Chapter

1

Drugs

Preview: *Pharmacology is an essential basic medical science that provides the foundation of clinical disciplines. The current CBME curriculum stresses more clinical-oriented Pharmacology. In this inaugural topic, students refresh the brief outlook of drug-related terminologies, asked during an assessment. The basic concept helps to assess a better understanding of exercises as recommended in different sections.*

The drug is used to prevent, diagnose, treat, and cure disease. Pharmacology is the discipline of medical science concerned with the scientific study of every aspect of a drug. Thus, drugs and pharmacology are complements of each other. This medical stream drives the international pharmaceutical industries to make mega profits.

PHARMACOLOGY

The word pharmacology is derived from the Greek word **pharmakon** (an active principle or drug) and **logos** (discourse in, science, treatise, study, or knowledge). Pharmacology is the science that deals with the **study of drug** and their interaction with the living system. Pharmacology is concerned with the study of all the aspects of the drug. This scientific discipline builds the intelligence to use the drug for good clinical practice.

Two main pillars of pharmacology are—pharmacokinetics (PK) and pharmacodynamics (PD). A substance (ingredient) that follows the principles of both criteria is considered pharmacologically active.

- **Pharmacokinetics** (*Kinesis* is a Greek word meaning *movement*)—pharmacokinetics is the study of the absorption, distribution, biotransformation, and excretion of drugs, i.e. **"What the body does to the drug"**. PK also denotes the relation between the dose and concentration of the drug, i.e. "**Dose-concentration"**. In brief, PK represents the journey of a drug in the body 'in, through and out'.
- **Pharmacodynamics** (*Dynamics* is a Greek word meaning *power*)—pharmacodynamics is the drug's physiological, biochemical, and therapeutic effects on the body and its mechanism of action, i.e. "**What the drug does to the body"**. PD also denotes the relation between plasma concentration and the effect of the drug, i.e. **"Concentration—effect"**.

DRUG

The drug is derived from the French word **drogue,** meaning a dry herb. WHO defines—A drug as any substance or product that is used or intended to be used to modify or

explore a physiological system or pathological state for the benefit of the recipient. Clinically, a drug is a substance used for the "diagnosis, prevention, treatment, and cure" of a disease.

Drug Vs Medicine

In clinical practice, both the terms 'drug and medicine' are commonly interchangeable but there is a minor difference. **Drug** is a broad term and includes all the pharmacologically active substances (natural, synthetic, or endogenous) used for prevention, diagnosis, cure, and treatment. **Medicine** is mainly used for the treatment of diseases and the clinical relief of patients. It includes both pharmacologically active 'drug' as well as pharmacologically inactive or inert substance 'placebo'. The word drug is linked with addiction in society. For all clinical purposes medicine is more appropriate.

Action Vs Mechanism of Action

There is a slight difference between action and mechanism of action. Better explained by the example—insulin is a hypoglycemic hormone that decreases blood glucose, this is action. But how does this happen? Insulin increases the utilization (uptake) of glucose by tissues via specific insulin receptors, this is the mechanism of action.

SOURCES OF DRUGS

Drugs are obtained from several sources—both natural and synthetic. From a commercial point of view, the majority of drugs are synthetic in nature.

Natural Sources

I. **Plants:** Atropine, morphine, quinine, digoxin.
II. **Animals:** Insulin, heparin, gonadotropins.
III. **Human:** Immunoglobulin, hCG.
IV. **Micro-organisms:** Antimicrobials like penicillin and cephalosporins.
V. **Minerals:** Iron, calcium carbonate, radio-isotopes.

Synthetic Sources

I. **Recombinant DNA technology:** Human insulin vaccines, factor VIII, interferon.
II. **Hybridoma technology:** Monoclonal antibodies (mab).
III. **Cell culture:** Urokinase.
IV. **Semi-synthetic:** Tetracycline, homatropine.
V. **Synthetic:** Fluoroquinolones, proton pump inhibitors.

