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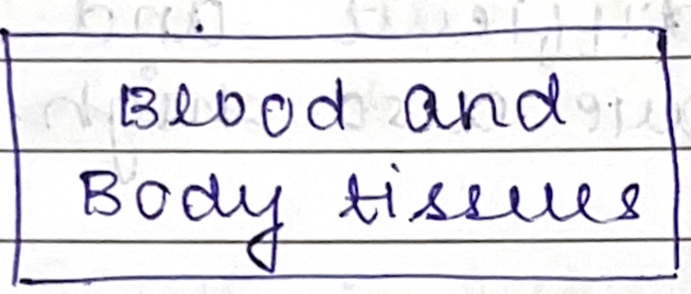
## ONE COMPARTMENT OPEN MODEL (IV BOLUS):

- When drug is given by rapid IV injection, it distributes rapidly and takes about one to three minutes for complete circulation
- This neglects its rate of absorption.




- General expression:

$$\frac{dx}{dt} = \text{Rate in} - \text{Rate out}$$

Here, Rate-in an assumption is absent.
The equation becomes:

$$\frac{dx}{dt} = -\text{Rate out}$$

∴ If rate-out follows first order kinetics, then:

$$\frac{dx}{dt} = -k_e x \quad \text{---(1)}$$

where,
$k_e$ = 1st order elimination.
$x$ = Amt. of drug in body

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## Pharmacokinetic parameters :

(1) Elimination rate constant -

Integration of eq (1)

$$\ln x = \ln x_0 - k_{EL} \quad \text{— (2)}$$

Express eq (2) in expanential form :

$$x = x_0 e^{-k_{Et}} \quad \text{— (3)}$$

Transforming eq (3) into common logarithms (log base 10), we get :

