Introduction to Pharmacology

Pharmacology:
Pharmacology is a branch of science that deals with the study of drugs that interact with the living systems through chemical processes, especially by bindings to regulatory molecules and activating or inhibiting normal body processes.

Clinical Pharmacology:
It evaluates the pharmacological action of drug, preferred route of administration and safe dosage range in human by clinical trials.

Branches of Pharmacology:

Pharmacognosy: It is a branch of Pharmacology which deals with-

- Source
- Identification
- Isolation
- Purification
- Standardization of drugs

Pharmacy: It is a branch of Pharmacology which deals with-

- Preparation
- Quality Control
- Dispensing of drugs

Pharmacokinetics: It is a branch of Pharmacology which deals with- (ADME)
("i.e what the body does to the drug").

- Absorption
- Distribution
- Metabolism
- Excretion

Pharmacodynamics: It is a branch of Pharmacology which deals with the effects of drug and the M/A ((i.e, "what the drug does to the body"). Effects may be-

- Beneficial effect (Therapeutics)
- Adverse effect (Toxicology)

Pharmacotherapeutics: It is a branch of Pharmacology which deals with the proper selection and use of drugs for the prevention and treatment of disease.

Toxicology: It's the science of poisons. Many drugs in larger doses may act as poisons. Poisons are substances that cause harmful, dangerous or fatal symptoms in living substances.

Pharmacogenetics:

When changes in the gene is directly related to the pharmacological action of the drug then it is called pharmacogenetics/ genetics. Pharmacogenetics typically refers to effects involving a limited number of genes, often involving drug metabolism. Pharmacogenetics is the study of genetic causes of individual variations in drug response.

Eg. CYP 2C19 gene encode CYP2C19 enzyme. If mutation of CYP 2C19 gene occur then it will change the pharmacological action of clopidogrel.

Pharmacogenomics:

When changes in the genome is directly related to the pathophysiology of the disease then it is called pharmacogenomics. pharmacogenomics involves the study of complex multigene patterns within the genome. Genetic polymorphisms are variants in individual genomes and remain constant throughout a person's lifetime. pharmacogenomics deals with the simultaneous impact of multiple mutations in the genome that may determine the patient's response to drug therapy.

Example: Wilm's tumor, Cancer.

Chemotherapy: It is a branch of Pharmacology which deals with the effects of drugs upon microorganisms, parasites and cancer cell.

Drugs: According to the WHO-
A drug is any substance or product that is used or intended to be used to modify or explore physiological systems or pathological states for the benefits of the recipient.
The aim of the drug is to improve the quality of life.

Use of drugs:
Diagnosis- $BaSO_4$ for GIT lesion
Prevention- Vaccine, contraceptives
Suppression/Control: Insulin for DM, Antihypertive drugs
Treatment: antibiotics for infection, diuretics for edema, analgesic for pain

Pharmacopoeia: An official code containing a selected list of the established drugs and medical preparations with descriptions of their physical properties and tests for their identity, purity and potency e.g. Indian Pharmacopoeia (I.P), British Pharmacopoeia (B.P) and United States Pharmacopoeia (USP).

Medicine: Medicines are the drugs which have been studied for its activity, dose and toxic effect and are recommended for therapeutic uses against diseases.

Differences between **Drug** and **Medicine**

Drug	Medicine
API of the medicine	Combination of API and excipients
Biologically active, prepared by a chemist.	Biologically active, prepared by a pharmacologist/pharmacist.
Can be cured for many purposes.	Used only for curing diseases.
M/A, dose, toxic effect, P/A are not established and are carrying through.	These parameters are not well established.

Sources of drugs

Common sources:

1. **Natural sourses:**
   - Plant sourses: Atropine
   - Animal sourses: Insulin, Heparin
   - Mineral sourses: $FeSO_4$
2. **Synthetic sourses:** Aspirin, Paracetamol
3. **Sesynthetic sourses:** Tetracycline.

Dose: The amount of drug or other remedy which is to be taken all at a time or in a fractional amount within particular time to get the biological response is called dose.

