Pharmacokinetics: The Effect of the Body on the Drug

Understanding
ADME

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Introduction to Pharmacokinetics

- Definition:
- Pharmacokinetics is the study of how the human body affects the drug, including
  - the processes of absorption, distribution, metabolism, and excretion - ADME).
- Importance: Understanding pharmacokinetics is crucial for determining
  - drug dosage, timing, and potential side effects

- **Visuals**: Diagram of the ADME process (simplified body diagram showing drug absorption, metabolism, distribution, and excretion).

Key Processes of Pharmacokinetics

- Absorption: How the drug enters the bloodstream
- Distribution: How the drug spreads through the body's tissues
- Metabolism: How the body breaks down the drug, usually in the liver
- Excretion: How the drug or its metabolites are removed from the body

Absorption

- Definition: The process by which a drug passes from its site of administration into the bloodstream
  - Factors Affecting Absorption:
  - Route of administration (oral, IV, etc.)
  - Drug formulation
  - Blood flow to the absorption site
  - Gastric pH

Distribution

- Definition: The dispersion of a drug throughout the fluids and tissues of the body

- Factors Influencing Distribution:
  - Plasma protein binding
  - Tissue permeability
  - Blood flow to organs
  - Volume of distribution (Vd)

Metabolism

- Definition: The chemical alteration of the drug in the body, often in the liver
- Phase I Reactions: Oxidation, reduction, hydrolysis (usually cytochrome P450 enzymes)
- Phase II Reactions: Conjugation (glucuronidation, sulfation)
- First-pass effect: Liver metabolism reduces the drug’s concentration before it reaches systemic circulation

Excretion

- Definition: The removal of drugs and their metabolites from the body, primarily via the kidneys
- Routes of Excretion:
  - Renal (urine)
  - Biliary (feces)
  - Others: sweat, saliva, exhalation

Key Pharmacokinetic Parameters

- Half-life (t½): Time it takes for the plasma concentration of a drug to reduce by half.
- Clearance (Cl): The rate at which a drug is removed from the body.
- Bioavailability (F): The proportion of the drug that reaches systemic circulation.
- Volume of distribution (Vd): The apparent volume in which the drug is distributed.

Half-life (t1/2) Calculation

- **Content**:
  - Formula: $t_{1/2} = 0.693 \times Vd/Cl$
  - Explanation of each variable.
  - Example calculation of half-life with real data.
- **Visuals**: A graphical representation of drug concentration falling over time, highlighting the half-life

Volume of Distribution (Vd) Calculation

- **Content**:
- Formula: Vd=Dose/C0
- Explanation: Where C0 is the initial drug concentration.
- Example calculation with practical data.
- **Visuals**: Illustration of how drugs are distributed into body compartments.

Clearance (Cl) Calculation

- **Content**:
- Formula: Cl=Dose/AUC
- Explanation: AUC (Area Under the Curve) represents the total drug exposure over time.
- Example calculation with a plot showing the AUC.
- **Visuals**: A drug concentration vs. time graph with the AUC shaded.

Bioavailability (F) Calculation

- **Content**:
- Formula: $F = \frac{AUC_{oral}}{AUC_{IV}} \times 100$
- Explanation: Comparing the bioavailability of oral administration vs. intravenous (IV).
- Example calculation with different AUCs.
- **Visuals**: Two AUC graphs side by side (oral vs. IV).

