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Diploma in Pharmacy 2nd Year
Pharmacology
Chapter 1 : General Pharmacology

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Chapter 1

General Pharmacology

Introduction

Pharmacology is derived from Greek word

Pharmacon means ***drug***

logos means to study

Pharmacology means to study about drug and its action.

Definition

Pharmacology is a branch of science in which we study about drugs and their Interaction with the living organism.

Or

It can be defined as " Pharmacology is a branch of science in which we study about Pharmacokinetic and Pharmacodynamics "

Pharmacokinetics :

- It is a Greek word which means the " the action of body on the drugs "
- Pharmacokinetic Involves the study of drug's absorption, distribution, metabolism, and excretion .

Pharmacodynamic :

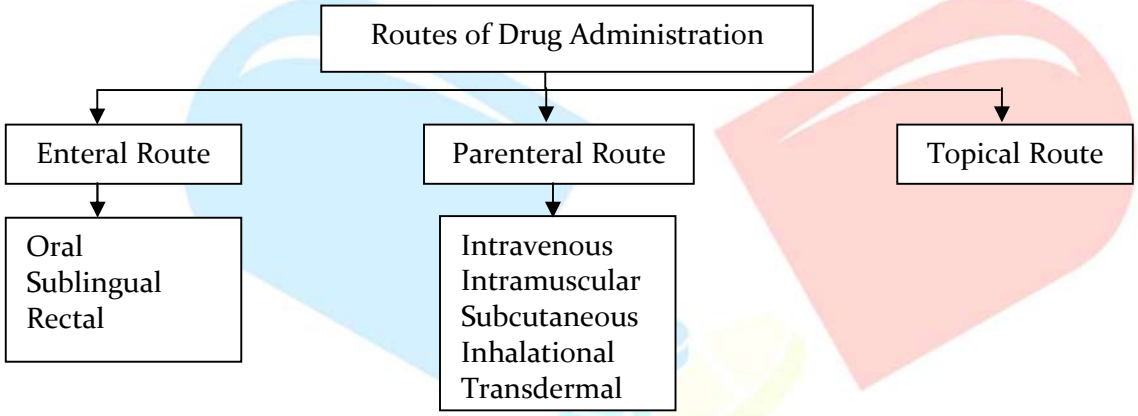
- It is also a Greek word which means " the action of drugs on the body "
- Pharmacodynamics involves the study of concentration of drugs on the site of action , result of effect , timing of drug's action , adverse effect etc.

Scope Of Pharmacology

- **Pharmacotherapeutics :** A person who has knowledge of Pharmacology can treat the patients , because he Knows selection of appropriate drugs , their dosage , and half life .
- **Preclinical Clinical trails :** A pharmacologist can work in the field of preclinical trails .
- **Clinical Trails :** A pharmacologist can work in the field of clinical trails .
- **Drug discovery :** A pharmacologist can go in the field of research and discover many of new drugs .
- **Toxicology :** A pharmacologist can reduce the toxicity effect, and turn adverse effects .

Various Route of Drug Administration

- Route of drug administration is the path by which the drug is introduced into the body.
- For the treatment of a disease, the drug is introduced into the body through a specific site.
- The choice of route for the drug administration depends on:
    - Properties of the drug like water or lipid solubility, ionisation, etc.
    - Therapeutic objectives, i.e., rapid onset of action or long-term administration or restricted to a local site.



Enteral Route

- It is the safest, most economical, and convenient route of drug administration.
- Tablets, capsules, powders, mixtures, emulsions and gels are taken orally.
- Solution form of drug gets rapidly absorbed through enteral route.

Oral Route

- In this route the drug is placed in oral cavity and is swallowed along with water or milk etc.
- Drug is administered through mouth.
- It is also known as per oral (p.o.).
- The main advantages of this route are that the patient is able to self-administer drug and chances of systemic infection are reduced.
- Activated charcoal (antidote) is used in the treatment of toxicities or overdose related problems of oral route.

Advantages

- Safe, convenient and painless method therefore most preferred.
- Economical, sterilisation is not required.
- For oral drug administration any assistance is not required.
- Less chances of acute drug reaction.