Dosage form: The form in which drug is taken is called dosage form. E.g. injection, tablet, syrup, liquid etc.

Dosage: Dosage is the determination of the amount, frequency and amount of doses of drug for a patient is called dosage.

Posology: Posology is a branch of medical science which deals with the doses or quantity of drugs which can be administered to produce the pharmacological effects.

Median lethal dose or LD50: This is the dose (mg/kg), which would be expected to kill one half of a population of the same species and strain.

Median effective dose or ED50: This is the dose (mg/kg), which produces a desired response in 50 per cent of test population.

Therapeutic index or therapeutic ratio: It is an approximate assessment of the safety of the drug. It is the ratio of the median lethal dose and the median effective dose. Also called as therapeutic window or safety.

$$\boxed{\text{Therapeutic ratio} = \frac{\text{LD}_{50}}{\text{ED}_{50}}}$$

The larger the therapeutic index, the safer is the drug. Penicillin has a very high therapeutic index, while it is much smaller for the digitalis preparation.

MEC (Minimum effective concentration): The minimum amount of drug required to produce desired pharmacological effect is known as MEC.

MTC (Maximum therapeutic concentration or minimum toxic concentration): It is the concentration of a drug above which the drug shows its therapeutic activity or it the concentration of a drug above which the drug shows its toxic effect.

Over The Counter Drugs (OTC): Drugs which are available without prescription are called OTC drugs.

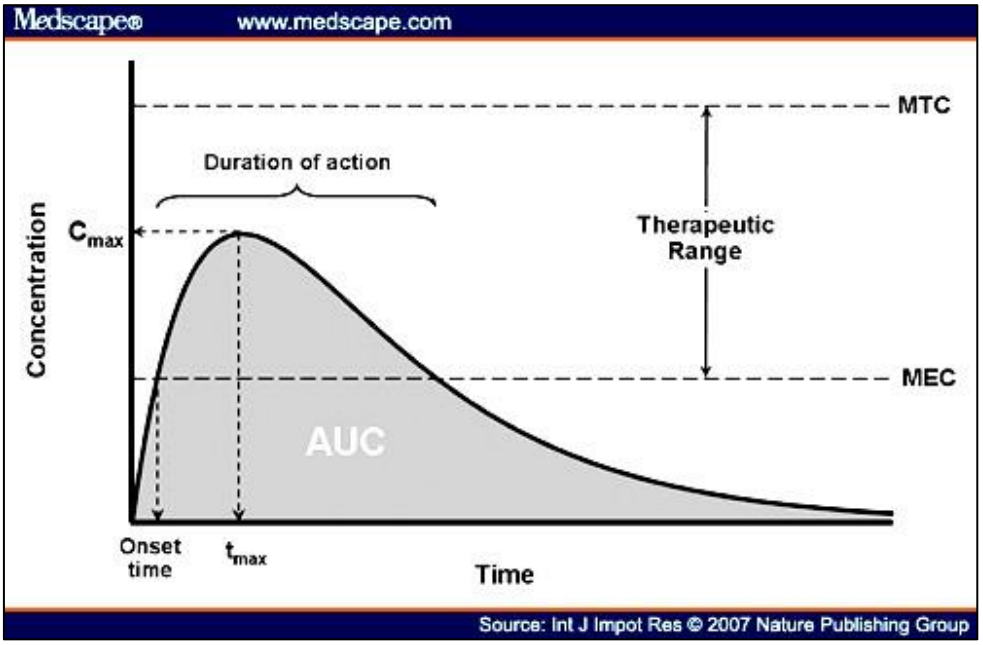
E.g. Paracetamol, vitamin tablet, iron tablet etc.

Prescription drugs: Drugs which are available with prescription are called prescription drugs. These drugs are prescribed by registered physician.

Control drug: Drugs which can never be dispersed without prescription. E.g. Narcotics, pathidine, heroine etc.

Official drugs: Drugs which are included in pharmacopoeia.

