

Monophasic Liquid Dosage FormGargles

- Gargles are aqueous solutions used for treating throat infection.
- Supplied in concentrated forms with directions of dilution with warm water before use.
- They are used into intimate contact with the mucous membrane of throat for few seconds, before they are thrown out of the mouth.
- They are used to relieve soreness in mild throat infection.
- They are also used for their antiseptics, antibiotics and anesthetics.

Mouth wash

- These are aqueous solutions with pleasant or acceptable taste & odour.
- These are used to make clean & deodorise the buccal cavity or used for oral hygiene.
- They mainly contain antibacterial agent, alcohol, glycerin, sweetening agent, flavoring agent and colouring agent.

## Throat Paint

- Throat paints are viscous liquid preparations used for mouth & throat infections.
- Glycerin is commonly used as a base because being viscous it adheres to mucous membrane for long period and it possess a sweet taste.

## 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 infection.
- Main solvents are water, glycerin.  
The viscous glycerin vehicle permits the drug to remain in the ear for a long time.

## Nasal drops

- Solutions of Drugs that are instilled into the nose from a dropper.
- They are usually aqueous. Because oily drops inhibit movement of cilia in the nasal mucosa and if used for longer periods may reach the lungs and cause lipoidal pneumonia.
- The drug may have a local effect.  
eg - antihistamine, decongestant.

## Enemas

- Aqueous or oily preparations that are introduced into the rectum for cleansing, diagnostic or therapeutic purposes.
- Enemas meant for cleansing are used to evacuate faeces in constipation or before an operation.
- They act by following methods:

### \* By stimulating peristalsis

- Enemas stimulate peristaltic movement of intestine and thus help to evacuate faeces by causing osmotic retention of water.

### \* By lubricating impacted faeces

- Enemas meant for therapeutic purpose are used as sedatives, anti helminthics, anti-inflammatory agents.
- Enemas should be freshly prepared, diluted the strong solution with warm water before use.

## Elixirs

- It is clear, pleasantly flavoured, sweetened, hydroalcoholic liquid preparations meant for oral use.
- Contains potent drugs such as antibiotics, antihistamines, sedatives. Very stable. (generally)
- The composition of elixirs contained mainly as ethyl alcohol, water, glycerin, propylene glycol, colouring agent etc.
- Elixirs are more fluid than syrups due to the use of less viscous ingredients such as alcohol & the minimal use of viscosity improving agents such as sucrose.
- They should be stored in tightly closed & light resistant containers in cool place.



## Syrup

→ Syrups are concentrated, viscous, aqueous solutions of sugars. or a sugar substitute and medical substances in water. (or any other kind of solvent)

→ 3 types

\* When purified water is used alone in making the solution of sucrose. (simple syrup)

\* When contains drug, called medicated syrup.

\* Those containing aromatic or flavoured substances are known as flavoured syrup.

→ Syrups are also used to apply sugar coating to tablets.

→ Syrups can undergo crystallisation. It can be prevented by adding polyhydric alcohols, sorbitol, glycerin. These can also help to increase solubility of added ingredients.

## Adv

⇒ Helps in masking the bitter taste of drugs.

→ Better absorbed, beneficial for paediatric and geriatric patients.

## Disadv

→ Short storage life.

→ Dilute solution of sucrose supports microbial growth.

→ Crystallisation occurs due to the presence of sucrose.



## Elixirs Liniments

- Liniments are liquid or semi-liquid preparations meant for external application to the skin.
- They are usually applied to the skin with friction or rubbing.
- Are usually alcoholic and oily liquid preparations.
- Alcoholic liniments are generally used for their rubefacient, counter irritant, mildly astringent and penetrating effect.
- Such liniments penetrate the skin more readily than those with an oil base.
- The oily liniments are milder in their action and may function solely as protective coatings and are more useful when massage is required.
- Liniments should not be applied to skin that are bruised or broken because they would be irritating.
- The label should carry the warning "Not to be applied to wounds or broken skin" and "for external use only".

## Lotions

- Are usually aqueous or alcoholic preparations.
- They are intended for external application without friction or rubbing to the affected area.
- Usually applied gently by dabbing or after spreading on a dressing.
- It is generally used to provide cooling, soothing and protective & antiseptic action.
- About half of the official lotions are solutions.
- Their main ingredients are simple salts, such as copper and zinc sulphates and lead subacetate, which are soluble in water or salicylic acid, for which alcohol is the solvent.
- All lotions are labelled "For external use only."

