

Pharmacokinetics

One-Compartment Open Model

- The one-compartment open model is the simplest and most commonly used pharmacokinetic model.
- It assumes that the entire body behaves as a single, homogenous unit where the drug distributes instantaneously and uniformly after administration.
- The term "open" refers to the fact that the drug can leave the system (elimination), typically via metabolism or excretion.

Key Assumptions:

1. The body is represented as a **single, homogenous compartment**.
2. Drug **equilibrates instantly** within the compartment after administration.
3. Elimination follows **first-order kinetics**, meaning that the rate of elimination is proportional to the drug concentration.
4. Drug is removed **irreversibly** (hence, it is an "open" system).
5. There is no consideration of separate compartments for tissues or organs.

Mathematical Representation:

- The drug concentration C at time t is given by:

$$C = C_0 e^{-k_e t}$$

- Where:
 - C_0 = Initial drug concentration
 - k_e = Elimination rate constant
 - t = Time
- This equation shows that the drug concentration decreases exponentially over time.

Types of One-Compartment Models Based on Drug Administration Route

- The one-compartment model can be adapted for different drug administration routes:
 1. **Intravenous bolus**
 2. **Intravenous infusion**
 3. **Extravascular administration** (e.g., oral, subcutaneous, or intramuscular)

Parameters Calculated from the Model:

- **Volume of distribution (Vd):** Relates dose to initial plasma concentration

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

- **Elimination rate constant (K_e):** Slope of log concentration vs. time plot
- **Half-life ($t_{1/2}$):**

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

- **Clearance (Cl):**

$$Cl = K_e \cdot V_d$$

Advantages:

- Simplicity makes it suitable for clinical applications.
- Easy to apply for IV bolus studies.
- Useful for drugs that distribute rapidly and homogenously.

Limitations:

- Not suitable for drugs with **slow distribution** or **multi-phase elimination**.
- May oversimplify the pharmacokinetics of drugs with extensive tissue binding or nonlinear kinetics.

Intravenous Injection (Bolus)

Definition

- An intravenous (IV) bolus injection involves administering a known dose of a drug directly into the bloodstream in a single, rapid injection (usually over seconds to a minute).
- This method allows the drug to bypass absorption barriers, resulting in immediate and complete bioavailability (100%).

Process:

1. A known **dose (D)** of the drug is injected **directly into the vein**.
2. Since the drug is delivered directly into systemic circulation, **there is no absorption phase**.
3. The drug is **immediately available** for distribution and elimination.
4. The body is assumed to act as a **single compartment** where the drug disperses **instantly**.

Pharmacokinetics of IV Bolus:

A. Initial Concentration

- Immediately after injection, the initial plasma drug concentration (C_0) is given by:

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

- Where:
 - C_0 = Initial plasma concentration
 - D = Dose administered
 - V_d = Apparent volume of distribution

B. Elimination Phase

- After administration, the drug undergoes **elimination** (metabolism and/or excretion), typically following **first-order kinetics**:

$$C_t = C_0 e^{-k_e t}$$

- Where:
 - C_t = Drug concentration at time t
 - k_e = Elimination rate constant
 - t = Time after injection
- In a **one-compartment model**, the drug concentration decreases **exponentially** over time due to elimination.

Concentration–Time Curve

- The plasma concentration rises sharply to C_0 immediately after injection.
- It then declines **exponentially** as elimination proceeds.
- When plotted on a semi-logarithmic graph, the curve appears as a straight line, enabling easy calculation of pharmacokinetic parameters such as half-life ($t_{1/2}$), clearance (Cl), and AUC (Area Under Curve).

Pharmacokinetic Parameters

- From the IV bolus data, the following parameters can be determined:
 - C_0 (Initial concentration) → helps calculate V_d
 - **AUC (Area Under the Curve)** → indicates overall drug exposure
 - **Clearance (Cl)** and **half-life ($t_{1/2}$)** → derived from concentration-time data

Advantages

- **Immediate onset of action** — ideal for emergency situations (e.g., cardiac arrest, severe pain).
- **100% bioavailability** — bypasses absorption and first-pass metabolism.
- **Precise dose control** — exact amount delivered into circulation.

Disadvantages / Limitations

- **High risk of toxicity** due to sudden high peak plasma levels.
- **Irreversible administration** — once injected cannot be withdrawn.

- **Unsuitable for irritating or slow-release drugs.**
- **Requires sterile technique** and trained personnel for safe administration.

Clinical Applications

- **Emergency medications** — e.g., epinephrine, morphine.
- **Anesthetics** or other drugs requiring rapid onset.
- **Situations demanding immediate therapeutic effect** or precise control over plasma levels.

Intravenous Infusion

Definition

- An intravenous (IV) infusion is a method of administering a drug directly into the bloodstream at a controlled rate over an extended period.
- Unlike an IV bolus (which delivers a single, rapid dose), IV infusion allows gradual and continuous drug delivery, helping to maintain a steady plasma concentration (steady-state level) over time.

Purpose and Clinical Use

- IV infusion is used when:
 - A **constant therapeutic level** must be maintained.
 - **Precise control** over plasma drug concentration is required.
 - **Rapid peaks and fluctuations** (as seen with bolus dosing) should be avoided.
- Commonly applied in:
 - Continuous drug therapy (e.g., insulin, dopamine, antibiotics).
 - Maintenance of drugs with a **narrow therapeutic index**.
 - IV sedation, anesthesia, or total parenteral nutrition (TPN).

Types of IV Infusion

1. Zero-Order Infusion (Most Common):

- The drug is infused at a **constant rate** (rate of input does not change with time).
- Example: Controlled infusion via an IV pump.

2. First-Order Infusion (Rare):

- The rate of infusion is **proportional to the drug concentration**.

Pharmacokinetics of IV Infusion

A. Drug Input and Concentration-Time Relationship



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