UNIT-I: General Pharmacology

As per syllabus Unit-1, Chapter A (Half)

(A) Introduction, definition and scope of Pharmacology

❖ DEFINITION OF PHARMACOLOGY

- **Pharmacology** is the science of drugs (Greek: Pharmacon—drug; logos—discourse in) which deals with interaction of exogenously administered chemical molecules (drug) with living systems.
- Two important and interrelated areas are: pharmacodynamic and pharmacokinetics.
  - i. ***Pharmacodynamic*** (**what drug does with the body**) are the study of the molecular, biochemical, and physiological effects of drugs on cellular systems and their mechanisms of action.
  - ii. ***Pharmacokinetics*** (**what body does with the drug**)-(**ADME**)- deals with the absorption, distribution, metabolism and excretion of drugs.

❖ SCOPE OF PHARMACOLOGY (Only brief study)

A. History

- ✓ It is of intellectual interest to know how drugs are discovered and developed. Often in the past, this was based on folklore or intelligent observation (e.g. digitalis leaf, penicillin). Nowadays, new drugs are mostly developed by the organic chemist working with a pharmacologist, increasingly from basic knowledge about key molecular targets. Usually some sort of biological screen is used to select among organic molecules for optimum pharmacological activity.

1. ***Francois Magendie*** **(1783-1855)**, a French physiologist laid down the dictum "Facts and facts alone are the basis of science." Experimental procedures with animals are the testing grounds for determination of drug action.
2. ***Claude Bernard*** **(1813-1878)**, investigated the plant extract curare and proposed a site of action for this agent.
3. ***Rudolph Buchheim*** **(1820-1879)**. In 1847 Buchheim established the first laboratory devoted to experimental pharmacology in the basement of his home in Dorpat which is known as the cradle of experimental pharmacology.
4. ***Oswald Schmiedeberg*** **(1838-1921)**. In 1872 set up an institute of pharmacology in Strasbourg, France (Germany at that time) which became a mecca for students who were interest in pharmacological problems.
5. ***J.N. Langley*** **(1852-1925 and Sir Henry Dale (1875-1968)** pioneered pharmacology in England, taking a physiological approach.
6. ***John J. Abel*** **(1857-1938)** established the first chair of pharmacology in the U.S.A. (U. Michigan, 1891) after training in Germany. Able went to Johns Hopkins in 1893, and trained many U.S. pharmacologists. He is known

as *"The Father of American Pharmacology"*.

7. The ***Second World War*** was the impetus for accelerated research in pharmacology (the war time antimalarial program) in the U.S., and introduced strong analytical and synthetic chemical approaches.

B. Chemistry

- ✓ Chemical structures of drugs can provide information about mechanism of action, pharmacokinetics, stability, and metabolic fate.

1. ***Structure-Activity Relationship:*** A modification of the chemical structure of a drug may accentuate or diminish its pharmacological effects, often providing clues as to the mechanism of action. A picture of the biological reactive site (the receptor) can be developed in such studies. Also, drugs are metabolized by body systems, which may convert the parent drug to a more active or a less active form. The drug structure can be modified to enhance or diminish the rate of metabolic conversion.
2. ***Sites of Action:*** The organ or cellular target of drug action.
3. ***Drug Receptors:*** Macromolecules in cells or cell membranes with which drugs interact to exert their effects. Usually the interacting forces are reversible ionic and Van der Waals bonds of relatively low energy, but sometimes covalent bonds are formed (e.g. organophosphate insecticides).

C. Pharmacodynamic

- ✓ The effect of the drug on the body. Pharmaco-dynamics is the study of the relationship of drug concentration and the biologic effect (physiological or biochemical).
- ✓ For most drugs it is necessary to know the site of action and mechanism of action at the level of the organ, functional system, or tissue. For example, the drug effect may be localized to the brain, the neuromuscular junction, the heart, the kidney, etc. Often the mechanism of action can be described in biochemical or molecular terms. Most drugs exert effects on several organs or tissues, and have unwanted as well as therapeutic effects. There is a dose-response relationship for wanted and unwanted (toxic) effects.
- ✓ Patient factors affect drug responses - age, weight, sex, diet, race, genetic factors, disease states, trauma, concurrent drugs, etc.

D. Pharmacokinetics

- ✓ The effect of the body on the drug. To produce its characteristic effects, a drug must be present in appropriate concentrations at its sites of action. Thus, it is important to know the interrelationship of the absorption, distribution, binding, biotransformation, and excretion of a drug and its concentration at its locus of action. E.g. This includes physiological and biochemical effects of drugs and their mechanism of action at organ system/subcellular/macromolecular levels, e.g.—Adrenaline → interaction with adrenoceptors → G-protein mediated stimulation of cell membrane bound adenylyl cyclase → increased intracellular cyclic 3′,5′AMP → cardiac stimulation, hepatic glycogenolysis and hyperglycaemia, etc.

1. ***Absorption*** (oral or parenteral)**:** A drug must be absorbed and achieve adequate concentration at its site of action in order to produce its biological effects. Thus, when a drug is applied to a body surface (e.g., G.I. tract, skin, etc.), its rate of absorption will determine the time for its maximal concentration in plasma and at the receptor to

produce its peak effect.