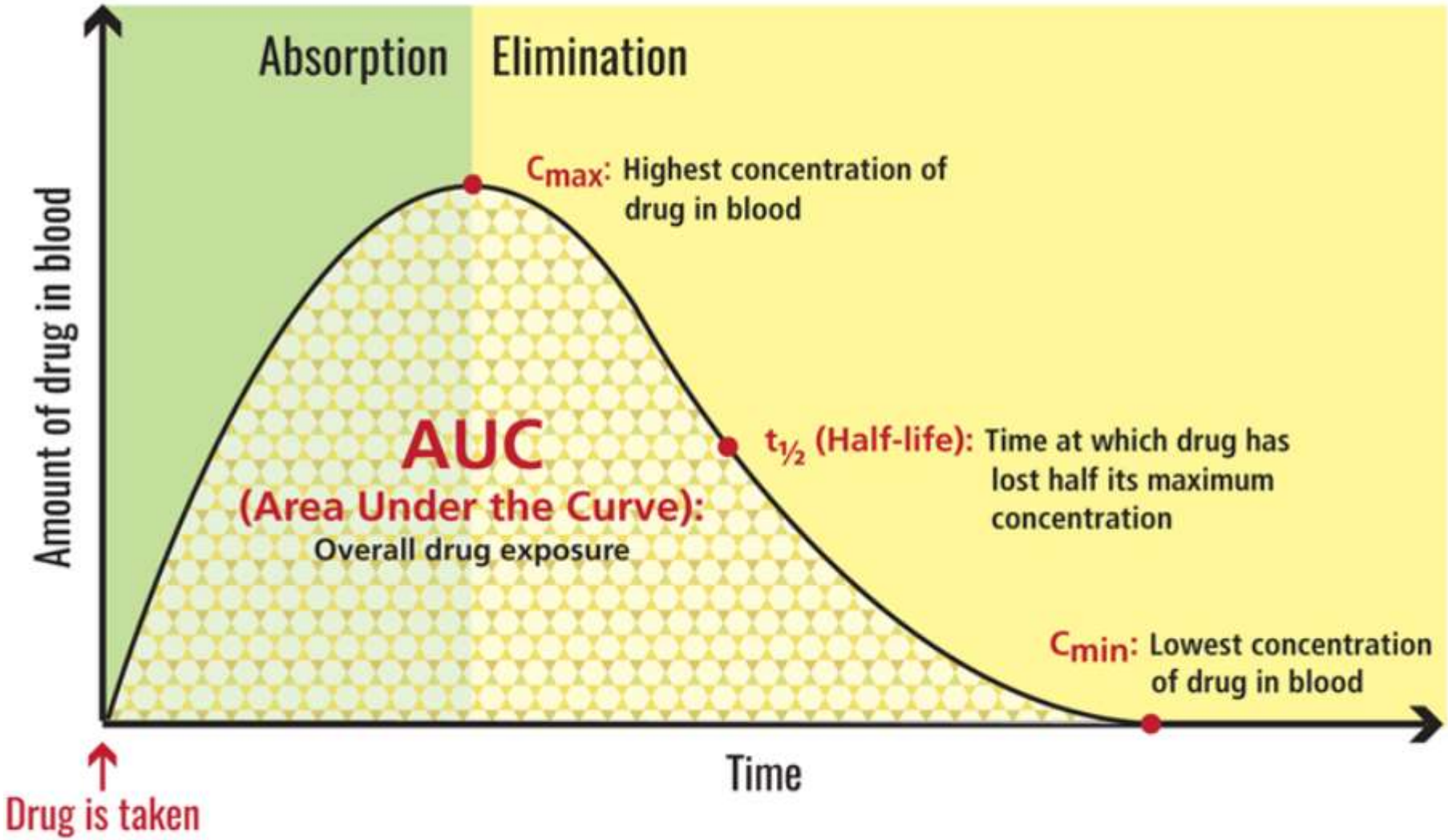
Maintenance Dose Calculation

- **Content**:
- Formula: Maintenance Dose=Css×Cl/F
- Explanation: Css is the steady-state concentration of the drug.
- Example calculation.
- **Visuals**: Diagram showing steady-state concentration.

Loading Dose Calculation

- **Content**:
- Formula: Loading Dose=Css×Vd/F
- Explanation: Initial higher dose to quickly achieve a therapeutic concentration.
- Example calculation.
- **Visuals**: Graph comparing loading dose vs. maintenance dose over time.

