DOSAGE FORMS

A dosage form is the physical form of a drug product in which a drug is produced and administered to patients for diagnosis, prevention, or treatment of disease.

It is the combination of the drug (active ingredient) and excipients (inactive ingredients), formulated to ensure safety, stability, accuracy of dose, and patient acceptability.

Drugs cannot usually be administered in their pure chemical state because:

- They may be unstable.
- They may have poor solubility or bioavailability.
- They may irritate tissues.
- Accurate dosing may not be possible.

To overcome these issues, drugs are formulated into **dosage forms**.

Dosage forms help in:

- Accurate administration of dose.
- Protection of drug (from light, air, gastric acid).
- Masking unpleasant taste/odor.
- Providing controlled release (sustained, delayed).
- Improving patient compliance.

Classification of Dosage Forms

Dosage forms can be classified in different ways:

1. Based on Physical State

- **Solid dosage forms**: Tablets, Capsules, Powders, Granules, Lozenges, and Suppositories.
- **Liquid dosage forms**: Solutions, Syrups, Elixirs, Emulsions, Suspensions, and Drops.
- **Semi-solid dosage forms**: Ointments, Creams, Gels, and Pastes.
- **Gaseous dosage forms**: Inhalers, Aerosols, and Nebulizers.

2. Based on Route of Administration

- **Oral**: Tablets, Capsules, Syrups, Suspensions.
- **Parenteral (injections)**: Intravenous (IV), Intramuscular (IM), Subcutaneous (SC).
- **Topical**: Ointments, Creams, Gels, Lotions.
- **Inhalation**: Aerosols, Nebulizers, Inhalers.
- **Rectal**: Suppositories, Enemas.
- **Vaginal**: Pessaries, Vaginal tablets, Creams.

- **Ocular (Eye)**: Eye drops, Eye ointments.
- **Nasal**: Nasal drops, Nasal sprays.
- **Otic (Ear)**: Ear drops.

3. Based on Release Pattern

- **Immediate release dosage forms**: Conventional tablets, capsules, syrups.
- **Modified release dosage forms**:
  - *Sustained release* (release over longer time).
  - *Controlled release* (predictable & constant rate).
  - *Delayed release* (release at specific site, e.g., enteric-coated tablets).
  - *Targeted drug delivery systems* (e.g., nanoparticles, liposomes).

Tablets

Definition

Tablets are **solid unit dosage forms** of medicaments or excipients, prepared by **compression or molding**, and intended for **oral, sublingual, buccal, or other routes of administration**. They usually contain a **precisely measured amount of drug** with suitable excipients to ensure stability, accuracy of dose, and acceptability to the patient.

Description

- Tablets are the **most popular dosage form** worldwide, accounting for about **70–80% of total drug formulations**.
- They are **stable, convenient to carry, easy to administer, cost-effective**, and can be manufactured in large quantities using modern machines.
- They may be **uncoated, coated, or modified release** to suit therapeutic needs.
- They can be swallowed, chewed, dissolved in the mouth, or even inserted into body cavities depending on the type.

Types of Tablets

A. Based on route of administration:

1. **Oral tablets** – swallowed with water (e.g., Paracetamol tablet).
2. **Buccal tablets** – placed in buccal pouch for absorption (e.g., Nicotine tablet).
3. **Sublingual tablets** – placed under the tongue for quick absorption (e.g., Nitroglycerin tablet).
4. **Chewable tablets** – chewed before swallowing (e.g., Antacid tablets).
5. **Effervescent tablets** – dissolve in water releasing CO_2 (e.g., Dispirin effervescent tablet).

B. Based on formulation design:

1. **Uncoated tablets** – simple compressed tablets.

2. **Coated tablets** – film coated, sugar coated, or enteric coated for protection/taste masking.
3. **Modified release tablets** – sustained release, controlled release, or delayed release.
4. **Multilayer tablets** – containing two or more layers of different drugs.

C. Based on purpose of use:

1. **Immediate release** (conventional tablets).
2. **Dispersible tablets** – rapidly disintegrate in water.
3. **Soluble tablets** – dissolve in water before administration.
4. **Hypodermic tablets** – used to prepare injectable solutions (obsolete type).