2. ***Distribution:*** The blood, total body water, extracellular, lymphatic and cerebrospinal fluids are involved in drug movement throughout the body. Depending upon its chemical and physical properties, the drug may be bound to plasma proteins or dissolved in body fat, delaying its progress to its sites of action or excretory mechanism.
3. ***Metabolism:*** This is how certain drugs are handled by the body in preparation for their elimination and includes the fate of drugs-biotransformation (e.g., hydrolysis, conjugation, oxidation-reduction).
4. ***Excretion:*** The kidney is the most important organ for drug excretion but the liver, lung and skin are also involved in drug elimination. Drugs excreted in feces are mostly derived from unabsorbed, orally ingested drugs or from metabolites excreted in the bile and not reabsorbed by the intestine. The physical and chemical properties, especially the degree of ionization of the drug, are important in the rate of excretion.
5. ***Biological Factors Modifying Pharmacokinetic Aspects:*** Normal variations occur in population pharmacokinetic constants (absorption rates, elimination rates). Other factors include age, weight, obesity, edema, concurrent diseases, other drugs (various interactions including effects on protein binding or metabolic rate), diet, dose interval and route of administration, genetic variations in elimination rate.

Some Important Aspects

Clinical Pharmacology and Therapeutics

1. ***Posology*:** It is an archaic term describing dosage regimens. Consideration of dosage schedules is a part of pharmacokinetics.
2. ***Bioavailability:*** The fraction of drug administered which is actually absorbed and reaches the systemic circulation following oral dosing. Preparations of the same drug by different manufacturers may have a different bioavailability.
3. ***Drug Nomenclature:*** In addition to its formal chemical name, a new drug is usually assigned a code name by the pharmaceutical manufacturer. If the drug appears promising and the manufacturer wishes to place it on the market, a United States Adopted Name (USAN) is selected by the USAN Council which is sponsored by:

    i. The American Medical Association

    ii. The American Pharmaceutical Association

    iii. The United States Pharmacopoeial Convention

    Types:

    A drug generally has three categories of names:

    (a) **Chemical name:** It describes the substance chemically, e.g. 1-(Isopropylamino)-3-(1-naphthyloxy) propan-2-ol for propranolol. This is cumbersome and not suitable for use in prescribing. A code name, e.g. RO 15-1788 (later named flumazenil) may be assigned by the manufacturer for convenience and simplicity before an approved name is coined.

    (b) **Non-proprietary name:** It is the name accepted by a competent scientific body/authority, e.g. the

United States Adopted Name (USAN) by the USAN council. Similarly, there is the British Approved name (BAN) of a drug. The nonproprietary names of newer drugs are kept uniform by an agreement to use the Recommended International Nonproprietary Name (rINN) in all member countries of the WHO.

(c) **Proprietary (Brand) name:** It is the name assigned by the manufacturer(s) and is his property or trade mark. One drug may have multiple proprietary names, e.g. ALTOL, ATCARDIL, ATECOR, ATEN, BETACARD, LONOL, TENOLOL, TENORMIN for atenolol from different manufacturers. Brand names are designed to be catchy, short, easy to remember and often suggestive, e.g. LOPRESOR suggesting drug for lowering blood pressure.

Toxicology

- ✓ The aspect of Toxicology deals with the adverse effects of chemical agents.
- ✓ Toxicology is concerned not only with drugs used in therapy but also with the other chemicals that may be responsible for household, environmental or industrial intoxication.

1. **Forensic Toxicology:** Addresses medicolegal aspects of the use of chemicals that are harmful to animals or man. Analytical chemistry and fundamental toxicological principles are hybridized to underlie this aspect of toxicology. Nonetheless accidental poisoning with drugs is a health problem of major significance. More than 1/4 of the fatalities and about 1/2 of all poisonings occur in children under 5 years of age. All common household articles that are poisonous should be made unavailable to children, and poisonous rodenticides and insecticides should not be placed in the home.
2. **Clinical Toxicology:** Focuses on toxic events that are caused by or are uniquely associated with drugs or other chemicals

ESSENTIAL MEDICINES (DRUGS) CONCEPT

The WHO has defined Essential Medicines (drugs) as "those that satisfy the priority healthcare needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost effectiveness. Essential medicines are intended to be available within the context of functioning health systems at all times and in adequate amounts, in appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. It has been realized that only a handful of medicines out of the multitude available can meet the health care needs of majority of the people in any country, and that many well tested and cheaper medicines are equally (or more) efficacious and safe as their newer more expensive congeners. For optimum utilization of resources, governments (especially in developing countries) should concentrate on these medicines by identifying them as Essential medicines. The WHO has laid down criteria to guide selection of an essential medicine.

(a) Adequate data on its efficacy and safety should be available from clinical studies.

(b) It should be available in a form in which quality, including bioavailability, and stability on storage can be assured.

(c) Its choice should depend upon pattern of prevalent diseases; availability of facilities and trained personnel; financial resources; genetic, demographic and environmental factors.

(d) In case of two or more similar medicines, choice should be made on the basis of their relative efficacy, safety, quality, price and availability. Cost-benefit ratio should be a major consideration.

(e) Choice may also be influenced by comparative pharmacokinetic properties and local facilities for manufacture and storage.

(f) Most essential medicines should be single compounds. Fixed ratio combination products should be included only when dosage of each ingradient meets the requirements of a defined population group, and when the combination has a proven advantage in therapeutic effect, safety, adherence or in decreasing the emergence of drug resistance.

(g) Selection of essential medicines should be a continuous process which should take into account the changing priorities for public health action, epidemiological conditions as well as availability of better medicines/formulations and progress in pharmacological knowledge.

(h) Recently, it has been emphasized to select essential medicines based on rationally developed treatment guidelines.

