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UNIT - III

★ Monophasic liquids :-

Monophasic liquid dosage form is a liquid preparation containing two or more components in one phase system. It is represented by a true solution.

→ A ~~true~~ true solution is clear homogenous mixture that is prepared by dissolving solute in a suitable solvent.

① 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.

→ Containers: clear glass bottles with plastic screw cap.

→ Labelling: For external use only.

# Method of preparations :-

They are usually prepared by dissolving all ingredients in solvents and then make up the volume as required.

# Advantage :-

→ Easy to use for the treatment of infection of pharynx just by gargling the solution using air from the lungs.

→ Relieve soreness in mild throat infection.

→ Supplied in conc. for so reduce container size.

→ Suitable for variety of drugs like antibiotic, antiseptic etc. (40)

### # Disadvantages :-

- Temporary effect of drugs.
- Not suitable for patients having respiratory problems
- They might be swallowed.

### ② Mouthwashes :-

→ These are non-sterile aqueous solution with pleasant taste and odour used for oral hygiene (clean and deodorize buccal cavity) and to treat infection of the mouth.

- Container: white fluted bottles

- Labelling: "Not to be swallowed in large amount"

### # Method of preparation :-

- Solution method where most of the ingredients are dissolved in solvent or co-solvent mixture to form clear solution.

### # Advantages :-

→ Utilized to remove loosen debris and food from the mouth.

→ provide deodorant, refreshing, analgesic or astringent effects.

→ Sometimes used to treat the mouth infection by using antibacterial agent.

### # Disadvantage :-

- If pH not monitored properly then may damage mouth tissues.

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### ③ Throat paint:-

- Viscous liquid preparation used for mouth and throat infection.
- Paints can be applied onto skin and mucous membranes. But all paints cannot be used for application onto mucous membrane.

Container - airtight, coloured fluted bottle.

Labelling - For external use only.

#### # Method of preparation:-

- Simple solution method with the aid of heat.

#### # Advantage:-

- Used for treatment of throat infection and mouth infection.
- Highly viscous solution so retain to the applied place for longer period of time.
- Glycerine used as a solvent which provides viscosity and turns liquid sweet.

#### # Disadvantage:-

- Applied with the help of brush or small cotton piece.
- They initiate salivation, hence patient has to spit.

#### ④ Ear Drops :-

Ear drops are liquid preparations meant for instillation into the ear.

- These are generally used for cleaning the ear, softening the wax & for treating the mild infections.

#### # Preparation of the ear drop :-

→ In these preparations, the drug is usually dissolved or suspended in a suitable solvent such as, propylene glycol, polyethylene glycol, glycerol, alcohol and water or a mixture of these.

Example :- Chloramphenicol Ear drops

- Chloramphenicol - 5g
- propylene glycol 9.5 to 100ml.

Chloramphenicol ear drops may be prepared by dissolving chloramphenicol in sufficient quantity of propylene glycol and finally making up the final volume with it.

#### ⑤ Nasal Drops :-

Nasal drops are liquid preparations intended for instillation into the nostrils usually with the help of a dropper.

→ Administered through the nose to obtain local effect, used during nasal congestion and upper-respiratory tract problem.

## # Preparation of Nasal drop :-

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### - Ephedrine Nasal Drops

- Ephedrine hydrochloride - 0.5g

Chlorbutol - 0.5g

Sodium chloride - 0.5g

Purified water q.s to 100ml

- The drops may be prepared by first dissolving chlorbutol in small quantity of hot water followed by cooling the solution to room temperature.
- Other ingredients are then dissolved in the solution, which is filtered and the final volume is made up with water.

## ⑥ Enemas :-

Enemas are liquid preparation meant to be introduced into the rectum for cleansing therapeutic or diagnostic purposes.

→ Evacuation enemas are rectal injections employed to evacuate the bowel in constipation or before an operation.

Eg. Enema of soap, sodium phosphate enema, olive and arachis oil enemas etc.

## ⑦ Syrup :-

→ Syrups are sweet viscous concentrated aqueous solution of sucrose in purified water.