Remarks

Based on physical and chemical properties, plant products are categorized as:

- **Alkaloids:** Basic insoluble substances that combine with acid to form a soluble salt, e.g. morphine sulfate.
- **Glycosides:** Combination of sugar with non-sugar (aglycone), e.g. digoxin, aminoglycoside, contains amino sugar.
- **Oils:**
  - **Fixed oils** (fat obtained from seeds with calorific value), e.g. castor oil.
  - **Volatile oils** (non-fat obtained from leaves, flowers, etc. without calorific value), e.g. turpentine oil.
  - **Mineral oils** (hydrocarbon mixture obtained from petroleum), e.g. paraffin.

- **Others:**
  - Tannins (non-nitrogenous, astringent compounds), e.g. catechu.
  - Resins (plant exudates, soluble in alcohol), e.g. oleoresin.
  - Gums (plant secretion form mucilaginous collides with water), e.g. gum acacia.

DRUG NOMENCLATURE

Every drug has three names.

i. Chemical Name

- Full chemical description of the drug.
- Usually lengthy, complex, and unsuitable for prescribing.
- Follow the rules issued by IUPAC (International Union of Pure and Applied Chemistry).

ii. Generic Name

- **Nonproprietary/approved/official name:** Assigned by a competent scientific authority such as USAN (United States of Adapted Name), BAN (British Approved Name), or an official agency like WHO (World Health Organization).
- Internationally accepted by WHO. After inclusion in the pharmacopeia, it becomes the official name.
- That could be the same all over the world.
- Similar spelling and pronunciation, so confusion does not arise.
- Convenient to prescribe.
- Economical (no promotional expenditure).
- Difficult for FDC, which has more than two ingredients.
- Quality control—sometimes may be substandard.

iii. Brand Name

- **Proprietary/trade/commercial name:** The name given by the manufacturer.
- Manufacturer is confined to ownership of the particular brand.
- The same drug may have different commercial names.
- Different brand names in different countries.
- Short, catchy, or smart name, but sometimes confusing.
- Suitable for FDC of several ingredients.
- Costly due to promotion and marketing of the brand.

Examples

- Para-acetyl aminophenol, N-acetyl para aminophenol (chemical name).
  Paracetamol, acetaminophen (generic name).
  Crocin, Metacin, Calpol, T-98 (brand name).
- 2-acetoxy benzoic acid (chemical).
  Aspirin, also called acetyl salicylic acid (generic name).
  Disprin, Majoral (brand name).

Name in Special Circumstances

Code name

- Coined during a clinical trial for simplicity, secrecy, and convenience.
- Denoted by alphabet letters (AXPZ) or some numbers (917) or both (MH49P).

Generic name

- Originally refers to genus or class, e.g. penicillins, benzodiazepines, etc. but later it is used as a synonym for the nonproprietary name.
- Usually, the generic name is universal throughout the world but there is some variation due to different systems used earlier. Some of the drugs still have two names, e.g. epinephrine (USAN) is also named adrenaline (BAN), similarly frusemide (furosemide) and lignocaine (lidocaine).
- Acetaminophen and paracetamol both generic names are commonly interchangeable. Paracetamol is British approved name. Paracetamol is derived from its chemical name **para acetyl aminophenol** (BAN) while Acetaminophen is derived from the chemical name **N-acetyl para aminophenol** (USAN)
- A generic version (other than the generic name) of the newly developed molecule is available after the expiry of the original patent.
- Branded generic drugs are those which have been given the commercial name. Such a drug has gone through the ANDA process of clinical trial after patent expiration.

Look-Alike and Sound-Alike (LASA) Name

- Also known as sound-alike and look-alike (SALA) name.
- Many medications appeared very similar when written(spelling) or spoken (phonetics).
- Can be classified as orthographic pairs (similar spellings) and phonological pairs (similar-sounding)
- Sometimes the names of different brands of drugs are very close to each other. Such sound-alike names create confusion, e.g. Allegra (fexofenadine) and Viagra (sildenafil).
- Some medications share similar letters, referred to as look-alike medication, e.g. DTap (diphtheria, tetanus toxoids, acellular pertussis), Tdap (tetanus, reduced diphtheria toxoids, acellular pertussis).
- These confusing names are one of the main causes of medication errors.

