UNIT 1 CHAPTER 1.2
DOSAGE FORM: INTRODUCTION TO DOSAGE FORMS, CLASSIFICATION AND DEFINITIONS

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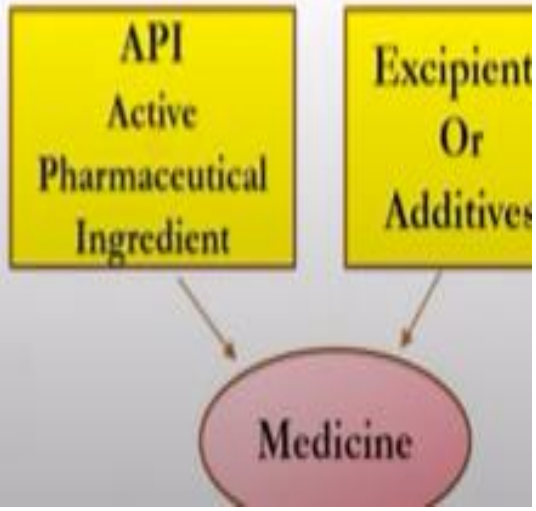
INTRODUCTION OF DOSAGE FORM

- Dosage forms are the career/medium through which drug molecule are delivered to the site of action within the body.

- Every dosage form is a combination of drug and non-drug components called Excipients.



Need of dosage form

Protection

1. Protection from external environment eg. coated tablets and sealed ampoules.
2. Protection from degradation because of gastric juice.

To improve therapeutic activity

1. To provide optimal drug action directly to the site of action eg ointments.
2. To place the drug directly in to the orifices eg. Rectal and vaginal dosage forms
3. To provide optimal drug action in the blood stream eg Injections
4. To provide rate controlled drug action eg modified release dosage forms
5. To improve Bioavailability of drugs with narrow absorption window eg. Gastro retentive dosage forms

To improve patient compliance

1. To maintain accuracy of dose eg. Unit dosage forms
2. Reduction in frequency of dosing eg Sustained Release and Controlled Release.
3. To improve the physical properties of drugs eg coated dosage forms
4. Ease of handling & administration

API (Active pharmaceutical ingredient) and excipients

API are the chemical compound that are actually used for diagnosis, treatment & prevention of disease.

Excipients are used to give particular shape to the formulation, to increase stability, palatability and to make the preparation more elegant.

The active substance is paracetamol. Each tablet contains 500mg of paracetamol. The other ingredients are, maize starch, potassium sorbate, purified talc, stearic acid, povidone, and soluble starch.

EXCIPIENT TYPES

- Coloring agents
- Sweetening agents
- Flavoring agents
- Solubilizing agents
- Antioxidants
- Preservatives
- Suspending agents
- Binding agents
- Solvents & Lubricants
- Perfumes

Classification of dosage form

They are classified according to:

Route of administration

- Oral
- Topical
- Rectal
- Parenteral
- Vaginal
- Inhaled
- Ophthalmic
- Otic

Physical form

- Solid
- Semisolid
- liquid

Classification and example

Dosage Forms

Solid

Unit dosage form

- Tablet
- Capsule
- Powder
- Pills

Bulk dosage forms

- Fine powders & Granules
- Dusting powder
- Insufflations
- Dentifrice

Liquid

Monophasic

- Syrups
- Elixirs
- Linctus
- Drops

Biphasic

- Emulsions
- Suspensions

Semi solid

Internal

- Suppositories
- Pessaries

External

- Ointments
- Creams
- Paste
- Jellies

Others

Gaseous Prepn

- Inhalers
- Aerosols

Tablets

Is solid pharmaceutical dosage forms containing drug substances with or without suitable diluents and prepared either by compression or molding methods

- Tablets may differ greatly in size and weight depending on the amount of drug substance present and the intended method of administration.

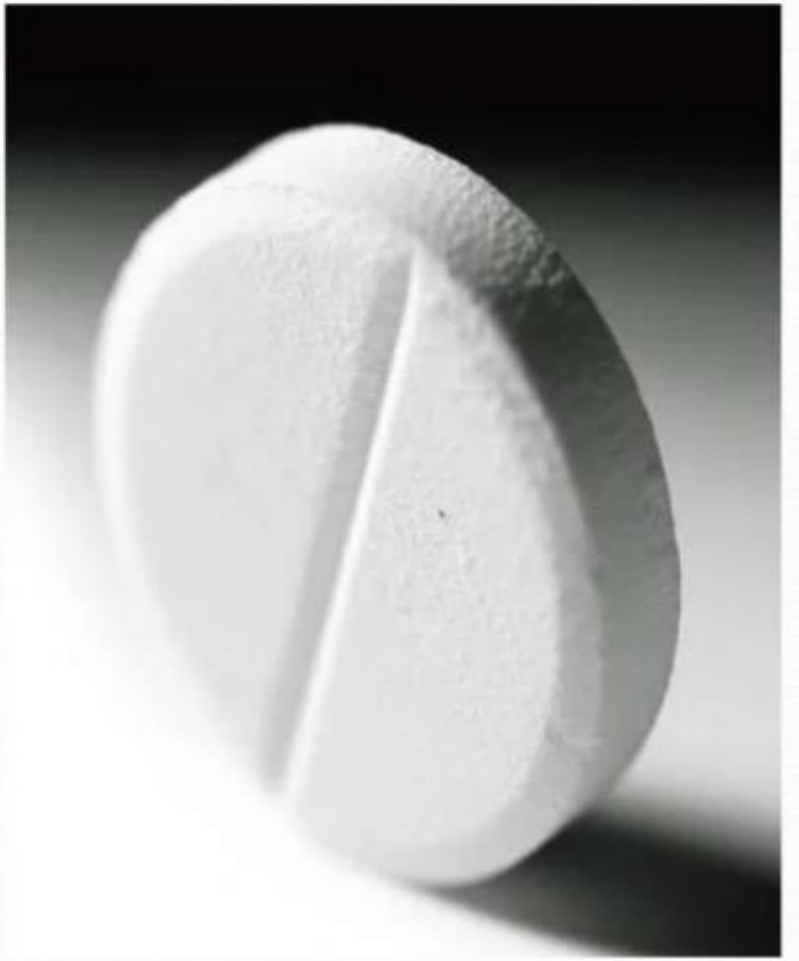
- They are divided into two general classes, whether they are made by compression or molding.