→ Simple Syrup I.P contains 66.7% w/w sucrose in purified water (100ml)

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→ Simple Syrup USP Contains 85% w/v Sucrose in purified water (100ml).

Medicated Syrup: Contains a therapeutic or medicinal agent  
e.g. Cough Syrup.

Flavoured Syrup: Contains flavouring agent but no medicinal substances e.g. Cherry Syrup.

# Method of preparation :-

The choice of particular method depends on the physical and chemical characteristics of the substance being used.

# procedure :-

① Hot process :-

- Weighed Sucrose is taken in beaker.
- Purified water is added.
- Heated on water bath (less than 70°C) till a solution is obtained.
- Product is filtered.
- Volume is made upto q.s.

② Precolator :-

- Sucrose is placed in percolator.
- Water is passed through sucrose slowly.
- Neck of percolator is packed with cotton.
- Rate of precolation regulates rate of dilution.
- After complete dissolution final volume is made upto q.s.

## ⑧ Elixirs :-

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Elixirs are defined as clear, aromatic, sweetened hydroalcoholic solution with or without medical substance, intended for oral use.

### # method of preparation :-

- Elixirs are prepared by simple dissolution with agitation or by mixing two or more liquids.
- Ingredients are dissolved in their respective solvent.  
EX. alcohol soluble ingredient in alcohol, water soluble in water.
- Alcoholic strength is maintained by adding the aqueous solution to the alcoholic solution.
- The mixture is then made up to the desired volume (q.s).
- Then elixir allowed to stand for some time.
- Then elixir is filtered.

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## ⑨ Liniments :-

- Liquid or semi-liquid preparation meant for application to the skin.
- The liniments are usually applied to the skin with friction and rubbing of skin (on the affected area).
- In alcoholic preparation, alcohol helps in the penetration of medication to the skin and also increases its counter irritation effect and subfacient action.
- Some lubricant may contain soap which spreads more easily on the skin.

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→ Liniment should not be applied on broken skin because it may cause excessive irritation.

Formulation: Turpentine liniment.

- Soft Soap - 9 gm
- Camphor - 5 gm
- Turpentine oil - 65 ml
- Purified water - q.s to 100 ml

10 Lotion :-

→ Topical preparation with a low to medium viscosity, use to moisturize dry skin.

Eg. Calamine lotion, baby lotion.

→ Lotions are liquid preparations meant for external use without friction.

→ Lotions are applied for antiseptic action, astringent action.

preparation of lotion :-

Lotion are prepared by triturating the ingredients to a smooth paste and then adding the remaining liquid phase with trituration.

Formula - Calamine lotion -

- Calamine - 15 gm
- Zinc oxide - 5 gm
- Bentonite - 3 gm
- Sodium Citrate - 0.5 gm
- Glycerin - 5 ml
- Liquid phenol - 0.5 ml

- Rose water - q.s to 100 ml.



## ★ Biphasic Liquids :-

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## ★ Suspensions :-

suspension is a two-phase system consisting of a finely divided solid particles dispersed in liquid (solid drug in liquid vehicle).



Continuous phase  
(Dispersion medium)

Dispersed phase  
(insoluble drug)

## # Classification of Suspension :-

### ① Based on General Classes :-

- oral Suspension
- Externally applied Suspension
- parenteral Suspension.

### ② Based on proportion of solid particles :-

- Dilute Suspension (2 to 10% w/v solid)
- Concentrated Suspension (50% w/v solid)

### ③ Based on Electrokinetic Nature of solid particles :-

- Flocculated Suspension
- Deflocculated Suspension

### ④ Based on Size of solid particles

- Colloidal Suspension (< 1 micron)
- Coarse Suspension (> 1 micron)
- Nano Suspension (10 ng)

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### # Advantage of suspension :-

- Suspension can improve Chemical stability of certain drug.  
Eg. Procaine penicillin G.
- Drug in suspension exhibits higher rate of bioavailability than other dosage forms.  
- bioavailability is in following order.