Shapes and Sizes

- **Shapes:** Round, oval, oblong, square, triangular (chosen for identification and branding).
- **Sizes:**
  - Small (4–5 mm) – for pediatric use.
  - Medium (6–12 mm) – most common oral tablets.
  - Large (>12 mm) – high-dose tablets (sometimes scored to break easily).
- **Markings:**
  - **Scored tablets** – have a groove to break into equal halves.
  - **Embossed tablets** – carry symbols, letters, or company logo for identification.

Advantages of Tablets

- Accurate and uniform dose.
- Easy to carry, transport, and store.
- High stability compared to liquids.
- Mask unpleasant taste using coating.
- Can be designed for **immediate or controlled release**.

Disadvantages of Tablets

- Not suitable for patients with **dysphagia (difficulty in swallowing)**.
- Drugs with **poor compressibility** cannot be easily made into tablets.
- Some drugs may get **inactivated by gastric fluids** unless coated.

Example Formula – Paracetamol Tablet (500 mg)

- **Paracetamol** – 500 mg (Active drug)
- **Starch** – 30 mg (Binder, disintegrant)
- **Microcrystalline cellulose** – 20 mg (Diluent)
- **Magnesium stearate** – 5 mg (Lubricant)
- **Talc** – 2 mg (Glidant)

Capsules

Definition

Capsules are **solid unit dosage forms** in which one or more drug substances, with or without excipients, are enclosed in a **hard or soft soluble shell**, usually made of gelatin. They mask unpleasant tastes/odors and allow easy swallowing.

Types of Capsules

1. **Hard Gelatin Capsules (HGC):**
   - Two-piece capsule (body + cap).
   - Contain powders, granules, pellets.
   - Example: Ampicillin capsule.
2. **Soft Gelatin Capsules (SGC):**
   - One-piece, flexible, hermetically sealed.
   - Contain liquids, semi-solids, or oils.
   - Example: Vitamin A soft gel.
3. **Modified Capsules:**
   - Enteric-coated capsules.
   - Sustained release capsules.

Sizes of Hard Gelatin Capsules

- Ranging from **000 (largest ~ 1.4 g fill)** to **5 (smallest ~ 60 mg fill)**.
- Pediatric doses usually use sizes 4 or 5.

Advantages

- Masks taste and odor.
- Smooth, easy to swallow.
- Flexible (suitable for powders, oils, pastes).
- Better bioavailability for poorly soluble drugs (with soft gels).

Disadvantages

- Hygroscopic drugs may cause capsule shell to become brittle.
- Not suitable for very soluble ionic drugs (may cause gastric irritation).
- Expensive compared to tablets.

Example Formula – Ampicillin Capsule (250 mg)

- **Ampicillin trihydrate** – 250 mg (Active drug)
- **Lactose** – q.s. (Diluent)
- **Magnesium stearate** – 5 mg (Lubricant)
- **Encapsulated in size 2 HGC shell**

Syrups

Definition

Syrups are **concentrated aqueous solutions of sugar (usually sucrose 60–80%) containing active medicaments**. They are clear, sweet, viscous liquid dosage forms.

Description

- Used for children and patients who cannot swallow solid forms.
- High sugar concentration provides **sweetness, stability (preservative effect), and viscosity**.
- Can be flavored and colored to improve palatability.

Types

1. **Medicated Syrups** – contain active drug (e.g., Paracetamol syrup).
2. **Flavored Syrups** – vehicle for extemporaneous compounding (e.g., Simple Syrup IP).
3. **Non-sucrose Syrups** – use sorbitol, glycerol, or artificial sweeteners for diabetics.

Advantages

- Easy to administer.
- Masks bitter taste.
- Rapid absorption.

Disadvantages

- Risk of microbial growth if not properly preserved.
- Not suitable for diabetic patients (unless sugar-free).