CHARACTERTICS OF TABLET:

- The tablet is an essentially tamperproof dosage form.
- They are unit dose form and offer the greatest capabilities of all oral dosage forms for greater dose precision.
- Lightest and most compact of all oral dosage form.
- Their cost is low.
- Easiest and cheapest to package and shipping.
- Product identification is simple.
- Provide greatest ease of swallowing with the least tendency for hang up, above stomach.
- They may be enteric or delay release.
- Better suited for large scale production.
- They have the best combination properties of chemical, mechanical and microbiological stability than other oral dosage forms.
- Tablets have accurate dose.

Disadvantages

- Some drugs resist compression into dense compacts
- Drugs with poor wetting, slow dissolution, intermediate to large dosages may be difficult or impossible to formulate and manufacture as a tablet that provide adequate or full drug bioavailability
- Bitter taste drugs, drugs with an objectionable odor, or sensitive to oxygen or moisture may require encapsulation or entrapment prior to compression or the tablets may require coating



A coating may be applied to:

1- hide the taste of the tablet's components.

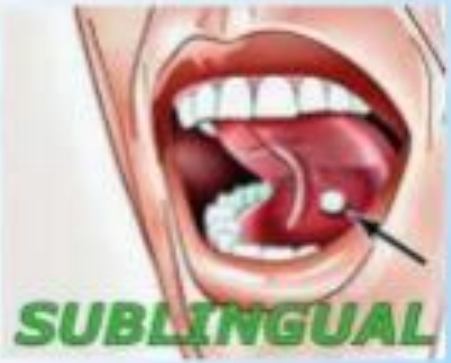
2- make the tablet smoother and easier to swallow .

3- make it more resistant to the environment.

4- extending its shelf life.

BUCCAL AND SUBLINGUAL TABLETS

* Sublingual and buccal medications are administered by placing them in the mouth, either under the tongue (sublingual) or between the gum and the cheek(buccal).
* The medications dissolve rapidly and are absorbed through the mucous membranes of the mouth, where they enter into the blood stream.



Effervescent tablet

* 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 di oxide.
* They are intended to be dissolved or dispersed in water before use providing:
  * Very rapid tablet dispersion and dissolution.
  * Pleasant tasting carbonated drink.

Chewable tablet

- They are tablets that chewed prior to swallowing.
- They are designed for administration of drugs to children e.g. vitamin products.
- Antacid formulations.

Lozenges

* Lozenges are solid preparations consisting of sugar and gum, the latter giving strength and cohesiveness to the lozenge and facilitating slow release of the medicament.
* It is used to medicate the mouth and throat for the slow administration of indigestion or cough remedies.

Pastilles

* Pastilles are solid medicated preparations designed to dissolve slowly in the mouth.
* They are softer than lozenges and their bases are either glycerol and gelatin, or acacia and sugar.

Pills

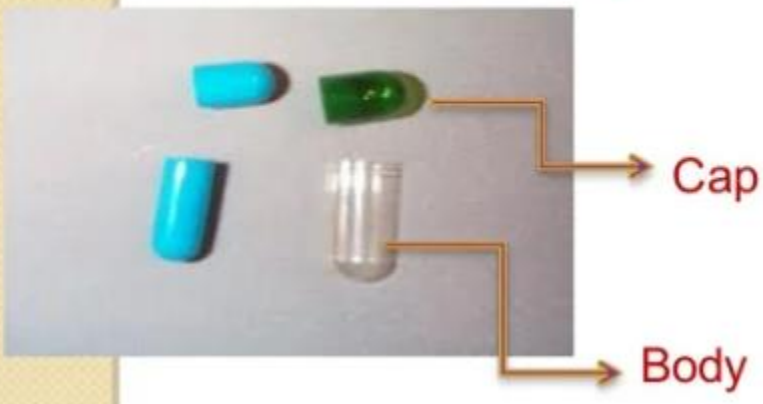
- These are small, rounded solid dosage forms containing medicaments intended for oral use.
- The medicaments are mixed with excipients to forms a firms plastic mass.
- The mass is rolled to uniform pill pipe, which cut into numbers of uniform pills. The pills are spherical in shape & produced by rolling them under wooden pill rounder.
- Sometimes pills are coated with varnish, gold leaf, etc to improve finish, unpleasant taste & stability.
- Now a days pills are outdated preparations because of number of disadvantages such as -

- Disintegration time of pill is uncertain means freshly prepared pills are disintegrates readily rather than old dried pills.
- It is difficult to prepare pills of uniform size & weight.

