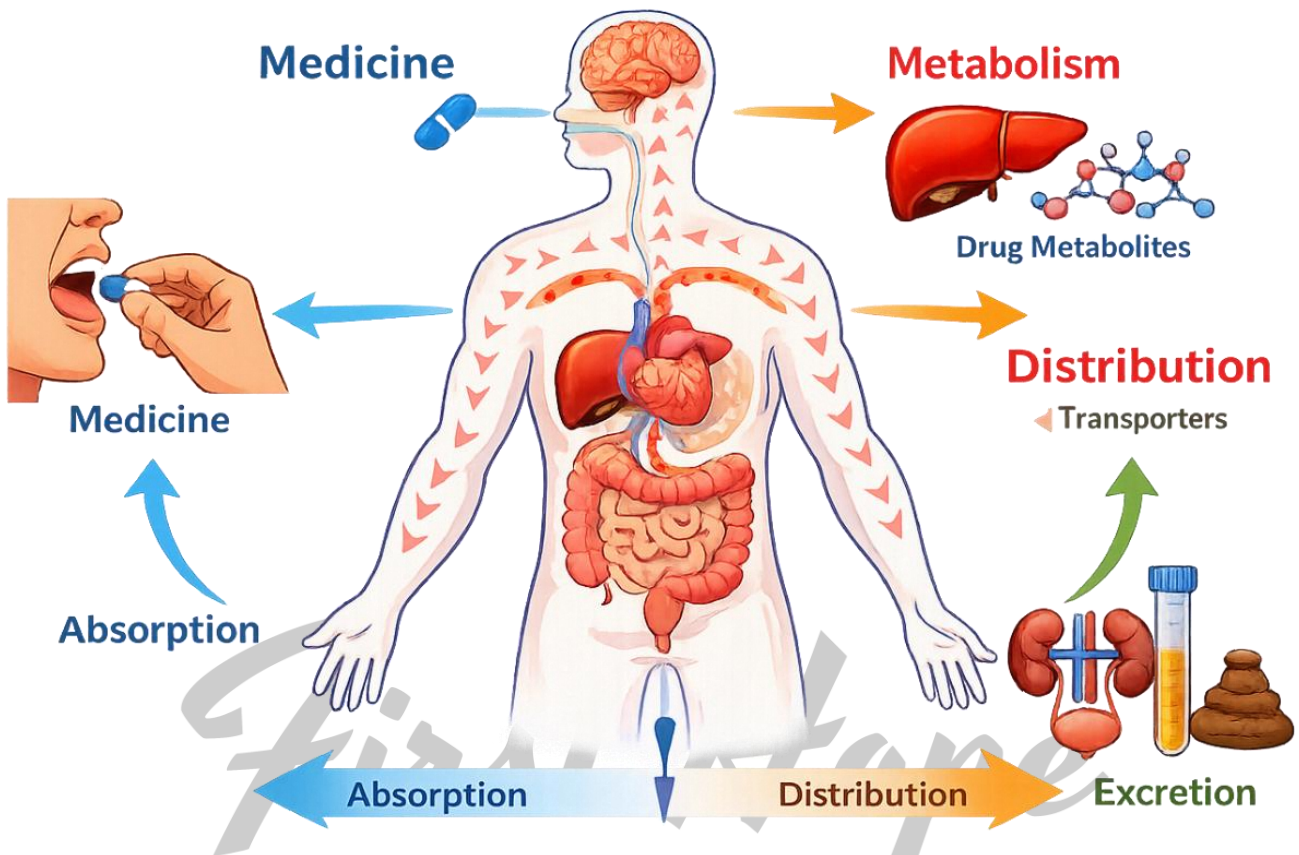


Pharmacokinetics

Pharmacokinetics: Basic Considerations

- Pharmacokinetics (PK) describes what the body does to a drug over time.



- It explains how a drug moves through the body using four main processes: **ADME (Absorption, Distribution, Metabolism, Excretion)**.

Absorption

Absorption is how a drug enters the bloodstream from its site of administration it is Important for all routes except IV (because IV goes directly into blood).

Factors affecting absorption:

- **Route of administration:** Oral, IV, IM, subcutaneous, etc.
- **Blood flow:** More blood flow = faster absorption.
- **Surface area:** Larger surface area (like intestine) increases absorption.
- **Drug properties:**
 - Lipid-soluble drugs cross membranes easily
 - Ionized drugs cross poorly
- **pH and pKa:**
 - Weak acids absorb better in acidic environments
 - Weak bases absorb better in basic environments

Distribution

Distribution is how the drug **spreads from blood to tissues**.