Example Formula – Paracetamol Syrup (125 mg/5 mL)

- **Paracetamol** – 125 mg
- **Sucrose** – 65% w/v
- **Sodium benzoate** – 0.1% (Preservative)
- **Glycerin** – 5% (Co-solvent, preservative action)
- **Flavor and color** – q.s.
- **Purified water** – up to 5 mL

Suspensions

Definition

Suspensions are **biphasic liquid dosage forms** consisting of finely divided **insoluble solid drug particles dispersed in a liquid vehicle**, stabilized by suspending agents.

Types

1. **Oral suspensions** – e.g., Antacid suspensions.
2. **Topical suspensions (lotions)** – e.g., Calamine lotion.
3. **Parenteral suspensions** – e.g., Depot corticosteroid injection.

Advantages

- Good for insoluble drugs.
- Taste can be masked.
- Flexible dosing.

Disadvantages

- Sedimentation & caking.
- Need to shake before use.
- Less stable than solutions.

Example Formula – Paracetamol Suspension (250 mg/5 mL)

- **Paracetamol** – 250 mg
- **Sodium CMC** – 0.5% (Suspending agent)
- **Sorbitol** – 70% (Sweetener & thickener)
- **Sodium benzoate** – 0.1% (Preservative)
- **Flavor, color** – q.s.
- **Purified water** – up to 5 mL

Ointments

Definition

Ointments are **semisolid preparations** intended for external application to the skin or mucous membranes, usually containing medicaments dissolved or dispersed in a suitable base.

Description

- Provide local effect (antibacterial, anti-inflammatory) or systemic absorption (e.g., nitroglycerin).
- Ointment bases can be oleaginous, absorption, water-removable, or water-soluble.

Types

1. **Medicated ointments** – e.g., Neomycin ointment.
2. **Non-medicated ointments** – used as emollients/protectives (e.g., Vaseline).

Advantages

- Provide prolonged contact time with skin.
- Easy application.
- Soothing effect.

Disadvantages

- Greasy, sticky.
- Less patient compliance compared to creams.

Example Formula – Neomycin Ointment (0.5%)

- **Neomycin sulfate** – 0.5 g
- **White soft paraffin** – 99.5 g (Base)

6. Inhalers (Aerosols)

Definition

Aerosols are **pressurized dosage forms** containing one or more active ingredients, packed with a propellant, and released as a fine spray or mist for inhalation or topical use.

Description

- Mainly used in **asthma, COPD** (metered-dose inhalers, dry-powder inhalers).
- Provides **rapid drug action in lungs**.

Types

1. **Metered-dose inhalers (MDIs)** – deliver a fixed dose per actuation.
2. **Dry powder inhalers (DPIs)** – drug in powder form inhaled by patient effort.
3. **Nebulizers** – convert liquid solution into aerosol mist.

Advantages

- Rapid onset of action.
- Lower dose needed (direct to lungs).
- Fewer systemic side effects.

Disadvantages

- Technique-dependent efficacy.
- Costly compared to tablets.

Example Formula – Salbutamol Inhaler (100 µg per actuation)

- **Salbutamol sulfate** – 100 µg/dose
- **Propellant (HFA-134a)** – q.s.
- **Metered-dose valve container**

Tablet: A solid unit dosage form prepared by compression, containing one or more drugs with or without excipients.

Capsule: A solid dosage form in which drug is enclosed in a hard or soft gelatin shell.

Powder: A dry, finely divided form of drug intended for internal or external use.

Granules: Agglomerates of powder particles used for better flow and compressibility.

Syrup: A concentrated aqueous solution of sugar, containing drug and flavoring agents.

Suspension: A biphasic liquid dosage form containing insoluble solid particles dispersed in a liquid medium.

Emulsion: A biphasic liquid dosage form consisting of two immiscible liquids (oil and water) stabilized by emulsifying agents.

Ointment: A semi-solid preparation intended for external application to skin or mucous membranes.

Cream: A semi-solid emulsion (oil-in-water or water-in-oil) for external application.

Gel: A semi-solid system with drug dispersed in a water-soluble or alcohol-based gel base.

Suppository: A solid dosage form intended for insertion into body cavities (rectum, vagina), where it melts or dissolves to release drug.