Capsule

- Capsules are solid unit dosage forms in which one or more medicaments enclosed within a shell.
- Capsules mainly divided in to two parts namely as –

  I) Body (Longest part of capsule shell), II) Cap (Smallest part of capsule shell)
- The capsule are generally prepared by gelatin.
- Depending on their formulation, two types of gelatin are used namely as – I) Hard gelatin, II) Soft gelatin.



Dusting Powders

- Dusting powders are applied externally to skin, so they should be applied in very fine state to avoid local irritation. Hence dusting powders should be passed through sieve no 80 to obtained fined powders.
- Dusting powders are prepared by mixing of more than one ingredients in which either starch, kaolin, or talc are used in their formulation. Generally talc or kaolin are used because they are inert in nature.
- Dusting powders are used for antiseptic, astringent, absorbent, antiperspirant etc.
- Dusting powders are of two sub type they are as

  I) Medical dusting powder

  II) Surgical Dusting powders

Medical Dusting Powders

- Medical Dusting powders are used to increase superficial condition of skin.
- These are not applied on wounds, burns etc
- Medical dusting powders must be free from dangerous pathogenic micro- organism.

Surgical Dusting Powders

- Surgical dusting powders are used in body cavities and also on major wounds like as burns etc.
- They should be sterilized before use.
- They are mainly used for their antiseptic, absorbent action.

Insufflations

- These are medicated dusting powders meant for introduction into body cavities (nose, throat, ear, vagina etc) with the help of an apparatus known as a insufflator.
- It sprays the powders (in a state of fine particles) on site of application.
- Now a days insufflations are also available in pressure aerosols. This pressure aerosols are used for administration of potent drug.
- They are used in the treatment of ear, nose, throat infections with antibiotics to produce local effect of drugs.

Snuffs

- These are finely divided solid dosage forms of medicaments which are inhaled into nostrils.
- They are mainly used for their antiseptic, bronchodilator and decongestion action.

Granules

- Granulation is the process in which primary powder particles are made to adhere to form larger multiparticle or large particles entities called **granules.**
- The bitter, nauseous, unpleasant powders can not be given tablets, capsule due to bulk quantity are required to be taken, as well as they are not given in liquid dosage forms due to their stability such powders are given in the granules forms.
- These powders are mixed with suitable exicipent along with granulating agent, prepare a coherent mass then dried & passed through the sieve to obtained desired size of granules.
- E.g. Effervescent granules

Effervescent Granules

- Effervescent granules are meant for internal use.
- They contained medicaments mixed with citric acid, tartaric acid & sodium bi carbonates, sometime saccharin or sucrose may be added for sweetening taste.
- Before, administration desired quantity of granules are dissolved in water, the acid & bicarbonate reacts with each other to produce effervescence.
- Effervescent granules are prepared by two methods, namely as, I) Heat method, II) Wet method

Heat method

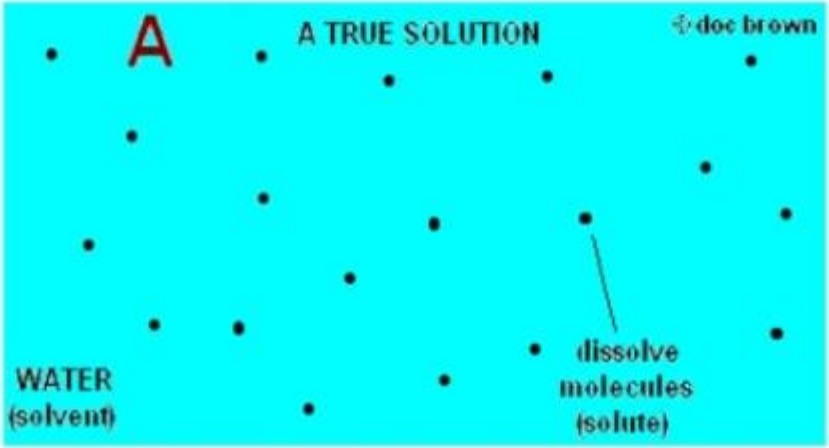
- A large porcelain or stainless steel evaporating dish is placed over the boiling water bath.
- The dish must be sufficiently hot (generally heating takes place for 1 – 5 min.) before transferring the powders into it, to ensure rapid liberation of water of crystallization from citric acid.
- If heating of the dish is delayed then the powder which is added to it, will heat up slowly & liberated water of crystallization will also be liberated simultaneously.
- As a result, sufficient water will not be available to make a coherent mass.
- This coherent mass will pass through the sieve to obtained suitable size of granules, dry it in oven at 60^0c then packed in air tight container.

Wet method

- In this methods all the ingredients are mixed thoroughly
- This powders mixture make moistened with non – aqueous vehicle (e.g. alcohol), to prepare a coherent mass which is then passed through sieve no 8 to obtained suitable granules.
- Then dried in oven at 60^0c. The dried granules are again passed through the sieve to break the lumps which may be formed during drying.
- The dried granules are packed in air tight container.

