Drug Absorption

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💊 Notes on Drug Absorption
(Pharmacokinetics & Pharmacodynamics)

🌟 Definition

Absorption is the process by which a drug molecule crosses the biological membrane and moves from its site of administration into the systemic circulation (central compartment).

🔷 It determines how much and how fast a drug becomes available at its site of action.

⚙️ Key Factors in Drug Absorption

Parameter	Description
Rate of Absorption	Speed at which the drug enters circulation
Extent of Absorption (Bioavailability)	Fraction of the administered dose that reaches systemic circulation
Routes of Administration	Oral, IV, IM, SC, transdermal, inhalation, etc.
Biological Membrane	The lipid barrier drugs must cross to reach the bloodstream

🧠 Mechanisms of Drug Absorption

Drugs can cross biological membranes via several mechanisms, depending on their chemical nature, size, and lipid solubility.

1. Passive Membrane Transport

No energy required ⚡ — movement is down the concentration gradient.

Type	Mechanism	Examples / Notes
Simple Diffusion	Movement from high → low concentration through lipid bilayer	Most lipid-soluble drugs
Filtration / Aqueous Diffusion	Passage through aqueous pores or channels	Small water-soluble drugs
Bulk Flow	Movement with body fluids (blood, lymph)	IV fluids, capillary filtration

🏵️ 2. Active Membrane Transport

Energy-dependent ⚡, carrier-mediated transport against the concentration gradient.

Type	Description	Notes
Primary Active Transport	Directly uses ATP (e.g., Na^+/K^+ ATPase pump)	Seen in renal tubules, liver
Secondary Active Transport	Uses ion gradient (e.g., Na^+ gradient drives glucose uptake)	Indirectly energy-dependent
Endocytosis	Engulfing of large molecules into vesicles	For macromolecules like insulin

🔷 Characteristics:

- Carrier mediated 🧬
- Energy dependent ⚡
- Works against gradient
- Shows selectivity, specificity, and saturation

3. Specialized Membrane Transport

Type	Mechanism	Example
Facilitated Diffusion	Carrier-mediated but no energy used; moves down concentration gradient	Glucose transport in RBCs

📌 Used by endogenous substances (e.g., glucose, amino

acids, vitamins).

🔬 Detailed Explanations

🧪 Simple Diffusion

- Based on the natural tendency of molecules to move from high → low concentration.
- Important for lipid-soluble drugs (e.g., steroids, alcohol).
- Sites: Jejunum, kidney, stomach, urinary bladder.

🧭 Determinants:

- Concentration gradient
- Lipid solubility (↑ solubility → ↑ absorption)
- Membrane surface area
- Thickness of membrane

💧 Filtration (Aqueous Diffusion)

- Movement through aqueous pores within membranes

or capillary endothelium.

- Common in intramuscular and capillary absorption sites.

- Independent of drug pH and pKa.

- Dependent on:

    - Blood flow
    - Hydrostatic pressure
    - Size of the pores

🧠 Example: Small hydrophilic drugs passing through renal glomeruli.

👊 Bulk Flow

- Drugs move with the flow of fluids (blood or lymph).

- Does not depend on lipid solubility or charge.

- Common in capillaries and tissues with high perfusion.

🧭 Flowchart: Overview of Drug Absorption Mechanisms

Drug Absorption

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Passive Transport → *Simple Diffusion* → *Filtration / Bulk Flow*

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Active Transport → *Primary* → *Secondary* → *Endocytosis*

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Specialized Transport → *Facilitated Diffusion*

🏁 Key Exam Points

📚 Remember:

- Passive transport = no energy, no carrier (except facilitated).
- Active transport = energy, carrier, selectivity, saturation.
- Filtration depends on blood flow, not pH/pKa.
- Endocytosis allows transport of large molecules like

vitamin B_{12} and proteins.

Summary Table

Mechanism	Energy	Carrier	Direction	Example
Simple Diffusion	✗	✗	High → Low	Lipid-soluble drugs
Filtration	✗	✗	High → Low	Small water-soluble drugs
Facilitated Diffusion	✗	✓	High → Low	Glucose transport
Active Transport	✓	✓	Low → High	Na^+/K^+ pump
Endocytosis	✓	✗	Variable	Insulin uptake

Facilitated Diffusion

Facilitated diffusion is a *carrier-mediated* transport mechanism in which drugs move down their concentration gradient with the help of specific carrier proteins — but without energy expenditure ⚡.

Characteristics

- ✓ Down concentration gradient (high → low)
- ⚡ No energy required
- Carrier-mediated (shows selectivity and

specificity)

- 🔁 Saturable process (limited number of carriers)

Examples:

- Glucose and ions across cell membranes

🧭 Comparison of Major Transport Mechanisms

Property	Simple Diffusion	Facilitated Diffusion	Active Transport
Gradient	Down	Down	Against
Energy Requirement	✗ None	✗ None	✅ Required
Carrier Involvement	✗ None	✅ Present	✅ Present
Specificity	Non-specific	Specific	Specific
Saturability	Not saturable	Saturable	Saturable
Type of Drugs	Lipid-soluble	Non-diffusible	Lipid-insoluble

💡 Examples of Absorption Mechanisms

Mechanism	Type	Examples

Passive Transport	Simple Diffusion	Aspirin, Warfarin
Active Transport	Carrier-mediated (ATP/ion gradient)	Levodopa, 5-Fluorouracil
Endocytosis	Vesicular transport	Vitamin B_{12} with Intrinsic Factor
Facilitated Diffusion	Carrier-mediated (no energy)	Glucose, Ions

🧩 Flowchart: Overview of Absorption Mechanisms

Drug Absorption

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Passive Transport → *Simple Diffusion* → *Filtration / Bulk Flow*

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Active Transport → *Primary (ATP)* → *Secondary (Ion Gradient)* → *Endocytosis*

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Specialized Transport → *Facilitated Diffusion (Carrier, No Energy)*

🌡️ Factors Affecting Drug Absorption

Drug absorption depends on both drug-related and body-related factors. Each plays a key role in determining rate, extent, and bioavailability of a drug in systemic circulation.