Examples

- Cycloserine (antibacterial) and cyclosporin (immunosuppressant) .
- Cotrimoxazole (antibacterial) and clotrimazole (antifungal).
- Eltroxin (thyroxin) and Althrocin (erythromycin).
- Nasivion (decongested) and Evion (vitamin).
- Livogen (iron and folate) and Levozin (levocetirizine).

DRUG TERMINOLOGIES

Prototype Drug

- A drug that represents a **particular group or class**.

- Prototype drug is the ancestral drug from which other drugs of the same class are developed.
- Characteristics or properties of other agents are based on the reference from the prototype drug.
  For example, morphine is a prototype drug of the narcotic analgesic group. Other agents, like codeine and pethidine are concerning morphine.

Drug Generation

- It is a group of pharmacologically similar or related drugs developed or produced in a **particular period**.
- The next group developed after a certain time interval with some modifications from the previous group.
- New group is generally more advanced than a prior counterpart given safety, coverage, and side effects.
- The only limitation is cost and sometimes doubtful safety profile of newer inclusion.
  For example, cephalosporins—I, II, III, IV,V generation; sulphonylureas—I, II generation.

Drug Choice

- Preference is given to the **particular drug**, based on maximum therapeutic benefits.
- Described as **first choice** (preference) or **next choice** (maybe second, third …. as per declined benefits).
  For example, penicillin is a drug of the first choice for the treatment of syphilis. Other drugs are the next choice in case of contraindication and are less effective than the first choice.

Drug Line

- Preference is given to the **group of drugs** based on the maximum therapeutic benefits and fewer adverse effects.
- Described as the **first-line** (more efficacy, fewer side effects) or **second-line** (less efficacious and more toxic than the first line) or third-line, e.g. anti-tubercular drugs—isoniazid, rifampicin, pyrazinamide, and ethambutol are used initially as the first line. Second-line macrolides, fluoroquinolones, aminoglycosides, etc. will be indicated under special conditions.

SPECIAL DRUG TERMS

Designer Drug

This term is used for illegal, lab-made synthetic drugs that mimic the existing drug by molecular modification. It mostly includes psychoactive drugs, that are not only illegal but also harmful to society. Thus, designer drugs are synthetic substitutes for commonly used recreational drugs, produced in small clandestine labs (clandestine means done secretly or kept secret). They are functional analogs, that have been designed to mimic the pharmacological effects of existing original drugs while avoiding being kept under illegal drugs. They are also designed to bypass the drug rules governing manufacturing and marketing. Because the efficacy and safety of these substances have not been evaluated in clinical trials, their use may result in unexpected outcomes.

A new designer opioid China white, developed from a modification of fentanyl, was several times more potent as well as dangerous than its original counterpart. (Insulin analogues are popular as designer insulin, not a designer drug but named designer as produced by modification of the basic design of insulin.)

Club Drug

Also known as '**rave or party drugs'** are used by youths or dancers in nightclubs, bars, concerts, and parties for pleasure and mood, e.g. LSD, MDMA, PCP, ketamine, etc., more often in combination with illegal sedative-hypnotics. Club drugs become even more dangerous and potentially fatal when combined with alcohol.

Me-Too Drug

A drug structurally similar to a prototype or other known drug with an identical mechanism of action but is now marketed by a new pharmaceutical company and is considered a new drug in terms of efficacy, compliance and side effects. It is also known as a '**follow-on drug**'. Thus, it is similar to a pre-existing drug usually by making minor modifications to prototype profiles and used to treat the same clinical condition. Beta-blockers, PPI, and ACEI are commonly used.

Hit and Run Drug

The medications whose duration of action is quite longer than their stay in the body are called "hit and run drugs", e.g. reserpine, PPI . Reserpine acts by combining with the storage vesicle of nerve endings and depletes noradrenalin from vesicles. Its action returns only when new vesicles are synthesized, which takes time. Similarly, PPI has a short half-life but irreversibly inhibits (paralyzes) the pump longer, thus their action persists for one day.