Solution > Suspension > Capsule > Compressed Tablet > Coated tab

- Duration and onset of action can be controlled.  
Eg. Protamine Zinc-Insulin suspension.
- Suspension can mask the unpleasant/bitter taste of drug  
Eg. Chloramphenicol palmitate.

### # Disadvantage :-

- physical stability, sedimentation and compaction can cause problems.
- It is difficult to formulate.
- Uniform and accurate dose can not be achieved unless suspension are packed in unit dosage form.

## \* Preparation of Suspension:

↓  
Reduced particle size by Levigation Method - wet grinding

↓  
Finely divided particles are added to dispersion medium

↓  
Wetting agent is added.

↓  
Uniform dispersion of deflocculated particles

↓  
Add Structured Vehicle

↓  
Addition of flocculating agent

↓  
Deflocculated Suspension in Structured Vehicles as final product

↓  
Flocculated Suspension as final product.

## # Flocculated Suspension:

- Flocculation is a process whereby small particles in suspension are caused to aggregate, giving large clusters (flocs) that are much more easily separated than the original particles.

→ particles form light fluffy conglomerates called flocs.

→ Since the flocs are group of particles, rate of sedimentation is fast.

→ The sediment is loosely packed and presents a scaffold like structure with entrapped liquid. The sediment does not form a dense hard cake.

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- In flocculated Suspension Sediment volume is high.
- The Supernatant liquid becomes clear at a shorter time since small particles are entrapped within the flocs and settle along with flocs rapidly.
- Redistribution of the sedimented particles by shaking the container is easy.

### # Deflocculated Suspension :-

Suspension in which particles settle slowly, and eventually form a sediment in which aggregation occurs with the resultant formulation of a hard cake which is difficult to resuspended.

- The particles in the suspension remain individually.
- Since the particles are small and remain separately, the rate of sedimentation is slow.
- The sediment formed become eventually a hard cake.
- The Supernatant liquid remains cloudy for a longer time as very small particles (approaching colloidal dimension) take very long time to settle.
- Redistribution of the sedimented particles by shaking the container is difficult.
- The suspension has a pleasing appearance.

# ★ Stability problems and Method to overcome

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<u>Problem</u>	<u>Cause</u>	<u>Remedies</u>
① Cap locking ⇒ Here dispersed particle crystallised on the thread of Bottle Cap (Interfere with Cap removal).		- Suitable Vehicle, Glycerine, Glucose, Sorbitol used to overcome this problem.
② Colour Change ⇒ Light sensitive preparation affected by Sunlight direct contact (Change in colour)		- Should be kept in Dark to avoid change in colour and degradation.
③ <u>Crystal Growth</u> :- During storage of suspension	→ change in pH Flow Soluble Impurity	- Avoid temp. change - Adjusting the pH & solubility of particle.
④ Change in flavour:- During long long storage agent is <u>volatile change in flavour</u> because flavouring agent is volatile.		- Add sufficient quantity of flavouring agent
⑤ Change in viscosity:- after long term storage viscosity change		- Add suitable viscosity enhancing agent
⑥ <u>Caking</u> :-	Solid particle form a hard cake	- modify particle size.

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## ★ Emulsion:

# Definition: An emulsion is a two phase system consisting of two incompletely miscible liquid, one of which is dispersed as fine globules in the other. The particle size of the globules range from 0.25 to 25  $\mu\text{m}$ .

## # Classification:

(A) Simple emulsion (macro emulsion)

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

(B) Multiple emulsions

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

(C) Micro emulsion

- oil-in-water micro emulsion
- water-in-oil micro emulsion

## # Emulsifying agent:

① Natural:

(a) Vegetable Source: Gum acacia, tragacanth, agar, starch, pectin.

(b) Animal Source: wool fat, egg yolk, gelatin.

② Semi Synthetic:

methyl Cellulose, Na Carboxy methyl Cellulose.

### ③ Synthetic :-

- (a) Anionic: Sodium Lauryl Sulphate
- (b) Cationic: Cetrimide, benzalkonium chloride.
- (c) Non-ionic: Glyceryl ester-glyceryl monoesters etc.

④ Inorganic :- Milk of Magnesia, Mg oxide, Mg trioxide etc.