Injection (Parenteral): Sterile preparations intended for administration through needle and syringe into the body (IV, IM, SC).

Inhalers/Aerosols: Dosage forms delivering drug directly to lungs via inhalation.

PRESCRIPTION

A prescription is an official written order prepared by a physician, a dentist, or any other authorized medical practitioner. This written order is addressed to the pharmacist and directs them to compound and dispense a specific medication that is intended for an individual patient. Along with this order, the prescription also contains accompanying instructions, both for the pharmacist who prepares or dispenses the medication and for the patient who has to consume the medicine.

The term "prescription" itself originates from the Latin word *praescriptus*. This Latin word is made up of two distinct parts: *prae*, which is a prefix meaning "before," and *scribere*, which means "to write." Thus, the literal meaning of the word prescription can be understood as "to write before."

1. Types of Prescription

There are two broad types of prescriptions:

1. **Pre-compounding prescription**: This refers to a prescription where the drug being prescribed is already prepared and manufactured by pharmaceutical companies. The pharmacist is not required to prepare the drug but simply dispenses it. For example, a prescription written for *Capsule Ciprofloxacin 500 mg* is considered a pre-compounding prescription since the medicine already exists in a prepared form.
2. **Extemporaneous prescription**: This type of prescription involves a situation where the pharmacist prepares the medication according to the specific instructions and directions given by the physician regarding the drugs and their dosages. However, this practice of extemporaneous compounding is largely not in use in modern times, since most drugs are already available in ready-made dosage forms.

2. Parts of a Prescription

A prescription generally consists of several important parts. These are:

1. Date of the prescription
2. Name, Age, and Sex of the patient
3. Superscription
4. Inscription
5. Subscription
6. Signature or signa (directions to the patient)
7. **Signature, Address, and Registration Number of the Prescriber**
8. **Renewal Instruction**

1. Date

The date is always written on the prescription by the prescriber. It serves multiple purposes.

- It helps to know the exact time when the medicines were last dispensed to the patient.
- It is an important measure to prevent misuse of drugs by patients.
- Prescriptions which include narcotics or other habit-forming drugs must compulsorily bear the date. This is essential to avoid the misuse of the prescription, especially in cases where the patient might attempt to present the same prescription multiple times to obtain the drug repeatedly.

2. Name, Age, Sex, and Address of the Patient

This information helps in properly identifying the prescription.

- Particularly in the case of children, recording the age and sex is very important. This helps the pharmacist in cross-checking the dose prescribed by the physician to ensure it is safe and accurate for the specific patient.
- If any of these details are missing in the prescription, the pharmacist is allowed to include the missing details after making the necessary enquiry directly from the patient.

3. Superscription

- The superscription is represented by the symbol **Rx**.
- Rx is an abbreviation derived from the Latin word *recipe*, which literally means "take thou" or "you take."
- In ancient times, the symbol was believed to have originated from the sign of Jupiter, the Roman god of healing. The symbol was used by the ancients in the hope of invoking divine assistance for the quick recovery of the patient.

4. Inscription

This is considered the **main part of the prescription order**. It contains the **names and quantities** of the prescribed ingredients. The name of each ingredient is written separately along with its quantity.

In complex prescriptions that contain several ingredients, the inscription can be divided into the following parts:

- **Base**: The active medicament responsible for the therapeutic action.
- **Adjuvants**: Substances added to enhance the action of the medicament or improve its palatability.
- **Vehicle**: The substance used to dissolve the medicament or increase the volume of the preparation.

In modern practice, most drugs are prescribed in ready-made dosage forms. The pharmacist is usually required to dispense the prepared form of drugs, and therefore, **compounding of prescriptions has almost been eliminated**.

5. **Subscription**

- This part of the prescription contains the prescriber's directions to the pharmacist.
- It usually includes instructions about the type of dosage form that has to be prepared and the number of doses that should be dispensed.

