Pharmaceutical Dosage Forms
Introduction

• What is a drug?
• Drug is any agent whether natural or synthetic having therapeutic and medicinal properties and used in the diagnosis, cure, treatment or prevention of disease in man and other animals.

• Usually the drug is referred to as Active pharmaceutical ingredient - API.

• Drug substances are rarely administered as a pure chemical substance, but are almost always given in a formulated preparation in combination with one or more nonmedicinal agents, referred to as pharmaceutical ingredients or excipients, in a form of dosage form.
• Therefore dosage forms are the means by which drug molecules are delivered to sites of action within the body.

- Pharmaceutical dosage form consists of:
  - Active Drug Substance
  - Excipients

• The dosage forms can vary from simple solutions to complex drug delivery systems, through the use of the appropriate excipients.
• The general area of study concerned with the formulation, manufacture, stability, and effectiveness of pharmaceutical dosage forms is termed **pharmaceutics**.

• The proper design and formulation of a dosage form requires consideration of the physical, chemical, and biologic characteristics of all of the drug substances and excipients to be used in fabricating the product.
Direct clinical use of the active drug substances „as they are“ is rare due to a number of good reasons:

• API handling can be difficult or impossible (e.g., low mg and µg doses).

• Accurate drug dosing can be difficult or impossible.

• API administration can be impractical, unfeasible or not according to the therapeutic aims.

• Some API can benefit from reducing the exposure to the environmental factors (light, moisture...), or they need to be chemically stabilised due to the inherent chemical instability.
• API can be degraded at the site of administration (e.g., low pH in stomach)

• API may cause local irritations or injury when they are present at high concentrations at the site of administration

• API can have unpleasant organoleptic qualities (taste, smell – compliance!)

• Administration of active substance would mean to have no chance for modification (improvement) of its PK profile
excipients

• The successful formulation of a stable and effective dosage form depends on the careful selection of the proper excipient.

• These excipients are usually used to solubilize, suspend, thicken, dilute, emulsify, stabilize, preserve, color, flavor, and improve the compressibility of drug substance to form the various dosage form.
excipients

- Coloring agents
- Sweetening agents
- Flavoring agents
- Surfactants
- Solubilizing agents
- Antioxidants
- Preservatives
- Thickening agents
- Suspending agents
- Binding agents
- Solvents
- Lubricants
- Perfumes
- Fats and oils
The Need for Dosage Forms

• Provides the mechanism for the safe and convenient delivery of accurate dose.

• Protects the drug substance from the destructive influences of atmospheric oxygen or humidity (coated tablets, sealed ampuls).

• Protects the drug substance from gastric juice (HCL), e.g. enteric coated tablets.

• Masking unpleasant taste (bitter, salty, or offensive taste) or odor of a drug substance (capsules, coated tablets, flavored syrups).
• Provides liquid preparations of substances that are either insoluble or unstable in the desired vehicle (suspensions).

• Provides clear liquid dosage forms of substances (syrups, solutions).

• Provides rate-controlled drug action (various controlled-release tablets, capsules, and suspensions).
• Provides maximum drug action from topical administration sites (ointments, creams, transdermal patches, and ophthalmic, ear, and nasal preparations).

• Provides placement of drugs directly in the bloodstream or body tissues (injections)

• Provides optimal drug action through inhalation therapy (inhalants and inhalation aerosols)
Pharmaceutical preparation (PP)

- particular pharmaceutical product containing active and inactive pharmaceutical ingredients (excipients) formulated into the particular dosage form.

- Two major types of PP according the origin:
  - **Manufactured** in large scales by pharmaceutical industry (original and generic preparations).
  - **Compounded** individually in compounding pharmacies
General considerations in PP

• The drug and excipients must be compatible with one another to produce a drug product that is stable, efficacious, attractive, easy to administer, and safe.

• The product should be manufactured with appropriate measures of quality control and packaged in containers that keep the product stable.

• The product should be labeled to promote correct use.

• The product should be stored under conditions that contribute to maximum shelf life.
Dosage forms are classified into:

- **Route of administration**
  - Oral
  - Topical
  - Rectal
  - Parenteral
  - Vaginal
  - Inhaled
  - Ophthalmic
  - Otic

- **Physical form**
  - Gas
  - Liquid
  - Semi solid
  - Solid
Gases

- They are mainly inhalation and aerosols.

- Medicinal gases:
  - inhalation/volatile anaesthetics (vaporised before administration by inhalation)

- Aerodispersions
  - of solid particles: (e.g., antiasthmatic inhalations)
  - or liquid particles (antiasthmatic inhalations or sprays)
Liquids

• Solutions
• Suspensions
• Emulsions
• **Solutions**
  - Clear Liquid preparations (one homogenous phase), prepared by dissolving one or more solutes in a suitable vehicle

• **Types of solutions:**
  - **Syrup:**
    - It is a concentrated aqueous solution of a sugar, usually sucrose to which medicaments are added.
    - Flavored syrups are a convenient form of masking disagreeable tastes
  - **Linctuses:**
    - are viscous, liquid oral preparations that are usually prescribed for the relief of cough.
    - They usually contain a high proportion of syrup and glycerol which have a soothing effect on the membranes of the throat.
Types of solutions....

• **Aromatic waters:**
  Aromatic waters are clear, aqueous solutions saturated with volatile oils or other aromatic or volatile substances.

