Bioavailability of Drugs

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💊 Definition

Bioavailability refers to the fraction of an active drug in any dosage form that reaches its site of action or the systemic circulation in unchanged form.

- Simplified: How much of the drug actually becomes available in the body to produce its effect.

- Key points:

    - Fraction of dose reaching systemic circulation
    - Remains unchanged/active
    - Relevant for all routes of administration

📏 Calculation of Bioavailability

Bioavailability (%F) is usually calculated using AUC (Area Under the Curve):

Formula:

Bioavailability (F) = AUC ORAL / AUC IV × 100

Where:

- AUC Oral = Drug exposure after oral administration
- AUC IV = Drug exposure after intravenous administration (100% bioavailable)

Interpretation:

- Measures extent of bioavailability
- Helps in dose adjustment

⚡ Factors Affecting Bioavailability

1. Factors Affecting Absorption
    - Solubility, pH, GI motility, food interactions
2. First Pass Metabolism (FPM)
3. Route of Administration

4. Pharmaceutical / Quality Control Factors

- Particle size
- Inert ingredients in formulation
- Compression pressure
- Moisture content
- Polymorphism

Flowchart: Factors Affecting Bioavailability

Drug Formulation / Administration

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Absorption from site of administration

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First-pass metabolism (liver / gut wall / other tissues)

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Systemic circulation (Bioavailable fraction)

First Pass Metabolism (FPM)

Definition:

- Also called pre-systemic metabolism
- Drug is metabolized before reaching systemic circulation
- Reduces bioavailability

Sites of First Pass Metabolism:

Site	Examples
Liver	Nitroglycerine, Lignocaine, Propranolol, Cimetidine
Intestinal mucosa	Chlorpromazine, Levodopa, α-methyldopa
Bronchial mucosa	Prostaglandins, Nicotine, Isoprenaline

Variations:

- Hepatic disease → may require dose adjustment

- Route of administration → e.g., sublingual or IV bypasses FPM

Example Drugs:

- Diazepam, Clonidine → 95–100% metabolized
- Lidocaine → 35% metabolized

Flowchart: First Pass Metabolism

Oral Drug

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Absorption in GI tract

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Intestinal metabolism → ↓ bioavailability

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Portal vein → Liver metabolism → ↓ bioavailability

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Systemic circulation (active drug fraction)

💊 Routes of Administration and Bioavailability

- IV → 100% bioavailability
- Oral → reduced by FPM
- Sublingual / Buccal / Rectal / Inhalational → partial or complete bypass of FPM

🏭 Pharmaceutical or Quality Control Factors

- Particle size: Smaller → faster dissolution → higher absorption
- Inert ingredients: Can enhance or reduce solubility
- Compression pressure: Affects tablet disintegration
- Moisture content: Can degrade sensitive drugs
- Polymorphism: Different crystalline forms → variable

solubility

📌 Clinical Significance

Changes in bioavailability can lead to:

Effect	Clinical Implication	Examples
Therapeutic failure	Life-saving drugs may not work	Antimicrobials, Antihypertensives
Toxicity	Drugs with low therapeutic index	Anti-cancer, Anticoagulants

Flowchart: Clinical Impact of Bioavailability Changes

Change in bioavailability

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↓ Therapeutic effect → Therapeutic failure
↑ Toxic levels → Drug toxicity

🔬 Equivalence of Drug Formulations

1. Chemical Equivalence

- Two drug products are chemically equivalent if they contain the same amount of the same active ingredient, in the same chemical form, and meet the same standards of purity, strength, and quality.

- 🧪 Example: Two tablets each contain 500 mg of paracetamol, even if made by different companies.

2. Bioequivalence

- Two drug products are bioequivalent if they show the same rate and extent of absorption (i.e., same bioavailability) when given at the same molar dose under similar conditions.

- 💊 Example: Brand A and Brand B paracetamol tablets reach the same plasma concentration curve (Cmax and AUC) in the body.

3. Therapeutic Equivalence

- Two drug products are therapeutically equivalent if they produce the same clinical effect and have the same safety profile when administered to patients under the same conditions.

- ♡ Example: Both brands relieve pain equally well and have similar side effects.

Flowchart: Types of Drug Equivalence

Formulations of a drug

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Chemical equivalence → Same drug content

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Bioequivalence → Same absorption / systemic availability

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Therapeutic equivalence → Same clinical effect