$$\log x = \log x_0 - \frac{k_{Et}}{2.303} \quad \text{— (4)}$$

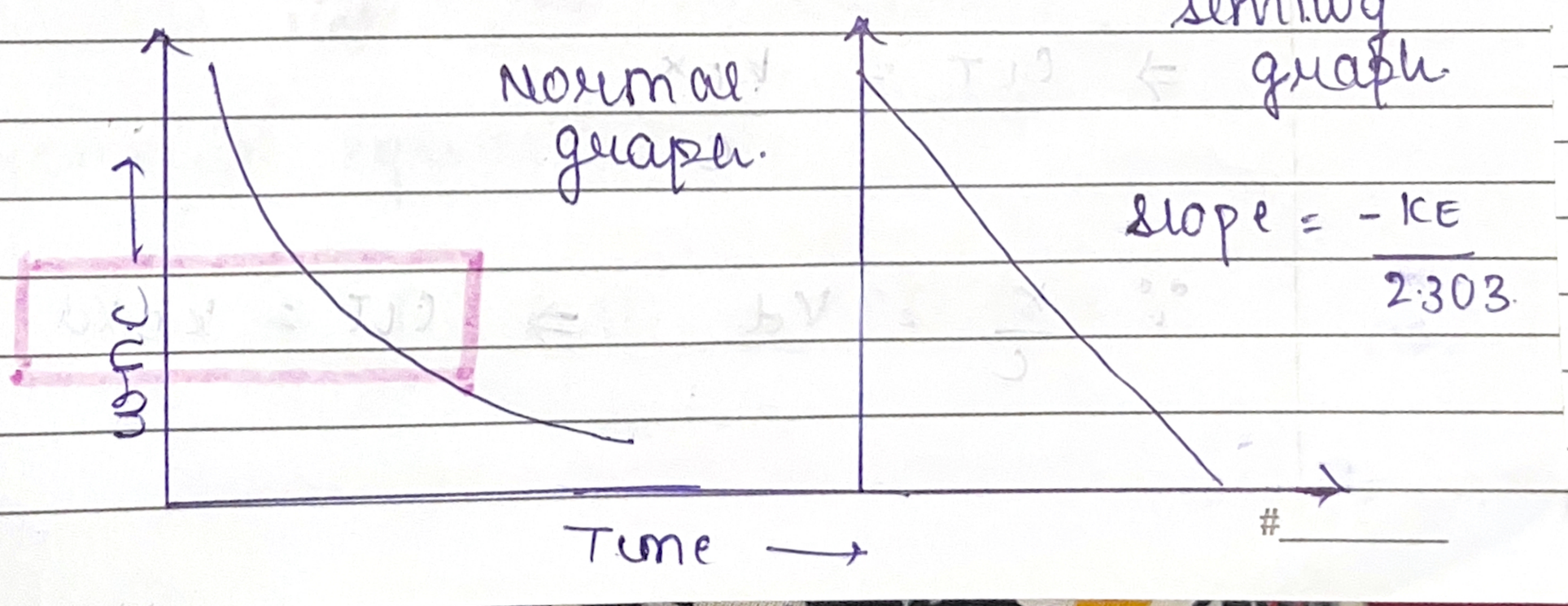
Here,

$x = C$

$x_0 = C_0$

$\therefore$

$$\log C = \log C_0 - \frac{k_{Et}}{2.303} \quad \text{— (5)}$$

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(2) Elimination half-life:

The time taken for the amount of drug in body as well as plasma concentration to decline to half of its initial value

$$t_{1/2} = \frac{0.693}{K_E}$$

(3) Clearance:

Hypothetical volume of body fluids containing the drug which is completely removed in a given period of time.

$$Cl_r = \frac{\text{Rate of elimination}}{PDC.}$$

$$= \frac{dx/dt}{C.}$$

$\because \frac{dx}{dt} = k_E X$

$\Rightarrow C_LT = \frac{K_E X}{C.}$

$\because \frac{X}{C} = V_d \Rightarrow C_LT = K_E X V_d$

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## ONE COMPARTMENT OPEN MODEL (IV INFUSION):

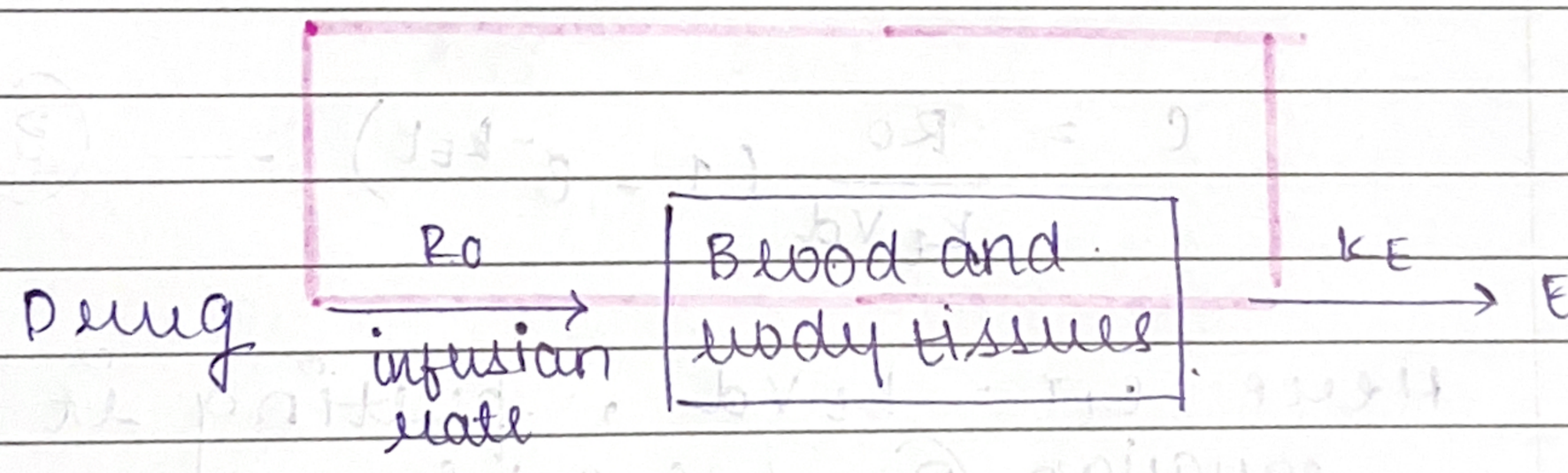
- Sometimes, IV Bolus is unsuitable where the drugs can precipitate toxicity.

- IV infusion is suitable when you require steady-state concentration. In such a situation, the drug is given at a constant rate (zero-order) by IV infusion.