Disadvantages

- Sometimes complete drug is not absorbed.
- First-pass metabolism takes place in liver where drug reaches through the portal vein.
- Gastric mucosa irritation by certain drugs leads to nausea and vomiting.
- Not effective in emergencies.
- Unpleasant taste of drugs.
- Route not preferred in unconscious and uncooperative patients.
- Low gastric pH, digestive and liver enzymes destroy drug, before its distribution into circulation.

Sublingual/Buccal Route

- Drug (small size tablet) is kept beneath the tongue (without water) to disintegrate and get absorbed in mouth, e.g., nitroglycerine tablets.
- The drug enters the systemic circulation through diffusion into the capillary network.
- In buccal route drug kept within the mouth around the cheeks or buccal cavity, where it disintegrates and get absorbed.

Advantages

- Rapid absorption of drugs due to highly vascularised site therefore fast onset of action.
- Stomach enzymes and acids are not involved so the drug remains stable.
- Drugs do not undergo first-pass metabolism.
- In case of any side effects drug can be withdrawn.
- Drugs can be administered easily.
- Less chances of infection.
- No involvement of GI environment.

Disadvantages

- It is sometimes inconvenient to keep drug in mouth.
- Small doses are required to keep in mouth.
- Drugs having high molecular weight cannot be absorbed (e.g., insulin).
- Unpleasant, distasteful, irritant drugs cannot be administered through this route.

Rectal Route

- Suppositories are drugs that are administered through rectal route.
- Drug is formulated with waxy additives in which drug is dissolved or liquefy on insertion into the rectum.
- Drug absorbance occurs directly through thin, highly vascularised wall of rectum.
- This route is used to avoid the destruction of drug by intestinal enzymes or by low pH of stomach.
- The drug is administered in the form of suppositories, through rectal route, when patient is not able to take drug orally (due to vomiting, in consciousness) or have restrictions on eating (mostl after surgery).

Advantages

- Useful when patient is suffering from nausea and vomiting.
- By-pass first pass metabolism can be avoided, since absorption occurs from external haemorrhoidal veins.
- Gastric irritant drugs are administered through this route.

Disadvantages

- Rectal inflammation.
- Irregular absorption.

Parenteral Route

→ All the route of drug administration other than the enteral route comes under parenteral route.

→ but this route mainly includes subcutaneous, intramuscular, an intravenous injections.

→ This route is useful when:

1) Drug is poorly absorbed from the gut,
2) Digestive enzymes destroy the drug,
3) To avoid first pass metabolism by liver
4) Rapid action of drug desired.

Intravenous (IV) Route

- In this Route the drug is directly injected into Vein through injection.
- Which absorbed directly into blood stream.
- Injection Inject at a angle of 25°

Advantages

- 100% bioavailability.
- Large quantities.
- Emergency situations.
- Diarrhoea and vomiting.
- No first-pass metabolism.

Disadvantages

- Inconvenient and painful causing irritation, cellulitis and thrombophlebitis.
- Repeated injections not suitable.
- Safety level is very low.
- Technical and trained person required.
- Infection may occur.
- Costly.

Intramuscular (IM) Route

- The drug is injected into muscles than the drug reach into Blood Circulation.
- Injection Inject at a angle of 90°

Advantages

- Uniform absorption.
- Onset of action is fast.
- Prevent first pass metabolism.
- No GIT related factors.

Disadvantages

- Only 10ml drug may be administered.
- Local pain and infection.
- Expensive.

Subcutaneous (SC) Route

- Drug is deposited into loose subcutaneous tissue which is richly supplies by nerves.

Advantages

- Self-administering.
- Onset of action is fast.
- Prevent first pass metabolism.
- No GIT related factors

Disadvantages

- Painful.
- Irritant drugs cause tissue damage.
- Maximum 2ml of dose may be injected.

