Pharmacology by Mahmoud Nazih

Nazih Table: Lecture 4 - Pharmacokinetics I (Absorption & Distribution)

Section	Key Points/Details	Examples/Notes	Important Questions
Definition	- Pharmacokinetics: What the body does to the drug (ADME: Absorption, Distribution, Metabolism, Excretion). - Pharmacodynamics: What the drug does to the body.	**Nazihiat**: **"K for Kinetics = Body to Drug", " D for Dynamics = Drug to Body."**	**Q1:** What does pharmacokinetics mean? **A:** What the body does to the drug.
Routes of Administration	- **Enteral**: Oral, sublingual, rectal. - **Parenteral**: IV, IM, subcutaneous. - **Others**: Inhalational, topical, transdermal.	Examples: - Oral: Common but subject to first-pass effect. - IV: 100% bioavailability.	**Q9:** Which route has 100% bioavailability? **A:** Intravenous.
Oral Absorption	- Most drugs absorbed in the small intestine (large surface area, long residence time). - Subject to first-pass metabolism in liver.	- **Weak acids:** Absorbed in stomach (low pH). - **Weak bases:** Absorbed in intestine (higher pH).	**Q10:** What best describes drug absorption? **A:** Weak acidic drugs are non-ionized in the stomach.
First-Pass Effect	- Orally administered drugs metabolized by intestinal and hepatic enzymes **before** entering systemic circulation. - Reduces bioavailability.	Example: - High first-pass effect: Propranolol.	**Q5:** What is the first-pass effect? **A:** Drug is metabolized by intestinal and hepatic enzymes before circulation.
Bioavailability	- **Fraction** of administered drug reaching systemic circulation unchanged. - Influenced by absorption and first-pass metabolism.	**IV administration: 100%** bioavailability. Oral drugs: Reduced bioavailability.	**Q8:** What is bioavailability? **A:** The proportion of the drug that reaches systemic circulation.
Mechanisms of Absorption	- **Passive Diffusion**: Driven by concentration gradient, no energy required. - **Facilitated Diffusion**: Passive but uses carriers, no energy. - **Active Transport**: Against gradient, requires energy. - **Endocytosis**: Bulk transport.	Examples: - Passive: Lipid-soluble drugs. - Facilitated: Vitamin B12. - Active: Glucose.	**Q7:** What is true about facilitated diffusion? **A:** Does not require energy.
Factors Affecting Absorption	- **Physicochemical Properties**: Solubility, pKa, lipid solubility. - **Surface Area**: Higher in small intestine. - **Blood Flow**: Enhances absorption. - **Food**: May delay or reduce absorption.	**Nazihiat**: **"SALT-BF"** (Solubility, Area, Lipid solubility, Transport, Blood Flow, Food).	**Q3:** Which best describes pharmacokinetics properties? **A:** Most orally administered drugs are absorbed in the small intestine.
Blood-Brain Barrier (BBB)	- Restricts polar/ionized drugs. - Lipid-soluble, unionized drugs can cross BBB. - Example: Thiopental crosses BBB for rapid anesthesia induction.	Mnemonic: **"LLC"** (Lipid-soluble, Low-ionized Cross).	**Q4:** What is true about the BBB? **A:** Highly lipid-soluble drugs readily cross the BBB.
Drug Distribution	- **Volume of Distribution (Vd)**: Apparent volume required to contain drug at plasma concentration. - **Factors Affecting Distribution**: Lipid solubility, protein binding, blood flow.	Examples: - Low Vd: Heparin (4L). - High Vd: Amiodarone (4200L).	Mnemonic: **"Vd = Volume Delivers."**
Key Graph Concepts	- Ionized vs. Non-Ionized: Non-ionized drugs are lipid-soluble and cross membranes. - Henderson-Hasselbalch Equation: Determines ionization at a given pH.	**Nazihiat**: **"Unionized = Universal Entry."**	**Q6:** What describes a pharmacokinetic property? **A:** Orally administered drugs are absorbed in the small intestine.

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Summary Table: Routes of Drug Administration

Route	Features	Advantages	Disadvantages
Oral (Enteral)	- Most common, convenient, and non-invasive. - Absorbed in the GI tract (mainly small intestine). - Subject to first-pass metabolism in the liver.	- Easy and safe. - Suitable for self-administration. - Cost-effective.	- Variable absorption. - Not suitable for unconscious or vomiting patients. - First-pass metabolism reduces bioavailability.
Sublingual	- Absorbed through capillaries under the tongue. - Bypasses the GI tract and liver.	- Rapid absorption. - Avoids first-pass metabolism.	- Limited to small, lipophilic drugs. - May cause irritation under the tongue.
Rectal (Enteral)	- Absorbed via rectal mucosa. - Partial avoidance of first-pass metabolism.	- Useful for patients who **cannot swallow.** - Partially bypasses first-pass metabolism.	- Inconsistent absorption. - May be uncomfortable for patients.
Intravenous (IV)	- Drug directly injected into the bloodstream. - 100% bioavailability. - Rapid onset of action.	- Immediate effect. - Suitable for emergencies. - Precise dosing.	- Irreversible. - Requires trained personnel. - Risk of infection.
Intramuscular (IM)	- Drug injected into the muscle. - Absorption depends on blood flow to the injection site.	- Allows depot (slow-release) formulations. - Useful for moderate-volume drugs.	- Painful. - Absorption can vary depending on site and blood flow.
Subcutaneous (SC)	- Drug injected under the skin. - Absorption slower than IV or IM.	- Suitable for slow, steady drug release. - Can be self-administered (e.g., insulin).	- Limited to small-volume drugs. - Risk of irritation or necrosis at the injection site.
Inhalational	- Rapid absorption via the large surface area of respiratory mucosa. - Direct action on respiratory diseases.	- Fast onset of action (almost as quick as IV). - Targeted delivery for respiratory diseases (e.g., asthma).	- Limited to specific drugs (e.g., gases, aerosols). - Requires proper technique.
Topical	- Applied directly to skin or mucosal surfaces. - Local action (e.g., creams, ointments).	- Minimizes systemic side effects. - Direct action at the site of application.	- Limited to local effects. - Risk of skin irritation.
Transdermal	- Drug delivered across the skin for systemic effect. - Uses patches.	- Sustained release. - Avoids first-pass metabolism. - Convenient for chronic conditions (e.g., nitroglycerin patches).	- Limited to lipophilic drugs. - Potential for skin irritation.
Intrathecal	- Injected into cerebrospinal fluid (CSF). - Bypasses the blood-brain barrier (BBB).	- Direct access to the central nervous system (CNS).	- Invasive. - Requires skilled personnel. - Risk of infection or nerve damage.

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- **Fast Routes: IV > Inhalational > Sublingual.**
- **Avoids First-Pass Metabolism: Sublingual, Rectal (partial), IV, Transdermal, Inhalational.**