## Biphasic Liquids

### Suspension

→ Suspensions are the biphasic liquid dosage form of medicament in which the finely divided solid particles ranging from 0.5 to 5.0 micron are dispersed in a liquid or semisolid vehicle.

→ The solid particles act as disperse phase whereas liquid vehicle acts as the continuous phase.

→ Suspensions are generally taken orally or by parenteral route.

### Qualities of a Good Suspension

→ It should settle slowly and should be readily re-dispersed on gentle shaking of the container.

→ The suspension should pour readily and evenly from its container.

→ It should be chemically inert.

→ The suspended particles should not form a cake.

→ It should be free from large particles which spoil its appearance, give a gritty taste to oral preparations.

→ And also cause irritation to sensitive tissues when applied externally.



## Classification

- ① Oral suspensions
- ② Parenteral suspensions.
- ③ Ophthalmic suspensions
- ④ Suspension for external use.

### ① Oral suspensions

→ These suspensions are to be consumed by the patient by oral route.

→ Oral suspensions generally contain flavouring agent and sweetening agent to mask the bitter taste of the drug.

→ They are also made palatable by using a suitable derivatives of drugs.

→ E.g: Chloramphenicol palmitate suspension is prepared to mask the bitter taste of chloramphenicol.

### ② Parenteral suspensions

→ The suspensions which are administered by parenteral route.

→ These suspensions are required to fulfil the following qualities :-

⊗ The particle size of the drug should be such that it can be easily pass through the needle of the syringe.

⊗ There should not be any crystal growth in the suspension during its storage.

⊛ The concentration of solid particles in the suspension should be between 0.5 to 30%.

⊛ The viscosity of the suspension should not interfere with its flow through the syringe needle.

⊛ The suspensions should be sterilised.

### ③ Ophthalmic suspensions

→ These are not commonly used as compared to eye-drops.

→ These are prepared only in those cases, when the drug is insoluble in the desired solvent or unstable in liquid form.

→ These suspensions must fulfil the following conditions —

① The particle size of the eye-suspensions should be fine enough so that it should be non-irritating to the eye.

② The suspensions should be sterilised.

③ These suspension should be isotonic

④ These should have desired viscosity.

⑤ The suspension should be packed in a suitable container, so that it can be easily instilled into the eye.

## ④ Suspensions for external use

- These suspensions are meant for external use. eg- lotions, inhalations, ear drops etc.
- These suspensions contain very small particles to avoid grittiness.
- Lotion containing suspended particles evaporate when applied to the skin leaving a light deposit of medicament on the surface.
- Lotions are easier to apply and less messy than many other semi-solid external preparations.
- Calamine lotion is a suspension type preparation which is applied on the skin to provide protective effect.
- Lotions which are meant for application on broken or inflamed skin should be free from harmful microorganisms.

### Advantages

- It is easy to swallow the suspended insoluble medicaments.
- The insoluble derivatives in suspensions is more palatable than soluble derivatives in solution.
- Some drugs are better absorbed in liquid form than in solid.



## Disadvantage

- All suspensions are required to be shaken before measuring a dose.
- The accuracy of dosage is less reliable as compared to solution.
- The storage of suspension may lead to changes in disperse system, especially when there is fluctuations in temperature.

## Flocculated and Non-flocculated Suspensions

- The suspensions are said to be flocculated, when the individual particles are in contact with each other and form a network like structure.
- Whereas in case of non-flocculated suspensions, the individual particles exist as a separate entity.

### Flocculated

- Particles form loose aggregates and form a network like structure.
- The rate sedimentation is high.
- Sedimentation is rapidly formed.
- Sediment is easy to redispense.
- Sediment is loosely packed and does not form a hard cake.
- Supernatant liquid is clear.
- The flocules stick to the sides of the bottle.
- Suspension is not pleasing in appearance.

### Non-flocculated

- Particles exist as separate entity.
- The rate of sedimentation is slow.
- Sediment is slowly formed.
- Difficult to redispense.
- Very closely packed and a hard cake is formed.
- Supernatant liquid is not clear.
- Do not stick to the bottles.
- Suspension is pleasing in appearance.

# Formulation of suspension

## ① Flocculating agents

→ In suspensions, the solid particles are well dispersed in dispersion medium.

→ The dispersion can be improved by adding a flocculating agent.

→ They are added to floc the drug particles.

eg- Sodium lauryl sulphate, tweens, carbowaxes etc.

## ② Thickening agents

→ These are hydrophilic colloids which form colloidal dispersions with water and increases the viscosity of the continuous phase.

→ So that the solid particles remain suspended in it for a sufficient long time to measure a uniform accurate dose.

eg- Graftan acacia, tragacanth, methyl cellulose.