• **Spirits:**
  Volatile drug dissolved in alcoholic or hydroalcoholic solutions

• **Elixir:** (Sweetened/ flavored spirit)
  It is pleasantly flavored clear liquid sweetened hydroalcoholic oral reparation.
  -The vehicle may contain a high proportion of ethanol or sucrose together with antimicrobial preservatives which confers the stability of the preparation.

• **Tinctures:**
  •Solution made by extracting from the crude (plant or vegetable) source those constituents of a drug that are soluble in alcohol.
Types of solutions....

• **Gargles:**
  • They are aqueous solutions used in the prevention or treatment of throat infections.
  • Usually they are prepared in a concentrated solution with directions for the patient to dilute with warm water before use.

**Mouthwashes:**
• These are similar to gargles but are used for oral hygiene and to treat infections of the mouth.
• **Collodion**
  - liquid preparations of nitrocellulose in a mixture of ether and ethanol used as a topical protectant, applied to the skin to lose small wounds, abrasions, and cuts, to hold surgical dressings in place, and to keep medications in contact with the skin.

• **Vaginal douches**
  - It introduces a stream of water into the body for medical or hygienic reasons.

• **Enemas**
  - An enema is the procedure of introducing liquids directly into the colon.
• **Emulsions**
• a dispersion system consisting of stabilized two immiscible liquids
• o/w or w/o
• cloudy appearance
• **Suspensions:**
  • A dispersion system where solid particles (dispersed phase) are dispersed in liquid phase (dispersion medium).

  • According to the size of dispersed particles (1 nm-0.5 mm) a molecular, colloidal and coarse dispersions can be distinguished.

  • May require shaking before administration.

• **Lotions:**
  • These are suspensions (aqueous) for external application without friction.
Semisolid dosage forms
1- Unshaped (without specific physical shape)

• Gels:
• A semisolid systems in which a liquid phase is constrained within a 3D cross-linked matrix (consisting of natural or synthetic gum) having a high degree of physical or chemical cross-linking.
• **Creams:**
  - semisolid emulsion systems containing more than 10% of water.
  - They are divided into
    - **o/w creams** - which are composed of small droplets of oil dispersed in a continuous aqueous phase.
    - more comfortable and cosmetically acceptable as they are less greasy and more easily water washable.

    - **w/o creams** - which are composed of small droplets of water dispersed in a continuous oily phase.

Water-in-oil creams are more difficult to handle but many drugs which are incorporated into creams are hydrophobic and will be released more readily from a water-in-oil cream than an oil-in-water cream.

Water-in-oil creams are also more moisturising as they provide an oily barrier which reduces water loss from the stratum corneum, the outermost layer of the skin.
• **Ointments**: are semi-solid, greasy preparations for application to the skin.

• - The base is usually anhydrous and immiscible with skin secretions.

• - Ointments may be used as emollients or to apply suspended or dissolved medicaments to the skin.

• **Ointments** have a higher concentration of oil, compared to **creams**
Pastes:
- Pastes are basically ointments into which a high percentage of insoluble solid (> 25%) has been added.

- It consists of fatty phase (ex. Petrolatum) and > 25% solid substance for example zinc oxide.

- They provide a protective coating over the areas to which they are applied such as sunscreens.
Semisolid dosage forms

2- Shaped

Suppositories (for rectal administration)
- different shapes.
- Melts or dissolve at body temperature.
- Oleaginous (cacao butter) or aqueous (PEGs, glycerinated gelatin).

• Pessaries (vaginal suppositories)
  - Similar as above, PEGs or glycerinated gelatin are often used as base.
Solid dosage forms

• Powders and Granules
• Capsules and Tablets
• **Powders**: are solid dosage form of medicament meant for internal and external use.

• **Granules**: They consist of solid, dry aggregates of powder particles often supplied in single-dose sachets.
  
  - Some granules are placed on the tongue and swallowed with water, others are intended to be dissolved in water before taking.
  
  - Effervescent granules evolve carbon dioxide when added to water.
Capsule is a medication in a gelatin container.

- Advantage: mask the unpleasant taste of its contents.

- The two main types of capsules are:
  1- hard-shelled capsules, which are normally used for dry, powdered ingredients,
  2- soft-shelled capsules, primarily used for oils and for active ingredients that are dissolved or suspended in oil.
**Tablet:** is a hard, compressed medication in round, oval or square shape

**Effervescent tablets:** are uncoated tablets that generally contain acid substances (citric and tartaric acids) and carbonates or bicarbonates and which react rapidly in the presence of water by releasing carbon dioxide.

They are intended to be dissolved or dispersed in water before use providing:
A- Very rapid tablet dispersion and dissolution.
B- pleasant tasting carbonated drink.
**Chewable tablets:** they are tablets that chewed prior to swallowing.

- They are designed for administration to children e.g. vitamin products.

**Lozenges:** It is a solid preparation consisting of sugar and gum. It is used to medicate the mouth and throat.
Classification of pharmaceutical dosage forms according to the route of administration

- For systemic administration
  - Peroral (p.o)
  - Sublingual (S.L) and buccal.
  - Rectal
  - Parenteral
  - Transdermal
  - Inhalation
for local administration
• Topical (on the skin or mucosa)
  Into/onto - the eye, nose, ear
  - the oral cavity
  - the vagina, rectum
  - the skin
• Oral (local effect within GIT; antacids, adsorbents)
Generations of dosage forms

– 1\textsuperscript{st} gen. – traditional (unmodified) release of API
– 2\textsuperscript{nd} generation: sustained or prolonged
– 3\textsuperscript{rd} gen. – controlled release of API (CR)

![Graph showing plasma concentrations over time with different release patterns]