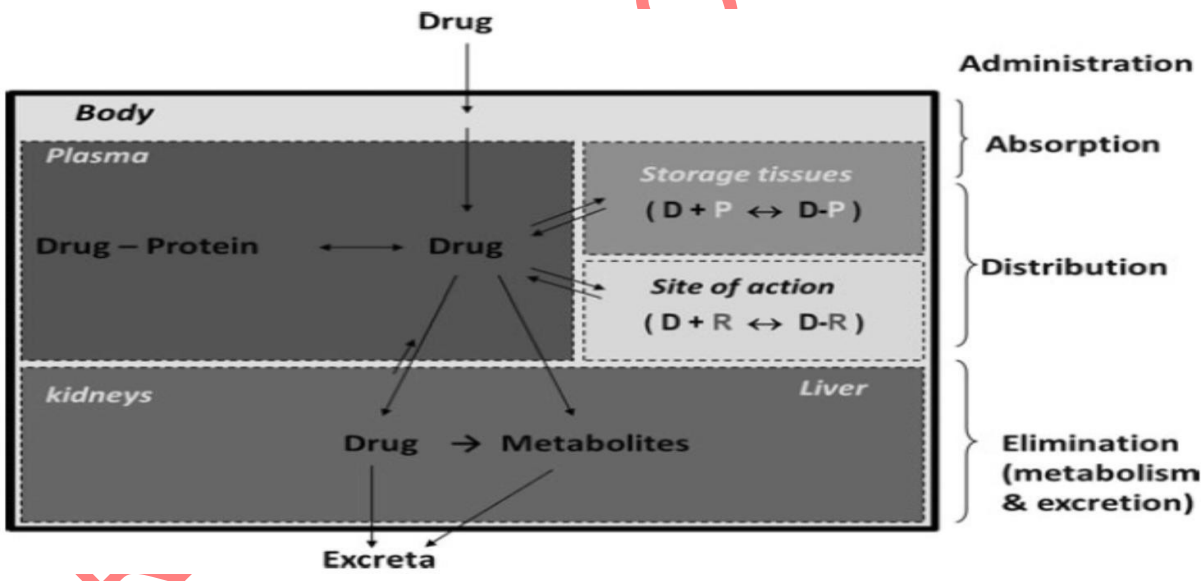
Pharmacovigilence

- ✓ The area of Pharmacovigilence that focuses on the effects of drugs on patient safety.
- ✓ It involves the characterization, detection, and understanding of adverse events associated with drug administration, including adverse drug reactions, toxicities, and side effects that arise as a consequence of the short- or long-term use of drugs.
- ✓ Adverse drug reactions, including drug-drug interactions, are estimated to be a major cause of mortality of inpatients and also lead to significant increases in duration of hospitalization. No drug is free of toxic effects. Some untoward effects of drugs are trivial, but others are serious and may be fatal. Side effects often are predictable from knowledge of the pharmacology of a particular drug.
- ✓ Examples of chemicals or drug-induced toxicities are given below:

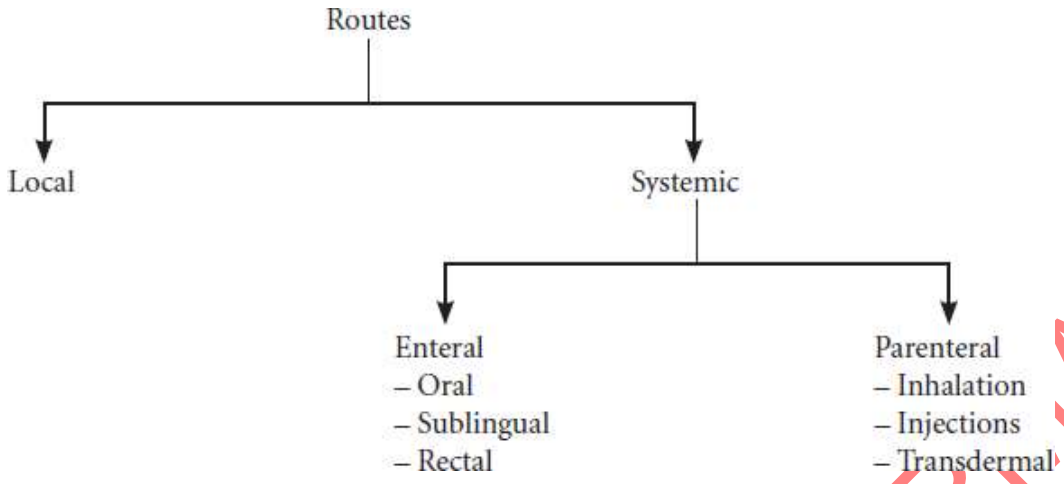
1. **Allergic reactions:** The number of serious allergic reactions to drugs involving antigen-antibody reactions is low but when they occur the physician must have sufficient knowledge to manage these problems.
2. **Blood dyscrasias:** These are very serious and sometimes fatal complications of drug therapy. They include: agranulocytosis, aplastic anemia, hemolytic anemia, thrombocytopenia and defects in clotting factors.
3. **Hepatotoxicity and nephrotoxicity:** Because many chemicals and drugs are eliminated and metabolized by the liver and kidney, damage to these organs is seen commonly.
4. **Teratogenic effects:** The thalidomide tragedy dramatically emphasized that drugs may adversely influence fetal development.
5. **Behavioral toxicity:** This is a term used to describe suppression of normal anxiety, reduction in motivation, impairment of memory and learning, distortion of judgement, impairment of reflexes, adverse effects on mood, etc.
6. **Drug dependence and drug abuse:** The repeated administration of some chemicals may lead to drug dependence. Drugs likely to be abused and upon which drug dependence may develop are the various psychopharmacological agents such as opiates, barbiturates, amphetamines, nicotine and ethanol. Dependence on tobacco (nicotine) is also well known.
7. **Carcinogenesis:** Carcinogenesis is a delayed type of toxicity with a latency of many years.
8. **Pharmacogenetic toxicities:** Certain genetically-predisposed individuals have a markedly toxic reaction to certain otherwise safe drugs. Examples are prolonged apnea after succinylcholine, or malignant hyperthermia associated with anesthetics.