AUC (area under the curve):



The therapeutic effect: is the primary effect intended that is the reason the drug is prescribed such as morphine sulfate in analgesia.

Side effect: secondary effect of the drug is one that unintended, side effects are usually predictable and may be either harmless

Drug toxicity: Drug toxicity is the deleterious effect of the drug on an organism or tissue, result from overdose or external use.

Drug allergy: Drug allergy is an immunological reaction to a drug.

Drug interaction: Drug interaction occurs when administration of one drug before or after effect of one or both drug.

Drug misuse: It is the improper use of common medications in way that lead to acute and chronic toxicity for example laxative, antacid and vitamins.

Drug abuse: It is an inappropriate intake of substance either continually or periodically.

Drug dependence: It is a person's reliance on or need to take drug or substance.

There are two type of drug dependence:

A. **Physiological dependence:** It is due to biochemical changes in the body tissue these tissue come to require substance for normal function.
B. **Psychological dependence**: It is emotional reliance on a drug to maintain a sense of wellbeing accompanied feeling of need.

Drug habituation: denotes a mild form of psychological dependence.

Illicit drug: Illicit drug use includes the non-medical use of a variety of drugs that are prohibited by international law. These drugs include: amphetamine, cocaine, heroin and other opioids. Also called **street drug** are those sold illegally.

Names of Drugs:

1. **The generic name:** It is given for the drug to being official name. Paracetamol
2. **The official name:** It is the name under which it is listed in one in the official publication. Paracetamol in BP; Acetaminophen in USP
3. **The chemical name:** It is the name by which the chemist knows it. e.g.: N-acetyl-p-aminophenol
4. **The trade mark or brand name (proprietary name):** It is name given by the drug manufacture. Example: Paracetamol in BP (official name) and NAPA, ACE (brand name)

Differentiate between Idiosyncrasy and Hypersensitivity or allergic drug reaction.

Idiosyncrasy	Hypersensitivity
Inherent quantitative abnormal reaction to a drug usually due to genetic abnormality	Inappropriate or excessive immune reaction which causes tissue damage

Idiosyncrasy has no subtypes e.g. In G-6-PO_4 dehydrogenase patient sulphonamide causes haemolysis.	Hypersensitivity has 4 subtypes **Type I:** Anaphylactic reaction e.g. Conjunctivitis, penicillin hypersensitivity **Type II:** Antibody dependent cytotoxic hypersensitivity e.g. Auto immune haemolytic anaemia **Type III:** Immune complex mediated hypersensitivity e.g. Rheumatoid arthritis **Type IV:** Cell mediated or delayed type hypersensitivity e.g. Leprosy

Routes of Drug Administration

The path taken by the drug to get into the body is known as the route of drug administration. A drug may be in ionized or unionized form.

SELECTION OF ROUTE

The ROA is determined by :

✓ **the physical characteristics of the drug**

✓ **the speed which the drug is absorbed and/ or released**

✓ **the need to bypass hepatic metabolism**

✓ **to achieve high conc. at particular sites**

✓ **Accuracy of dosage**

✓ **Condition of the patient**

❖ Classification:

1. Local routes
2. Systemic routes

❖ Local routes

1. Topical
2. Deeper tissues

3. Arterial supply

1. Topical or site specific route

Skin, eye, ear, nose, respiratory tract, vagina are included in the topical or site specific route. This route is often chosen to ensure that the **drug reaches a specific site with a minimum absorption into the systemic circulation with a view to reducing adverse effects**.

-Cutaneous administration

The drug is applied on the surface of the skin. The principle is to deliver a drug locally or to get systemic effect.

When the drug is applied on to the skin with the purpose of absorption, it is called transdermal administration. Scopolamine and glyceryl trinitrate can be administered though this route.

-Conjunctival administration

The ophthalmic drug in solution, suspension, ointment or solid dosage form is applied on to the surface of the conjunctiva with the purpose to get its local effect.