Gateway Drug

As the name indicates, a gateway drug is an introductory habit-forming drug that can lead to the subsequent use of other more addictive drugs. Alcohol and tobacco are commonly used. Marijuana (dried leaves of cannabis sativa/ganja) opens the gate for cocaine use.

Hard and Soft Drug

Hard drugs are liable to disable the individual as a functioning member of society by inducing severe psychological depression and physical dependence such as heroin or cocaine. **Soft drugs** are less dependence-producing. These results are mainly psychological but very little or less physical dependence on alcohol, tobacco, and sedatives.

Blockbuster Drug

A drug that generates huge profits for the pharmaceutical industry, is a major factor in the success of pharmaceutical companies. Tagamet, Lipitor, Advair, Humira, Vioxx, Zoloft and COVID-19 vaccines are some examples of all-time biggest blockbuster drugs.

Smart Drug

Substances commonly referred to as nootropics are claimed to improve human cognitive abilities, creativity, intelligence, and motivation. Such drugs, e.g. caffeine, ginseng, and

ginkgo is used to improve memory, thought, learning, and mood. Methylphenidate is commonly used by students, also called a **study drug**.

Truth Drug

Commonly known as 'truth serum', is a conversational name for a range of drugs used to obtain information from subjects who are unable or unwilling to provide it. Agents such as scopolamine, midazolam, and sodium thiopental are used for this purpose to make a person answerable. Legal and human rights issues are still there.

Auxilliary Drug

A drug that does take care of an important issue of the overall treatment, e.g. use of anesthetics during operation (an auxiliary label is a label added to a dispensed medication package to provide supplementary information regarding the safe administration and storage of medication).

Wonder Drug

A drug (usually newly discovered) that elicits a dramatic positive response in the clinical condition of a patient. Also known as a **miracle drug**, is highly effective with the least side effects and is most widely prescribed. Aspirin has often been called a wonder drug partly because of its effectiveness in many health problems. Penicillin during World War, because of its remarkable effects on infectious diseases.

Recreational Drug

Drug use alters the state of consciousness and creates feelings and emotions. LSD a hallucinogen is commonly used for this purpose. Some recreational agents like tobacco, alcohol, betel nut, gutkha, and caffeine are widely used worldwide.

Orphan Drug

Some drugs are meant for diagnosis, prevention, or treatment of 'rare disease '. A rare disease is called an orphan disease and sufferers as patients/health orphans (orphan receptors are receptors for which there is no endogenous ligand). Orphan drugs may be lifesaving but they are commercially difficult to obtain. There are several orphan diseases out of which about 80% are genetic. Approximately 1000 drugs have orphan status, e.g. miltefosine (kala-azar), anagrelide (polycythemia vera), and deferiprone (iron overload in thalassemia).

Orphan drugs are not easily available due to manufacturing reasons. Such drugs remain unattended due to economic reasons like the enormous cost of production. Manufacturers apathy and lack of interest due to limited demand and less profit. Drug development for such rare diseases may not be able to recover the cost incurred. Orphan drugs receive priority at all stages of drug development. Orphan drugs are developed by the government and offer incentives like tax relief and subsidies.

PHARMACEUTICAL PRODUCTS

The use of FDC is very popular, so students practice differentiating the rational or irrational combinations. Banned drugs and orphan drugs also need attention. Pharmacological particulars such as antimicrobials, hormones, vaccines, nutrients as well as counterfeit drugs and OTC drugs are very common in the pharmaceutical market.

FIXED DOSE COMBINATIONS

A large number of pharmaceutical preparations contain two or more drugs in a definite ratio. Such combinations are popularly known as 'fixed dose combinations (FDCs)'. FDCs are innovative forms of drug therapy that offer distinct advantages to patients as well as physicians. Rational combinations of FDC are efficacious but irrational combinations may be dangerous. WHO has approved authentic combinations in the Essential Medicine List (EML).