❖ Definition

- A route of administration in pharmacology and toxicology is the path by which a drug, fluid, poison, or other substance is taken into the body.
- Most of the drugs can be administered by different routes. Drug- and patient-related factors determine the selection of routes for drug administration. The factors are:
    1. Characteristics of the drug. Physical and chemical properties of the drug (solid/ liquid/gas; solubility, stability, pH, irritancy).
    2. Emergency/routine use.
    3. Site of action of the drug—local or systemic.
    4. Condition of the patient (unconscious, vomiting, diarrhoea).
    5. Age of the patient.
    6. Effect of gastric pH, digestive enzymes and first-pass metabolism.
    7. Patient's/doctor's choice (sometimes).
- Before consider the various routes of drug administration, let study of how drugs move within the body:-



(Schematic diagram showing the various pharmacokinetic processes following administration of a drug. D drug, P protein, R receptor)



1. LOCAL ROUTES

- It is the simplest mode of administration of a drug at the site where the desired action is required. Systemic side effects are minimal.

i. ***Topical:*** Drug is applied to the skin or mucous membrane at various sites for local action.

a) ***Oral cavity:*** As a suspension, e.g. nystatin; as a troche, e.g. clotrimazole (for oral candidiasis); as a cream, e.g. acyclovir (for herpes labialis); as ointment and jelly, e.g. 5% lignocaine hydrochloride (for topical anaesthesia); as a spray, e.g. 10% lignocaine hydrochloride (for topical anaesthesia).

b) ***GI tract:*** As tablet that is not absorbed, e.g. neomycin (for sterilization of gut before surgery).

c) ***Rectum, Vaginal and analcanal:***

- **As an enema** (administration of drug into the rectum in liquid form):

- *Evacuant enema* (for evacuation of bowel): For example, soap water enema—soap acts as a lubricant and water stimulates the rectum.
- *Retention enema:* For example, methylprednisolone in ulcerative colitis.

- **As a suppository** (administration of the drug in a solid form into the rectum), e.g. bisacodyl— for evacuation of bowels.

✓ *Advantages*

- Used in children.
- Little first pass effect.
- Can be given in vomiting.
- Can be given in unconscious patient.
- Higher therapeutic concentrations of drug are achieved rapidly in rectum.
- For rapid evacuation of bowel, usually during gut sterilization before any surgical or radiological procedure.

✓ *Disadvantages*

- Inconvenient.
- Drug absorption is slow and erratic.
- Irritation or inflammation of rectal mucosa can occur.

d) ***Eye, ear and nose:*** As drops, ointments and sprays (for infection, allergic conditions, etc.), e.g. gentamicin eye/ear drops.

e) ***Bronchi:*** As inhalation, e.g. salbutamol (for bronchial asthma and chronic obstructive pulmonary disease). Gases, volatile liquids and solids (in the form of finely divided powders) are inhaled for systemic and local effects. Inhalation of solids is called insufflation.

✓ *Advantages*

- Rapid absorption of the drug due to large surface area.
- First pass effect is avoided.
- Rapid local effects.

✓ *Disadvantages*

- Only few drugs can be administered.
- May produce irritation of pulmonary mucosa.
- Inconvenient procedure.
- Chances of cardiotoxicity.

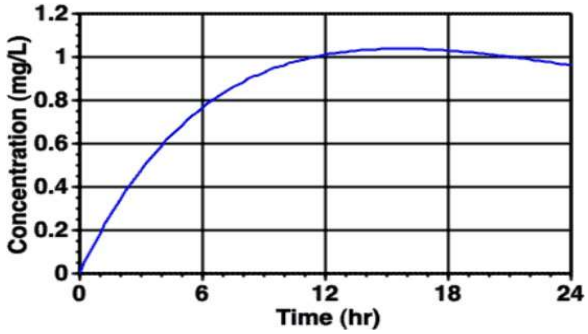
f) ***Skin:*** As ointment, cream, lotion or powder, e.g. clotrimazole (antifungal) for cutaneous candidiasis.

g) ***Transdermal***: Transdermal patches can provide prolonged or controlled (iontophoresis) drug delivery. Systemic absorption (Transdermal) is better with low dose, low MWt, lipid soluble drugs

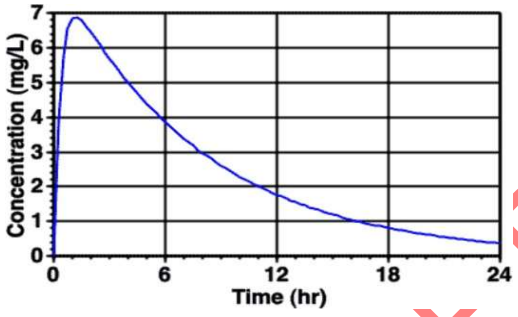
ii. ***Intra-arterial route:*** This route is rarely employed. It is mainly used during diagnostic studies such as coronary angiography and for the administration of some anticancer drugs, e.g. for treatment of malignancy involving limbs.

iii. ***Administration of the drug into some deep tissues by injection***, e.g. administration of triamcinolone directly into the joint space in rheumatoid arthritis.