Nowadays, the majority of prescribed drugs are already available in a suitable, ready-made formulation. Because of this, the pharmacist is usually only required to dispense the ready-made drug forms. The compounding of prescriptions, which was once a major part of pharmacy practice, has now been almost completely eliminated

6. **Signatura (often written as "Sig")**

- This section provides directions to the patient regarding how the drug has to be administered.
- It usually contains details such as the quantity of the medicine or the number of dosage units to be taken, how many times a day it should be taken, and at what time it should be administered.
- These directions must always be written on the label of the container to ensure the patient knows exactly how to use the medicine.

Common Latin terms:

- *Cochleare magnum* – one tablespoon
- *Ter in die* – three times a day
- *Post cibos* – after meals
- *Sumenda* – to be taken

7. **Signature, Address, and Registration Number of the Prescriber**

- Information about the physician or prescriber is essential because it allows the pharmacist or patient to contact the doctor in case of an emergency.
- Every prescription must be signed with the prescriber's own hand.
- The address and registration number of the prescriber must also be written, especially in the case of narcotics or other habit-forming drugs. This is an important measure to prevent misuse.

8. **Renewal Instruction**:

- The prescriber should indicate clearly on every prescription whether it can be renewed and, if so, how many times renewal is allowed.
- This instruction is especially important when the prescription involves **narcotic or habit-forming drugs,** as it prevents unnecessary and harmful misuse.

Handling of Prescription

The steps in handling a prescription include:

- Receiving the prescription
- Reading and checking the prescription
- Collecting the required materials
- Compounding
- Weighing
- Finishing

Receiving

- The prescription should always be received by the pharmacist themselves.
- This process includes reading and checking the prescription carefully.
- While receiving a prescription, the pharmacist should maintain a neutral facial expression. They should not show surprise or confusion, as such reactions may create unnecessary anxiety or suspicion in the patient.

Reading and Checking

- The prescription must be read completely and carefully from top to bottom.
- The pharmacist should check the nature of the dosage form and estimate the time required for its preparation.
- If a long time is required for compounding, the patient should be informed and asked to wait.
- Careful examination of the prescription should always be done behind the counter, not in front of the patient.
- If there is any doubt, unclear direction, or possible error in writing, the patient must not be made aware of it directly. Instead, the pharmacist should consult another pharmacist or the prescriber.
- Every word and abbreviation in the prescription must be correctly interpreted.
- A pharmacist should never guess the meaning of illegible or confusing words.
- The prescription should be checked for any possible incompatibility.

Collecting and Weighing the Material

- Materials required for compounding are collected and placed on the left side.
- A balance is kept in the center.
- The materials are then carefully weighed and checked.

Compounding, Labeling, and Packaging

- Compounding should be done for one prescription at a time to ensure accuracy.
- Accuracy, cleanliness, and proper technique should be followed.
- The quantity to be dispensed must be exact.

- Good quality paper and adhesive must be used for packaging.
- The label should be of appropriate size and must contain all required information and special directions for use.

- Incompatibilities should always be checked to ensure there are no pharmaceutical or therapeutic conflicts. Different medicines prescribed to the same patient must not interact with each other in a harmful way.
- For example, certain antibiotics should not be taken with meals since food can significantly decrease their absorption and therefore reduce their effectiveness.

Common Latin Prescription Terms

Some commonly used Latin prescription abbreviations include:

1. **ac (ante cibum)** – before meals
2. **bid (bis in die)** – twice a day
3. **gt (gutta)** – drop
4. **hs (hora somni)** – at bedtime
5. **od (oculus dexter)** – right eye
6. **os (oculus sinister)** – left eye
7. **po (per os)** – by mouth
8. **pc (post cibum)** – after meals
9. **prn (pro re nata)** – as needed
10. **q 3 h (quaque 3 hora)** – every three hours
11. **qd (quaque die)** – every day
12. **qid (quater in die)** – four times a day
13. **Sig (signa)** – write or label
14. **tid (ter in die)** – three times a day

Sources of Error in Prescription

Errors in prescriptions can lead to patient harm, treatment failure, or adverse effects. Therefore, it is crucial for pharmacists to carefully evaluate each prescription before dispensing. The **major sources of error** are as follows:

1. **Abbreviations**

Abbreviations may create confusion in interpreting the prescription.

