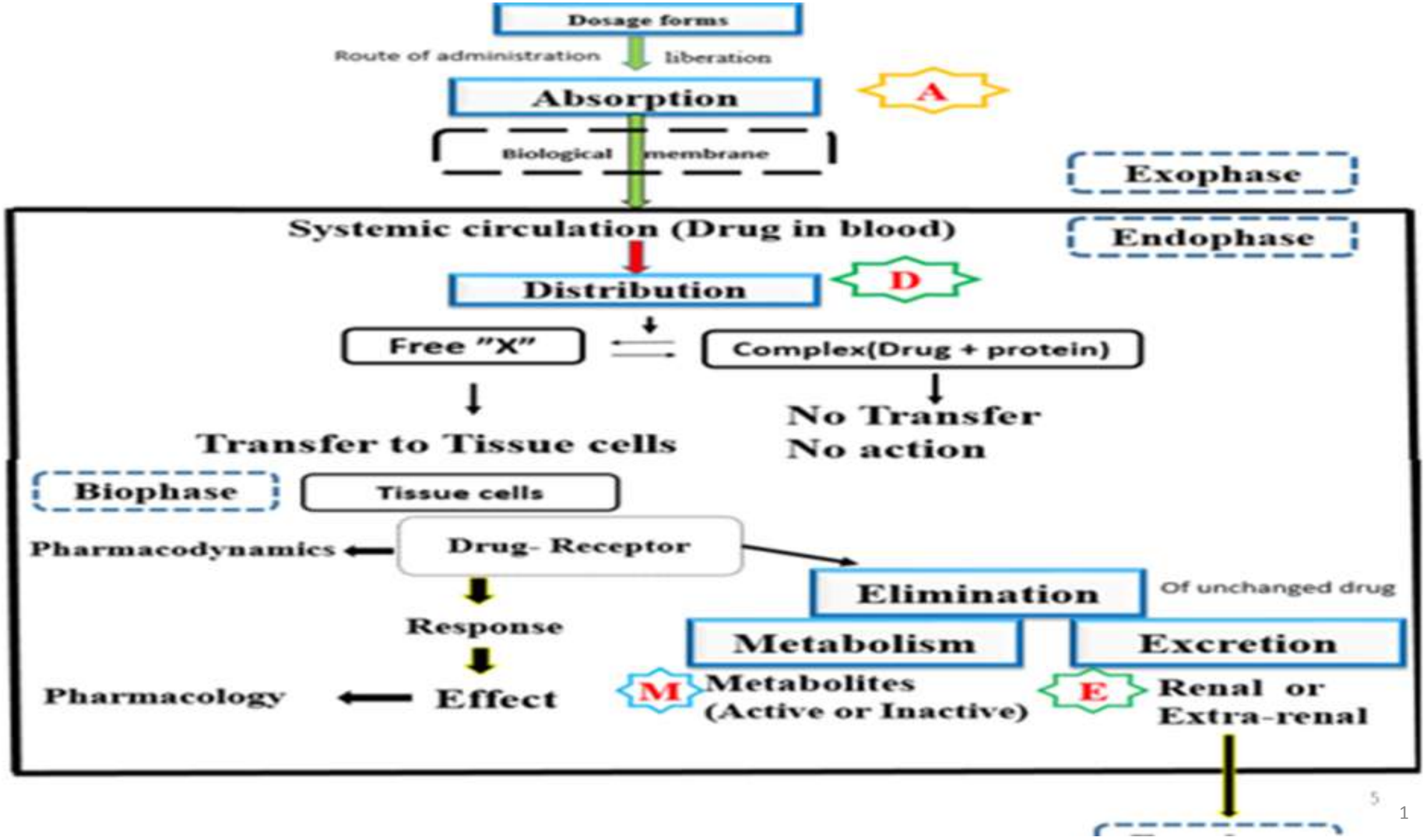

Dosage forms
Route of administration
liberation
Absorption
A
Biological membrane
Exophase
Systemic circulation (Drug in blood)
Endophase
Distribution
D
Free "X"
Complex(Drug + protein)
No Transfer
No action
Transfer to Tissue cells
Biophase
Tissue cells
Pharmacodynamics
Drug- Receptor
Elimination
Of unchanged drug
Response
Metabolism
Excretion
Pharmacology
Effect
M
Metabolites
(Active or Inactive)
E
Renal or
Extra-renal

Pharmacokinetics:

➢The study of factors that govern the time course of drug concentration in the body.

➢The study of the **rates of the transfer processes** associated with the **ADME** of a drug in the intact subject.