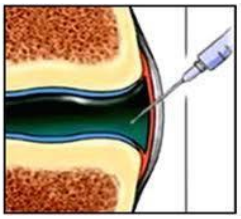
Since liquid preparation is quickly washed away by normal eye secretion, ointment is often used at night in order to retain the drug in the eye for a longer period.

2. Deeper tissue

Certain deep areas can be approached by using a syringe and needle, but the drug should be such that systemic absorption is slow.

Intra-articular route

Intra-articular route involves injection into the joint cavity/space. Corticosteroids may be injected by this route in rheumatic arthritis.



Intracardiac route

It means the injection of drug directly into the heart. Adrenaline is administered through this route after cardiac arrest.

Intrathecal route:

Intrathecal route involves the subarachnoid space (directly into the brain). Methotrexate is frequently administered for the management of leukemic involvement of the CNS. This technique requires special precautions.

Intraperitoneal route

Here, the drug is administered directly into the peritoneal cavity. Hypertonic solution may be used for peritoneal dialysis through this route. This solution removes waste products from plasma.

3. Arterial supply

Intraarterial route

The drug is administered directly into the artery. Sometimes it is preferred for the anticancer drugs such as floxuridine for the treatment of liver cancer.

❖ Systemic routes

- ✓ Oral
- ✓ Sublingual
- ✓ Buccal
- ✓ Rectal
- ✓ Inhalation
- ✓ Nasal
- ✓ Parental

a. <u>Oral Route</u>:

- Oral route is the most common route of drug administration and most of the drugs are administered by this route. It may be in the form of tablets, capsules, syrup, emulsions or powders. E.g. ampicillin, aspirin, isoniazid etc.
- Some drugs are absorbed from stomach; however, duodenum is the major site of drug absorption due to its larger absorptive surface.
- Most drugs absorbed from GI tract enter the portal circulation and encounter the liver before they enter into systemic circulation.
- Ingestion of drug with food or other drugs can influence drug absorption

Advantages:

- <u>Convenient</u> - self- administered, pain free, easy to take
- <u>Absorption</u> - takes place along the whole length of the GI tract
- <u>Cheap</u> - compared to most other parenteral routes

Disadvantages:

- ✓ Slow onset of action.
- ✓ Not suitable for unconscious and non-cooperative patients.
- ✓ Sometimes inefficient - only part of the drug may be absorbed
- ✓ First-pass effect occur
- ✓ Irritation to gastric mucosa - nausea and vomiting
- ✓ Discoloration of the teeth

✓ Not suitable for bitter tasting drug

✓ destruction of drugs by gastric acid and digestive juices

✓ Not suitable for emergencies

Most biotransformation occurs at some points between the absorption of drug into the general circulation and its renal circulation. However, some drugs may be metabolized in the stomach, intestinal wall, liver or in the lungs before being absorbed into systemic circulation. This phenomenon is known as first-pass effect or biotransformation.

First Pass Effect / first pass metabolism

It is also called pre-systemic metabolism.

Pre-systemic / First pass metabolism

Metabolism of the drug in the stomach, intestinal wall and liver or in the lung before being available into the systemic circulation is called Pre-systemic / First pass metabolism.

Hepatic first pass metabolism

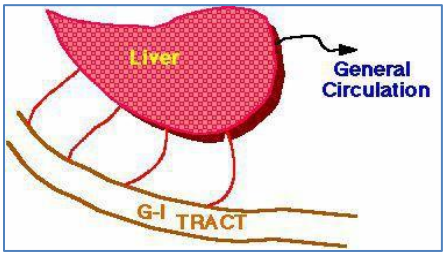
Metabolism of the drug in the liver before being available into the systemic circulation is called hepatic first pass metabolism.

Drugs undergoing first- pass biotransformation are chlorpromazine, glyceryl trinitate, imipramine, levodopa, lidocine, metoprolol, morphine, propranolol, salbutamol, verapamil etc.

Greater the first pass effect, less amounts of the drug reach the systemic circulation.

Only 20 mg of a 100 mg oral dose of propanolol reaches systemic circulation.