As the name indicates, a fixed-dose combination is a formulation of two or more active ingredients (in a fixed ratio) combined in a single dosage form, e.g. drug A + B + C ... in a single preparation.

Common FDCs in clinical practice are anti-microbial, antitubercular, anti-diarrheal, anti-HIV, anti-hypertensive, analgesics, antacids, cough mixtures, nutrients combinations (hematinic, multivitamins and tonics), etc.

Criteria of Drug Combination

- The basis for combining drugs must be sound.
- Each drug component must have an independent mode of action.
- Cannot affect pharmacokinetics as well as pharmacodynamics of each other.
- Combination must be synergistic, antagonistic, or complementary in their effect.
- Both components should have different side effects; preferably one may counter the other.

Advantages

- Better patient compliance.
- Convenience in terms of reduced frequency of administration.
- Synergistic combinations improve therapeutic potential, e.g. addition of clavulanic acid in amoxicillin.
- Prevention of drug resistance, commonly seen with single-drug therapy after prolonged use, e.g. antimicrobial.
- Enhances efficiency and ensures when more than one agent has to be administered, e.g. anti-tubercular, anti-HIV.
- Side effects of one component may be counteracted by another, e.g. combination of potassium-sparing and losing diuretic.
- Only one expiry date simplifies dosing, whereas single products may have different expiry dates.

Disadvantages

- Pharmaceutical irrational combinations.
- Effects of pharmacokinetics and pharmacodynamics of each other.
- Antagonism of action.
- Additional adverse effects.
- Difficult to adjust the individual dose or flexibility in dose.
- Interaction among different components.
- Different time courses of action and inappropriate dose intervals.
- Difficult to trace out causative agents during drug reactions.

- Contraindication to any component means contraindication of FDC.
- Confusion of the therapeutic aims and false sense of superiority due to the addition of agents in combination.
- Additional cost burden, if a patient does not need all the ingredients in combination.

Regulation of FDC

New drug discovery and clinical trials are very costly affairs. A newly invented drug fails even at phase III of the trial and this puts a huge financial burden on the pharmaceutical company. The introduction of FDC is the least expensive. When well-known drugs combine as an FDC, the new formulation just requires approval and license from the authority. The introduction of a new FDC is more economical and profitable for pharmaceutical companies, in place of spending huge amounts on clinical trials. An FDC is treated as a new drug because combining two or more drugs' safety, efficacy, and bioavailability of individual ingredients may change. WHO approved only a few rational combinations in the latest essential medicine list.

COUNTERFEIT DRUGS

Despite official regulation, fraudulent drugs are flooding the pharmaceutical market worldwide and present a serious health problem. Such drugs are popularly termed counterfeit, spurious, or imitation drugs. Spurious drugs are formulations manufactured concealing the true identity of the product and made to resemble another drug, especially in some popular brands to deceive the buyer and cash on the popularity of original products. Some common practices are:

- Correct ingredient but less quantity (tablet paracetamol 500 mg contains less).
- False label—wrong or low-cost ingredient (strip of ofloxacin has ciprofloxacin inside).
- Non-bioequivalence (poor quality of correct ingredients with correct amount)
- No active ingredient at all (use of placebo).
- Adulteration—something is added to an active drug.

Preventive measures are enforcement of the Drug Regulation Act and quality control of preparation. Regular check-ups and raids by drug inspectors.

OVER-THE-COUNTER DRUGS

Drugs that a person can buy without a prescription. Such easily available non-prescription drugs are known as, over-the-counter (OTC) or more commonly OTC drugs (explained in communication pharmacology).

SOME INTERESTING TERMS

Drug holiday (drug vacation, medication vacation): It stands for deliberate interruption of long-term therapy to restore effectiveness or reduce the risk of tolerance or toxicity. Discontinuation for three weeks may temporarily improve responsiveness in some conditions. The concept is not useful in practice due to fear of resistance (anti-tubercular drugs) or aggravation of symptoms (anti-angina, antiepileptic). The patient sometimes starts their drug holiday for compliance.