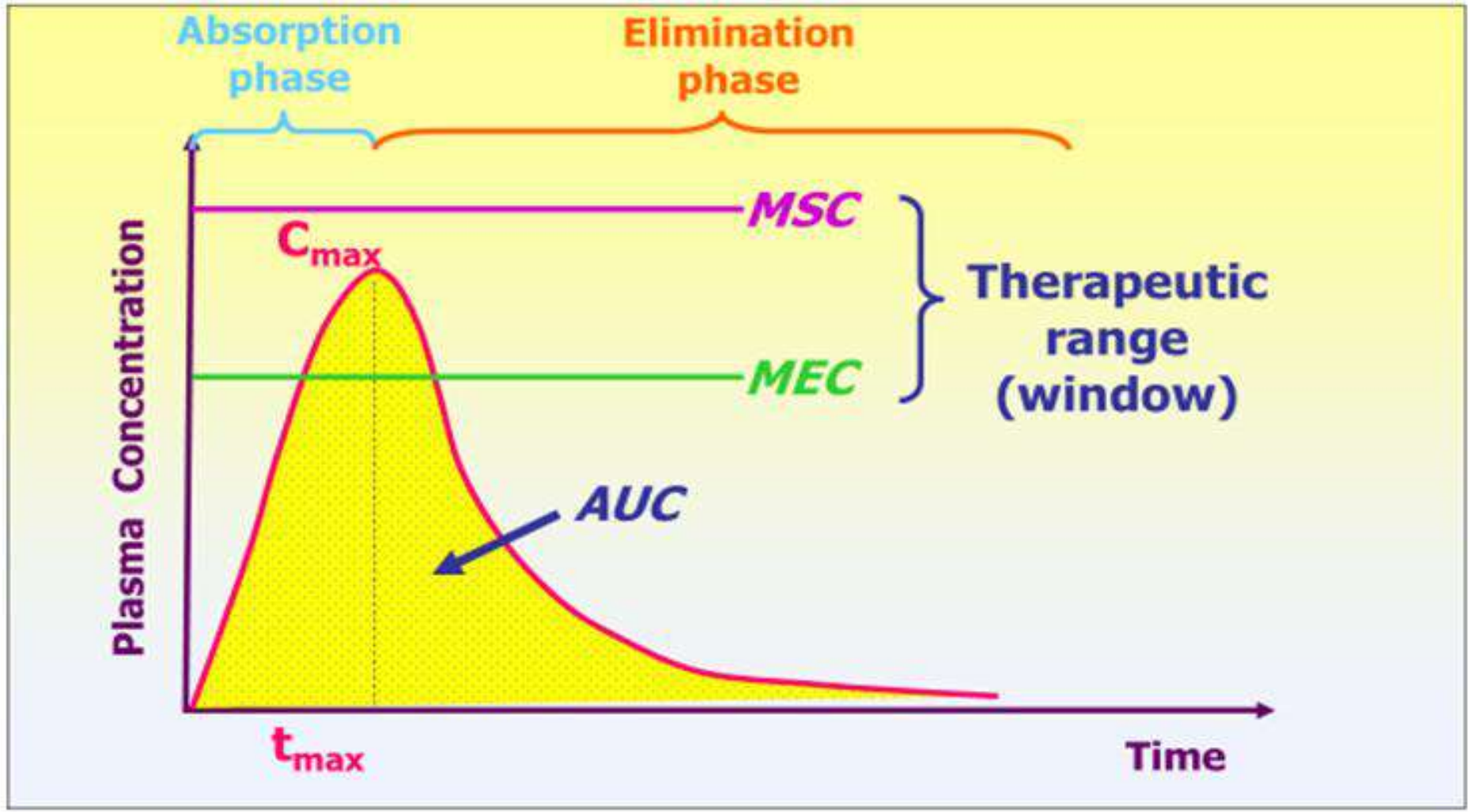


Figure: A typical blood plasma concentration-time curve obtained following the IM administration.

- **Drug Product Performance Parameters:**

1) **Minimum effective concentration (MEC):** Minimum conc. of drug needed at the receptor site to produce the desired pharmacologic effect.

2) **Minimum toxic concentration (MTC):** Minimum drug conc. needed to produce a toxic effect.

3) **Onset time:** The time required for the drug to reach the MEC.

4) **Duration of action:** The difference between onset time and the time for the drug to decline back to the MEC.