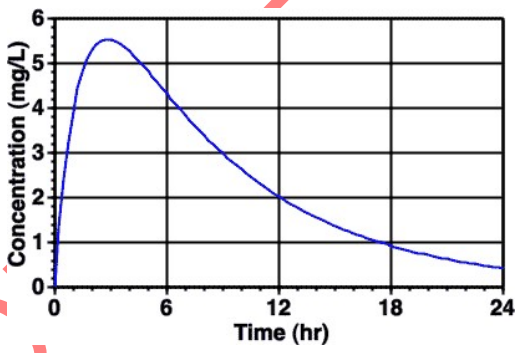
- ***Typical Plot of Concentration versus Time after Topical Administration***



- *Typical Plot of Concentration versus Time after Inhalation Administration*



- *Typical Plot of Concentration versus Time after Rectal Administration*



2. a) Systemic Routes (Enteral)

- Drugs administered by this route enter blood and produce systemic effects. **Enteral Routes** It includes (i) ***Oral route,*** (ii) ***Buccal*** or ***Sublingual route*** and (iii) ***Rectal route***.

i. ORAL ROUTE

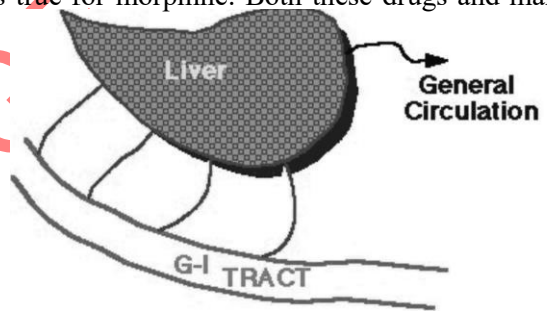
✓ It is the most common and acceptable route for drug administration. Dosage forms are tablet, capsule, syrup, mixture, etc., e.g., paracetamol tablet for fever, omeprazole capsule for peptic ulcer are given orally.

✓ ***Advantages:***

- Convenient - portable, safe, no pain, can be self-administered.
- Cheap - no need to sterilize (but must be hygienic of course)
- Variety of dosage forms available - fast release tablets, capsules, enteric coated, layered tablets, slow release, suspensions, mixtures
- Convenient for repeated and prolonged use.

✓ ***Disadvantages:***

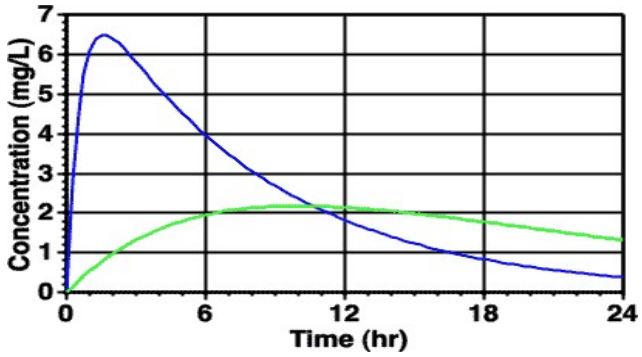
- *Sometimes inefficient* :- high dose or low solubility drugs may suffer poor availability, only part of the dose may be absorbed. Griseofulvin was reformulated to include the drug as a micronized powder. The recommended dose at that time was decreased by a factor of two because of the improved bioavailability.
- *First-pass effect* :- drugs absorbed orally are transported to the general circulation via the liver. Thus drugs which are extensively metabolized will be metabolized in the liver during absorption. e.g. the propranolol oral dose is somewhat higher than the IV, the same is true for morphine. Both these drugs and many others are extensively metabolized in the liver.



First Pass Effect

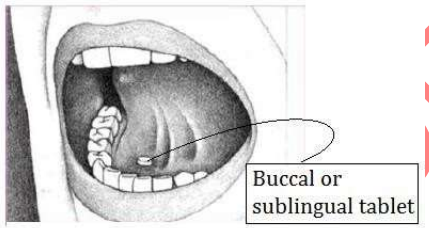
- *Food* :- Food and G-I motility can effect drug absorption. Often patient instructions include a direction to take with food or take on an empty stomach. Absorption is slower with food for **tetracyclines** and **penicillins**, etc. However, for **propranolol** bioavailability is higher after food, and for **griseofulvin** absorption is higher after a fatty meal.
- *Local effect* :- Antibiotics may kill normal gut flora and allow overgrowth of fungal varieties. Thus, antifungal agent may be included with an antibiotic.
- *Unconscious patient* :- Patient must be able to swallow solid dosage forms. Liquids may be given by tube.