Precaution:

The pharmacist should interpret abbreviations carefully and never guess the meaning of any ambiguous abbreviation. If there is doubt, clarification must be obtained from the prescriber.

- **Example:**

- Writing “Dispense Achromycin” for “Achro” may cause confusion if the prescriber intended “Achrostatin.”

2. Name of the Drug

Certain drug names look or sound similar, which may lead to dispensing the wrong drug.

- **Examples:**
  - **Digitoxin** vs **Digoxin**
  - **Prednisone** vs **Prednisolone**
- **Precaution:**
  - Pharmacists must read carefully and confirm with prescriber in case of doubt.

3. Strength of the Preparation

Many drugs are available in different strengths. If the strength is not mentioned, it may result in underdosing or overdosing.

- **Example:**
  - Dispensing **paracetamol 500 mg** when the prescription does not specify strength may be incorrect.
- **Precaution:**
  - The strength must be clearly stated in the prescription.

4. Dosage Form of the Drug Prescribed

Several medicines are available in multiple dosage forms (e.g., tablets, capsules, liquids, suppositories).

- **Precaution:**
  - The prescriber should specify the **pharmaceutical dosage form** in the prescription to avoid ambiguity.

5. Dose

Unusually high or low doses can be dangerous. Paediatric doses may be difficult to calculate and require careful consultation. Even correct doses can be harmful if administered too frequently.

- **Example:**
  - A sustained-release formulation prescribed **every 4 hours** is inappropriate (usually given 2–3 times/day).
- **Precaution:**
  - Pharmacists should verify doses and consult paediatric posology or contact prescriber when necessary.

6. Instructions for the Patient

Instructions in prescriptions are often incomplete or missing.

- **Required Details:**
  - Quantity of drug per dose
  - Frequency & timing of administration
  - Route of administration
- **Precaution:**
  - All instructions must be clear to avoid confusion and ensure proper use.

7. Incompatibilities

There may be **pharmaceutical** (physical/chemical) or **therapeutic** (drug-drug interaction) incompatibilities.

- **Examples:**
  - Some antibiotics should not be taken with meals as food decreases absorption.
- **Precaution:**
  - Pharmacists must check all prescribed drugs for incompatibilities and potential interactions before dispensing.

Posology

The term **Posology** is derived from the Greek words: **"Posos"** = *how much* **"Logos"** = *study*

Definition

Posology is the branch of medical science and pharmacy that deals with the study of doses of drugs and medicines. It involves determining the **right dose** of a drug required to produce the desired therapeutic effect in patients, without causing toxicity.

It is an important concept because **the same drug can act as a life-saving medicine in proper dose, but may turn toxic or even fatal in higher dose**.

In short Posology = *Science of drug dosage*

Factors Affecting Posology

Posology is the branch of medical science that deals with the study of dosages of medicines and drugs. It focuses on the amount of drug required to produce a therapeutic effect without causing toxicity.

The dose of a drug varies greatly depending on multiple factors, both patient-related and drug-related.

1. **Age**
   - The pharmacokinetics of many drugs change with age.

- **Newborn infants (pediatric patients)** are abnormally sensitive to certain drugs due to the immature state of their hepatic and renal functions. These organs are responsible for inactivating and eliminating drugs from the body.
- Failure to detoxify and eliminate drugs in infants leads to **drug accumulation in tissues** and may result in toxicity.
- **Elderly patients** are also more sensitive to some drugs. For example, hypnotics may produce a state of confusion in them.