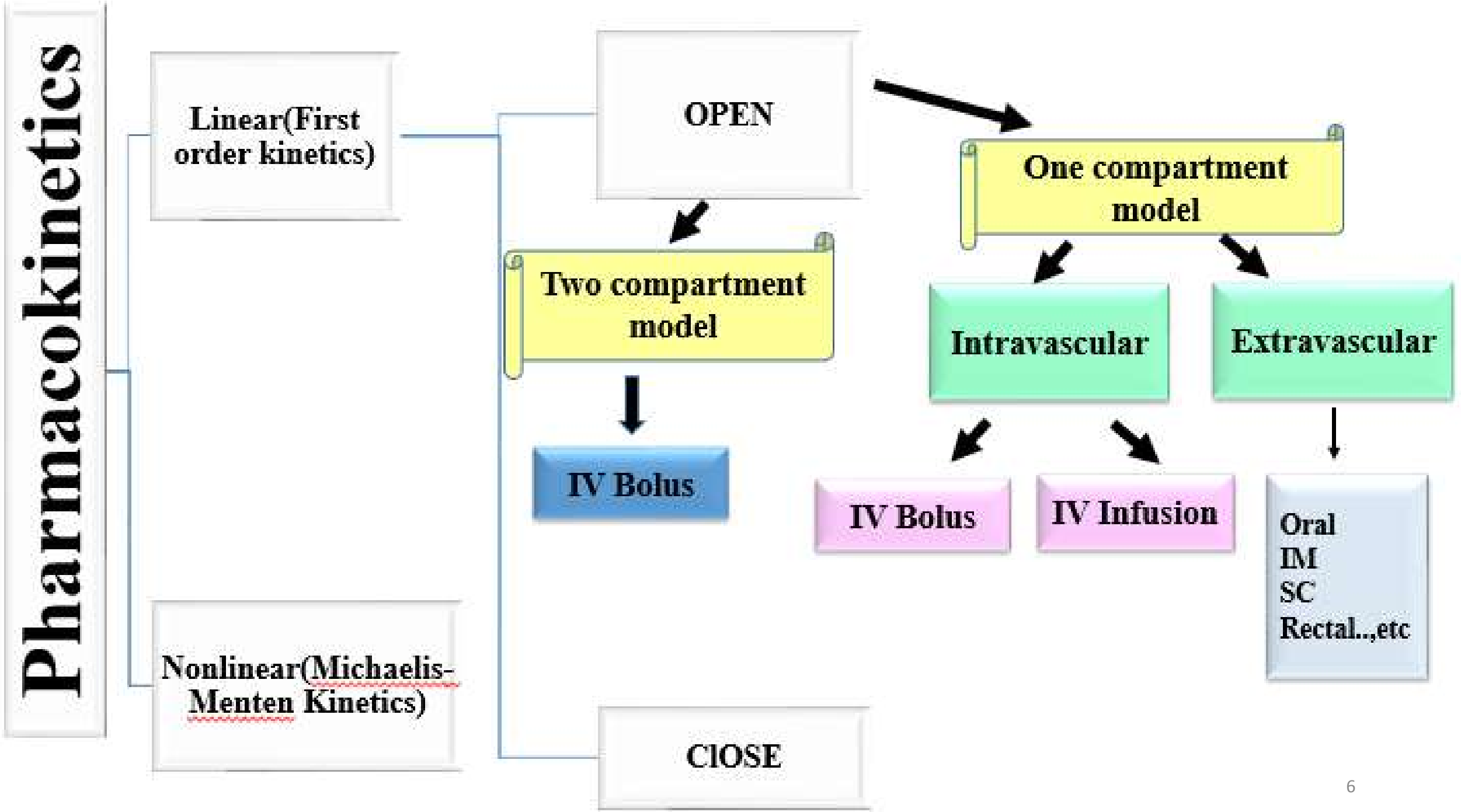
5) **Tmax:** The time at which maximum drug conc. observed in plasma. It is proportional to the rate of drug absorption.

6) Cmax: The maximum drug conc. observed in plasma at a particular time.

7) AUC: It is related to the amount of drug absorbed systemically.

8) Therapeutic range or window: A range of plasma drug concentrations over which the desired response is obtained and toxic effects are avoided.

9)The intensity of pharmacological effect is proportional to the number of drug receptors occupied, which is reflected in the observation that higher plasma drug concentrations produce a greater pharmacologic response.


Pharmacokinetics
Linear(First order kinetics)
Nonlinear(Michaelis-Menten Kinetics)
OPEN
ClOSE
Two compartment model
IV Bolus
One compartment model
Intravascular
Extravascular
IV Bolus
IV Infusion
Oral
IM
SC
Rectal..,etc

Compartment

- **Definition**: An entity which can be described by a definite volume and a concentration of drug contained in that volume.
- It is a group of tissues with similar blood flow and similar drug affinities.

Pharmacokinetics models:

- It is a mathematical model devised to simulate the rate processes of drug absorption, distribution, and elimination.
- These mathematical models make possible the development of equations to describe drug conc. In the body as a function of time.

