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BIOPHARMACEUTICS AND PHARMACOKINETICS

UNIT 1
PART 1

TOPIC :

- **Introduction to Biopharmaceutics**

Absorption : Mechanisms of drug absorption through GIT, factors influencing drug absorption through GIT, absorption of drug from Non per oral extra-vascular routes,



Biopharmaceutics

→ Biopharmaceutics is the branch of pharmacy that studies how the physical and chemical properties of a drug, dosage form, and route of administration affect the rate and extent of drug absorption into the bloodstream.

→ It explains:

- How a drug is released from the dosage form
- How the drug dissolves
- How it reaches the blood circulation
- How formulation affects drug action

→ Biopharmaceutics helps in the development of safe, effective, and stable dosage forms such as tablets, capsules, syrups, injections, and ointments.

Pharmacokinetics

Pharmacokinetics is the study of the movement of drugs inside the body over time. It describes what the body does to the drug after administration.

It includes four main processes:

1. **Absorption** – Entry of drug into blood
2. **Distribution** – Movement of drug to body tissues
3. **Metabolism** – Chemical conversion of drug in the body
4. **Excretion** – Removal of drug from the body

These processes are commonly called ADME.

Pharmacokinetics helps in determining:

- Dose of drug
- Frequency of administration
- Duration of therapy

- Drug concentration in blood

Applications of Biopharmaceutics and Pharmacokinetics

Applications of Biopharmaceutics

- Helps in designing suitable dosage forms
- Improves drug absorption and bioavailability
- Enhances therapeutic effectiveness
- Reduces side effects caused by poor absorption
- Assists in formulation development
- Helps in selecting proper route of administration
- Supports quality control of pharmaceutical products

Applications of Pharmacokinetics

- Determines safe and effective dose
- Predicts drug concentration in blood
- Helps in maintaining therapeutic drug levels
- Prevents toxicity and adverse effects
- Decides dosing interval and duration
- Useful in clinical trials and drug development
- Helps in dose adjustment in liver and kidney diseases
- Explains drug interactions in the body

Absorption

- Absorption is defined as the movement of a drug from its site of administration into the systemic circulation (bloodstream).
- The drug must reach the bloodstream to produce its therapeutic effect, except in cases where the drug is directly administered into blood such as intravenous (IV) injection.
- For proper absorption, most drugs should be lipid soluble because biological membranes are mainly made of lipids. Lipid soluble drugs can easily cross these membranes.
- For example:
 - A drug given through the oral route must cross:
 - Gastrointestinal membrane
 - Blood vessel membrane
 - Therefore, the drug should be in lipid soluble form for better absorption.

Nature of Drugs

Most drugs available in the pharmaceutical market are:

- Weak acids
- Weak bases

This is because weak acidic and weak basic drugs can exist in:

- Unionized form
- Ionized form

The unionized form is more lipid soluble and can easily cross biological membranes.

Therefore, drugs are absorbed better when they remain in their unionized form.

Absorption of Weak Acidic and Weak Basic Drugs

Weak Acidic Drugs

→ Weak acidic drugs are better absorbed in an acidic medium such as the stomach.

Reason:

- In acidic pH, weak acids remain mostly unionized
- Unionized drugs are more lipid soluble
- Hence absorption increases

Examples:

- Aspirin
- Phenobarbital

Weak Basic Drugs

→ Weak basic drugs are better absorbed in a basic medium such as the intestine.

Reason:

- In basic pH, weak bases remain mostly unionized
- Unionized form increases lipid solubility
- Hence absorption becomes better

Examples:

- Atropine
- Ephedrine

Mechanism of Drug Absorption Through GIT

→ Drug absorption through the gastrointestinal tract (GIT) refers to the process by which drugs move from the site of administration into systemic circulation.

→ The following mechanisms are involved in drug absorption:

1. Passive Diffusion

→ Passive diffusion is the most common mechanism of drug absorption.

In this process:

- Drug moves from higher concentration to lower concentration
- No energy is required
- Lipid soluble drugs are absorbed easily

Characteristics:

- Simple process
- Does not require carrier proteins
- Depends on concentration gradient

Example:

- Most oral drugs

2. Facilitated Diffusion

→ Facilitated diffusion is the movement of drugs across membranes with the help of carrier proteins.

Characteristics:

- Carrier mediated process
- No energy required
- Movement occurs from higher to lower concentration

Example:

- Vitamin transport

3. Active Transport

→ Active transport is the movement of drugs against the concentration gradient with the help of carrier proteins and energy (ATP).

Characteristics:

- Requires energy
- Carrier mediated
- Selective process

Example:

- Absorption of amino acids and glucose

4. Pore Transport / Filtration

→ In this mechanism, small water-soluble drugs pass through pores or channels present in membranes.