Inhalational Route

- It delivers drug throughout the respiratory tract, mucous membranes and pulmonary epithelium, as well as giving fast effect as intravenous injections.
- Gases or aerosol forms of drugs like anaesthetics are administered through this route.
- This route is effective in treatment of patients with respiratory complications such as asthma, or chronic obstructive pulmonary disease.
- Systemic side effects related to drugs (e.g., albuterol and corticosteroids fluticasone) can be minimised in this route.

Advantages

- Surface area of the respiratory endothelium is large causing rapid absorption.
- Instant absorption of drug and rapid onset of action.
- No hepatic first-pass metabolism of drug.

Disadvantages

- Specialised equipment required for drug delivery, e.g., inhalers.
- Bioavailability of drug depends on the patient's inhaler technique and drug particle size of drug.
- Due to use of inhaler dose regulation is difficult.

Transdermal Route

- Transdermal patches are employed to deliver systemic effect of drug through skin.
- The rate of absorption depends on physical characteristics of the skin and application site.
- Transdermal patch provides sustained delivery of drugs,
- e.g., antianginal drug (nitro-glycerine), antiemetic (scopolamine), and contraceptive patch.

Advantages

- Sustained effect.
- No hepatic first-pass metabolism.
- Convenient and good patient compliance.

Disadvantages

- Relatively slow onset.
- Excessive absorption may give inflamed, rough, abraded on skin.
- This route is preferred for highly lipophilic drugs.

Topical Route

- In topical route drug is applied on the surface of skin (epidermis) or mucous membrane, by means of special formulations, e.g., creams, ointments, gels, lotions, sprays, powders, and aerosols.
- By the topical route local (affecting a small area) to systematic (affecting the entire body) effects can be obtained.
- The drug is absorbed through the pores present in skin (e.g., sweat glands and hair follicles, etc.).
- These dosage forms treat skin infections, minimise inflammation, and protect skin.

Advantages

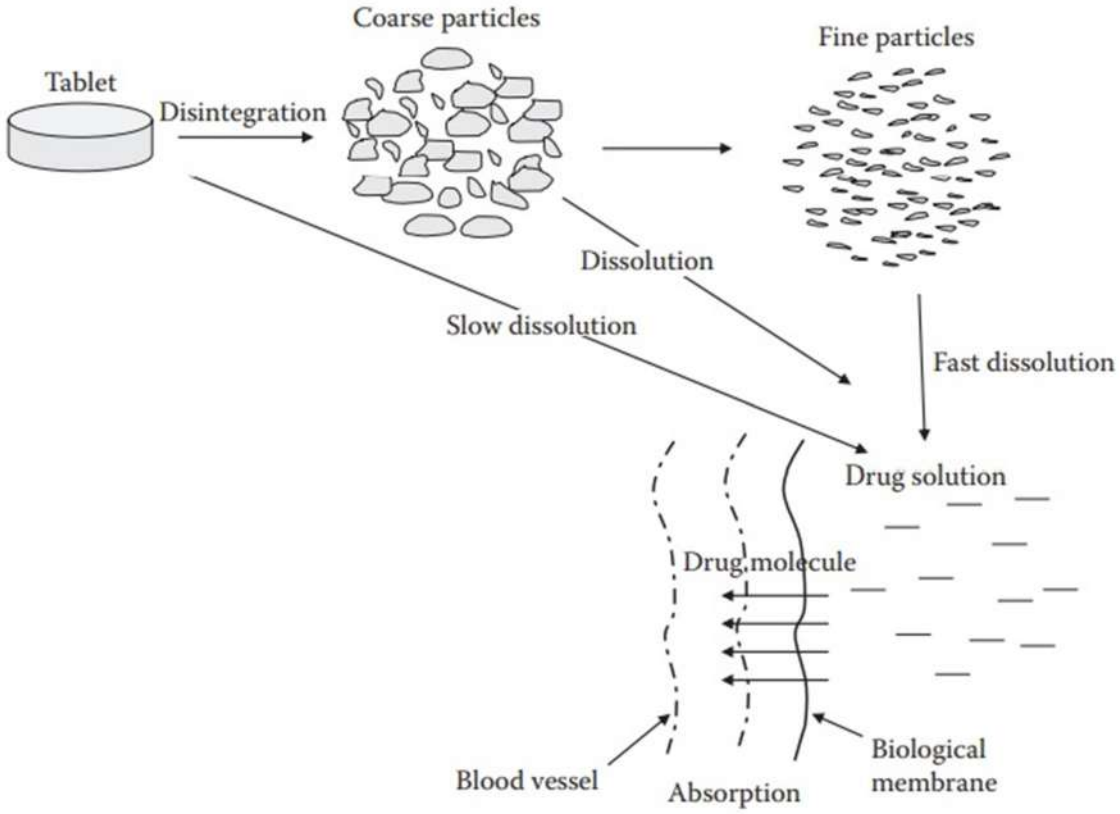
- Drug can be applied easily.
- Less complication than oral delivery as drugs poorly absorbed systemically.
- Fast action on application site.