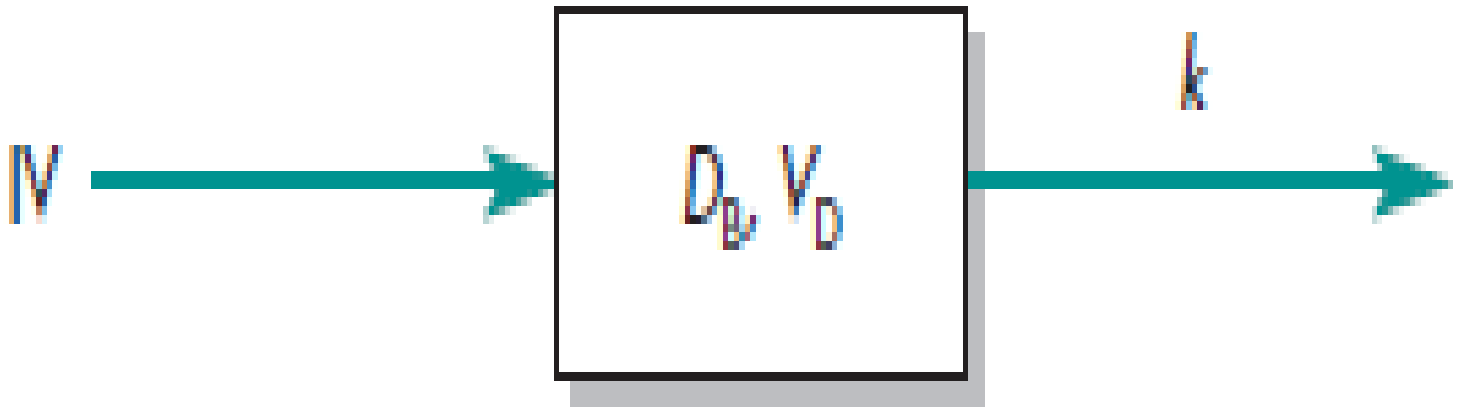
Pharmacokinetic models

Intravascular

Extravascular

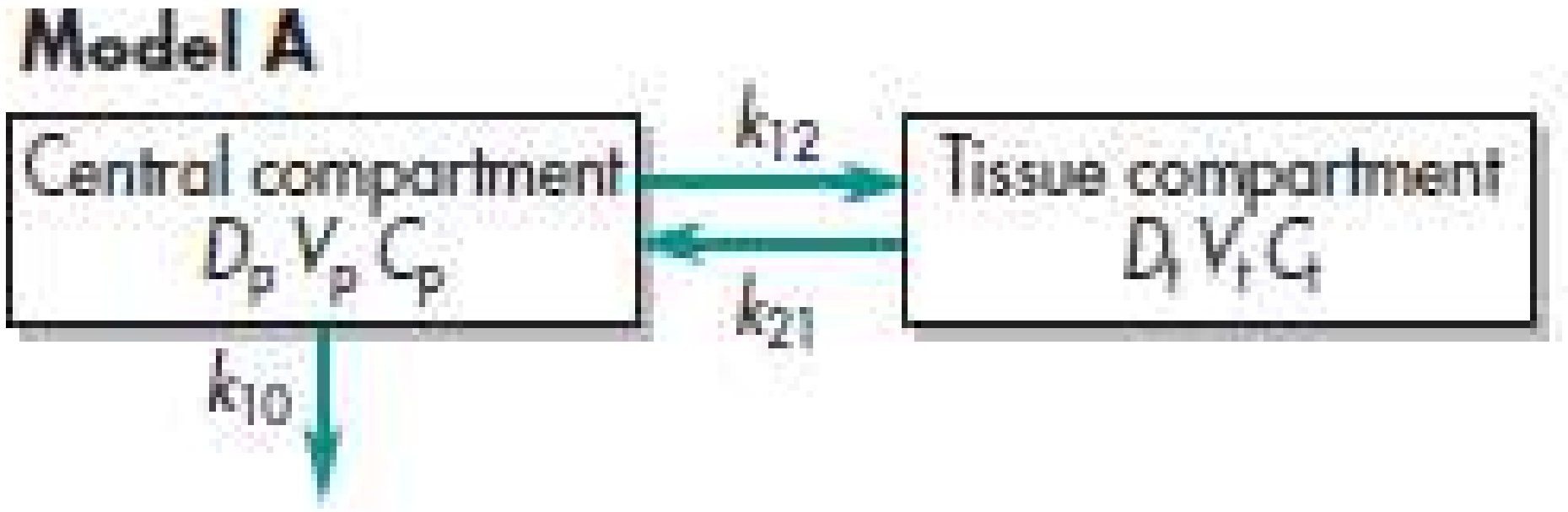
➢ Intravascular administration:

Case 1: One compartment open model



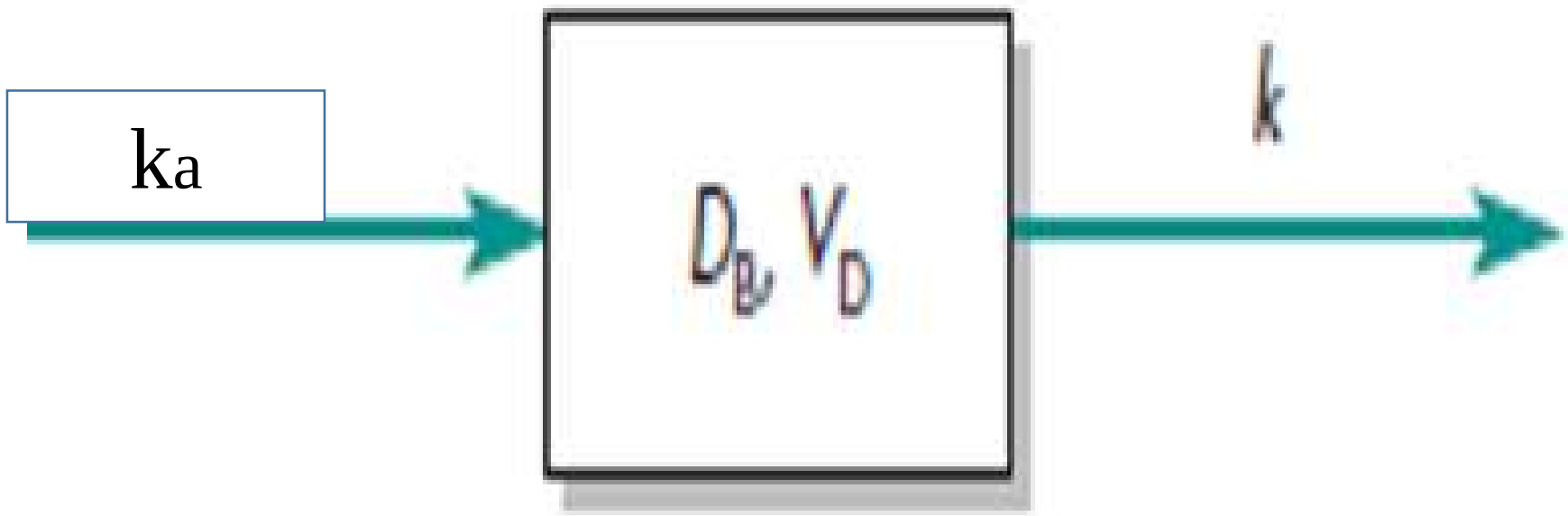
➢ Intravascular administration:

- Case 2: Two compartment open model



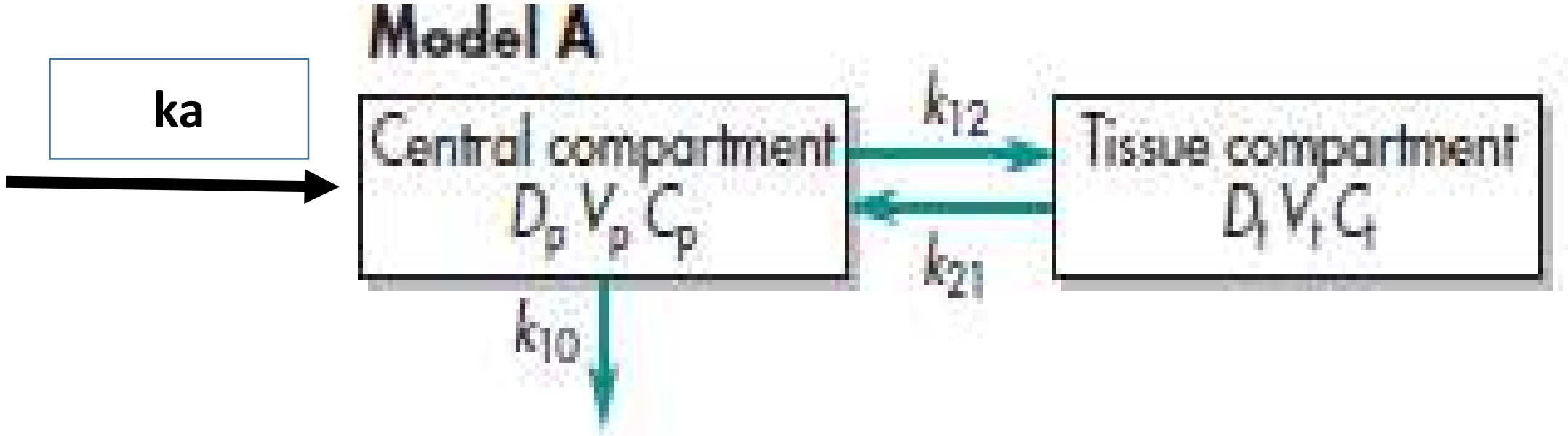
➢ Extravascular administration:

- **Case 1**: One compartment open model with first order absorption:



➢ Extravascular administration:

- **Case 2**: Two compartment open model with first order absorption:



➢Uses of Pharmacokinetic models:

1. Predict plasma, tissue, and urine drug levels with any dosage regimen.
2. Calculate the optimum dosage regimen for each patient individually.
3. Estimate the possible accumulation of drug and/ or metabolites.
4. Correlate drug conc. with pharmacological or toxicological activity.
5. Explain drug interactions.
6. Evaluate differences on the rate or extent of bioavailability between formulations.
7. Give a good picture concerning protein binding.
8. Describe how changes in physiology or disease affect the absorption, distribution, or elimination of the drug.

1. One compartment open model

A. Intravascular administration:

A drug is directly injected into a vein.

❖Advantages:

1.The drug enters into circulation in active form.

2.Desired blood concentration can be obtain.

3.Quick and immediate effect is produced.

4.It is useful in case of emergency.

5.It is useful in an unconscious patient.