✓ ***Typical Plot of Concentration versus Time after Oral Administration Fast and Slow Release Dosage Forms***



ii. BUCCAL and SUBLINGUAL ROUTE (SL)

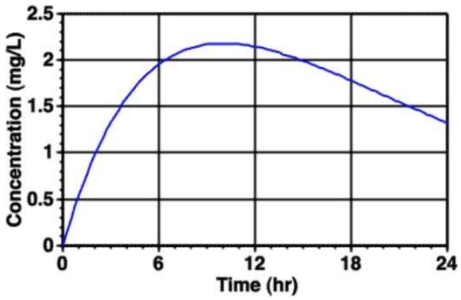
- ✓ Some drugs are taken as smaller tablets which are held in the mouth or under the tongue.
- ✓ These are buccal or sublingual dosage forms.
- ✓ Buccal tablets are often harder tablets [4 hour disintegration time], designed to dissolve slowly. Nitroglycerin, as a softer sublingual tablet [2 min disintegration time], may be used for the rapid relief of angina.
- ✓ This Route of administration is also used for some steroids such as testosterone and oxytocin. Nicotine containing



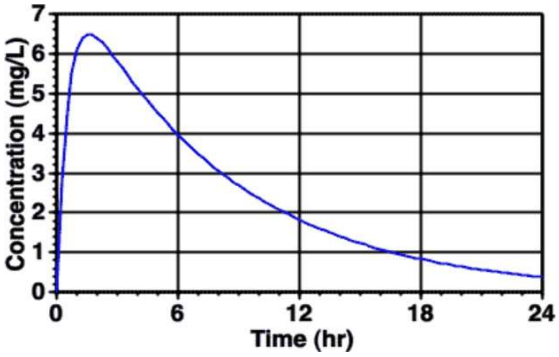
chewing gum may be used for cigarette smoking replacement.

- ✓ ***Advantages:***
  - Quick onset of action.
  - Action can be terminated by spitting out the tablet.
  - Bypasses first-pass metabolism.
  - Self-administration is possible.
- ✓ ***Disadvantages***
  - It is not suitable for bitter tasting and unpalatable drug.
  - It is not suitable for Irritant and lipid-insoluble drugs.
  - cannot give to unconscious patient.
  - Large quantities cannot be given.
  - Cannot be given in severe vomiting.

✓ ***Typical Plot of Concentration versus Time after Buccal Administration***



✓ ***Typical Plot of Concentration versus Time after Sublingual Administration***



iii. RECTAL ROUTE

✓ Drugs can be given in the form of solid or liquid.

- ***Suppository:*** It can be used for **local** (topical) effect as well as **systemic effect**, e.g. indomethacin for rheumatoid arthritis.
- ***Enema:*** Retention enema can be used for local effect as well as systemic effect. The drug is absorbed through rectal mucous membrane and produces systemic effect, e.g. diazepam for status epilepticus in children.

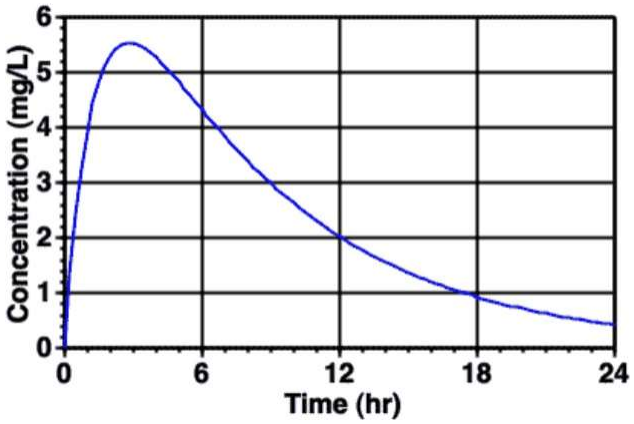
✓ ***Advantages***

- Used in children.
- Little first pass effect.
- Can be given in vomiting.
- Can be given in unconscious patient.
- Higher therapeutic concentrations of drug are achieved rapidly in rectum.
- For rapid evacuation of bowel, usually during gut sterilization before any surgical or radiological procedure.

✓ ***Disadvantages***

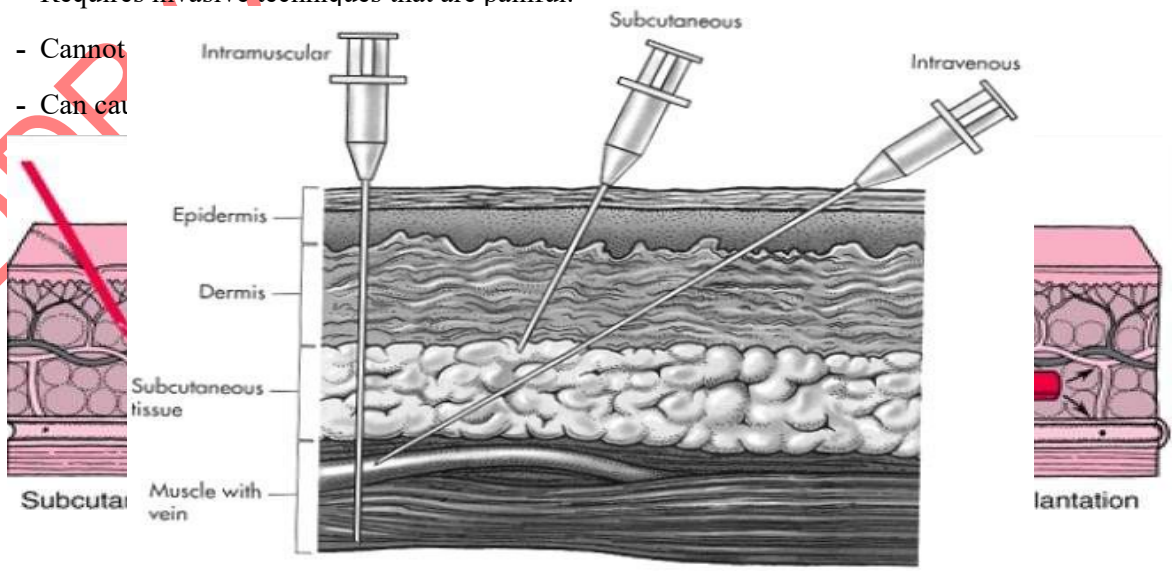
- Inconvenient, not well accepted. May be some discomfort
- Drug absorption is slow and erratic.
- Irritation or inflammation of rectal mucosa can occur

