

Pharmaceutical Dosage Forms

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Learning objectives:

Following the lesson presentation students will be able to:

1. Describe the science of Pharmaceutics
2. Describe the reasons we need dosage forms
3. Describe how dosage forms are classified
4. Describe dosage forms according to their physical forms
5. Describe dosage forms according to their route of administration

Pharmaceutical Dosage Forms

Pharmaceutics is Science of dosage form design. Pharmaceutical Dosage Forms are consisted of Active Drug Substance (active pharmaceutical ingredient) and Excipients. Active Drug Substances (active pharmaceutical ingredients, API) are chemical compounds with pharmacological intended for use in diagnosis, treatment or prophylaxis of diseases. Excipients or additives are Inactive pharmaceutical ingredients including diluents/fillers, binders, lubricants, coatings, preservatives, colorants, flavouring agents and disintegrants.

Direct clinical use of the active drug substances “as they are” is rare due to the 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 therapeutically 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)

Dosage forms are classified according to physical form or route of administration.

Classification according to physical properties of dosage forms

According to the overall physical properties of dosage forms dosage forms can be classified to:
Gaseous dosage forms, Liquid dosage forms, Semisolid dosage forms and Solid dosage forms.

A) Gases

- 1) Medicinalgases, inhalation/volatile anaesthetics (vaporised before administration by inhalation)
- 2) Aerodispersions of solid or liquid particles (Metered dose inhaler or Dry powder inhaler)

B) Liquids

- 1) Solutions – one homogenous phase, prepared by dissolving one or more solutes in a solvent
- 2) Emulsions- a dispersion system consisting of two immiscible liquids (o/w or w/o) which has cloudy appearance
- 3) Suspensions- a dispersion system where solid particles are dispersed in liquid phase which not intended for systemic administration of drugs with high potency

C) Semisolids

- 1) Unshaped (without specific physical shape) which consisted of
 - i) Gels -A semisolid systems in which a liquid phase is constrained within a 3D cross-linked matrix
 - ii) Creams – semisolid emulsion systems (o/w, w/o) containing more than 10% of water

iii) Ointments – semisolid dosage forms with the oleaginous (hydrocarbon), water-soluble or emulsifying base

2) Shaped: including suppositories (for rectal administration) which have different shapes and dissolves at body temperature. They can have oleaginous (cacao butter) or aqueous (PEGs, glycerinated gelatine) base.

D) Solid

1) Unshaped (powders for external/internal use)

2) Shaped (tablets, capsules, implantates, transdermal patches and ...)

Classification according to the administration route of dosage forms

Another way to classify drug dosage forms are based on route of administration which is including: systemic administration (oral, sublingual, buccal, rectal, parenteral, transdermal, inhalation) and local administration (skin, mucosa, eye, nose, ear, oral cavity, vagina, rectum, brochi)

Dosage forms for systemic administration

A) **Oral solid dosage forms:** 1) Powders 2) Granules 3) Tablets and 4) Capsules

1) **Powders:** Powder is a mixture of finely divided drugs and/or chemicals in dry form.

2) **Granules:** Granules are agglomerates of powdered materials prepared into larger, free flowing particles.

3) **Tablets:** There are several types of tablets including:

- Compressed Tab: Standard uncoated tablets are manufactured by compression.

- Multiple compressed Tab (e.g. ACA): Multiply compressed tablets are prepared by subjecting the fill material to more than a single compression. The result may be a multiple-layer tablet or a tablet within a tablet, the inner tablet being the core and the outer portion being the shell.

- Sugar coated (S.C.) Tab (dragé): Compressed tablets may be coated with a colored or an uncolored sugar layer. The coating is water soluble and quickly dissolves after swallowing. The sugar coat protects the enclosed drug from the environment and provides a barrier to objectionable taste or odor. The sugar coat also produces an elegant, glossy, and widely utilized in preparing multivitamin and multivitamin mineral combination. Sugar coating doubled the tablet weight.

- Film coated Tab (F.C.): This is an attractive method within one or two hours. Polymers such as hydroxyl propyl cellulose, hydroxyl propyl methyl cellulose, and colloidal dispersion of ethyl cellulose are commonly used in forming a skin like film. A 30% dispersion of ethyl cellulose is known as aqua coat. The film is usually colored and has the advantage over sugar coatings in that it is more durable, less bulky, and less time-consuming to apply. By its composition, the coating is designed to rupture and expose the core tablet at the desired location in the gastrointestinal tract.

- Enteric coated (EC) Tab: An oral dosage form in which a tablet is coated with a material to prevent or minimize dissolution in the stomach but allow dissolution in the small intestine.

