95 L/hr.

62. Based on your calculations, which of the following processes surely involved in the excretion of antibiotic (QAZ)
A) Glomerular filtration B) Active secretion C) Reabsorption
D) A&C E) All of the above

63. If we want to achieve an average drug concentration at steady state ($Cp_{(av)ss}$) of 1.45 ug/mL, what is the appropriate maintenance dose for this drug to be taken every 8 hr?

A) 200 mg. B) 500 mg. C) 40 mg. D) 250 mg.

(For questions 64-69) Kinetocin is a drug which follows a one-compartment kinetic model. The total body clearance = 145 mL/min, volume of distribution (V_d) = 99.6 L, and therapeutic range of the drug is 1.6-4.7 mg/L. Intravenous bolus doses of 800 mg of the drug are administered every 8 hr to a patient. Please estimate the following parameters:

64. The plasma half life
A) 0.5 hr. B) 2 hr. C) 7 hr. D) 8 hr.

65. The maximum concentration after the first dose
A) 1 mg/L. B) 3 mg/L. C) 7 mg/L. D) 8 mg/L.

66. The minimum concentration after the first dose (after tau)
A) 1 mg/L. B) 2 mg/L. C) 4 mg/L. D) 8 mg/L.

67. The minimum concentration at steady state
A) 1 mg/L. B) 2 mg/L. C) 4 mg/L. D) 8 mg/L.

68. The average steady state concentration
A) 11.5 mg/L. B) 23 mg/L. C) 15.78 mg/L. D) 7.48 mg/L.

69. The loading dose to reach steady state immediately
A) 1800 mg. B) 700 mg. C) 1600 mg. D) 800 mg.

(For questions 70-75) The following coefficients and rate constants were obtained by the method of residual after a single IV bolus dose (250 mg) of kinetolol, a drug with a two-compartment kinetic model: A = 27.4 µg/mL, B = 3.85 µg/mL, α = 0.04 min^{-1} and β = 0.02 min^{-1}. Calculate the following kinetic parameters:

70. Beta half-life ($\beta_{1/2}$)
A) 0.2 hr. B) 0.3 hr. C) 0.6 hr. D) 0.8 hr.

71. Alpha half-life ($\alpha_{1/2}$)
A) 0.2 hr. B) 0.3 hr. C) 0.6 hr. D) 0.8 hr.

72. The plasma concentration at 2.8 hr from drug administration
A) 177 µg/L. B) 167 µg/L. C) 0.17 µg/L. D) 0.18 µg/L.

73. The plasma concentration at time zero (Cp_0)
A) 36 µg/mL. B) 31 µg/mL. C) 26 µg/mL. D) 22 µg/mL.

74. The volume of central compartment (Vd_c)
A) 1 L. B) 2 L. C) 5 L. D) 8 L.

75. The plasma AUC
A) 12.2 mg.hr/L. B) 16.4 mg.hr/L. C) 14.6 mg.hr/L. D) 18.9 mg.hr/L.

Equations for the pharmacokinetic Class

For any first order process

$$t_{1/2} = \frac{\ln 2}{k} = \frac{0.693}{k}$$

$$TBC = k\,vd$$

After a bolus iv administration:

$$Cp_0 = \frac{Dose}{Vd} \quad \text{or} \quad \Delta Cp = \frac{Dose}{Vd}$$

$$AUC\Big|_{t=0}^{t=\infty} = \frac{Cp_0}{k}$$

During first order elimination:

$$\log Cp = \frac{-kt}{2.303} + \log Cp_o$$

$$Cp = Cp_o\, e^{-kt}$$

After oral administration of the drug:

$$Cp = \frac{F D k_a}{Vd\,(k_a - k)}(e^{-kt} - e^{-k_a t})$$

$$t_{max} = \frac{\ln k_a - \ln k}{k_a - k} = \frac{\ln (k_a / k)}{k_a - k}$$

Cp versus time plot after a single oral dose

$$y\text{-intercept} = \frac{F D k_a}{Vd\,(k_a - k)}$$

The area under the curve (AUC) :

$$AUC\Big|_{t=0}^{t=\infty} = \frac{F\,Dose}{k\,Vd} = \frac{F\,Dose}{TBC}$$

The Renal and Metabolic Excretion of Drugs:

$$\frac{\Delta A_e}{\Delta t} = k_e\, A_{t\,mid} = k_e\, Vd\, Cp_{t\,mid}$$

$$\frac{\Delta A_e / \Delta t}{Cp_{t\,mid}} = k_e\, Vd = \text{Renal Clearance}$$