Pharmacokinetics



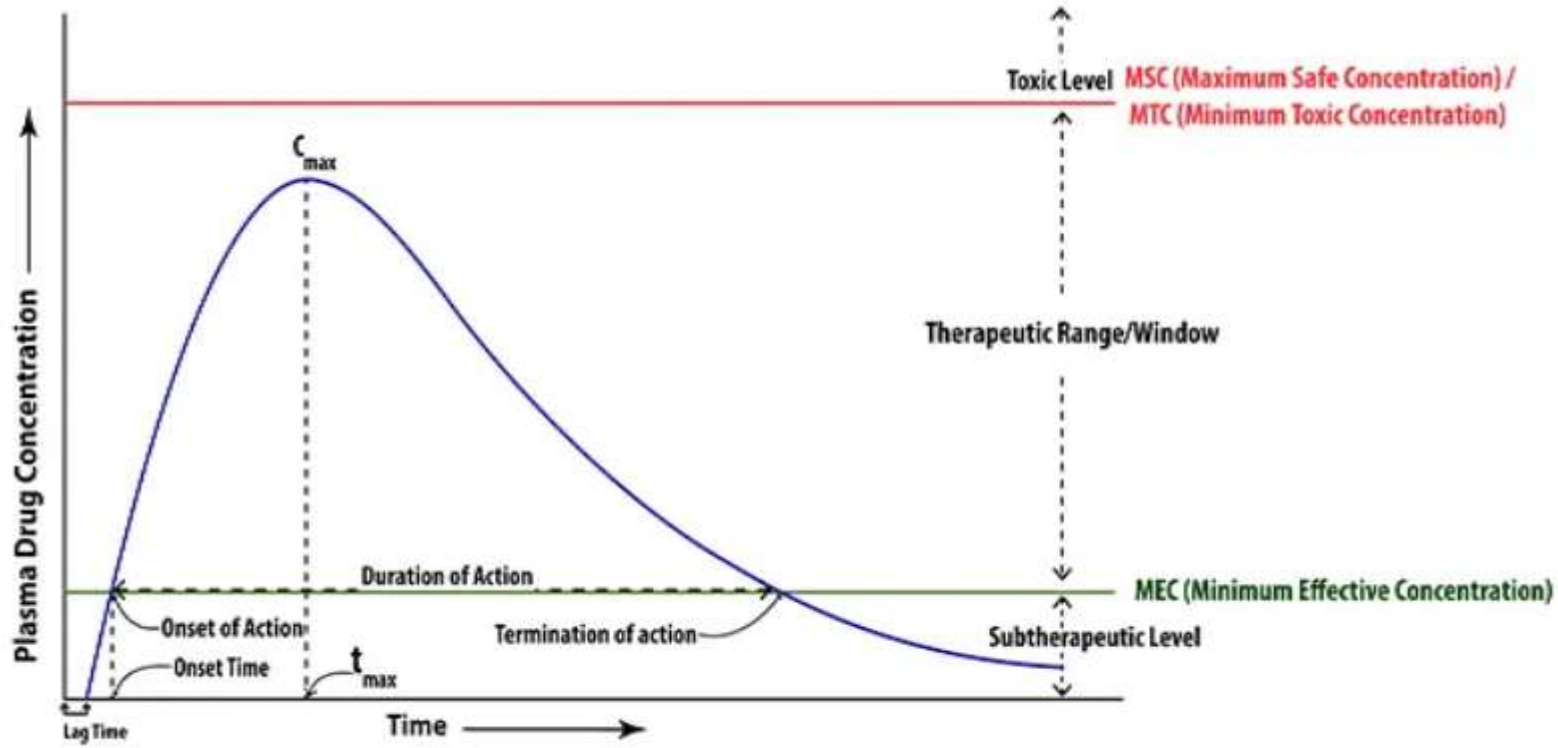


Figure: Plasma level time curve of immediate release dosage forms after oral administration of a single dose

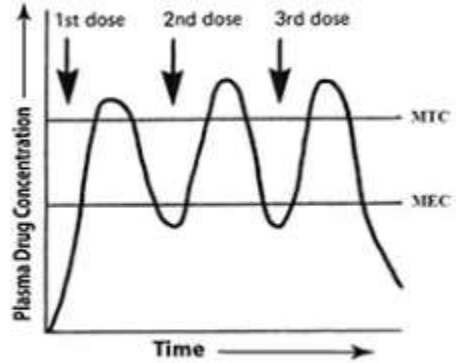


Figure: Drug concentration vs time graph of multiple doses of immediate-release dosage forms