Drug honeymoon (honeymoon period/effect/phase): A time span during which problems known to exist are either not manifest or are ignored, just like the **honeymoon period** during which newlywed couples are most cordial and passionate with each other. In medical science, the honeymoon period is a brief period of disease remission, which follows the diagnosis of a disease and before its impact is felt (as seen in Type I diabetes during which no insulin therapy is required). The **honeymoon effect** is an initial period of temporary efficacy followed by a loss of effectiveness (as seen with antiepileptics in epilepsy). The **honeymoon phase** is a term for the early stage of illicit drug use before the development of addiction, during which the abuser is enjoying the buzz without recognizing his growing dependence.

Drug bank: A comprehensive freely accessible online unique bioinformatics resource. The database contains detailed information on drug (chemical, pharmacological, pharmaceutical) data with comprehensive drug targets (protein, sequence, structure). Data was released at an interval of 2 years. The first version was released in 2006. The most recent is the 5.0 version which contains approximately 15000 drug entries.

Bioterrorism: Some agents have the potential to be used as biological weapons. Such stable agents have been produced easily and kept to be used when required against mankind. *Yersinia pestis*, *Bacillus anthracis*, *Clostridium botulinum*, *Brucella*, and *Francisella tularensis* can result in plague, anthrax, botulism, brucellosis, and tularemia, respectively. The most recent incident is a worldwide pandemic of coronavirus-induced COVID-19 that resulted in a global lockdown.

EXERCISE

The inclusion of general consideration aims to imprint an image in the brain about all possible drug-related terminologies, commonly used in day-to-day practice. Although this is an addition, it helps in the memorization of students. A brief overlook definitely adds to the getting more scores because of its content frequently asked during an oral examination.

Chapter

2

Routes of Drug Administration

Preview: *The route of administration is the way by which drug formulations, fluids, and other substances are introduced into the body. Knowledge of routes is important for the administration of various dosage forms (an exercise of the new curriculum).*

There is a correlation between medicinal formulation and their application in the body. For the proper delivery of various dosage forms (the forms in which a drug is administered), there is a need for a specific route of administration. Selection criteria for routes depend on:

1. **Drug properties:**
   - **Nature:** Solids (orally), gases (inhalation), liquid (oral as well as parenteral route).
   - **Solubility:** Water-soluble drug (oral route), oily drug (IM), irritant drug (IV route).
2. **Amount:**
   - **Large volume:** IV route via infusion.
     Oral, inhalation, topical, and enema according to indications.
   - **Small volume:** All routes.
3. **Therapeutic indication:**
   - **Site:** GIT (oral), lung (inhalation), and skin (topical).
   - **Need:** General (oral), emergency (parenteral).
4. **Patient clinical condition:**
   - Conscious, cooperative—oral route.
   - Unconscious, irritable, severe emesis, breathlessness, shock—parenteral route.

A drug formulation can be administered in the body by following major routes—**enteral**, **parenteral,** and **topical.** Administration routes can be divided according to drug action. **Systemic action** is produced by the enteral and parenteral routes while **local action** is by the topical route.

ENTERAL ROUTE

- Most natural and accepted mode of drug administration.
- Drug is mainly given by oral route (PO), which enters into GIT (*Enteron = intestine*).
- Sublingual (buccal) and rectal modes are also considered under the enteral route, but the drug does not enter directly into GIT.

- Drugs used by the SL route are lipophilic in nature with short onset of action.
- Dosage forms are both solid such as tablets (DT, SR, EC, MD), capsules, powders, etc., and liquid like drops, syrups, suspensions, mixtures, linctus, elixirs, etc.

Advantages

- Safe and convenient.
- Self-administration (no need for assistance).
- Non-invasive, painless.
- Economical (does not need devices).
- Drugs intended for local GIT action, e.g. anthelmintic and laxative are better utilized orally (neither absorbed nor destroyed).