$$\text{Renal Cl} = TBC\,\frac{A_{e\,\infty}}{Dose} = \frac{A_{e\infty}}{AUC_{iv}}$$

$$\frac{\Delta A_e}{\Delta t} = k_e\, A = k_e\, A_o\, e^{-k t_{mid}}$$

$$\text{Absolute } F = \frac{A_{e\,\infty\ Oral}}{A_{e\,\infty\ iv}}$$

$$\text{Relative } F = \frac{A_{e\,\infty\ (test)}}{A_{e\,\infty\ (reference)}}$$

AUC by the trapezoidal rule:

$$AUC = (1/2)(C_0+C_1)(t_1-t_0) + (1/2)(C_1+C_2)(t_2-t_1) + \text{+ area under the tail}$$

$$\text{Area under the tail} = \frac{Cp_{last}}{k}$$

After Oral Administration:

$$\text{Absolute } F = \frac{AUC_{oral}}{AUC_{iv}}$$

$$\text{Relative } F = \frac{AUC_{test}}{AUC_{reference}} = \frac{F_{test}}{F_{reference}}$$

During constant rate iv infusion:

$$Cp_{ss} = \frac{K_o}{kVd} \text{ and } L.Dose = Cp\ Vd$$

At s.s. during multiple administration:

$$Cp_{ss.max} = \frac{FD}{Vd\,(1 - e^{-k\tau})}$$

$$Cp_{ss.min} = Cp_{ss.max}\, e^{-k\tau}$$

$$Cp_{ss.max} - Cp_{ss.min} = \frac{FD}{Vd}$$

At steady state:

$$Cp_{average} = \frac{FD}{k\,Vd\,\tau} = \frac{AUC}{\tau}$$

$$R_{accum} = 1/k\tau$$

In patients with renal dysfunction:

$$D_{failure} = D_{normal}[f\,(KF-1)+1]$$

$$t_{1/2\,failure} = \frac{t_{1/2\ normal}}{[f\,(KF-1)+1]}$$

where:

$$KF = \frac{GFR_{failure}}{GFR_{normal}} = \frac{Cr\,Cl_{failure}}{Cr\,Cl_{normal}}$$

$$Cr\,Cl = \frac{(140 - age)(wt\text{ in kg})}{72\ (S.Cr\text{ in mg/dl})}$$

* **For drugs that follow two compartment pharmacokinetic model :**

$$Cp = A\ e^{-\alpha t} + B\ e^{-\beta t}$$

$$\beta = \frac{0.693}{\beta_{t\,1/2}} \qquad \alpha = \frac{0.693}{\alpha_{t\,1/2}} \qquad V_c = \frac{Dose}{Cp_o} = \frac{Dose}{A+B}$$

$$AUC\Big|_o^\infty = \frac{A}{\alpha} + \frac{B}{\beta}$$

$$TBC = \frac{Dose}{AUC\Big|_o^\infty} \qquad TBC = K_{10}\, V_c$$

$$K_{10} = \frac{TBC}{V_c} \qquad K_{21} = \frac{\alpha \cdot \beta}{K_{10}} \qquad K_{12} = (\alpha + \beta) - (K_{21} + K_{10})$$

$$Vd_{ss} = V_c\left(1 + \frac{K_{12}}{K_{21}}\right) \qquad Vd_\beta = \frac{TBC}{\beta} = \frac{V_c \cdot K_{10}}{\beta}$$

** **For nonlinear kinetics:**

$$t_{1/2} = \frac{0.693\ Vd}{V_{max}}(K_m + Cp_{ss}) \qquad \frac{V_{max}}{K_m + Cp_{ss}} = TBC$$

*** **After drug administration by short iv infusion:**

For the first dose:

$$C_p = \frac{K_0}{V\,K}\left(1 - e^{-k\,t'}\right)$$

For multiple doses before achieving steady state:

$$C_p = \frac{K_0}{V\,K}\left(1 - e^{-k\,t'}\right) + Cp_x\, e^{-K\,t'}$$

At steady state:

$$Cp_{max\,ss} = \frac{K_0\left(1 - e^{-k\,t'}\right)}{K\,V_d\left(1 - e^{-k\,\tau}\right)}$$

$$Cp_{min\,ss} = Cp_{max\,ss}\, e^{-K(t - t')}$$