- The half life ($t_{1/2}$) of infusion longer than that of IV Bolus.

Advantages:

(1) Ease of control of rate of infusion
(2) Prevents fluctuating plasma levels
(3) Other drugs, electrolytes and nutrients can be conveniently administered.




General equation.

$$\frac{dx}{dt} = \text{Rate in} - \text{Rate out}$$

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$$\therefore \frac{dx}{dt} = R_0 - K_E X \quad \text{—— (1)}$$

Integrate the above equation — (1)

$$x = R_0 / K_E \left(1 - e^{-K_E t}\right)$$

— (2)

By volume of distribution.

$$x = V_d C.$$

Putting values of $x$ in (2), we get:

$$V_d C = \frac{R_0}{K_E} \left(1 - e^{-K_E t}\right)$$

$$C = \frac{R_0}{K_E V_d} \left(1 - e^{-K_E t}\right) \quad \text{—— (3)}$$

Here $C_L T = K_E V_d$, putting it in equation (3) we get:

$$C = \frac{R_0}{C_L T} \left(1 - e^{-K_E t}\right) \quad \text{—— (4)}$$

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At steady-state, the rate of change of amount of drug in the body is zero $\left(\frac{dx}{dt} = 0\right)$

$$\therefore \quad \frac{dx}{dt} = R_0 - K_E X$$

$$0 = R_0 - K_E X$$

But

$$X = X_{ss} \text{ (steady state)}$$

$$\therefore \quad \boxed{0 = R_0 - K_E X_{ss}} \quad \text{——— (5)}$$

By rearranging the above equation, we get:

$$K_E X_{ss} = R_0$$

$$X_{ss} = R_0 / K_E$$

we know, $X_{ss} = C_{ss}$

$$X_{ss} = V_d C_{ss}.$$

$$\therefore \quad C_{ss} = \frac{R_0}{K_E V_d} \Rightarrow K_E V_d = C_{LT}.$$

$$\therefore \quad \boxed{C_{ss} = R_0 / C_{LT}} \quad \text{——— (6)}$$

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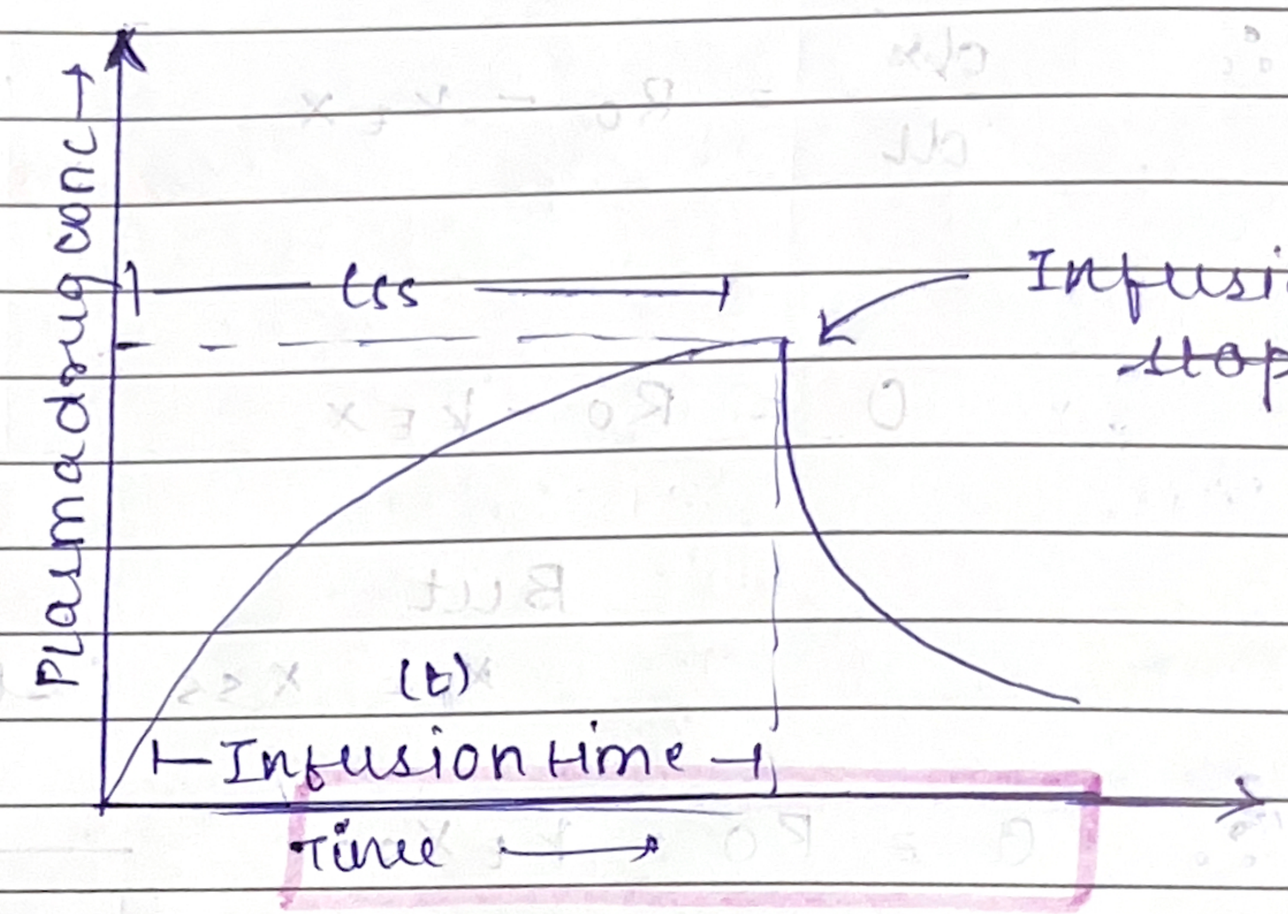
$\Rightarrow$ Css = $\frac{\text{Rate of infuse}}{\text{Total clearance.}}$