Characteristics:

- Suitable for small molecules
- Depends on pore size
- No energy required

Example:

- Urea, Water

5. Ion Pair Transport

→ In ion pair transport, ionized drugs combine with oppositely charged ions to form neutral complexes which can cross lipid membranes.

Characteristics:

- Helps absorption of ionized drugs
- Increases lipid solubility temporarily

Example:

- Certain quaternary ammonium compounds

6. Endocytosis

→ Endocytosis is the process in which the cell membrane engulfs drug particles and transports them inside the cell.

Characteristics:

- Used for large molecules
- Requires energy

Types:

- Phagocytosis
- Pinocytosis

Example:

- Absorption of vitamins and proteins

Factors Affecting Drug Absorption

→ Drug absorption is influenced by various physiological, physicochemical, and pharmaceutical factors. These factors affect the rate and extent of drug absorption into the bloodstream.

1. Lipid Solubility of Drug

→ Drugs that are more lipid soluble can easily cross biological membranes made of lipids.

- Lipid soluble drugs show better absorption
- Water soluble drugs are absorbed slowly

Example:

- Diazepam is highly lipid soluble and rapidly absorbed

2. pH of Medium

The pH of the absorption site affects ionization of drugs.

- Weak acidic drugs are better absorbed in acidic medium
- Weak basic drugs are better absorbed in basic medium

Reason:

- Unionized drugs are more lipid soluble and cross membranes easily

Example:

- Aspirin absorbs in stomach
- Atropine absorbs in intestine

3. pKa of Drug

pKa is the pH at which a drug exists equally in ionized and unionized forms.

- Drugs remain more unionized when environmental pH favors them
- Unionized form shows better absorption

Thus, pKa influences drug absorption significantly.

4. Surface Area for Absorption

Greater surface area increases absorption.

- Small intestine has very large surface area due to villi and microvilli
- Therefore, most drugs are absorbed mainly from intestine

5. Blood Flow to Absorption Site

Good blood supply maintains concentration gradient and increases absorption.

- Increased blood flow → faster absorption
- Reduced blood flow → slower absorption

Example:

- Intramuscular injections absorb faster in well-perfused muscles

6. Dosage Form of Drug

Different dosage forms release drugs at different rates.

Order of absorption:

Solution > Suspension > Capsule > Tablet > Coated tablet

- Liquids are absorbed faster than solids
- Enteric-coated tablets dissolve slowly

7. Particle Size of Drug

Smaller particle size increases surface area and dissolution rate.

- Fine particles dissolve rapidly
- Faster dissolution leads to better absorption

8. Concentration of Drug

Higher drug concentration increases absorption rate.

Reason:

- Greater concentration gradient enhances passive diffusion

9. Gastric Emptying Time

The time taken by stomach contents to enter intestine affects absorption.

- Faster gastric emptying increases absorption
- Delayed emptying slows absorption

Most drugs absorb mainly from intestine.

10. Presence of Food

Food may either increase or decrease drug absorption.

Food can:

- Delay gastric emptying
- Interact with drugs
- Change stomach pH

11. Route of Administration

Different routes show different absorption rates.

Examples:

- IV route gives immediate effect
- Oral route shows slower absorption

12. Drug Interactions

Some drugs affect absorption of other drugs.

Examples:

- Antacids reduce absorption of certain antibiotics
- Iron preparations interfere with tetracycline absorption

13. Gastrointestinal Motility

Movement of GIT affects contact time of drug with absorption surface.

- Increased motility reduces absorption
- Decreased motility may increase absorption

14. Disease Conditions

Diseases can alter drug absorption.

Examples:

- Diarrhea decreases absorption
- Malabsorption syndrome reduces drug uptake

15. First Pass Metabolism

Some orally administered drugs are metabolized in liver before reaching systemic circulation.

This reduces bioavailability.

Example:

- Nitroglycerin
- Propranolol

Absorption of Drug from Non-Per Oral Extravascular Routes

- Non-per oral extravascular routes are routes of drug administration other than oral route in which the drug is not directly injected into the bloodstream.
- In these routes, the drug must cross biological membranes before entering systemic circulation.
- These routes are used when:
 - Oral administration is not suitable
 - Rapid action is needed
 - Drug is destroyed in GIT
 - Patient cannot swallow medicines

Types of Non-Per Oral Extravascular Routes

1. Sublingual Route

- In this route, the drug is placed under the tongue.
- The drug dissolves in saliva and is absorbed through the sublingual mucosa directly into blood circulation.