2. **Sex**
   - Women do not always respond to drugs in the same way as men.
   - Special care must be taken when administering drugs during **menstruation, pregnancy, and lactation**.
   - Strong purgatives such as **Aloes** should be avoided during menstruation.
   - Drugs that stimulate uterine smooth muscles, such as **drastic purgatives, antimalarial drugs, and ergot alkaloids**, are contraindicated during pregnancy.
   - Substances such as **alcohol, barbiturates, and narcotic drugs** can cross the placenta and affect the fetus.
   - During **lactation**, drugs like **morphine** and **tetracycline** should be avoided because they can adversely affect the baby through breast milk.
3. **Body Weight and surface area**
   - The average dose of a drug is often expressed in terms of **mg per kg body weight**.
   - Another method is to use a **total single dose** for an adult weighing between 50–100 kg.
   - However, this dose may not be applicable in cases of **obese patients, children, or malnourished individuals**. In such cases, doses should always be carefully calculated based on actual body weight.

$$\text{Dose} = \frac{\text{BSA } (\text{m}^2)}{1.7} \times \text{Average Adult Dose}$$

Where:

- ✓ **BSA (m^2)** → Patient's body surface area in square meters
- ✓ **1.7** → Standard average adult BSA (m^2)
- ✓ **Average Adult Dose** → Standard dose prescribed for an adult patient

4. **Route of Administration**
   - Intravenous (I.V.) doses of drugs are usually **smaller than oral doses**, as the drug directly enters systemic circulation and bypasses first-pass metabolism.
   - This also increases the chances of **drug toxicity**.
   - Therefore, the **effectiveness and safety** of a drug are greatly influenced by the route of administration.
5. **Time of Administration**

- The presence of food in the stomach can **delay drug absorption**, while an empty stomach allows more rapid absorption.
- However, rapid absorption does not always mean better effectiveness.
- Some drugs must be taken **after meals**, such as **iron, arsenic, and cod-liver oil**.
- Others, like **antacids**, should be taken **before meals**.

6. **Environmental Factors**
   - The **personality and behavior of a physician** may influence the therapeutic effect of drugs, especially in psychosomatic disorders.
   - Women, being generally more emotional than men, may require **lower doses** of certain drugs.
   - Inert dosage forms called **placebos**, which resemble real medicines, can produce therapeutic benefits in conditions such as **angina pectoris** and **bronchial asthma** due to psychological influence.
7. **Presence of Disease**
   - Diseases can alter the effect of drugs.
   - For example:
     - **Barbiturates** and **chlorpromazine** may have unusually prolonged effects in patients with **liver cirrhosis**.
     - **Streptomycin** may produce toxic effects in patients with **impaired kidney function**, as it is excreted mainly through the kidneys.
8. **Accumulation**
   - Some drugs, if administered repeatedly over a long period, may accumulate in the body and produce **toxic effects**.
   - Examples include **digitalis, emetine, and heavy metals**, which are slowly excreted from the body.
   - This phenomenon is called the **cumulative effect** of a drug.
9. **Additive Effect**
   - When two or more drugs are administered together, and their combined effect is **equal to the sum of their individual effects**, it is called an **additive effect**.
   - Example: **Ephedrine + Aminophylline** in the treatment of bronchial asthma.
10. **Synergism**

- When two or more drugs are given in combination to **increase or prolong their action** beyond what a single drug can achieve, the phenomenon is called **synergism**.
- Example: **Procaine + Adrenaline**. Adrenaline prolongs the duration of action of procaine.

11. **Antagonism**

- When the action of one drug is **opposed by another drug** on the same physiological system, it is called **drug antagonism**.
- Antagonism is very useful in the treatment of **poisoning**.
- Examples:
  - **Milk of Magnesia** is given in acid poisoning because its alkaline effect neutralizes the acid.

- **Adrenaline (vasoconstrictor)** and **Acetylcholine (vasodilator)** neutralize each other when given together.

12. **Idiosyncrasy**

- Idiosyncrasy is also referred to as **drug allergy**.
- It is an **unusual or abnormal response** to a drug, different from its normal pharmacological action.
- Examples:
  - A small dose of **aspirin** may cause gastric hemorrhage in sensitive individuals.
  - Some individuals are extremely sensitive to **penicillin** or **sulfonamides**, which may cause severe toxic effects.

13. **Tolerance**

- When an unusually **large dose of a drug is required** to produce the same effect that a normal therapeutic dose would ordinarily produce, it is called **drug tolerance**.
- Examples:
  - **Smokers** can tolerate high levels of nicotine.
  - **Alcoholics** can tolerate larger amounts of alcohol.
- Types of tolerance:
  - **True tolerance**: Produced by both oral and parenteral administration.
  - **Pseudo tolerance**: Produced only by the oral route.