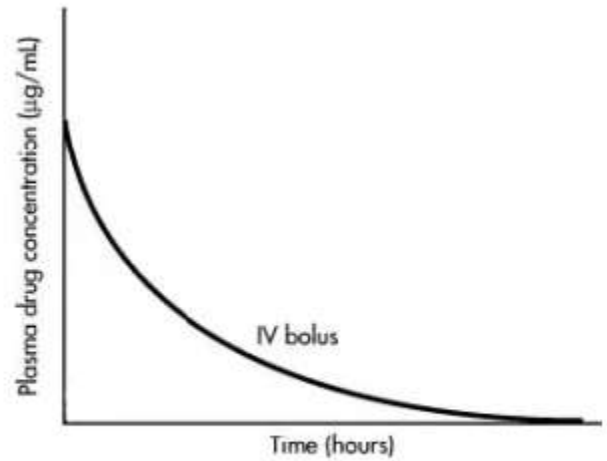


Figure: Plasma level time curve of a single intravenous bolus dose of a drug

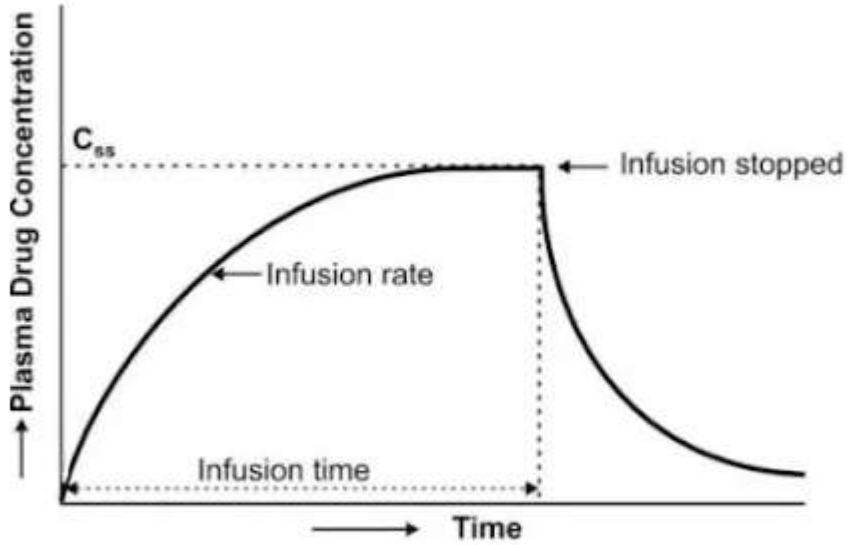


Figure: Plasma drug concentration-time profile for constant IV infusion

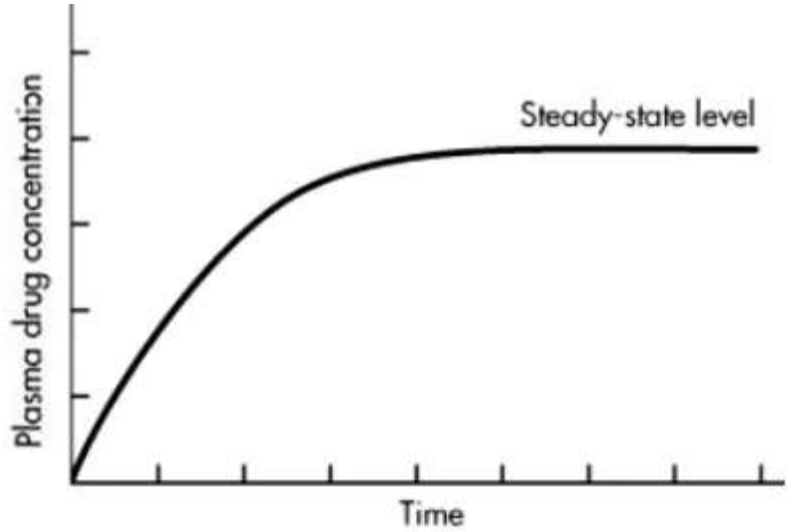
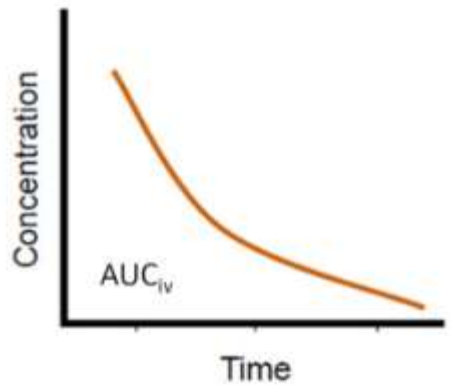


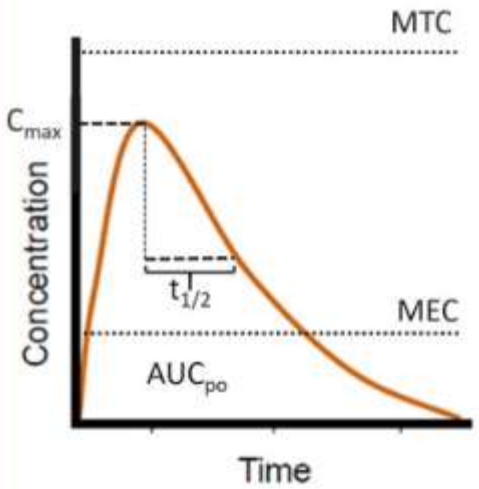
Figure: Drug concentration vs time graph of controlled release / sustained release dosage forms after administration of a single dose

Pharmacokinetic parameters of a plasma concentration time profile

Intravenous administration (iv)



Oral (po) or subcutaneous (sc) administration



CL	V_d	C_{max}	AUC	$t_{1/2}$	F
• **Clearance** • Reflects the rate of drug elimination	• **Volume of distribution** • Measure of the extent of distribution in organs and tissues	• **Maximum concentration** of drug in plasma	• **Area Under the Curve** • Describes the total exposure to a drug	• **Half-life** • The time needed to reach half of drug maximum concentration	• **Bioavailability** $F = \frac{AUC_{po}/dose_{po}}{AUC_{iv}/dose_{iv}}$

Clinical Relevance

- Dose adjustment: Based on pharmacokinetics, especially in patients with liver or kidney dysfunction.
- Therapeutic drug monitoring: Measuring drug levels in the blood to ensure efficacy and avoid toxicity.
- Drug interactions: How other medications can alter absorption, metabolism, or excretion.

Conclusion

- Summary: Pharmacokinetics helps determine how much of a drug should be administered and how frequently

- Final Thought: A comprehensive understanding of ADME processes is essential for optimizing therapeutic outcomes and minimizing adverse effects

Take home message

Pharmacokinetics = ADME

The effect of the body on the drug