- Sublingual (S.L) and buccal Tab: Buccal and sublingual tablets intended to be dissolved in the buccal pouch (buccal tablets) or beneath the tongue (sublingual tablets) for absorption through the oral mucosa. Drugs used by this route are for quick systematic action. They enable oral absorption of drugs that are destroyed by the gastric juice and/or are poorly absorbed from the gastrointestinal tract. Buccal tablets are designed to erode slowly, whereas those for sublingual use (such as nitroglycerin) dissolve promptly and provide rapid drug effects.

- Chewable Tab: These are intended to be chewed in the mouth before swallowing. These have a creamy base, usually of specially flavored and colored mannitol. Chewable tablets are especially useful for administration of large tablets to children and adults who have difficulty swallowing solid dosage forms.

- Effervescent Tab: Effervescent tablets are prepared by compressing granular effervescent salts (active ingredient with mixture of organic acid such as citric acid or tartaric acid and sodium bicarbonate) that release gas when in contact with water. These tablets generally contain medicinal substances that dissolve rapidly when added to water and produce a solution rapidly with the release of carbon dioxide. The “bubble action” can assist in breaking up the tablets and enhancing the dissolution of the active drug.

- Sustained release (S.R.)Tab or Retard Tab: Time release technology (also known as sustained-release, extended-release, controlled-release, retard and other synonyms) is a mechanism used in tablets to dissolve a drug over time in order to be released slower and steadier into the bloodstream while having the advantage of being taken at less frequent intervals than immediate-release formulations of the same drug.

- Scored and Double scored Tab: Tablets that can be broken in half or quarters will be scored by the manufacturer to make the process easier.

4) Capsules: Capsules are solid dosage forms in which the drug substance is enclosed in either a hard or soft, water soluble container or shell of gelatin.

- Hard gelatin capsules: A hard gelatin capsule consists of two pieces, a cap and a body, that fit one inside the other. They are produced empty and are then filled in a separate operation. Hard gelatin capsules are usually filled with powders, granules, or pellets containing the drug. After ingestion, the gelatin shell softens, swells, and begins to dissolve in the gastrointestinal tract. Encapsulated drugs are released rapidly and dispersed easily, leading to high bioavailability.

- Soft gelatin capsules: Soft gelatin capsules are prepared from plasticized gelatin; they are formed, filled, and sealed in a single operation. Soft gelatin capsules may contain a nonaqueous solution, a powder, or a drug suspension, none of which solubilize the gelatin shell. Emulsions should not be inserted into soft gelatin capsules, since they are unstable and crack the shell of the capsule when the water is lost in the manufacturing process. Extreme acidic and basic pH must also be avoided, since a pH below 2.5 hydrolyzes gelatin, while a pH above 9 has a tanning effect on the gelatin.

B) ORAL liquid dosage forms:

1) Solutions: Solutions are homogeneous mixtures of one or more solutes dispersed in a dissolving medium (solvent) which includes Syrups, Elixirs and Tinctures.

- Syrups: Aqueous solutions containing a sugar or sugar substitute with or without added flavoring agents and drugs are classified as syrups. Sucrose is the sugar most frequently employed

insyrups; in special circumstances it may be replaced in whole or in part by other sugars (eg, dextrose) or nonsugars(eg, sorbitol, glycerin, and propylene glycol).Most syrups consist of between 60 and 80% sucrose.Sucrose not only provides sweetness and viscosity to the solution; it renders the solution inherently stable(unlike dilute sucrose solutions, which are unstable).

- Elixirs: Sweetened hydroalcoholic (combinations of water and ethanol) solutions are termed elixirs. Elixirs are usually less sweet and less viscous than syrups. Since elixirs contain a lower proportion of sugar, they are consequently less effective than syrups in masking the taste of drugs. In contrast to aqueous syrups, elixirs are better able to maintain both water soluble and alcohol-soluble components in solution due to their hydroalcoholic properties. These stable characteristics often make elixirs preferable to syrups.All elixirs contain flavoring and coloring agents to enhance their palatability and appearance. Elixirs containing over 10-12% alcohol are usually self-preserving and do not require the addition of antimicrobial agents for preservation.

- Tinctures: A tincture is typically an alcoholic extract of plant. To qualify as an alcoholic tincture, the extract should have an ethanol percentage of at least 25–60%.

2) Emulsions: An emulsion is a thermodynamically unstable system consisting of at least two immiscible liquid phases, one of which is dispersed as globules (dispersed phase) in the other liquid phase (continuous phase), stabilized by the presence of an emulsifying agent.