1. One compartment open model

❖**Disadvantages**:

1. Drugs which precipitate blood constituents can not be administered.
2. Unwanted reaction , if occur, are immediate.
3. Withdrawal of the drug is not possible.
4. High risk of toxicity.
5. Special person.
6. Slow administration rate. example: **Pentothal.**

- **Example : Pentothal**

Duration of administration	LD 50%
1 sec	76
15 sec	98
30 sec	100
2 min	171
10 min	200

1**. One compartment open model**

Intravascular administration:

- Manners of administration:

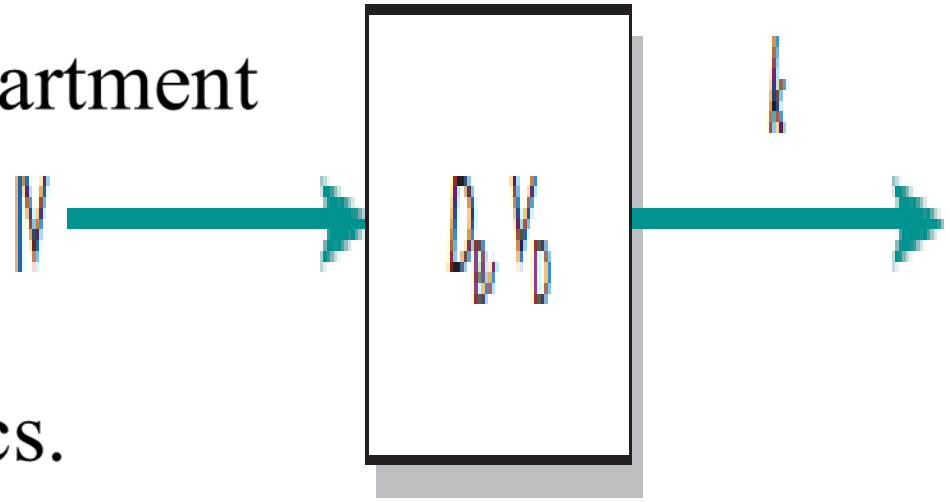
1.IV Bolus.

2.IV Infusion.