Disadvantages

- The pathway involved in drug absorption is more complicated.
- Lesser bio-availability (first-pass metabolism).
- Onset of action may be slow (not suitable for emergencies).
- Food, milk, and other drugs interfere with absorption.
- Non-palatable and irritant drugs cannot be administered.
- Difficult to use in patients with severe vomiting.
- Cannot be given to unconscious, non-cooperative, and bedridden patients.
- Demerits of the oral route can be minimized by specific modifications of formulation such as enteric-coated, sugar-coated, and sustained-release tablets.

PARENTERAL ROUTE

- As the name indicates, the parenteral route means all routes other than enteral or gastrointestinal *(per = beyond, the enteral = intestine).*
- Drug is administered directly into blood or body fluid to achieve maximum bio-availability.
- This route is used for drugs that are poorly absorbed, irritant, unstable, or degradable in GIT.

Advantages

- Rapid and predictable action.
- Gastric irritant drugs can be given.
- Maximum bioavailability (bypass first-pass metabolism).
- Used in patients with severe emesis and diarrhea.
- Can be used in unconscious and non-cooperative patients.

Disadvantages

- Poor patient compliance.
- Self-medication is difficult.
- Inconvenient, as it needs assistance and devices like a syringe, needle, etc.
- Risk of infection and local irritation at the injection site.
- Mandatory aseptic precaution.
- Injections are painful and not generally accepted.

- Injury to adjacent tissues possible.
- Immediate side effects can develop.
- Expensive.

Parenteral drugs are administrated by following major routes—injections, transmucosal, inhalational, and transdermal.

(i) Injections

Drug injected into specific tissue or site (vein, muscles, dermis, etc.) through a syringe and needle. Common modes are:

- **Intramuscular (IM):** In large skeletal muscles.
- **Intravenous (IV):** In a superficial vein (bolus or infusion).
- **Intradermal (ID):** In the dermis of the skin (very small quantity).
- **Subcutaneous (SC):** In subcutaneous space under the skin.

Special modes

- **Intra-arterial:** In the artery.
- **Intra-cardiac:** In the heart.
- **Intra-peritoneal:** In the peritoneal cavity.
- **Intra-thecal:** In the subarachnoid space.
- **Intra-articular:** In the joint.
- **Intra-medullary:** In the medulla of long bone.
- **Intra-lesional:** Directly into the lesion.
- **Others:** Intra-penile, intra-vesicle, and retro-bulbar, etc.

(ii) Transmucosal

Drugs are absorbed across the mucous membrane (rich blood supply). It includes three routes:

- **Sub-lingual/ buccal:** Drugs (lipid-soluble, nonirritant tablet) kept under the tongue.
- **Intra-nasal:** Drug introduced through the nostril by nasal spray.
- **Rectal:** The drug (irritant) can be put into the rectum by enema or by suppository (sublingual and rectal routes are also kept under the enteral route)

(iii) Inhalation

Drugs (gases, volatile liquids, aerosol, etc.) are directly given into the respiratory tract. Lungs provide a large surface area for absorption. Meanwhile, alveoli are thin and vascular, allowing the inhaled drug's rapid onset of action and maximum bioavailability. Common aerosol devices used as—metered-dose inhalers (MDI), nebulizers, dry powder inhalers (DPI), etc.

(iv) Trans-cutaneous (dermal)

Highly lipid-soluble drugs are applied over the skin for slow and sustained action. Common modes are **inunction, jet injector, and adhesive patches.**

TOPICAL ROUTE

- Drugs are applied on the skin or mucous membrane of nasal, aural, oropharyngeal, conjunctival, vaginal, and anal areas, etc. for localized actions.

- Effects depend upon lipid solubility, duration, and area of exposure.
- Hydrated skin has more permeability than dry skin.
- Dosage forms are cream, paste, gel, dusting powder, ointment, gargle, lotion, lozenges, paint, etc.

Advantages

- Convenient, self-application.
- Excellent patient compliance.
- None or very few systemic side effects.

Disadvantages

- Local hypersensitivity reactions.
- Risk of infection after prolonged use.

EXERCISE

Routes of drug administration are very important as per the therapeutic efficacy of a drug. This exercise can be clubbed with dosage forms for clarity of explanation. Students must know different types of routes, their advantages and disadvantages.