✓ ***Typical Plot of Concentration versus Time after Rectal Administration***



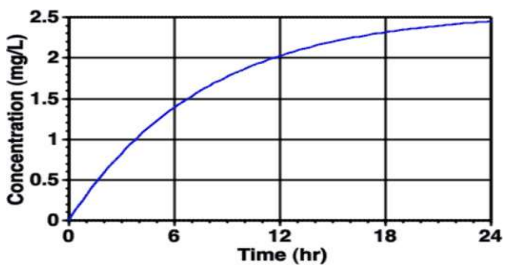
2. b) Systemic Routes (Parenteral)

- Routes of administration other than enteral route are called parenteral routes.
- *Advantages of parenteral routes*
  - Onset of action of drugs is faster; hence it is suitable for emergency.
  - Useful in:
  - Unconscious patient.
  - Uncooperative and unreliable patients.
  - Patients with vomiting and diarrhoea.
  - It is suitable for:
  - Irritant drugs.
  - Drugs with high first-pass metabolism.
  - Drugs not absorbed orally.
  - Drugs destroyed by digestive juices.
- *Disadvantages of parenteral routes*
  - Require aseptic conditions.
  - Preparations should be sterile and is expensive.
  - Requires invasive techniques that are painful.
  - Cannot
  - Can ca

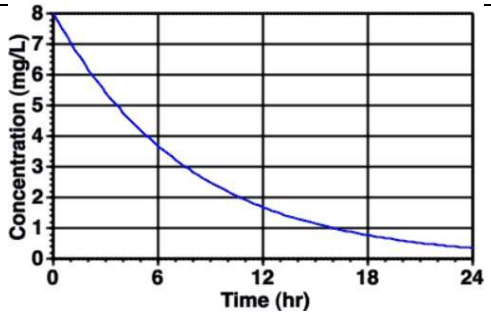


i. INTRAVENOUS (IV)

- Drugs may be given into a peripheral vein over 1 to 2 minutes or longer by infusion, or Drugs are injected directly into the blood stream through a vein.
- Drugs are administered as:
    a) ***Bolus:*** Single, relatively large dose of a drug injected rapidly or slowly as a single unit into a vein. For example, i.v. ranitidine in bleeding peptic ulcer.
    b) ***Slow intravenous injection:*** For example, i.v. morphine in myocardial infarction.
    c) ***Intravenous infusion:*** For example, dopamine infusion in cardiogenic shock; mannitol infusion in cerebral oedema; fluids infused intravenously in dehydration.
- **Advantages**
    - Bioavailability is 100%.
    - Quick onset of action; therefore, it is the route of choice in emergency, e.g. intravenous diazepam to control convulsions in status epilepticus.
    - Large volume of fluid can be administered, e.g. intravenous fl uids in patients with severe dehydration.
    - Highly irritant drugs, e.g. anticancer drugs can be given because they get diluted in blood.
    - Hypertonic solution can be infused by intravenous route, e.g. 20% mannitol in cerebral oedema.
    - By i.v. infusion, a constant plasma level of the drug can be maintained, e.g. dopamine infusion in cardiogenic shock.
- **Disadvantages**
    - Once the drug is injected, its action cannot be halted.
    - Local irritation may cause phlebitis.
    - Self-medication is not possible.
    - Strict aseptic conditions are needed.
    - Extravasation of some drugs can cause injury, necrosis and sloughing of tissues.
    - Depot preparations cannot be given by i.v. route.
- **Precautions**
    - Drug should usually be injected slowly.
    - Before injecting, make sure that the tip of the needle is in the vein.

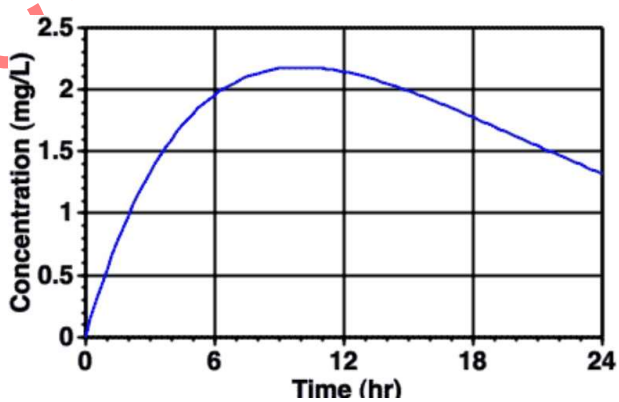


- **Typical Plot of Concentration versus Time during an IV Infusion Administration**
- **Typical Plot of Concentration versus Time during an IV Bolus Administration**



ii. SUBCUTANEOUS (s.c.) ROUTE

- The drug is injected into the subcutaneous tissues of the thigh, abdomen and arm, e.g. adrenaline, insulin, etc.
- **Advantages:**
  - Actions of the drugs are sustained and uniform.
  - Drugs can be given in presence of vomiting and diarrhea.
  - Drugs can be given to unconscious patients.
  - First pass effect is avoided.
  - Drugs that are not absorbed from G.I.T can be given.
  - Self-administration is possible (e.g. insulin).
  - Depot preparations can be inserted into the subcutaneous tissue, e.g. norplant for contraception.
- **Disadvantages**
  - Only non-irritant drugs can be given otherwise severe irritation, pain and necrosis of subcutaneous tissues can occur.
  - Absorption of the drugs is slow than I/M injection.
  - Expensive.
  - Danger of infection, if proper sterilization techniques are not used.
  - Large volumes of drug cannot be given.
- **Typical Plot of Concentration versus Time during subcutaneous Administration**