$\text{Slope} = \frac{-K_E}{2.303}$

Pharmacokinetic parameters:

(1) Half life

$t_{1/2} = 0.693 / K_E$

(2) slope $= -K_E / 2.303.$

(3) $AUC = \frac{R_0 T}{K_E V_d} = \frac{R_0 T.}{C_L T} = C_{ss} \cdot T.$

($\because C_{ss} = R_0 / C_{LT}$)

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## ONE COMPARTMENT OPEN MODEL EXTRAVASCULAR ADMINISTRATION :

- When a drug is given by an extra vascular route (Oral, IM, Rectal etc) the absorption of the drug is prequisite to its therapeutic activity.

OR

= Rate of Absorption $\propto$ Therapeutic activity of drug.

- It can be described mathematically

↙ ↘

**zero - order process** → Characterized by constant rate of absorption

**First - order process** → Characterized by decline in rate with ARA

$$\frac{dx}{dt} = \text{Rate of absorption} - \text{Rate of elimination}$$

$$\boxed{\frac{dx}{dt} = \frac{dx_{ev.}}{dt} - \frac{dx_E}{dt}} \quad \text{---- (1)}$$

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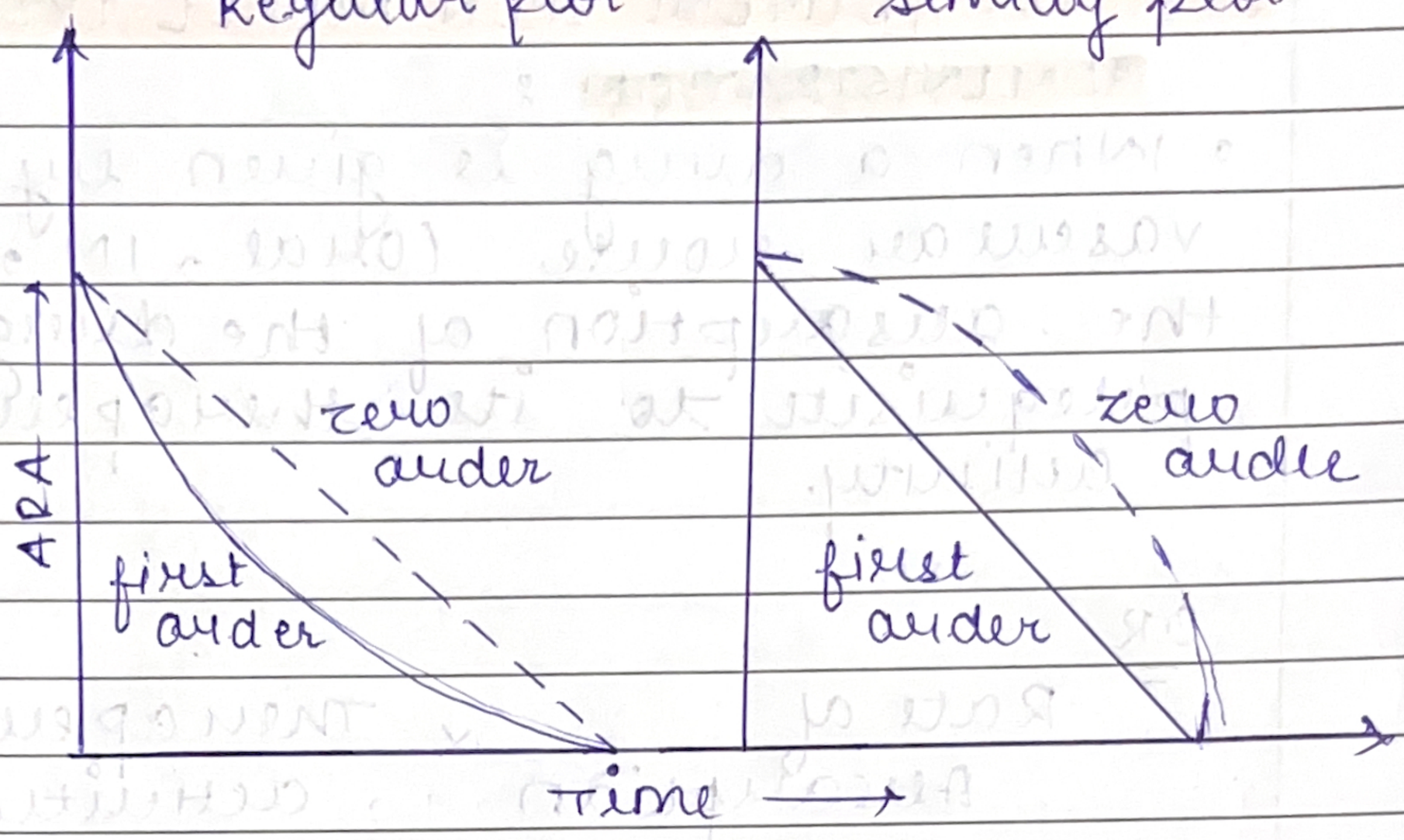
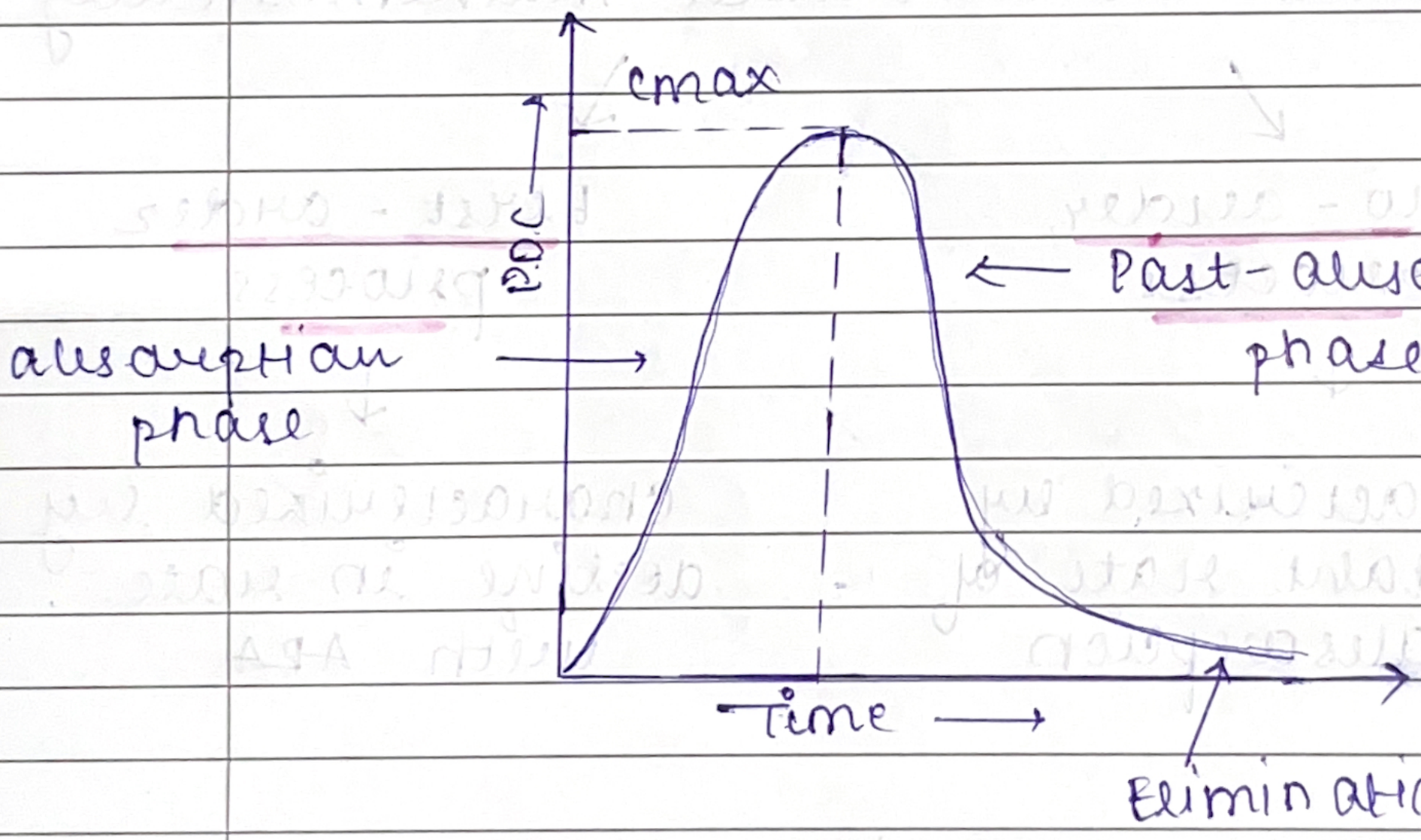
Regular plot