Introduction

- Monophasic dosage form refers to liquid preparation containing two or more components in one phase system, it is represent by true solution.
- A true solution is a clear homogenous mixture that is prepared by dissolving solute in a suitable solvent.



- The component of the solution which is present in a large quantity is known as "SOLVENT" where as the component present in small quantity is termed as "SOLUTE".

Advantage

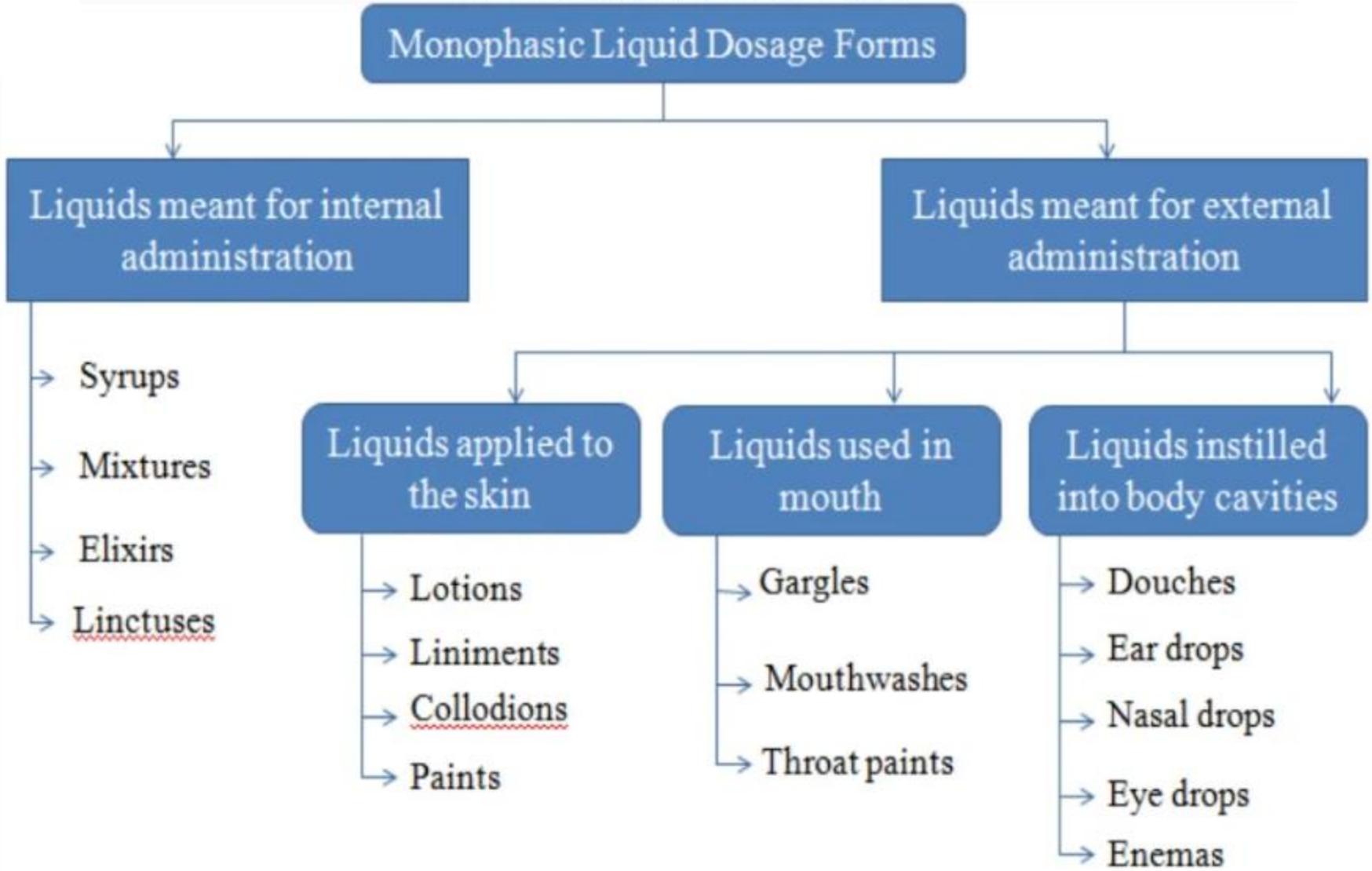
- It is easier to swallow, therefore easier for children and old age people.
- Facilitate absorption of drug faster than solid dosage form as drug is already in solution form.
- It is homogenous therefore give uniform dose than suspension or emulsion which need shaking.
- Simple and fast to formulate
- It can be administered by various routes :

  Oral, Parenteral (injection),enema for rectal use, otic(ear), nasal and ophthalmic preparation.

Disadvantage

- They are bulky, so difficult to transport and store.
- Water is commonly use vehicle, which is prone to microbial growth. So addition of preservative is needed.
- When expose to direct sunlight it may undergo hydrolysis, so need to store in cool and dark place.
- Drug stability reduce by hydrolysis or oxidation. So, they have shorter expire date than solid dosage form.
- Other major sign of drug instability are color change, Precipitation, microbial growth etc.