💊 I. Factors Related to the Drug

1 Lipid-Water Solubility

- The lipid-water partition coefficient determines the drug's ability to cross membranes.
- Higher lipid solubility → faster absorption.
- A thin water film on the epithelial surface must also dissolve the drug before absorption.

2 Particle Size

- Smaller particle size → larger surface area → faster absorption.
- *Inverse relationship* with absorption rate.

- Example: Micronized griseofulvin has better absorption than coarse particles.

3 Molecular Size

- Inverse relationship — smaller molecules cross membranes more easily.

4 Physical Nature of the Drug

- Solid → slower absorption
- Liquid → faster
- Gas → fastest
- Crystalloids absorb more readily than colloids.

5 Ionization of Drugs

Only unionized (lipid-soluble) forms of drugs can cross biological membranes.

For Weak Acids:

$AH \rightleftharpoons A^- + H^+$

For Weak Bases:

$B + H^+ \rightleftharpoons BH^+$

- pKa: The pH at which 50% of the drug is ionized.
- Henderson-Hasselbalch Equation:
  - $pKa - pH = \log [AH / A^-]$ *(for weak acids)*
  - $pKa - pH = \log [BH^+ / B]$ *(for weak bases)*

🔑 Clinical Significance:

- Explains absorption, distribution, and excretion patterns.
- Basis of ion trapping — drugs accumulate where they are more ionized (e.g., acidic drugs trapped in alkaline urine).

6 Chemical Nature of the Drug

- Determines route and stability.
- Example:

- Iron salts (require acidic medium)
- Heparin & penicillin (destroyed orally → given parenterally)

7 Dosage Form

- Disintegration → Dissolution → Absorption
- Controlled by drug formulation type:
  - Conventional
  - Sustained Release (SR)
  - Depot
  - Transdermal (TD)
  - Rapid-dissolving formulations
- Examples:
  - Nitroglycerine (sublingual, rapid)
  - Diclofenac (SR for prolonged action)

8 Formulation Components

- Diluents, binders, excipients affect drug release and absorption.

- Poor formulation = reduced bioavailability.

9 Drug Concentration

- Higher concentration increases concentration gradient, thus enhancing diffusion rate.

- Governed by Fick's Law of Diffusion:

Flux (molecules/unit time) =

$$[(C_1 - C_2) \times \text{Area} \times \text{Permeability Coefficient}] / \text{Thickness}$$

II. Factors Related to the Body

1 Area of Absorptive Surface

- Greater surface area = greater absorption.

- Intestine > Stomach (due to villi and microvilli).

- Surgeries removing intestinal sections ↓ absorption.

2 Vascularity

- Absorption rate depends on blood flow.

- IM > SC (higher vascularity).
- Decreased by shock or vasoconstrictors, increased by massage.

3 pH of the Medium

- Influences ionization → affects absorption.
- Weak acids absorb best in acidic medium (stomach).
- Weak bases absorb best in alkaline medium (intestine).

4 Presence of Other Substances

- Food & drugs can alter absorption:
  - Statins + grapefruit juice → ↓ absorption
  - Iron + tetracycline → chelation → ↓ absorption
  - Bile acid resins bind drugs → ↓ absorption
  - Epinephrine (local vasoconstrictor) → delays absorption.

5 Gastrointestinal Motility

- Decreased motility (opioids) → delayed absorption

- Increased motility (metoclopramide) → faster absorption but reduced contact time.

6 Functional Integrity of Absorptive Surface

- Conditions like intestinal edema or mucosal flattening ↓ absorption efficiency.

7 Diseases Affecting Absorption

System	Example	Effect
GIT	Diarrhea, malabsorption	↓ Absorption
Stomach	Achlorhydria	↓ Absorption of weak acids
Liver	Cirrhosis	Altered metabolism → altered absorption
Nervous system	Neuropathy	Alters GI motility
Lungs / Skin	Emphysema, lipodystrophy	↓ Absorption of inhaled/topical drugs

💡 Methods for Modifying Absorption

⏳ Delaying Absorption

- Formulation: Use sustained-release or depot

preparations.

- Local vasoconstrictors (e.g., epinephrine with local anesthetic).
- Significance: Prolongs duration, reduces side effects.

⚡ Enhancing Absorption

- Formulation modifications (improved solubility, nano-formulations).
- Massage or heat at injection site (↑ blood flow).
- Significance: Faster onset, useful in emergencies (e.g., nitroglycerine).

🧠 Quick Recap Flowchart

Factors Affecting Absorption

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Drug-related Factors → *Solubility, Particle size, Ionization, Dosage form, Concentration*

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Body-related Factors → *Surface area, Vascularity, pH, Motility, Disease states*

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Modification Methods → *Enhance (Massage, Heat) / Delay (SR forms, Vasoconstrictor)*

🏁 Key Takeaways

✅ Unionized, lipid-soluble drugs absorb best.

✅ Absorption is fastest in organs with high surface area & blood flow.