Disadvantages

- Skin irritation
- Improper absorption of certain drugs.
- Ointments have longer duration of action due to sticky and oily texture.

Drug Absorption

- → It is Defined as the movement of drug molecule from its site of administration to the systemic circulation in unchanged form.
- → When we take any drug through oral route it goes into stomach in which disintegrants and dissolution takes place then drug reach into intestine.
- → Now after dissolution drug absorbed into blood from intesting through membrane.



Types of Drug Absorption

- ➢ Passive diffusion /simple diffusion
- ➢ Filtration / Pore transport
- ➢ Endocytosis .
- ➢ Facilitated diffusion .
- ➢ Active Transpor

- ❖ **Passive diffusion /simple diffusion :** In this type of absorption the drug is transported from higher concentration to low concentration.

- **Filtration / Pore transport :** In this type of absorption the drug molecules are pass through the space between tow cells.
- **Endocytosis :** In this type of absorption the cell membrane engulfs the drug molecule and take inside the cell.
- **Facilitated diffusion :** In this type of absorption a carrier protein helps in the entering of drug inside the cell or membrane from higher concentration to low concentration , and no energy required in this process.
- **Active Transport :** In this type of absorption the carrier molecule combines with drug molecule and transports it inside the membrane , and energy is required in this process.

Factors Affecting Absorption of Drugs

- **Physical State of Drug :** the liquids are betterly absorbed than solid medicaments .
- **Particle Size Smaller :** Particle size of drug absorbed easily .
- **Surface area of absorbing site :** Larger absorbing surface area provides greater absorption of drug .
- **Physical and mental state of the patient :** abnormal / disturbed physiological conditions affect the absorption of drugs like infection , fever ,emotional upset etc.
- **Functional condition of GIT :** Increased peristaltic movement of GIT decreases the absorption of drugs .
- **pH of drug Acidic :** drugs are rapidly absorbed in stomach while basic drugs are rapidly absorbed in intestine
- **Presence of food and other things in GIT :** The presence of food in GIT may reduce the absorption of drugs , because no direct connation with walls of GIT .

Bioavailability

→ Bioavailability is the friction of administered drug that reaches the systemic circulation.

→ Bioavailability is expressed as the fraction of administered drug that give access to the systemic circulation in a chemically unchanged form.

→ For Example

If 100 mg of a drug administered orally and 60 mg is this drug are absorbed unchanged the bioavailability 0.6 / 60 %

→ Bioavailability is defined as the rate and amount of absorption of unchandged drug from its dosage forms and become available at the site of action

→ Bioavailability is made up of two words

Bio means ***Living Organisms***

Availability means ***to be present (at site of action)***

Factors Affecting Bioavailability

- Physical State of Drug
- Particle Size
- Solubility of Drug
- PH of Fluid
- Effect of first pass metabolism

Distribution of drug

→ Distribution of drug means delivery/transportation of drug to body's tissues.

→ Body Fluid function s solvent for maximum drug, and the drugs reach their site of action by this solvent system.

Factors Affecting Drug distribution

- Age (fat content , skeletal muscles , Plasma protein)
- Pregnancy.
- Obesity.
- Disease conditions .
- Drug interaction.
- Diet.