The greater the first-pass effect, the less the agent will reach the systemic circulation when the agent is administered orally



b. *<u>Sublingual Route</u>*:

Sublingual route involves tablets placed under the tongue. The drug should be lipid soluble and small. Examples- nitroglycerin, isoprenaline and oxytocin. Nifedipine used for the treatment of hypertension in emergency is given by sublingual route.

Advantages:

- Rapid onset of action.
- Not destroyed by gastric juice
- Overcome the first pass effect.
- Economical
- Quick termination
- Drug absorption is quick

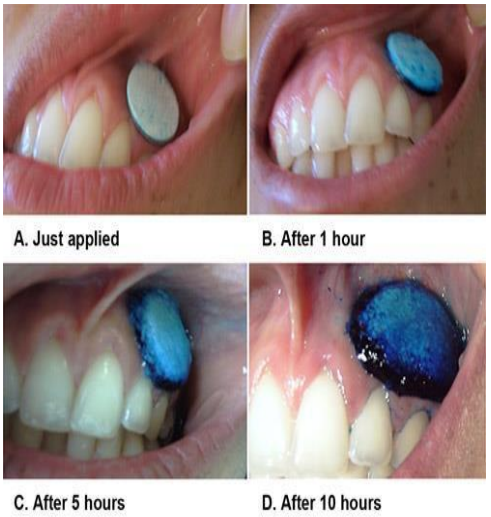
Disadvantages:

- Unsuitable for bitter drugs
- irritation of oral mucosa
- few drugs are absorbed
- Impossible to administer large volume of drug.
- Short duration of action.

c. Buccal Route

Buccal administration is where the dosage form is placed between gums and inner lining of the cheek

(buccal pouch) absorbed by buccal mucosa**.**



Advantages

- Avoid first pass effect
- Rapid absorption

Disadvantages

- Inconvenience
- advantages lost if swallowed
- Small dose limit

d. Rectal Route:

Rectal administration means the placement of drug in the rectum in the form of suppository, ointment or liquid for local or systemic effect. E.g. Analgesics (e.g. aspirin, paracetamol), antiemetics (e.g.

chlorpromazine) are used for systemic effect. Purgatives (laxatives) are administered in rectum for local

effect.

Advantages:

- Avoid gastric irritation.
- Not destroyed by gastric juice.
- Suitable for the patients who are unable to swallow.
- Used in children
- Little or no first pass effect
- Used in vomiting/unconscious
- higher concentrations rapidly achieved

Disadvantages:

- This route is generally not acceptable by the patients.
- Drugs given by rectal route have 50% first pass metabolism.
- Irritation of rectal mucosa may occur.
- Absorption is slow and incomplete.

e. Inhalation

The drug is inhaled into the lungs where the site of action may be local or systemic. Here the lung serves as the route of both administration and elimination.

Dosage form: Inhaler, Aerosol.

Advantages:

- Rapid absorption takes place.
- Rapid onset of action takes place.
- This route has minimum side effects.
- No first pass effect takes place.
- This method is easy.
- Self-medication is possible.

Disadvantages:

- Special apparatus is required.
- Irritation of the respiratory tract may take place.
- Cooperation of the patient is required.
- Airway must be patent.

f. Nasal administration

The drug in the form of drop or spray is administered into the nose. Xylometazoline is an example of a nasal decongestant.

Advantages:

- ✓ Local therapeutic effects
- ✓ lower risk of side effects
- ✓ Transdermal route offers steady level of drug in the system

g. Parenteral Route

It means the administration of drugs only by injection.

Parenteral route includes:

a. Subcutaneous Route (SC)

Subcutaneous route is injected into subcutaneous tissue (i.e. tissue layers beneath the skin).

The volume used is 2 ml. Insoluble suspensions like insulin and solids might be applied by this route. Example - insulin.

IMPLANT: A tablet or porous capsule is inserted into the loose tissues by incision of the skin, which is then stitched up. Example: certain hormonal drugs

Advantages:

- Absorption is slow and uniform,
- Self-medication is possible.