Semilog plot




(1) Absorption phase.

$$\frac{dx_{ev.}}{dt} > \frac{dx_E}{dt}$$

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(2) Post - absorption phase.

$$\frac{dX_{ev}}{dt} = \frac{dX_E}{dt}$$

(3) Elimination phase.

$$\frac{dX_{EV}}{dt} < \frac{dX_E}{dt}$$

⇒ Zero - order absorption :

Drug at ev site → (R.o ↓) → Blood and other tissues → ($k_E$) → Elimin$^n$

Zero order.

⇒ First - order absorption :

Drug at ev site → ($k_a$ ↓) → Blood and other tissues → ($k_E$) → Elimin$^n$.

first order

From eq — (1)

$$\frac{dx}{dt} = k_a X_A - K_E X \quad \text{——— (2)}$$

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Integrate equation (2) then we get:

$$X = \frac{k_a F X_0}{(k_a - k_E)} \left[ e^{-k_E t} - e^{-k_a t} \right]$$

Transforming into terms of conc°, we get:

$$C = \frac{k_a F X_0}{V_d (k_a - k_E)} \left[ e^{-k_E t} - e^{-k_a t} \right] \quad \text{---- (3)}$$

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## ABSORPTION RATE CONSTANT (Residual):

- It is used to resolve a multi-exponential curve into individual components.