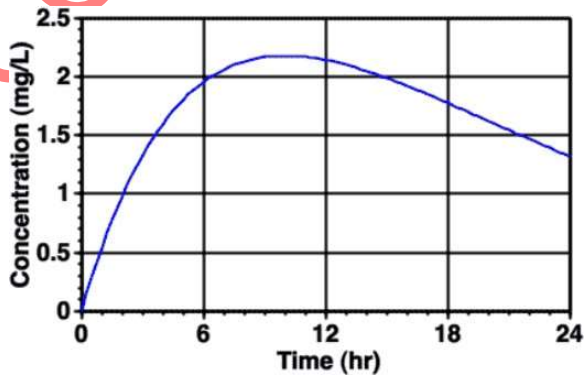


iii. INTRAMUSCULAR (i.m) ROUTE

- The drug is injected deep in the belly of a large skeletal muscle. The muscles that are usually used are detoid, triceps,

Gluteus,. Maximus, rectus, femurs depending on the specie of animal.

- The muscle is less richly supplied with sensory nerves, hence injecting a drug 1m is less painful.
- Absorption of drug from gluteal region is slow especially in females due to high fat deposition.
- Deep intramuscular injections are given at upper outer quadrant of buttock to prevent the injury to major nerves.
- Deep I/M injections are less painful than I/M injections on arm due to high fat content.
- Intramuscular injections are given at an angle of 90 degrees.
- **Advantages**
  - Rate of absorption is uniform.
  - Rapid onset of action.
  - Irritant substances can be given.
  - Drugs can be given to unconscious patients.
  - Accuracy of dosage is ensured.
  - Useful in emergency situations.
  - First pass effect is avoided.
  - Drugs producing gastric irritation can be given.
  - Drugs that are not absorbed from G.I.T can be given.
- **Disadvantages**
  - Small quantities up to 10 ml of the drug can be given at a time.
  - Local pain and abscess formation.
  - Technical person is needed, self-administration is difficult.
  - Expensive.
  - Danger of infection, if proper sterilization techniques are not used.
  - Chances of nerve damage.
- **Typical Plot of Concentration versus Time during Intramuscular Administration**



iv. INTRATHECAL ROUTE

- Drug is injected into the subarachnoid space (spinal anaesthetics, e.g. lignocaine; antibiotics, e.g. amphotericin B, etc.).

v. INTRA-ARTICULAR ROUTE

- Drug is injected directly into the joint space, e.g. hydrocortisone injection for rheumatoid arthritis. Strict aseptic precautions should be taken. Repeated administration may cause damage to the articular cartilage.

v. TRANSDERMAL ROUTE

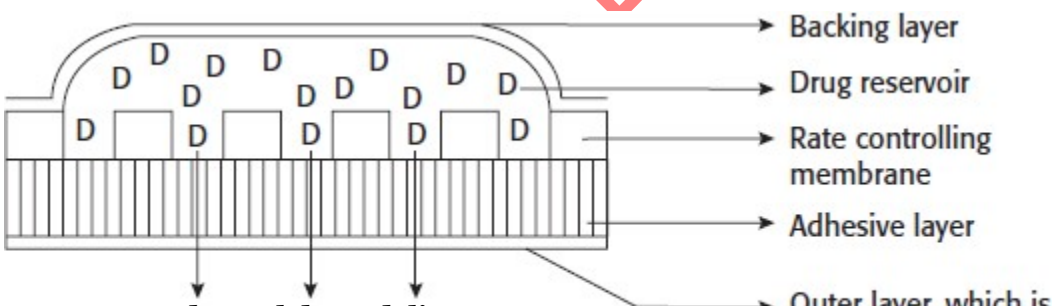
- The drug is administered in the form of a patch or ointment that delivers the drug into the circulation for systemic effect.
- For example, scopolamine patch for sialorrhoea and motion sickness, nitroglycerin patch/ointment for angina, oestrogen patch for hormone replacement therapy (HRT).

Advantages

- Self-administration is possible.
- Patient compliance is better.
- Duration of action is prolonged.
- Systemic side effects are reduced.
- Provides a constant plasma concentration of the drug.

Disadvantages

- Expensive.
- Local irritation may cause dermatitis and itching.
- Patch may fall-off unnoticed.



Transdermal drug-delivery system.

vi. INTRAPERITONEAL ROUTE

- Indication: Colon and Ovarian
- Peritoneal space has much surface area; may not be reached by IV chemo
- Catheters used: implanted port
- Chemotherapy agents used: Cisplatin, Taxol
- **Advantages:** less systemic side effects
- **Disadvantages:** infection, pain.

vii. INTRAPLEURAL

- Seeding of pleura
- Used as sclerosing agent to stop pleural effusions
- Injected by physician into chest tube and clamped. Patient changes position 15 min for 1 hour
- Chemotherapy agents used: Bleomycin, Adriamycin, Talc slurry
- **Side effects:** severe pain