3) Suspensions: Suspensions are dispersions of finely divided solid particles of a drug in a liquid medium in which the drug is not readily soluble. Suspending agents are added to suspensions to increase viscosity, inhibit agglomeration, and decrease sedimentation.

C) Rectal route dosage forms:

Rectal dosage forms (suppositories, gels, creams, enemas) can be used for both local and systemic drug administration. This form can bypass the liver; therefore there may be no first pass effect. When patient cannot swallow the drug, this form can be used. It is also useful for children. The disadvantages are it is uncomfortable (poor compliance), actual amount of drug absorbed is hard to predict and it causes local irritation of rectal mucosa.

D) Parenteral route dosage forms:

Parenteral dosage forms are a dosage form that breaks one's skin. These are in the form of injections. Because this is an injectable dosage form and it breaks the protective barrier of the skin, the product must be free of contamination. There are three different routes of injection for parenterals: intravenous, intramuscular, and subcutaneous. Intravenous injections go directly into the blood through a major peripheral vein which leads to a 100% bioavailability because the drug is administered directly to the central compartment or blood. The drug is injected as a solution directly into the blood, so a response may be seen immediately since dissolution does not occur.

Advantages: It can be an approach of choice in the case of problems with oral absorption, Problems with stability of API in GIT (pH, enzymes), Uncooperative patients (unconsciousness, vomiting...), Urgent need for rapid onset of action (emergencies)

Disadvantages: Non-compliance (phobias, children..), Pain/irritation at the site of injection, Certain degree of hemolysis may occur, Need for trained personnel using aseptic procedures, Higher risk of adverse severe adverse reactions (hypersensitivity)

Implants: Implants are used to control drug delivery for localized or systemic drug effects. In these systems, drugs are embedded into biodegradable or nonbiodegradable materials to allow slow release of the drug.

Advantages: largely overcomes problems with individual compliance

Disadvantages: mini-surgery is needed, uneasy to simply discontinue the therapy, local reactions

E) Transdermal Patches

Transdermal patches deliver drugs directly through the skin and into the bloodstream. In general, patches are composed of three key compartments: a protective seal that forms the external surface and protects it from damage, a compartment that holds the medication itself and has an adhesive backing to hold the entire patch on the skin surface, and a release liner that protects the adhesive layer during storage and is removed just prior to application.

Advantages: Elegant alternative to injectables, Pain and stress-free, No need for trained specialist, Long-term drug delivery with minimal fluctuations of drug concentrations, Good compliance, Unlike other controlled drug delivery systems the delivery of the API can be immediately discontinued

Disadvantages: Not feasible for all API, Local reactions, Need not be cost-effective

Dosage forms for local drug administration

Into/onto: Eye, nose, ear, Oral cavity, Vagina, rectum, Bronchi, Skin/hairs

A) Dosage forms for local drug administration into the eye

1) Eye liquid dosage forms: Drops (smaller volumes, 10-20 ml) and Lotions (up to 100 ml)

- Must be sterile (sterile ingredients/preparation) – proper handling, storage and administration to avoid contamination

- Isotonic with tears (to avoid eye irritation due to the hypotonic preparations)

Advantages: high local concentration, lower systemic adverse reactions, minor effects on vision

Disadvantages: local hypersensitivity, rapid tear wash-out

2) Eye semisolid drug formulation: Gels, creams and ointments

- MUST also be sterile and clear

- Direct application into the conjunctiva to avoid contamination (do not use fingers)

Advantages: API exposure is longer.

Disadvantages: Can hinder vision (useful for overnight treatment), dosage accuracy

B) Dosage forms for local drug administration into the nose/ear

- Usually isotonic

- Vehicles and API must be non-irritating

- Vehicle – isotonic aqueous solutions/oils

- When kept under lower temp, it should be warmed in hands before use (ear)

C) Dosage forms for local drug administration into the vagina

This route can be included Tablets (disintegrating in vagina), Capsules, Pessaries (vaginal suppositories), Foams and Creams. There are application devices for this route.

D) Dosage forms for local drug administration into the rectum

Suppositories, Ointments, creams, Enemas (procedure of introducing liquids into the rectum and colon via the anus)

E) Dosage forms for local drug administration onto the skin/hairs

Aerodispersion(sprays), Aqueous dosage forms (lotions, medicated shampoo), Semisolid dosage forms (Gels, Creams, Ointments) and Solid dosage forms (Powder)

MCQ: The absorption rate of a drug is most rapid when the drug is formulated as:

- A. Controlled-release product
- B. Hard gelatin capsule
- C. Compressed tablet
- D. Solution
- E. Suspension