For a drug that follows one-compartment kinetics and given EV, the conc. of drug in plasma is expressed by a biexponential eqn.

$$C = \frac{ka F X_0}{V_d (ka - K_E)} \left[ e^{-K_E t} - e^{-ka t} \right] \quad \text{— (1)}$$

If $\frac{ka F X_0}{V_d (ka - K_E)} = A$, a hybrid constant, then:

$$C = A e^{-k_E t} - A e^{-k_a t} \quad \text{— (2)}$$

During elimination when absorption is almost over and the value of $e^{-k_a t}$ approaches to zero, the eqn is reduced to:

$$\overleftarrow{C} = A e^{-K_E t} \quad \text{— (3)}$$

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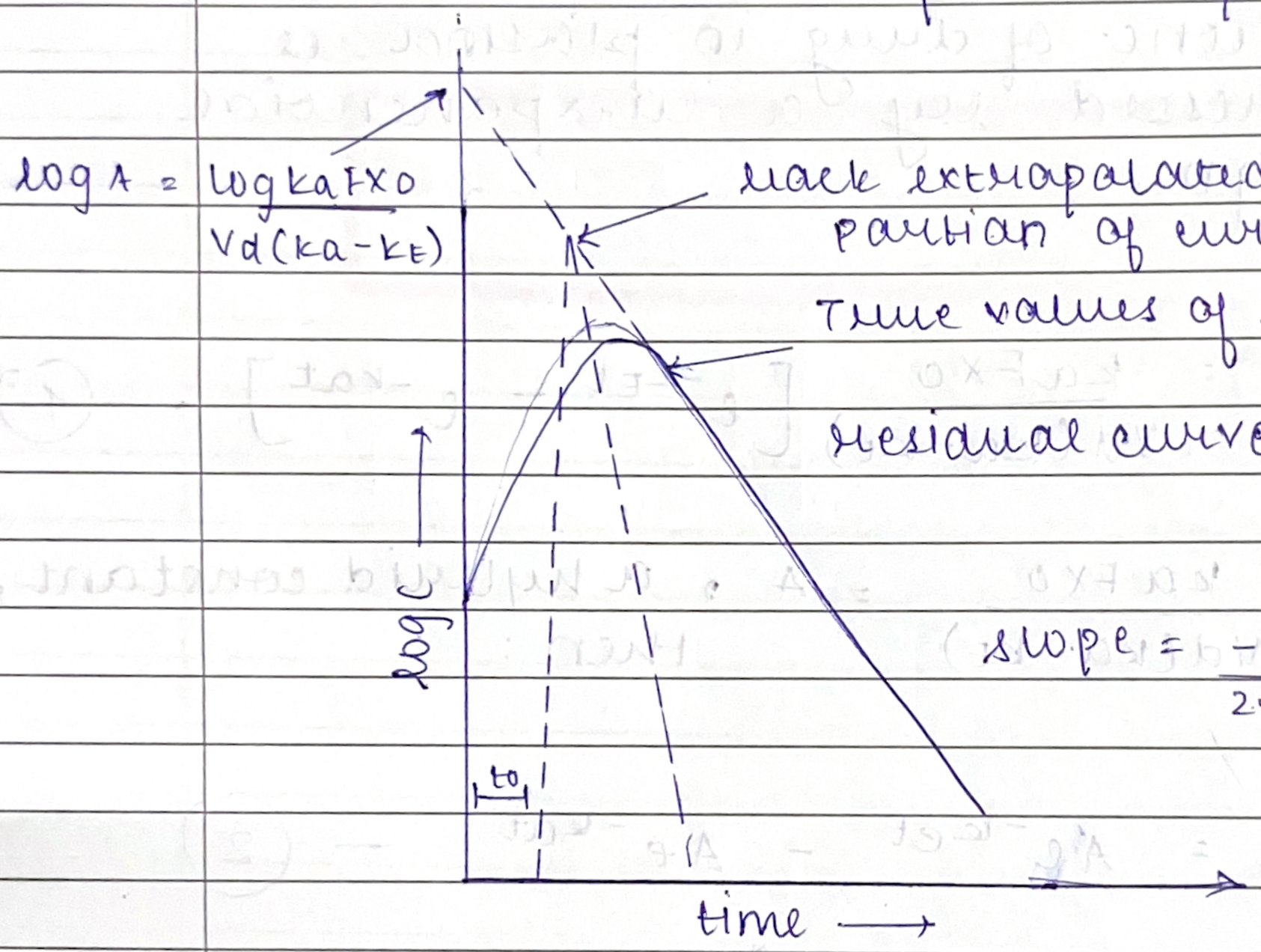
When expressing eqn (3) in log form:

$$\log \overleftarrow{C} = \log A - \frac{K_E}{2.303}$$

where,

$\overleftarrow{C}$ = back extrapolated plasma

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