Classification



Liquids meant for internal administrations

- **Syrup :** Aqueous preparations of 60% to 85% sucrose with or without flavoring agents and medicinal substances. e.g. Chlorpheniramine maleate syrup, Chloral hydrate .

- **Elixirs :** Clear, aromatic, sweetened hydro alcoholic solutions with or without medicinal substances, intended for oral use. Eg: Dexamethasone elixir .

- **Linctuses :** Viscous, liquid and oral preparations that are generally prescribed for the relief of cough. Eg: Codeine Linctus.

- **Mixtures: A mixture is a liquid preparation meant for oral administration in which medicament or medicaments are dissolved, suspended or dispersed in suitable vehicle**

Market available Syrup/Elixir/ Linctus

Liquids meant for external administration

Liquids used in the mouth

- **Gargles :**Aqueous solutions containing antiseptics or antibiotics used to treat throat infections. Available in concentrated form with direction for dilution with warm water before use. eg: Povidone Iodine gargle.
- **Mouthwash:** Aqueous solution with a pleasant taste and odor used to clean and deodorize the buccal cavity. Have antiseptic and astringent activity.eg: Antiseptics-phenol derivatives.
- **Throat paints :** Viscous liquid preparation used for mouth and throat infections. Eg: Phenol glycerine, Compound Iodine.

Market available Gargle, Mouthwash and Throat paints

Liquids meant for external administration

Liquids instill into body cavity

- **Eye drops:** Sterile, aqueous/oily solutions intended for instillation in eye. Eg: Timolol maleate eye drops.
- **Nasal drops** Administered through the nose to obtain local effect. Used during nasal congestion and upper-respiratory tract problem. Eg: Oxymetazolin Hydrochloride nasal drops.
- **Enemas:** Aqueous or oily solution that is introduced into the rectum and colon via the anus for cleansing, therapeutic or diagnostic purposes.

Market available Eye drop, Nasal drop and Enemas

Liquids meant for external administration

Liquid meant for skin

- **Liniments :** Oily liquid preparations, intended for external application with rubbing action to the affected area. Use to relief pain and stiffness, such as from muscles spasm and arthritis.
- **Lotions :** Topical preparation with a low to medium viscosity. Use to moisturize dry skin. Eg: Calamine Lotion, baby lotion

Market available Liniment, Lotion and Paint

Eye lotions

- These are the aqueous solutions used for washing the eyes.
- These are supplied in concentrated forms & are required to diluted with warm water immediately before use.
- They should be free from foreign particles to avoids irritation to the eye.
- They are required to prepared fresh & should not be stored for more than two days to avoid microbial contaminations.

Ear drops

- These are the solutions of drugs that are instilled into ear cavity with the help of dropper.
- These are generally used for cleaning the ear, softening the wax & for treating the mild infections.
- The solutions is generally prepared in water, glycerin, propylene glycol & dilute alcohol.

Sprays

- These are the preparations of drugs in media which may be aqueous, alcoholic, or glycerin.
- They are applied to the mucous membrane of throat or nose with an atomizer.
- The throat sprays must be sprayed from a special type of atomizer known as a nebulizer, which removes the large droplets by baffling system. Only precaution should be taken that the fine droplet will used to easily reach the lungs.

Nebulizer

Inhalations

- These are liquid preparations containing volatile substance & are used to relieve decongestion & inflammations of respiratory tract.
- The volatile substance in inhalations would be volatile at room temperature so that they should be placed on some adsorbent pad or handkerchief.
- In some cases inhalations will added to hot water (65^0c) then vapors will inhaled.

Biphasic liquid dosage forms

- The liquid which consist of two phases are known as a biphasic liquid dosage forms.
- They are sub categorized into two different forms namely as –

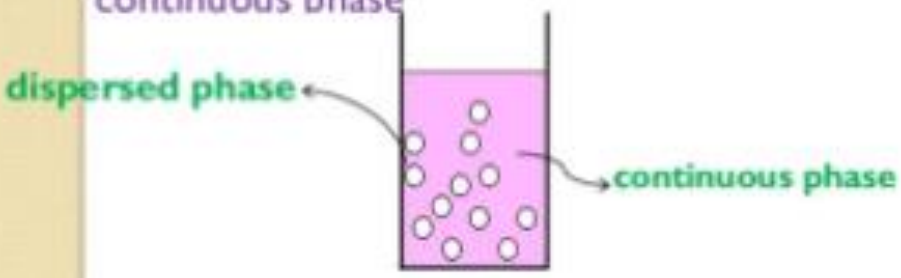
  I) Emulsion

  II) Suspension

- In emulsion both phases are available in liquid where as in suspension, finely divided solid particles are suspended in liquid medium.