## ③ Wetting agents

→ These are the substances which reduce the interfacial tension between the solid particles and liquid medium, thus producing a suspension of required quality.

→ This may be achieved by adding a suitable wetting agent which is adsorbed at the solid/liquid interface in such a way that the affinity of the particles for the surrounding medium is increased and the interparticulate forces are decreased.

eg- alcohol in tragacanth mucilage.



#### ④ Preservatives

- A suitable preservative is needed to preserve suspensions against bacterial growth.
- Preservatives selected should be effective against a wide range of microorganisms.
- Eg - Benzoic acid, sodium benzoate, methyl paraben.

#### ⑤ Organoleptic additives

- Colouring agents, sweetening agents and flavouring agents are generally incorporated in oral suspensions.
- A suitable perfume and colour is incorporated in suspensions which are meant for external use.

#### Evaluation of the stability of suspensions

##### ① Sedimentation method

- It is determined by keeping a measured volume of the suspension in a graduated cylinder in an undisturbed position for a definite period of time and noted the ultimate height ( $H_u$ ) of the sediment and initial height of the total suspension.
- The sedimentation volume  $F$  is the ratio of the ultimate height and initial height. ( $H_u/H_0$ ).
- The sedimentation volume can be plotted against time.
- A stable suspension shows a horizontal or less steep curve.
- The evaluation of redispersibility can also be determined by shaking the suspension and again find out the sedimentation volume ( $H_u/H_0$ ).



## ② Micromeritic method

- The stability of a suspension depends on the particle size of the disperse phase.
- The size of the particle in a suspension may grow and may ultimately lead to the formation of lumps or caking.
- So any change in particle size with reference to time will provide useful information regarding the stability of a suspension.
- A change in particle size distribution and crystal habit may be studied by microscopy and Coulter counter method.

## ③ Rheological method

- The viscosity of the suspension is studied at different time intervals by using a good quality of viscometer.
- It provides useful information about the stability of suspension.

#### ④ Electrokinetic method

→ The determination of surface electric charge or zeta potential of suspension is helpful to find out the stability of suspension.

→ Certain zeta potentials produce more stable suspensions because of controlled flocculation.

→ Zeta potential can be calculated from the migration velocities of the particles measured by the electrophoretic method.

# Emulsions

- An emulsion is a biphasic liquid preparation containing two immiscible liquids, one of which is dispersed as minute globules into the other.
- The liquid which is converted into minute globules is called the 'dispersed phase' and the liquid in which the globules are dispersed is called the 'continuous phase'.
- Normally, two immiscible liquids cannot be dispersed for a long period. So, an emulsifying agent is added to the system.
- It forms a film around the globules in order to scatter them indefinitely in the continuous phase, so that a stable emulsion is formed.
- The globule size in emulsion varies from 0.25 to 25  $\mu\text{m}$  diameter.
- Emulsion having large globules are called coarse emulsions while those having large globules ~~are~~ of 5  $\mu\text{m}$  are considered to be fine emulsions.



## Advantages

- Medicines having an unpleasant taste and odour can be made more palatable for oral administration in the form of an emulsion. eg - castor oil, cod-liver oil.
- Emulsion provides protection against drugs which are prone to oxidation or hydrolysis.
- Various external preparations such as creams, lotion and foam aerosols are formulated in emulsion.
- The sterile stable intravenous emulsions containing fats, carbohydrates and vitamins can be administered.
- Emulsions improve the absorption of oils when taken internally.

## Disadvantages

- Pharmaceutical emulsions are unstable and therefore must be formulated to stabilize the emulsion from separation.
- Pharmaceutical emulsion may be difficult to manufacture.

## Types of Emulsions

### ① Oil in water type (o/w)

→ For this type, the oil is in dispersed phase whereas water is in the continuous phase.

→ The o/w type emulsions are preferred for internal use.

### ② Water in oil type (w/o)

→ For this type, the water is in the dispersed phase whereas oil is in the continuous phase.

→ These are mainly used externally as lotions or creams.

## Tests for Identification of Type of Emulsion

### ① Dilution test

→ The emulsion is diluted with water.

→ In case, the emulsion remains stable after its dilution, it is o/w emulsion.

→ The w/o emulsion breaks on its dilution with water but remains stable when diluted with oil.

## ② Dye test

- The scarlet red dye is mixed with the emulsion.
- Place a drop of the emulsion on a microscopic slide, cover it with a cover slip and examine it under a microscope.
- If the disperse globules appear red and the 'ground' colourless, the emulsion is o/w type.
- The reverse condition occurs in w/o type emulsion i.e., the disperse globules appear colourless for the red 'ground'.