Characteristics

- Rapid absorption
- Bypasses first-pass metabolism
- Fast onset of action

Advantages

- Quick therapeutic effect
- Easy administration
- Useful in emergencies

Disadvantages

- Suitable only for small doses
- Drug must be lipid soluble

Examples

- Nitroglycerin



- Isosorbide dinitrate

2. Buccal Route

- The drug is placed between cheek and gum.
- Absorption occurs through buccal mucous membrane.

Characteristics

- Slow and sustained absorption
- Avoids first-pass metabolism

Advantages

- Easy to administer
- Useful for prolonged action

Disadvantages

- Limited drug absorption
- Patient discomfort possible

Examples

- Buccal tablets of nicotine



3. Rectal Route

- The drug is administered into rectum in the form of suppositories or enemas.
- Drugs are absorbed through rectal mucosa.

Characteristics

- Useful when oral route is not possible
- Partial avoidance of first-pass metabolism

Advantages

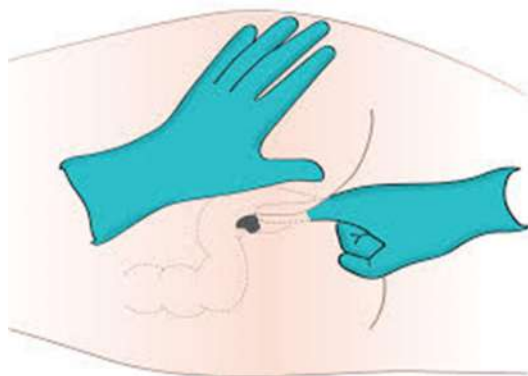
- Suitable for vomiting or unconscious patients
- Useful in children

Disadvantages

- Irregular absorption
- Patient discomfort

Examples

- Paracetamol suppository
- Diazepam rectal gel



4. Intramuscular Route (IM)

→ Drug is injected into muscle tissue.

→ Absorption occurs through blood capillaries present in muscles.

Characteristics

- Faster absorption than subcutaneous route
- Depends on blood flow

Advantages

- Suitable for oily preparations
- Moderate volume can be administered

Disadvantages

- Pain at injection site
- Risk of infection

Examples

- Streptomycin injection
- Vitamin B₁₂ injection



5. Subcutaneous Route (SC)

→ Drug is injected beneath the skin into subcutaneous tissue.

Characteristics

- Slow and sustained absorption
- Depends on local blood circulation

Advantages

- Suitable for self-administration
- Prolonged action possible

Disadvantages

- Small volume only
- Irritating drugs cannot be given

Examples

- Insulin
- Heparin



6. Inhalation Route

→ Drug is administered through lungs as gases, vapors, or aerosols.

→ Absorption occurs through alveolar membrane.

Characteristics

- Very rapid absorption
- Large surface area of lungs helps absorption

Advantages

- Rapid onset of action
- Direct effect on respiratory tract

Disadvantages

- Dose accuracy difficult
- Requires special devices

Examples

- Salbutamol inhaler
- General anesthetics



7. Nasal Route

→ Drug is administered through nasal cavity.

→ Absorption occurs through nasal mucosa.

Characteristics

- Rapid absorption
- Avoids first-pass metabolism

Advantages

- Easy administration
- Quick effect

Disadvantages

- Small dose only
- Nasal irritation possible

Examples

- Nasal decongestants
- Desmopressin nasal spray



8. Transdermal Route

→ Drug is applied on skin in the form of patches or ointments.

→ Drug slowly penetrates through skin into blood circulation.

Characteristics

- Slow and controlled absorption
- Long duration of action

Advantages

- Sustained drug release
- Improves patient compliance

Disadvantages

- Only potent lipid soluble drugs suitable
- Skin irritation possible

Examples

- Nicotine patch
- Fentanyl patch



9. Vaginal Route

→ Drugs are administered into vagina as creams, tablets, or pessaries.

Characteristics

- Local or systemic absorption possible

Advantages

- Useful for local infections
- Avoids first-pass metabolism

Disadvantages

- Variable absorption
- Patient discomfort

Examples

- Clotrimazole vaginal tablet



Factors Affecting Absorption from Non-Per Oral Extravascular Routes

- Blood flow at site
- Lipid solubility of drug
- Surface area available
- Drug concentration
- pH of medium
- Dosage form
- Condition of membrane
- Presence of disease

Advantages of Non-Per Oral Extravascular Routes

- Avoids gastrointestinal irritation
- Bypasses first-pass metabolism
- Faster onset of action possible
- Useful in unconscious or vomiting patients
- Suitable for sustained drug delivery

Disadvantages

- Some routes are painful
- Risk of infection
- Limited dose administration
- Absorption may vary
- Special techniques may be required