Emulsion

- Emulsion is a biphasic liquid preparations containing two immiscible liquid (Continuous Phase & dispersed phase) made missicible.
- The liquid which is converted into minute globules is called as dispersed phase & the liquid in which the globules are dispersed is called the continuous phase

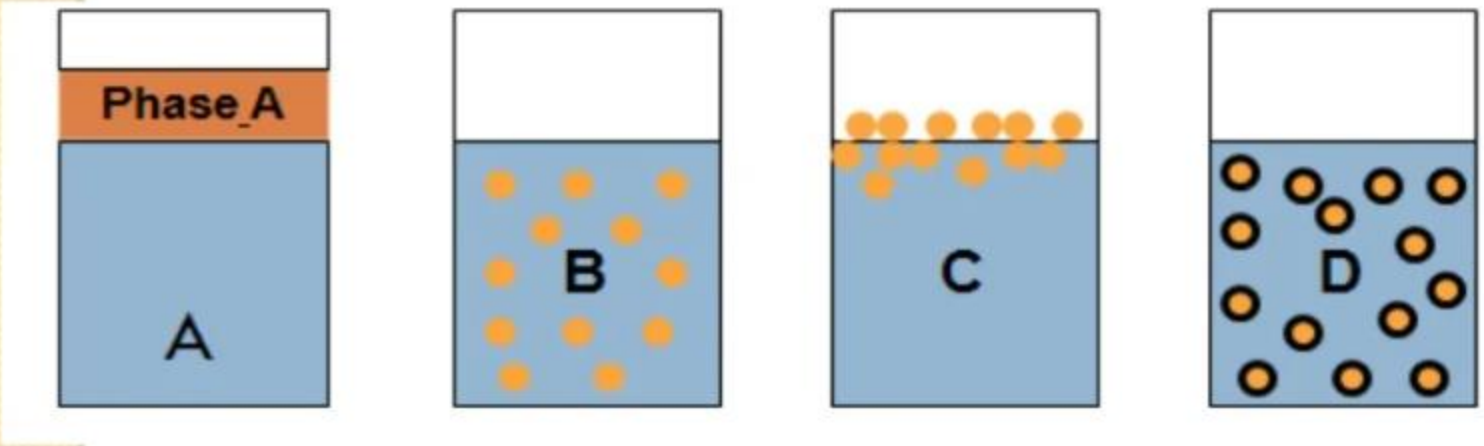


Two Immiscible Liquids

- **Dispersed Phase (Internal phase)**
- **Continuous Phase (External phase)**

- An emulsion is a thermodynamically unstable system consisting of at least two immiscible liquid phases one of which is dispersed as globules in the other liquid phase stabilized by a third substance called emulsifying agent.
- The globule size in emulsion varies from 0.25 to 25 μm.

- Examples for emulsions:- milk, rubber latex, crude oil etc.



A.: Two immiscible liquids not emulsified

B. An emulsion of phase B dispersed in Phase A

C. Unstable emulsion slowly separates.

D. The emulsifying agent (black film) places it self on the interface between phase A and phase B and stabilizes the emulsion.

Types of emulsions

Simple type

- Water in oil (w/o)
- Oil in water (o/w)

Depending on globule size

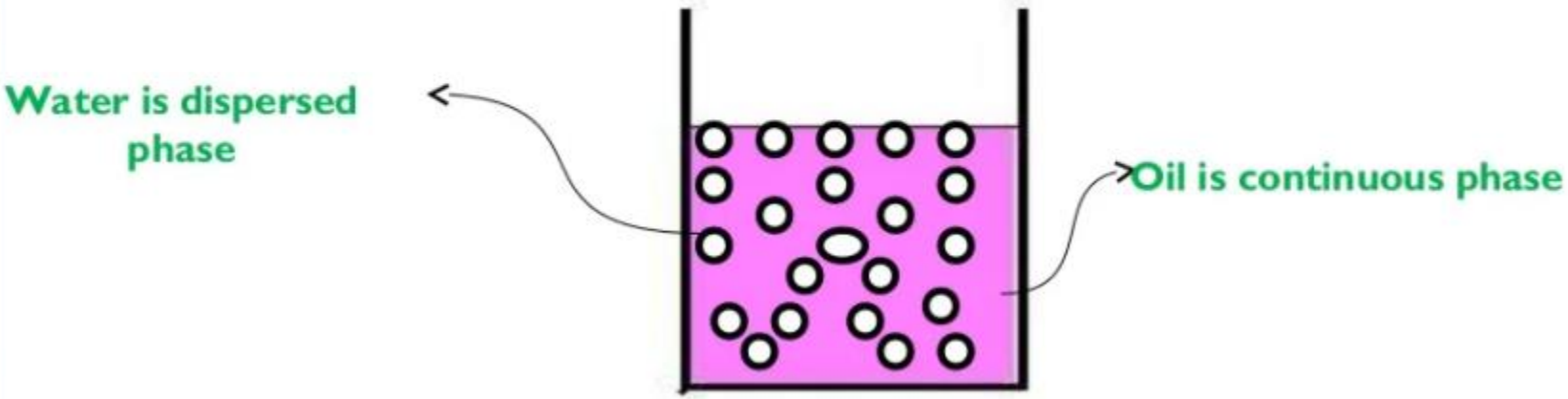
- Micro emulsion
- Fine emulsion

Special type

- Multiple emulsion (w/o/w, o/w/o)