⑤ Alcohols (polyols) :- Carbowax, cholesterol and lecithin.

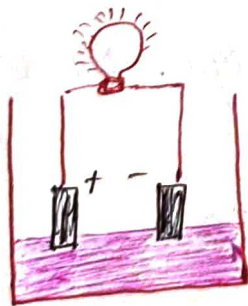
### # Test for the identification of type of emulsion :-

#### ① Dilution test :-

- In this test the emulsion is diluted either with oil or water.
- If the emulsion is o/w type and it is diluted with water, "it will remain stable as water is the dispersion medium" but if it is diluted with oil, the emulsion will break as oil and water are not miscible with each other.

#### ② Conductivity test :-

- water is good conductor of electricity whereas
- oil is non-conductor. Therefore, continuous phase of water runs electricity more than continuous phase of oil.



Bulb glows with o/w



Bulb doesn't glow with w/o

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③ Dye Solubility test :-

- Water Soluble dye (methylene blue) will be taken up by the aqueous phase where as oil Soluble dye will be taken by oily phase.
- When microscopically it is observed that water Soluble dye is taken up by the Continuous phase, it is o/w emulsion.
- If the dye is not taken up by the Continuous phase, test is repeated with oil Soluble dye, Colouring of Continuous phase Confirms w/o emulsion.
- This test Can fail if ionic emulsion are present.

④ Fluorescent test :-

- oils give fluorescence under Uv light, while water doesn't. Therefore, o/w emulsion shows spotty pattern while w/o emulsion fluoresces.
- when a w/o emulsion is exposed to fluorescent light under a microscope the entire field fluorescence. If the fluorescence is spotty, then the emulsion is of o/w type.
- However, all oils do not exhibit fluorescence under Uv light and thus the method does not have universal application.



## # Method of preparation of emulsion:-

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Preparation of emulsion depends on the scale at which it is produced.

# On small scale: Mortar and pestle can be used but its efficiency is limited. To overcome this drawback, small electric mixture can be used although care must be exercised to avoid excessive entrapment of air.

# For large scale: production ~~medi~~ mechanical stirres are used to provide controlled agitation and shearing stress to produce stable emulsion.

→ This the methods commonly used to prepare emulsion can be divided into two categories.

### (A) Trituration Method:-

This method consists of dry gum method and wet gum method.

#### (1) Dry Gum Method:-

→ In this method, the oil is first triturated with gum with a little amount of water to form the primary emulsion.

→ The trituration is continued till a characteristic 'clicking' sound is heard and a thick white cream is formed.

→ Once the primary emulsion is formed, the remaining quantity of water is slowly added to form the final emulsion.

#### (2) Wet Gum Method:-

- As the name implies, in this method first gum and water are triturated to form a mucilage.

→ The required quantity of oil is then added gradually in

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small proportion with thorough trituration to form the primary emulsion.

# Formulae for primary Emulsion:

	oil	Gum	water
For Fixed oil	4	1	2
For Volatile oleo resin	2	1	2
	1	1	2

# Stability problems in emulsion & methods to Overcomes:

- The following three change usually occurs during the storage of an emulsion -

① Cracking:

Cracking means the separation of two layers of disperse and continuous phase, due to the coalescence of disperse phase globules which are difficult to redisperse by shaking.

# Cracking occurs due to the following reasons:-

- Addition of emulsifying agent of opposite type.
- Decomposition or precipitation of emulgent.
- Addition of common solvent.
- microorganism.
- change in temperature.

② Creaming :-

Creaming may be defined as the upward movement of dispersed globules to form a thick layer at the surface of the emulsion.

→ Creaming is a temporary phase because it can be re-distributed by mild shaking.

- Creaming depend on - Radius of globules
- viscosity of the dispersion medium
- Storage condition.

③ Phase Inversion :-

- phase Inversion means the Change of one type of emulsion into the other type i.e oil in water emulsion change into water in oil type and vice versa.

- It may be due to following reason.

- By the addition of an electrolyte
- By changing the phase - volume ratio
- By temperature change
- By changing the emulsifying agent.