Key points:

- **Drugs travel in blood either:**
 - Free (active form)
 - Bound to plasma proteins (inactive form)

Factors affecting distribution:

- **Blood flow to tissues:** Brain, liver, kidney get drug faster
- **Capillary permeability:** Some tissues (brain) restrict entry (blood-brain barrier)
- **Protein binding:** Highly bound drugs stay in plasma
- **Tissue binding:** Some drugs accumulate in fat or bone

Metabolism (Biotransformation)

Conversion of drug into **more water-soluble forms for elimination** it is mainly occurs in the liver.

Two phases:

1. Phase I (functionalization):

- Oxidation, reduction, hydrolysis
- Often involves CYP450 enzymes

2. Phase II (conjugation):

- Drug combines with another molecule (e.g., glucuronide)
- Makes drug more water-soluble

Excretion

Removal of drug from the body.

Main routes:

- Kidneys (urine) – most important
- Bile (feces)
- Lungs (for gases)
- Sweat, saliva, breast milk (minor)

Important PK Parameters

1. Half-life ($t_{1/2}$)

- Time required for drug concentration to reduce by half

2. Clearance (Cl)

- Volume of plasma cleared of drug per unit time

3. Area Under Curve (AUC)

- Represents total drug exposure

Pharmacokinetic Models

- Pharmacokinetic models are mathematical representations used to describe and predict drug concentration over time in the body.

Pharmacokinetic Models

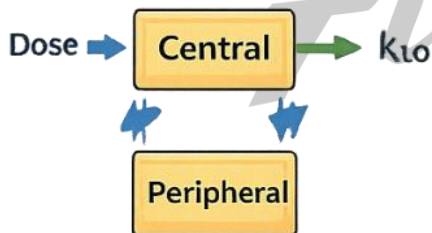
Compartmental Models



One-Compartment Model

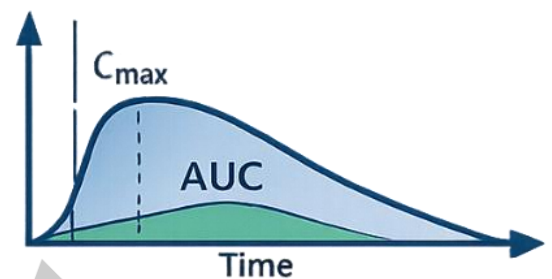


Two-Compartment Model

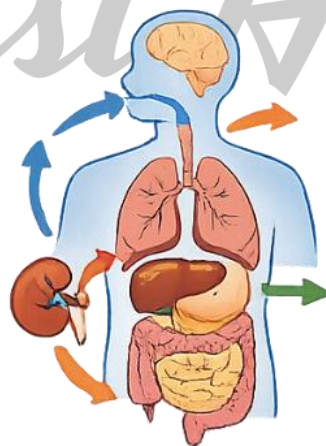


Two-Compartment Model

Non-Compartmental Analysis



Area Under the Curve (AUC)



Physiologically-Based PK (PBPK) Model

Why Models are Needed

- To understand drug behavior
- To design dosage regimens
- To predict concentration at different times

Types of Models

1. Compartment Models

- Body is divided into compartments
- Drug moves between compartments

2. Non-compartment Models

- Do not assume compartments
- Use statistical methods

Compartment Concept

- A compartment is not a real organ.
- It is a theoretical space where the drug concentration is assumed to be uniform.
- **Example:** Blood and highly perfused organs may form one compartment

Assumptions

- Drug distributes instantly within a compartment
- Drug elimination follows certain kinetics
- Compartments are connected

First Hope

One-Compartment Model

Compartment Modeling: One-Compartment Model

- In this model, the body is treated as a **single, uniform compartment** where the drug distributes **instantly and evenly** after administration.

Basic Idea

- Simplest pharmacokinetic model
- Assumes instant distribution throughout the body
- Drug concentration changes are governed mainly by absorption (if any) and elimination

One-Compartment Model: IV Bolus Administration

Definition

- A **single, rapid injection** of drug directly into the bloodstream.

Key Features

- Drug enters instantly
- No absorption phase
- Highest concentration occurs at **time = 0**

Concentration-Time Profile

- Concentration declines exponentially over time
- Decline is due to elimination only
- Forms a straight line on a semi-log plot

Equation

$$C = C_0 e^{-kt}$$

- Where:**
 - C** = concentration at time *t*
 - C₀** = initial concentration
 - k** = elimination rate constant

Important Pharmacokinetic Parameters

- Half-life (t_{1/2}):** Time required for concentration to reduce by half
- Clearance (CL):** Volume of plasma cleared per unit time
- Volume of Distribution (Vd):** Extent of drug distribution in the body

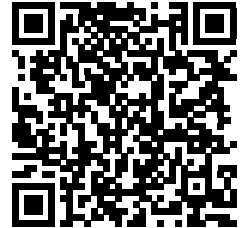


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