Pharmacokinetics

Pharmacokinetics: Definition and Introduction

Definition

- Pharmacokinetics (PK) is the branch of pharmacology that deals with the quantitative study of how a drug moves into, though, and out of the body over time.
- It answers the question: **"What does the body do to the drug?"**
- Pharmacokinetics focuses on four primary processes, collectively referred to as **ADME**:
    - **Absorption**
    - **Distribution**
    - **Metabolism**
    - **Excretion**

Importance of Pharmacokinetics

- Helps determine proper dosage regimens, frequency of administration, and the optimal route of drug delivery.
- Aids in predicting drug-drug interactions, avoiding toxicity, and optimizing therapeutic efficacy.

Key Aspects of Pharmacokinetics (ADME)

1. **Absorption**
    - ➢ The process of a drug entering the **bloodstream** from its site of administration.
2. **Distribution**
    - ➢ The dispersion of the drug throughout the **fluids and tissues** of the body.
3. **Metabolism (Biotransformation)**
    - ➢ The **biochemical modification** of the drug, mainly occurring in the **liver**.
4. **Excretion**
    - ➢ The removal of the drug and its metabolites, primarily via the **kidneys (urine)** or **bile (feces)**.

Mathematical Model in Pharmacokinetics

Overview

- A mathematical model in pharmacokinetics is a **quantitative framework** that describes how a drug is absorbed, distributed, metabolized, and eliminated (ADME) in the body over time.

- These models use equations and variables to simulate drug concentrations at various sites (like blood or tissues) to predict outcomes and guide dosage regimens.

Why Use Mathematical Models?

- To predict drug concentrations at any time point.
- To simulate different dosing scenarios (single dose vs. multiple doses).
- To optimize therapeutic efficacy and minimize toxicity.
- To aid in designing clinical trials and interpreting pharmacokinetic data.

Types of Mathematical Models

There are two broad categories:

A. Compartmental Models

- These treat the body as one or more "compartments" where the drug moves between.
- Simple but useful for most clinical applications.

B. Physiologically Based Pharmacokinetic (PBPK) Models

- These are complex models that incorporate real physiological parameters like organ sizes, blood flow rates, etc.
- Used in regulatory submissions and detailed simulations.

Basic Mathematical Elements

- **Differential Equations:** These describe the rate of change of drug concentration over time.
- **Rate Constants (k):** Represent processes such as absorption (ka), elimination (ke), and distribution (k12, k21).
- **Volume of Distribution (Vd):** The theoretical volume in which the drug would need to be uniformly distributed to produce the observed concentration.
- **Clearance (Cl):** The rate at which a drug is removed from the body.

Example Equation

- For a single-compartment model with first-order elimination:

$$C(t) = C_0 \cdot e^{-k_e t}$$

- Where:
  - $C(t)$= drug concentration at time t
  - C_0= initial concentration
  - k_e= elimination rate constant

Reaction Kinetics: Rate, Rate Constants, and Order

Basic Concepts

A. Rate of Reaction:

- Measures how fast reactants are converted into products. Influenced by **temperature**, **concentration**, **catalysts**, and **surface area**.

B. Rate Constant (k):

- A constant specific to a given reaction at a certain temperature.

C. Order of Reaction:

- Indicates how the **reaction rate depends on the concentration** of reactants.

General Rate Equation:

- For a reaction:

  aA + bB → Products

$$\text{Rate} = k[A]^m[B]^n$$

- **m & n:** Orders of the reaction with respect to A and B, respectively.
- **Overall Reaction Order =** m + n

Types of Reaction Kinetics

A. Zero-Order Kinetics

- Rate is **independent of reactant concentration**.
- Drug concentration **decreases linearly over time**.

Rate Equation:

$$\text{Rate} = k$$

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

$$t_{1/2} = \frac{[A]_0}{2k}$$

  - Half-life **depends on initial concentration**.

B. First-Order Kinetics

- Rate is **directly proportional** to the concentration of the drug.
- Drug elimination follows an **exponential decline**.

Rate Equation:

$$\text{Rate} = k[A]$$

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

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

- Half-life is **constant**, regardless of concentration.

Plasma Drug Concentration-Time Profile / Drug Levels in Blood

- Plasma drug concentration-time profiles (often referred to as **drug levels in blood**) represent how the concentration of a drug in the bloodstream changes over time.
- This data is essential for evaluating the **ADME** phases (Absorption, Distribution, Metabolism, and Elimination) and guiding clinical decisions regarding **dosage** and **therapeutic drug monitoring (TDM)**.