Disadvantages:

- Not suitable for large volume administration.
- Painful.
- Skin discoloration may occur.

b. Intramuscular route (IM)

Intramuscular route might be applied to the deep muscle. The volume used is 3 ml. Several drugs (e.g. benzylpenicillin, streptomycin, iron-dextran complex) are administered through this route.

Advantages:

- Rapid onset of action.
- Chosen for the patients who are intolerant of oral preparations
- Suitable for unconscious patients.
- Slow releasing drugs can be given by this route.
- Uniform absorption.
- Mild irritants can be given
- First pass avoided
- Gastric factors can be avoided

Disadvantages

- Self-medication not possible.
- Some drugs may cause tissue staining as in iron-dextran complex.
- Skilled person is needed.
- Sterility is needed.
- Painful and expensive.
- Only upto 10ml drug given
- Local pain and abscess
- Infection & nerve damage may happen

c. Intravenous injections (IV)

Intravenous injections might be applied through the veins. In case of acute bronchial asthma, aminophylline and in case of dehydration, saline are administered by this route. TPN or Total Parenteral Nutrition (containing nutrients and drugs) is administered by this route.

Advantages:

- Rapid onset of action.
- This route is preferred in emergency situations
- This route is preferred for unconscious patients
- Large volume of fluids might be injected by this route
- No first pass effect takes place.
- Administration of drug can be stopped if adverse effect develops.
- Bioavailability 100%
- Suitable for patients with vomiting & diarrhea
- Gastric manipulation avoided

Disadvantages:

- Self-medication is not possible.
- Skilled person is necessary.
- This method is not suitable for oily preparations
- irritation & cellulitis
- repeated injections not always feasible
- less safe
- technical assistance required
- danger of infection
- expensive
- painful and less convenient

d. Intradermal route

✓ Drug is given within skin layers (dermis)

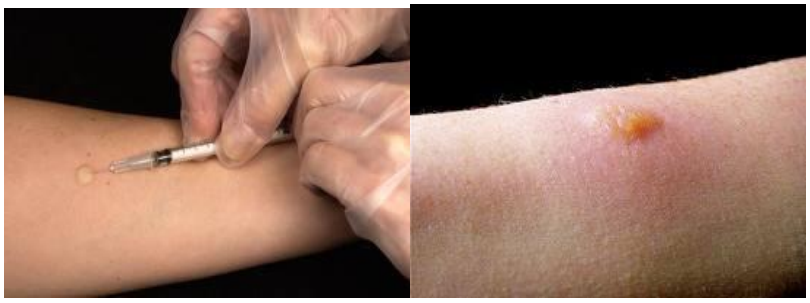
✓ Painful

✓ Mainly used for testing sensitivity to drugs.

E.g. penicillin, ATS (anti tetanus serum)

INOCULATION: administration of vaccine (like small pox vaccine)

The drug is injected into the dermis layer of the skin. This route is mostly used for diagnostic purposes. This route is usually painful.



e.

Route for administration
-Time until effect-

intravenous	**30-60 seconds**
inhalation	**2-3 minutes**
sublingual	**3-5 minutes**
intramuscular	**10-20 minutes**
subcutaneous	**15-30 minutes**
rectal	**5-30 minutes**
ingestion	**30-90 minutes**
transdermal (topical)	**variable (minutes to hours)**

ROA, Bioavailability & General Characteristics

Route	Bioavailability (%)	Characteristics
Intravenous (IV)	100	most rapid onset
Intramuscular (IM)	75 to ≤ 100	large volumes may not feasible; may be painful
Subcutaneous (SC)	75 to ≤ 100	smaller volumes than IM; may be painful; slower onset than IV or IM
Oral (PO)	5 to < 100	most convenient; first-pass effect may be significant
Rectal (PR)	30 to < 100	less first-pass effect than oral
Transdermal	80 to ≤ 100	usually very slow absorption; used for lack of first-pass effect; prolonged duration of