## ③ Conductivity test

- Water is a good conductor of electricity. whereas oil is non-conductor of electricity.
- The conductivity test can be performed by dipping a pair of electrodes connected through a low voltage bulb in the emulsion.
- If the bulb glows on passing the electric current, the emulsion is o/w type, because water is in the continuous phase.
- In case the bulb does not glow, the emulsion is w/o type, because oil is in the continuous phase.



#### ④ Fluorescence test

→ Certain fixed oils possess the physical property of fluorescing in the presence of ultraviolet radiation.

→ On microscopic observation of emulsion under ultraviolet radiation, the whole field fluorescence indicates that oil is present in continuous phase (w/o type emulsion) and droplets fluorescence indicates that oil is present in disperse phase (o/w).

#### Formulation of Emulsion

##### ① Emulsifying Agents

→ The emulsifying agents reduce the interfacial tension between two phases i.e., oily phase and aqueous phase and thus make them miscible with each other & form a stable emulsion.

→ They are also known as emulgents or emulsifiers.

→ There are large number of emulsifying agents which are available to prepare a stable emulsion.

→ But it is very difficult to select a proper emulsifying agent for the development of a stable emulsion.

→ No single emulsifying agent possesses all the properties required for the preparation of stable emulsion.

→ Therefore, sometimes it becomes necessary to use two or more than two emulsifying agents instead of one, to prepare a stable emulsion.

Properties (An ideal emulsifying agent should possess)

- It should be capable of reducing the interfacial tension between the two immiscible liquids.
- It should be compatible with other ingredients of the preparations.
- It should be non-toxic.
- It should be capable to produce and maintain the required consistency of the emulsion.
- It should be chemically stable.
- It should be capable of keeping the globules of dispersion liquid distributed indefinitely throughout the dispersion medium.

② Preservation of Emulsions

## Preparation of Emulsions

### ① Dry gum method

- Measure the required quantity of oil in a dry measure and transfer it into a dry mortar.
- Add the calculated quantity of gum acacia into it and triturate rapidly so as to form a uniform mixture.
- Add required quantity of water and triturate vigorously till a clicking sound is produced and the product becomes white or nearly white due to the total internal reflection of light.
- The emulsion produced at this stage is known as primary emulsion.
- Add more of water to produce required volume.



## ② Wet Gum Method

- Calculate the quantity of oil, water and gum required for preparing the primary emulsion.
- Powder the gum acacia in a mortar. Add water and triturate it with gum so as to form a mucilage.
- Add the required quantity of oil in small portions with rapid trituration until a clicking sound is produced and the product becomes white or nearly white.
- At this stage the emulsion is known as primary solution.
- Add more of water in small portions to the primary emulsion with trituration to produce the required volume. Stir thoroughly so as to form a uniform emulsion.

## ③ Bottle Method

Oil : Water : Gum  
2 : 2 : 1

- Used for the preparation of emulsions of volatile and other non-viscous oils.
- Measure the required quantity of the oil & transfer into a large bottle.
- Add the required quantity of powdered gum acacia.
- Shake the bottle vigorously, until the oil and gum are mixed thoroughly.

→ Add the calculated amount of water all at once.

→ Shake the mixture vigorously to form a primary emulsion.

→ Add more of water in small portions with constant agitation to produce the required volume.

#### ④ Other Methods

→ Various blenders and homogenisers are used for preparing emulsions.

→ Hand homogeniser, Silver mixer homogeniser and colloidal mill are used for the preparation of extemporaneous emulsions.

→ These homogenisers are based on the principle that the large globules in coarse emulsion are broken into smaller globules by passing them under pressure through a narrow orifice.

→ The emulsion is passed through a homogeniser many a times till an emulsion of desired satisfaction is produced.

→ The colloidal mills are used to produce a very fine emulsion having globule size less than one micron on a large scale manufacture.

## Stability of Emulsions

→ An emulsion is said to be stable if it remains as such after its preparation. i.e., the dispersed globules are uniformly distributed through out the dispersion medium during its storage.

→ The emulsion should be chemically stable and there should not be any bacterial growth during its shelf life.

The following three changes usually occurs during the storage of an emulsion —

① Cracking

② Creaming

③ Phase inversion

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 may occurs due to the following reasons:—

① By adding of emulsifying agent of opposite type

→ Soaps of monovalent metals produce o/w type emulsions whereas soaps of divalent metals produce w/o type emulsions.