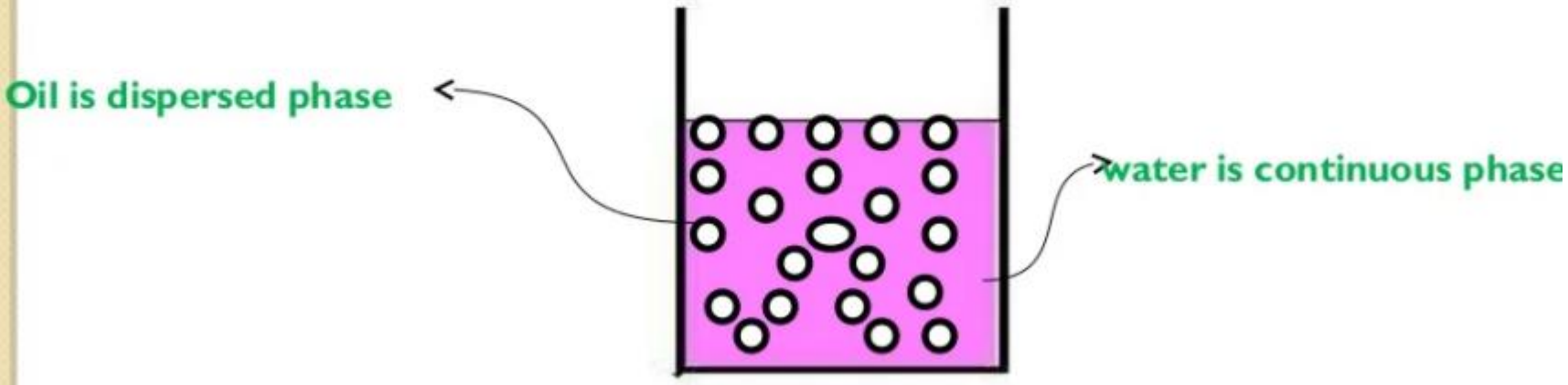
Water in oil (w/o)

- In this types of emulsion water is dispersed phase & oil is continuous phase
- w/o types of emulsion generally meant for External use.
- Examples are butter, lotions, creams etc.
- In rare case they are used internally.



Oil in water (o/w)

- In this types of emulsion oil is dispersed phase & water is continuous phase
- o/w types of emulsion meant for both Internal use & External use.
- Examples for internal use are Vitamin A in corn oil, liquid paraffin in water etc.
- Examples for External use are Benzyl benzonate emulsion.



Suppository

Suppositories are solid or stiffened semi solid dosage forms intended for insertion into body orifices (rectum, vagina, urethra) where they melt, soften, or dissolve and exert a local or systemic effect.

a. **Rectal suppositories** for adults weigh 2 gm and are torpedo shape.

- Children's suppositories weigh about 1 gm.

b. **Vaginal suppositories or Pessaries** weigh about 3-5gm and are molded in globular or oviform shape or compressed on a tablet press into conical shapes.

c. **Urethral suppositories** called bougies are pencil shape. Those intended for males weigh 4 gm each and are 100-150 mm long.

- those for females are 2 gm each and 60-75 mm in length.

d. **Nasal suppositories:** called nasal bougies or buginaria meant for introduction in to nasal cavity.

- They are prepared with glycerogelatin base.
- They weigh about 1 gm and length 9-10 cm.

e. **Ear cones:**

- Aurinaria and meant for introduction into ear.
- Rarely used
- Theobroma oil is used as base.
- Prepared in urethral bougies mould and cut according to size.

ADVANTAGES:

_ Can exert local effect on rectal mucosa.

_ Used to promote evacuation of bowel.

_ Avoid any gastrointestinal irritation.

_ Can be used in unconscious patients (e.g. during fitting).

_ Can be used for systemic absorption of drugs and avoid first-pass metabolism.

– Babies or old people who cannot swallow oral medication.

– Post operative people who cannot be administered oral medication.

– People suffering from severe nausea or vomiting.

- **DISADVANTAGES OF SUPPOSITORIES:**

- The problem of patient acceptability.
- Suppositories are not suitable for patients suffering from diarrhea.
- In some cases the total amount of the drug must be given will be either too irritating or in greater amount than reasonably can be placed into suppository.
- Incomplete absorption may be obtained because suppository usually promotes evacuation of the bowel.