Biotransformation of Drugs

→ Also known as drug Metabolism

→ It is Defined as the conversion of drug from one chemical form to another.

Or

→ The chemical alteration of the drug in the body , in which nonpolar drugs are converted into polar form and lipid soluble compounds are converted into lipid insoluble form.

Drug Metabolizing organs.

- Liver is the heart of metabolism
- Because of its relative richness of enzymes in large amount
- Schematic Chart of Metabolizing Organs
- Liver > Lungs > Kidney > Intestine > Placenta > Skin > Brain > Testes > Muscles > Spleen

Types of Biotransformation Reaction

⇨ Mostly Biotransformation are done by microsomal enzymes Such as Cytochrome P-450 Oxidose, Glucuronyl transferace.

⇨ It is divided into two types

- Phase 1 Reaction
- Phase 2 Reaction

Phase 1 Reaction

- In this reaction the drugs can be metabolized by Oxidation, Reduction, Hydrolysis and Increase polarity (Water Solubility) of drugs.
- So drugs can easily excreta from kidney.
- There are no-synthetic reaction.

- **Example :** Aspirin $\xrightarrow[\text{Hydrolysis}]{\text{Enzyme}}$ Salicylic acid

Phase 2 Reaction

- This Reaction is faster than phase 1 Reaction and also those not excreted after phase 1 Reaction can excreted through phase 2 Reaction
- It involve Conjugation with an endogenous substance such as glucuronic acid , sulfate etc. Acetylation , Methylation, Glycine.
- These Reaction are more polar.
- So the drugs can easily excreted by the kidney & Liver.
- **Example :** Salicylic acid $\xrightarrow[\text{Acid}]{\text{Glucumic}}$ Excreation

Factors Affecting drug Metabolism

- **Inhibitors :** certain drugs like omeprazole , ciprofloxacin inhibit enzymes that metabolise a drug .
- **Stimulators :** certain drugs like phenobarbitone , rifampicin can increase the activity of enzymes that metabolise a drug .
- **Age :** Young children show poor drug metabolism because metabolic enzymes are not developed properly in them .
- **Sex :** In comparison to males , females have lesser ability for drug metabolise .
- **Body Temperature :** High temperature of body provides fast metabolism of drugs .

Excretion of Drugs

- It is a process of body in which drugs or metabolites are removed from the body.
- Drug excretion is the removal of drug from the body either as a metabolite or unchanged drug.
- There are two types of excretion :

  Renal Excretion : Kidneys are main organs for excretion , and the excretion is done through kidneys is called renal excretion .

  Non- Renal Excretion : The excretions by all other organs except kidneys are called Non renal excretion . (lungs , intestine , salivary glands , sweat glands).
- It is the Last step of Pharmacokinetics

Route of Drug excretion

- There are many different route of excretion like
- **Urine**
  - Most of Drugs are excreted through the kidney by the process of urination
  - Water soluble drugs excreted out through this.
- **Milk**
  - It is also Known as mammary excretion.
  - A drug that is excreted in milk can enter to breast feeding infant and therefore it is significant.
- **Skin (Sweat)**
  - Some of Drugs is excreted in the form of sweat from skin
  - Sweat show the excretion of compound like Benzonic acid, Salicylic acid and Alcohol etc
- **Salivary Excretion**
  - This involves the excretion of drugs through the saliva.
- **Faeces**
  - Some of drugs in liver is absorbed in bile which further excreted through Faeces.
- **Lungs**
  - Some Drugs in the form of gases and volatile lipids are eliminated through exhalation by lungs.

General Mechanism of Drug Action

- Most of Drugs Produce their action by interacting with a target biomolecules like – Protein etc.
- How any drugs produce their action is known as Mechanism of Drug action
- The general Mechanism of action of drugs can be classified into the following four classes
  1. Transport Process
  2. Enzymes
  3. Ion Channels
  4. Receptors

Factors Modifying drug action

- Body Weight
- Age
- Sex
- Route of administration
- Time of administration
- Diet and environmental factors
- Genetic Factors
- Emotional Factors
- Presence of disease
- Metabolic disturbance