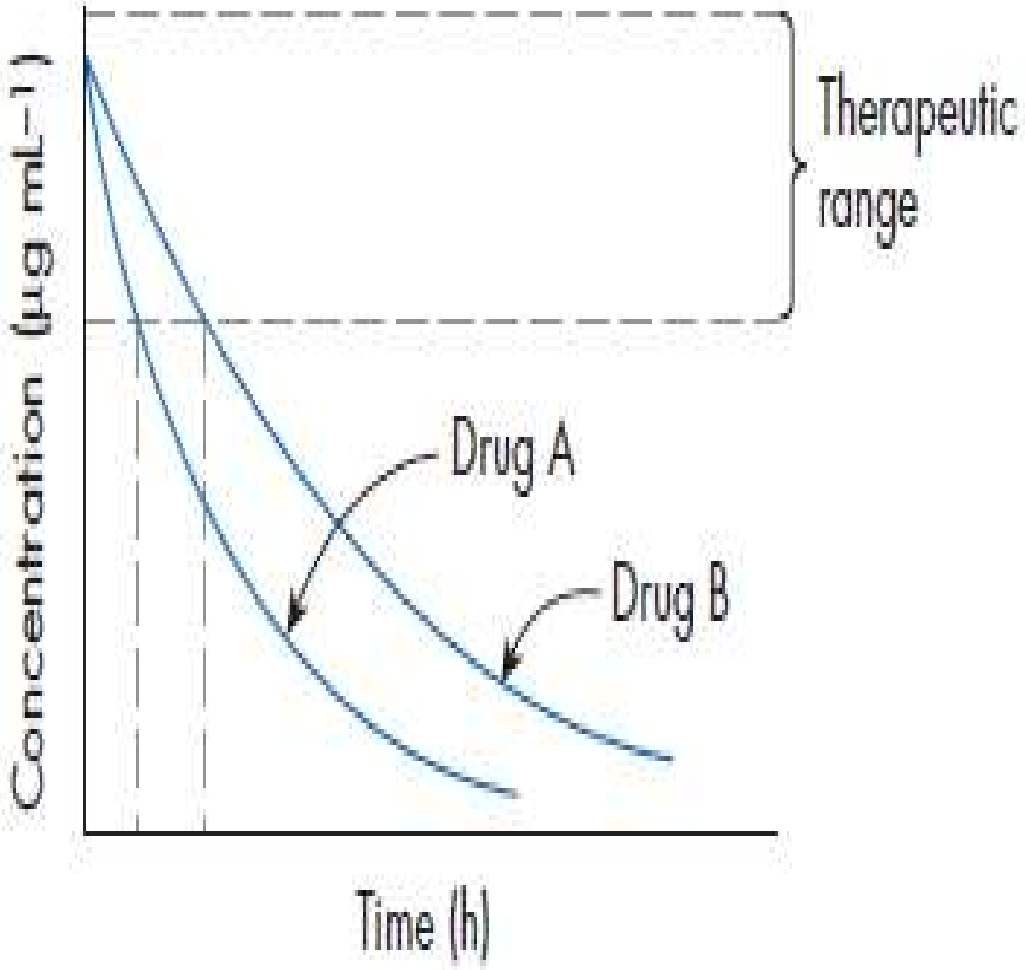
1- IV Bolus

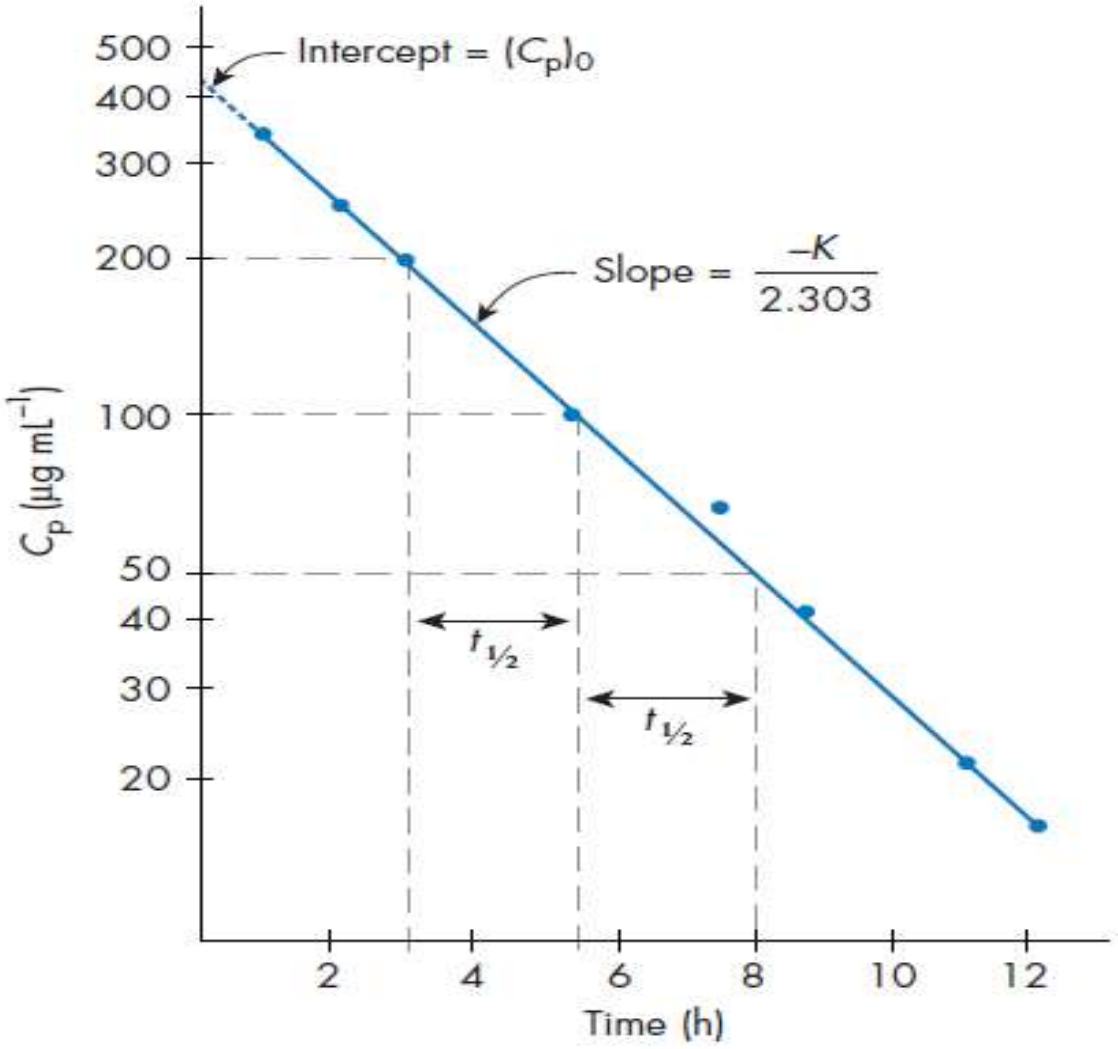
❖ **Assumptions:**

1. The body represented by a single compartment with Volume Vd. $Vd = \frac{Xt}{Ct}$
2. There is no distribution phase.
3. Drug is eliminated by first order kinetics.
4. Any changes that occur in plasma level of a drug reflect proportional changes in tissue drug level.
5. Biological fluids (Blood, Urine, Saliva) are used to determine drug conc.



1- IV Bolus





Semilogarithmic plot of plasma concentration (Cp) versus time following administration of the drug by intravenous bolus

1- IV Bolus

➢ **The elimination half life (t1/2) or "biological half-life":**

- the time (h, min, day, etc.) at which the mass (or amount) of unchanged drug becomes half (or 50%) of the initial mass of drug.
- **Determination of the elimination half life:**
- Equation below expresses the concentration of drug remaining in the plasma at a given time:

$$C_p = (C_p)_0 \, e^{-kt}$$

Rearranging this equation gives $\frac{C_p}{(C_p)_0} = e^{-kt}$

By definition, when $C_p = 0.5\,(C_p)_0$, time $(t) = t_{1/2}$,

hence $0.5 \frac{C_p}{(C_p)_0} = e^{-kt} \rightarrow 0.5 = e^{-kt}$ or $\text{Ln. } 0.5 = -k\, t_{1/2}$