14. **Tachyphylaxis**

- When a drug is administered repeatedly at short intervals, its **cell receptors become blocked**, and the pharmacological response decreases.
- This reduced response **cannot be reversed** even by increasing the dose.
- This phenomenon is called **tachyphylaxis** or **acute tolerance**.
- Example: **Ephedrine**, when repeatedly given at short intervals in bronchial asthma, produces much less response due to tachyphylaxis.

15. **Metabolic Disturbances**

- Changes in **water-electrolyte balance, acid-base balance, body temperature, and other physiological factors** can modify drug effects.
- Example: **Salicylates** reduce body temperature only when there is fever. They have **no antipyretic effect** if the body temperature is normal.

Pediatric dose calculations

Introduction

- Pediatric patients (newborns, infants, and children) are **not small adults**.
- Drug doses cannot simply be scaled down from adult doses because:

  - Body composition differs (higher water content, less fat).
  - Organs (liver, kidney) are immature → altered drug metabolism and excretion.
  - Drug response varies with growth and development.
- Hence, **specific formulae and methods** are used to calculate pediatric doses.

General Principles

1. Pediatric dose is usually derived from the **adult dose**.
2. Calculations are based on **age, weight, or body surface area (BSA)**.
3. **Safety margin** is always considered, as children are more vulnerable to toxicity.
4. Doses are expressed as **mg/kg body weight** or **mg/m² body surface area**.

Methods of Pediatric Dose Calculation

1. Young's Formula (Age-based)

$$Child\ Dose = \frac{Age\ (years)}{Age + 12} \times Adult\ Dose$$

- Simple and easy, but not very accurate.
- Example: A 6-year-old child, adult dose = 300 mg

$$\frac{6}{6 + 12} \times 300 = 100\,mg$$

2. Dilling's Formula (Age-based, for children above 2 years)

$$Child\ Dose = \frac{Age\ (years)}{20} \times Adult\ Dose$$

- Example: 10-year-old child, adult dose = 400 mg

$$\frac{10}{20} \times 400 = 200\,mg$$

3. Clark's Formula (Weight-based)

$$Child\ Dose = \frac{Weight\ (kg)}{70} \times Adult\ Dose$$

- Uses average adult weight = 70 kg.
- Example: 20 kg child, adult dose = 200 mg

$$\frac{20}{70} \times 200 = 57.14\,mg$$

4. Body Surface Area (BSA) Method (Most Accurate)

$$Child\ Dose = \frac{BSA\ (m^2)}{1.7} \times Adult\ Dose$$

- 1.7 m^2 = average adult BSA.
- BSA (Mosteller's Formula):

$$BSA(m^2) = \sqrt{\frac{Height(cm) \times Weight(kg)}{3600}}$$

- Example: Child height = 110 cm, weight = 20 kg, Adult dose = 300 mg

$$BSA = \sqrt{\frac{110 \times 20}{3600}} = \sqrt{0.611} = 0.78\,m^2$$

$$Child\ Dose = \frac{0.78}{1.7} \times 300 = 137.65\,mg$$

5. Fried's Formula (for infants <1 year old)

$$Infant\ Dose = \frac{Age\ (months)}{150} \times Adult\ Dose$$

- Example: 6-month-old baby, adult dose = 300 mg

$$\frac{6}{150} \times 300 = 12\,mg$$

---

6. Salisbury's Rule

$$Child\ Dose = \frac{Age\ (years) \times Adult\ Dose}{24}$$

Important Considerations in Pediatric Dosing

- **Neonates and infants** require extra care due to immature organs.
- Always consider **therapeutic drug monitoring (TDM)** for narrow therapeutic index drugs (e.g., digoxin, aminoglycosides).
- **Liquid dosage forms** (syrups, suspensions, drops) are preferred for children.
- Pediatric doses must be **rounded carefully** for practical administration (avoid overdosing)