UNIT – 3

Pharmacokinetics: Definition and Introduction

Definition: Pharmacokinetics is the branch of pharmacology that deals with the study of the time course of drug absorption, distribution, metabolism, and excretion in the body. It involves the quantitative analysis of drug concentration changes over time.

Introduction:

- **Drug Absorption:** Entry of a drug into the bloodstream after administration.
- **Drug Distribution:** Movement of drugs throughout the body.
- **Drug Metabolism:** Biotransformation of drugs into metabolites.
- **Drug Excretion:** Elimination of drugs and their metabolites from the body.

Compartment Models

Definition: Compartment models are mathematical representations used to describe the pharmacokinetic behavior of drugs in the body. These models assume that the body is divided into compartments, each representing a tissue or organ with specific drug characteristics.

1. **One-Compartment Model:**
    - **Assumption:** The entire body is considered as a single compartment.
    - **Parameters:**
        - Ct: Drug concentration at time t.
        - $0C0$: Initial drug concentration.
        - k: Elimination rate constant.
2. **Two-Compartment Model:**
    - **Assumption:** The body is divided into the central (bloodstream) and peripheral compartments.
    - **Parameters:** Include distribution and elimination rate constants.

Non-compartment Models

Definition: Non-compartment models are used when the pharmacokinetics of a drug cannot be adequately described by compartmentalization.

1. **Physiological Models:**
    - Incorporate physiological parameters to describe drug distribution and elimination.

One-Compartment Open Model

Intravenous Injection (Bolus):

- **Administration:** Direct injection into the bloodstream.

- **Parameters:**
    - Ct: Drug concentration at time t.
    - $0C0$: Initial drug concentration.
    - k: Elimination rate constant.

Intravenous Infusion:

- **Administration:** Continuous infusion into the bloodstream.
- **Steady State Concentration (Css):** Achieved when the rate of drug input equals the rate of elimination.
- **Parameters:**
    - Css: Steady-state concentration.
    - D: Infusion rate.
    - τ: Infusion duration.
    - Cl: Clearance.

Extra Vascular Administrations:

- **Routes:** Includes oral, intramuscular, subcutaneous, etc.
- **Absorption Rate Constant (*Ka*):** Describes the rate of drug absorption.

Pharmacokinetic Parameters

1. **Elimination Rate Constant (*k*):**
    - **Definition:** The fraction of drug eliminated per unit time.
    - **Significance:** Reflects the speed of drug elimination.
2. **Half-life ($1/2t1/2$):**
    - **Definition:** The time required for the drug concentration to decrease by half.
    - **Significance:** Indicates the duration of drug action and dosing intervals.
3. **Volume of Distribution (*Vd*):**
    - **Definition:** Theoretical volume in which the total amount of drug would need to be uniformly distributed to provide the observed concentration.
    - **Significance:** Describes the extent of drug distribution in the body.
4. **Area Under the Curve (AUC):**
    - **Definition:** Represents the total drug exposure over time.
    - **Significance:** Used to calculate bioavailability and assess drug efficacy.

5. **Absorption Rate Constant (*Ka*):**
    - **Definition:** Rate of drug absorption after extravascular administration.
    - **Significance:** Influences the speed at which drug concentrations increase.
6. **Clearance (*Cl*):**
    - **Definition:** The volume of plasma from which the drug is completely removed per unit time.
    - **Significance:** Describes the body's ability to eliminate the drug.
7. **Renal Clearance (*CLR*):**
    - **Definition:** The volume of plasma cleared of drug by the kidneys per unit time.
    - **Significance:** Reflects the renal excretion of drugs.

Understanding these pharmacokinetic parameters is crucial for designing effective drug regimens, predicting drug behaviour, and optimizing therapeutic outcomes. The values of these parameters can guide dose adjustments, frequency of administration, and the selection of appropriate routes of drug administration.