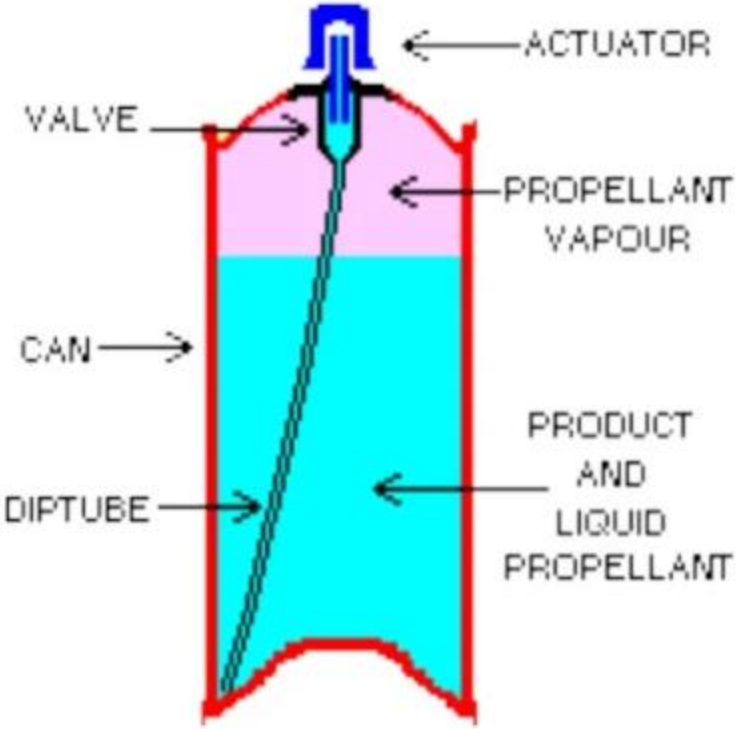
SHAPE OF SUPPOSITORIES

AEROSOL

- Aerosol or Pressurized package is defined as "A system that depends on the power of a compressed gas or liquefied gas to expel the contents from the container."
- Pharmaceutical Aerosol is defined as aerosol product containing active ingredients dissolved ,suspended or emulsified in a propellant or a mixture of solvent and propellant and intended for oral or topical administration or for administration into the eye, nose ,ear, rectum and vagina.
- In 1942 - First aerosol was developed. (insecticide)
- In1950 - Pharmaceutical aerosol for topical administration was developed.
- In 1955 - Aerosol for the local activity in the respiratory tract was developed (Epinephrine).

COMPONENTS OF AEROSOLS

- Propellant
- Container
- Valve and actuator
- Product concentrate



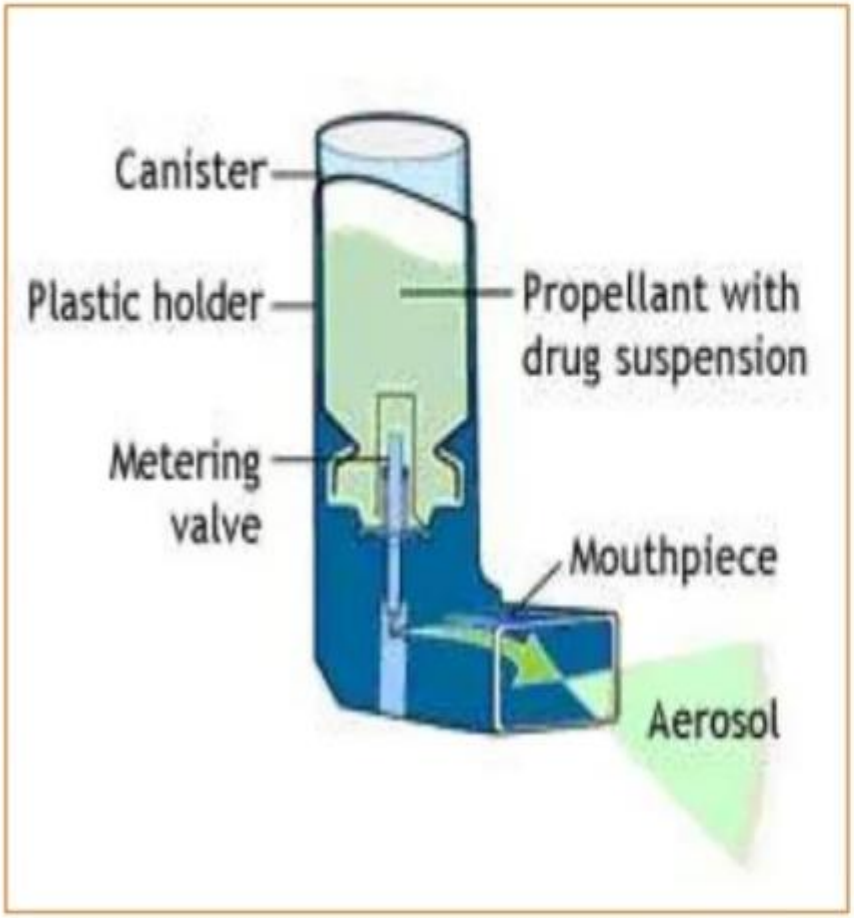
Advantages

- Rapid onset of action.
- Avoidance of gastrointestinal upset.
- Avoidance of intestinal and hepatic first-pass metabolism.
- A dose can be removed with out contamination of materials.
- Easy and convenience of application.
- The medication can be delivered directly to the affected area in desired form (localized action).

Disadvantages

- Expensive.
- Chlorofluorocarbon propellants cause Ozone layer depletion.
- Inflammability
- Toxicity
- Explosivity

Metered Dose Inhalers (MDIs)



METERED DOSE INHALERS

- Used to minimize the number of administration errors.
- To improve the drug delivery of aerosolized particles into the nasal passageways and respiratory tract.

Advantages of MDI:

- It delivers specified amount of dose .
- Portable and compact.
- Quick to use , no contamination of product.
- Dose-dose reproducibility is high.

Disadvantages of MDI :

- Low lung deposition ; high pharyngeal deposition .
- Coordination of MDI actuation and patient inhalation is needed.

MARKETED PHARMACEUTICAL AEROSOL PRODUCTS

Metered Dose inhalers :

BRAND NAME	DRUG	USE
Flovent Diskus	Fluticasone	Asthma
Advair	Fluticasone and Salmeterol	Asthma
Aerobid	Flunisolide	Asthma
Qvar	Beclomethasone	Asthma
Proventil	Albuterol	Bronchospasm