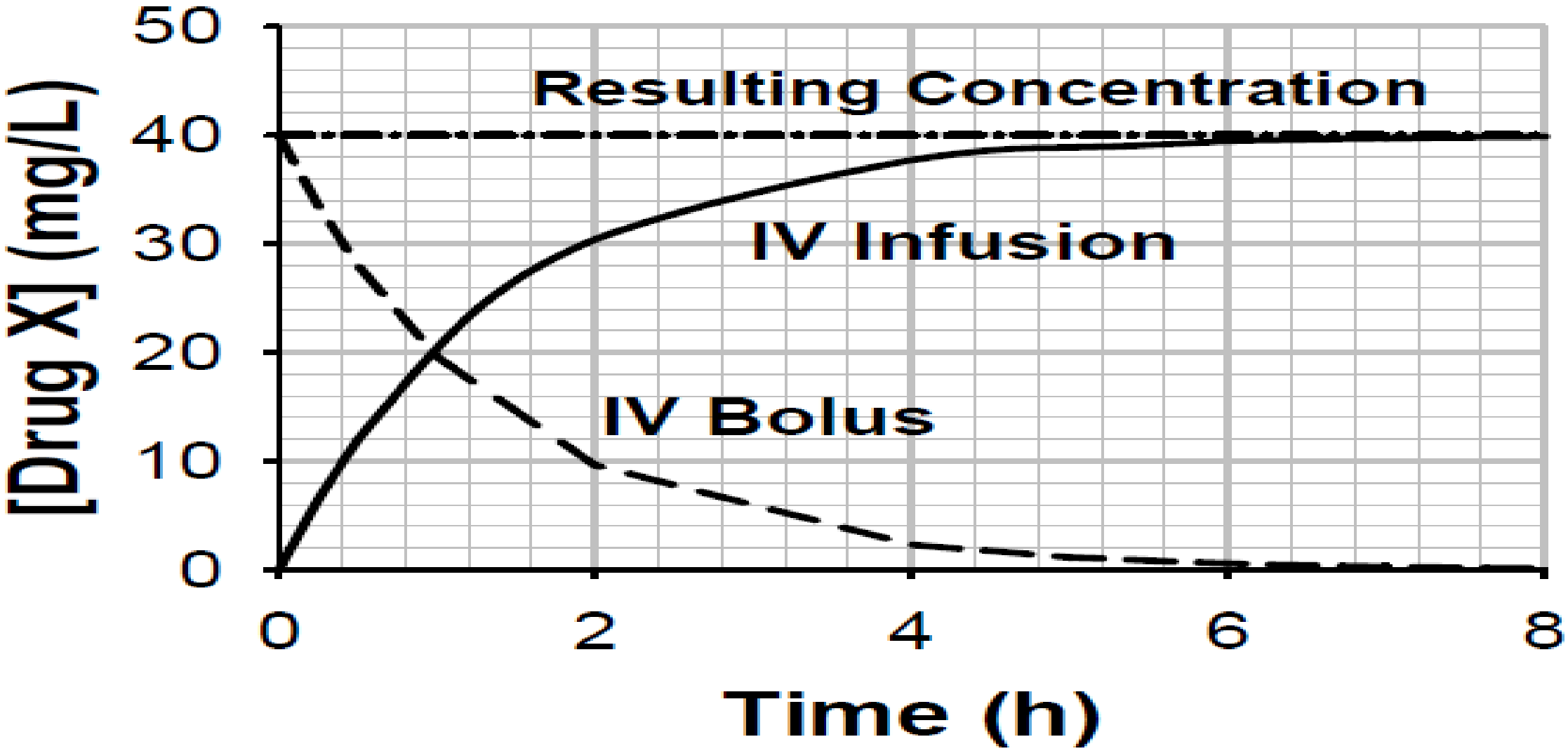
Converting from natural to common logarithms, $\text{Ln. } 0.5 = 2.303 \times \log 0.5$

Since Ln. $0.5 = 0.693 \rightarrow 0.693 = -k\, t_{1/2} \rightarrow t_{1/2} = 0.693/k$

1- IV Bolus

- **The elimination rate constant (k or k_{el})**
- $t_{1/2} = 0.693/ k \rightarrow k = 0.693/ t_{1/2}$
- Slope
- $$k = \frac{\ln (Cp)0 - \ln (Cp)}{(t - to)}$$

1- IV Infusion



2- IV Infusion

➢ **Ct1: ko> ke**

- V (infusion) = dx/dt= ko- ke. X_t
- X_t: total amount of drug in the body at time t.
- (At t=0 , X_o = 0 so ke. X_t =0)
- By integration:

$$Ct1 = \frac{ko}{ke.Vd}(1 - e^{-ke.t1})$$

2- IV Infusion

- **Ct_{ss}**: the conc. Of the steady state, ko= ke , Ct=C max= Css

$$Ct_{ss} = \frac{1}{Vd}(1 - e^{-ke.tss})$$

- **Ct_3 :** ke > ko, $Ct_3 = Ct_{ss} . e^{-ke.t3}$

$$Ct_3 = \frac{1}{Vd}(1 - e^{-ke.tss}) . e^{-ke.t3}$$

- **Ct_4 :** Ke>>Co , $Co_4 = Ct_1$

$$Ct_4 = C_{04} . e^{-ke.t4}$$

- $Ct_4 = \frac{ko}{ke.Vd}(1 - e^{-ke.t1}) . e^{-ke.t4}$