Phases of Drug in Blood

1. Absorption Phase

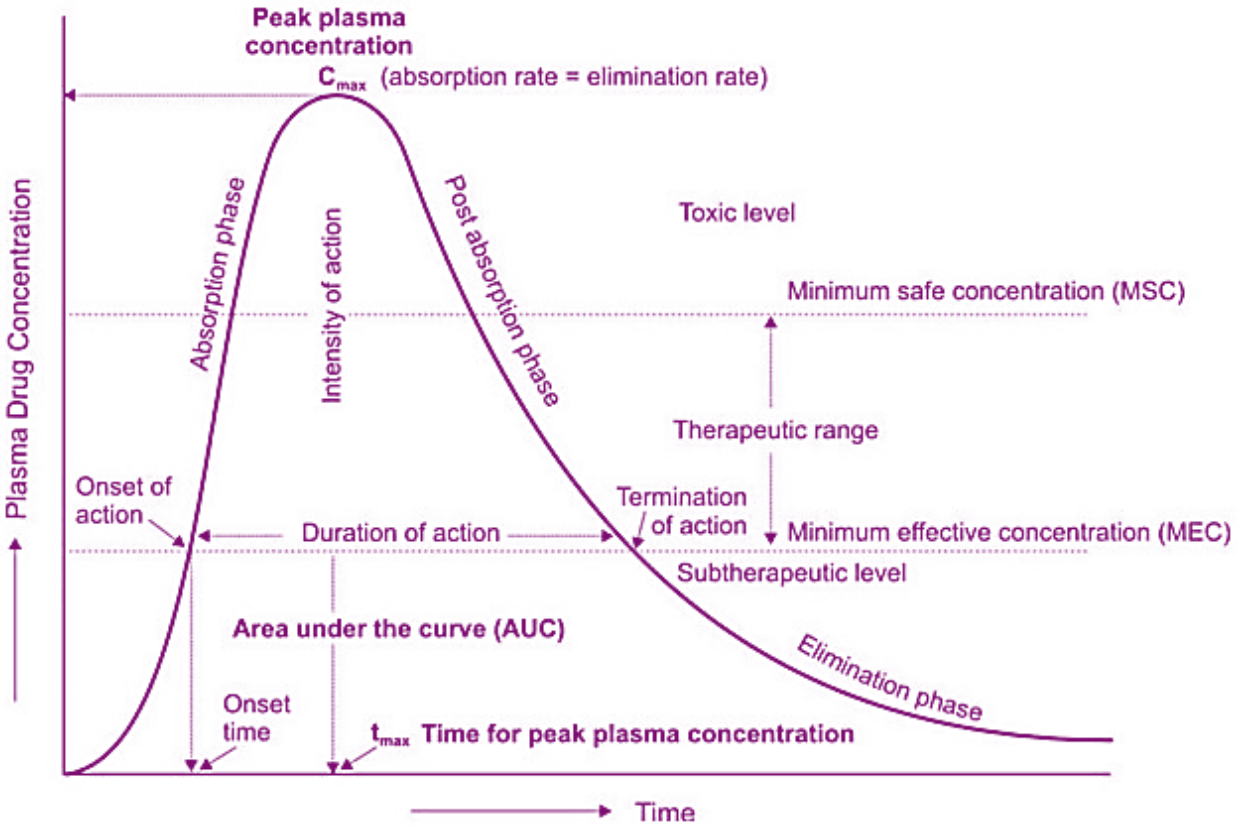
- Occurs after administration (especially non-IV routes).
- Drug levels increase as the drug enters systemic circulation.

2. Distribution Phase

- Drug begins to move from the blood into various tissues.
- Plasma levels may drop even though the total body drug amount is still high.

3. Elimination Phase

- Metabolism and excretion lower the drug concentration over time.



- Represents **total drug exposure** over time.
- Helps in determining **half-life ($t_1/_2$)**, **clearance (Cl)**, and **volume of distribution (Vd)**.

Key Pharmacokinetic Parameters

- **Cmax**: Peak plasma concentration achieved after administration.
- **Tmax**: Time taken to reach Cmax.
- **AUC (Area Under the Curve)**: Total drug exposure over time.
- **Half-life (t½)**: Time required for plasma concentration to reduce by 50%.
- **Clearance (Cl)**: Volume of plasma cleared of the drug per unit time.
- **Volume of Distribution (Vd)**: Theoretical volume linking the plasma concentration to the total amount of drug in the body.

Importance in Clinical Settings

- **Therapeutic Drug Monitoring (TDM):** Especially for drugs with narrow therapeutic windows (e.g., digoxin, lithium).
- **Dose Adjustment:** Based on individual metabolism, age, disease state, or drug interactions.
- **Bioavailability Assessment:** Compares drug levels between different formulations.

Drug Monitoring Techniques

- **Blood Sampling:** At specific time intervals.
- **Chromatographic Methods:** HPLC, LC-MS used for measuring drug levels.
- **Non-invasive Alternatives:** Under development (e.g., saliva, sweat analysis).

Pharmacokinetic Model

Definition

- A **pharmacokinetic model** is a conceptual and mathematical tool used to describe and predict the movement of drugs within the body over time.
- These models provide a simplified representation of complex physiological processes, aiming to quantify **absorption**, **distribution**, **metabolism**, and **excretion** (ADME) using parameters derived from experimental data.

Purpose of Pharmacokinetic Models

- To simulate how a drug behaves in the human body.
- To predict plasma and tissue concentrations over time.
- To estimate important pharmacokinetic parameters like **half-life**, **volume of distribution**, and **clearance**.

First Hope

FREE PREVIEW

Click here to visit our website

PHARMACY PREMIUM NOTES

Complete subject and semesters are available on FirstHope app only.

Scan or click here

Click here to get the app >

Available on Google Play

JOIN THE FIRSTHOPE COMMUNITY

Join our Telegram channel

Click here to join Telegram >

Scan or click here

@FirstHopeNotes

Instagram

@firsthope.official

Click here to follow >

YouTube channel

FirstHope-Pharmacy / Live streams

Click here to watch >

WhatsApp channel

Follow FirstHope on WhatsApp

Click here to join >

FirstHope website

firsthope.co.in

Click here to visit >

B.Pharm / D.Pharm / M.Pharm / Pharm.D

Preview notes. Complete subjects and semesters in the FirstHope app.