→ But the addition of monovalent soap to a divalent soap emulsion or a divalent soap to a monovalent soap emulsion leads to cracking of emulsion.



(b) By decomposition or precipitation of emulsifying agents?

→ When an acid is added to an alkali soap emulsion, it causes the decomposition of an emulsifying agent and thus leads to cracking.

→ Similarly, when sodium chloride is added to sodium or potassium soap emulsion, it leads to the precipitation of emulsifying agents and thus cracking of emulsion takes place.

(c) By microorganisms

→ If emulsions are not stored properly, they may develop bacterial & mould growth.

→ This may lead to destruction of emulsifying agent and cause cracking of emulsion.

→ Therefore, it is desirable that all emulsions which are required to be stored for a long period should be suitably preserved.

(d) By creaming

→ A creamy emulsion is more liable to crack than a homogenous emulsion.

→ It is therefore, necessary to take steps to retard creaming as far as possible.

## ① Changes in temperature

→ When emulsions are stored for a long time, an increase in temperature may reduce the viscosity of the emulsion and encourage creaming.

→ When emulsions are stored at a very low temp<sup>o</sup>, freezing of its water content into ice and subsequent melting of the ice and shaking may reform the emulsion.

## 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 or stirring to get again a homogenous emulsion.

→ As far as possible creaming of an emulsion should be avoided because it may lead to cracking with complete separation of two phases.

According to Stoke's law, the rate of creaming depends on the number of factors which can be explained by the following equation:—

$$V = \frac{2r^2(d_1 - d_2)g}{9\eta}$$

Where,

$V$  = rate of creaming

$r$  = radius of globules

$d_1$  = density of dispersed phase

$d_2$  = density of continuous phase

$g$  = gravitational constant

$\eta$  = Viscosity of the dispersion medium.

### ① Radius of globules

→ The rate of creaming is directly proportional to the radius of the globules.

→ Larger the size of the globules, the more will be creaming and smaller the size of the size of the globules, lesser will be creaming.

→ The small globules will rise less quickly than large globules.

→ Hence, creaming can be reduced by reducing the size of globules by passing the emulsion through a homogeniser.

$$V = \frac{2r^2(d_1 - d_2)g}{9\eta}$$



## (ii) Difference in density of disperse phase & cont. phase

→ The rate of creaming depends upon the difference between the densities of the disperse phase and continuous phase.

→ Greater the difference, more will be the creaming.

→ This difference can be reduced but it is not desirable because it is not required therapeutically.

## (iii) Viscosity of the dispersion medium

→ The rate of creaming is inversely proportional to the viscosity of the dispersion medium.

→ The viscosity can be increased by tragacanth and methyl cellulose.

→ But too much viscosity is undesirable because it may become difficult to ~~separate~~ separate the material which have settled at the bottom.

## (iv) Storage condition

→ The emulsion should be stored in a cool place because the rise in temp<sup>o</sup> reduces the viscosity which may lead to creaming.

→ The freezing should be ~~stored~~ avoided because it may lead to cracking.

### ③ Phase Inversion

→ Phase Inversion means the change of one type of emulsion into the other type i.e., oil in water emulsion changes into water in oil type and vice versa.

→ It may be due to following reasons:-

① By the addition of an electrolyte.

② By changing the phase-volume ratio.

③ By temperature change.

④ By changing the emulsifying agent.

→ The phase Inversion can be minimised by keeping the concentration of disperse phase between 30 to 60%.

↳ By storing the emulsion in a cool place.

↳ By using a proper emulsifying agent in adequate concentration.

# Differentiation between Emulsion and Suspension

## Emulsions

→ These are biphasic liquid preparations containing two immiscible liquids one of which is dispersed as minute globules into the other.

(i) The globule size of the dispersed liquid is in the range of 0.25 to 25  $\mu\text{m}$ .

(ii) The emulsifying agent is required to make a stable emulsion.

(iii) Emulsions are of two types, i.e., oil-in-water type & water-in-oil type.

(iv) There are several tests to confirm the type of emulsion.

(v) During storage, freezing should be avoided as it may lead to cracking of emulsion.

## Suspensions

(i) These are biphasic liquid dosage form of medication in which finely divided solid particles are dispersed in a liquid or semi-solid vehicle.

(ii) The particle size of the suspended solid is in the range of 0.5 to 5.0 micron.

(iii) The suspending agent is required to make a stable suspension.

(iv) Suspensions are of two types, i.e., flocculated & non-flocculated.

(v) There is no test to identify the type of suspension.

(vi) During storage, freezing should be avoided as it may lead to aggregation of the suspended particles.