BIPHASIC LIQUIDS

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- Liquid preparations having two phases are termed as biphasic liquids.
- These preparations have dispersed phase and dispersion medium.

1)Emulsion: These are biphasic liquid preparations of two immiscible liquids, with one liquid dispersed in the other liquid in the form of globules.

2) Suspensions: These are biphasic liquid preparations in which the finely divided drug particles are uniformly dispersed throughout the vehicle.

Suspensions:

Are biphasic liquid preparations containing finely divided 0.5-3 micron diameter solid drug particles dispersed or suspended throughout a liquid or semisolid vehicle.

Ideal properties of suspensions:

- The solid drug particles should not sediment . On slightly shaking of the suspension container, the sediment should immediately redisperse.
- The particles should not sediment to form cake.
- The suspension should be viscous enough to allow its easy pouring.
- The suspension should be chemically stable.
- The suspension should be palatable for oral administration, whereas, for external applications they should not contain gritty particles.

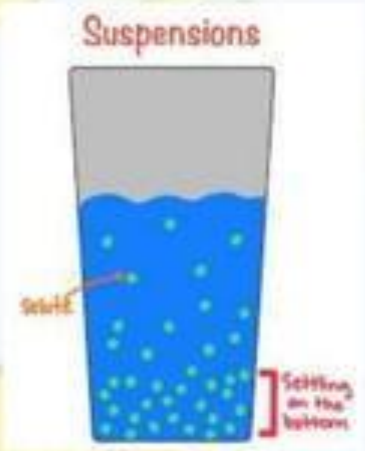
Adv:

- It is easy to formulate drugs having large doses, in the form of suspension, than the solid dosage forms like tablet and capsules.
- It is easy to swallow for children and geriatric patient.
- Bioavailability is greater

- Insoluble drugs can be formulated in the form of liquid dosage forms.

Disadvantages:

- Accuracy of dosage is less reliable.
- Dispersed drug particles may adsorb added flavors, colours, and preservatives making it difficult to formulate a suspension.
- The rate of absorption is slower than the solution dosage forms.



Classification of suspensions:

1) Suspensions are classified according to route of administration;

a) Suspensions for oral use:

- These are administered by oral route and are convenient for Paediatric and geriatric patients who have difficulty in swallowing solid dosage forms.
- The formulation of oral suspensions contains sweetening and flavoring agents to enhance their palatability.
- Suspension for oral use are also called as "**mixtures**".

Eg: Magnesium trisilicate mixture

b) Suspensions for topical use:

- These suspensions are meant for external use and applied on skin without rubbing.
- They are often referred as '**lotions**'.

Eg: Calamine lotion.

c) Suspensions for nasal use:

- These are termed as **inhalations** containing one or more volatile oils dispersed in water.
- A distributing agent such as light magnesium carbonate is used in these suspensions to adsorb the oil.

Eg: Menthol and eucalyptus oil inhalation

d) Suspensions for ophthalmic use:

- Drugs that are insoluble or unstable in water are formulated as suspensions for ophthalmic use.
- These suspensions should be sterile, isotonic and suitably viscous for retaining in the eye.

Eg: prednisolone acetate ophthalmic suspension

e) Suspension for parenteral use:

- Parenteral suspensions are formulated to provide prolonged release.
- The particle size of suspended drug should be such that it can easily pass through the needle of the syringe.
- These suspensions should be sterile.

2) Suspensions are classified according to the particle size of the dispersed phase

a)Colloidal suspension: have particle size between 1nm-500nm. These are therapeutically more effective than coarse suspensions.

b) Coarse suspensions:

Particle size more than 1 micron.

3)Suspensions are classified according to the properties of dispersed solid into four types;

a) Suspensions containing diffusible solids:

Many insoluble powders are light and easily wettable. They readily mix with water and on shaking diffuse evenly through the liquid for sufficiently long time, enough to ensure uniform withdrawal of each dose. Such substances are known as diffusible or dispersible solids.

Eg: light kaoline, Light magnesium carbonate.

b) Suspensions containing indiffusible solids:

- Indiffusible solids do not remain evenly distributed in the vehicle long enough to ensure uniformity of dose and hence require suspending agent.

Eg: Aspirin, chalk.

c) Poorly wettable solids:

- Some substances are insoluble in water and have poor wettability with water.
- While preparing aqueous suspensions of such substances, some particle form lumps in the liquid which are difficult to disperse while other remain on the surface and become attached to the upper part of the container.

d) Suspensions containing precipitate forming liquids:

- Certain liquid preparations contain resinous matter that precipitates out when added to water. They are insoluble in water and form indiffusible precipitates in the presence of salts.

4) Suspensions are classified according to properties of dispersed phase into two types,

a) Flocculated suspensions:

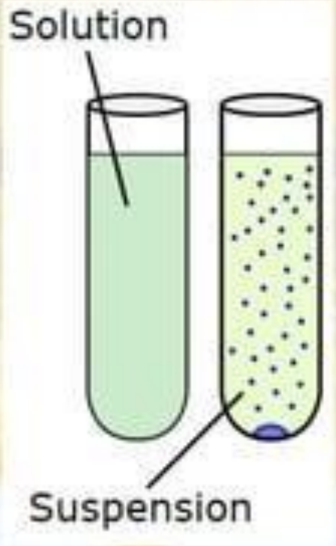
- A loosely bound structure of particles is called a flocculate or floccule.
- The flocculated particles tend to sediment at rapid rate, because each unit is composed of many individual particles.
- The volume of final sediment is large and easily redispersed by moderate agitation.
- In flocculated suspensions, the supernatant becomes clear.

b) Deflocculated suspensions:

- In this system, the dispersed particle remain as discrete units and the rate of sedimentation depends on the size of each unit.
- The rate of settling is slow.
- The supernatant of deflocculated system remains cloudy after shaking for an appreciable time due to very slow settling rate.

FLOCCULATED SUSPENSION	DEFLOCCULATED SUSPENSION
1. Particles are in the form of loose agglomerates.	1. Particles in the suspension exists as separate entities
2. Floccules are collection of particles, so rate of sedimentation is high.	2. Particles settle separately and hence rate of sedimentation is low.
3. The sediment is loosely packed. Thus sediment is easily redispersed.	3. The sediment is very closely packed. Thus the cake is nonredispersible.
4.The suspension shows a clear supernatant	4. The supernatant liquid is cloudy.

Methods of preparation of suspensions:



Suspensions are prepared by two methods;

1) Dispersion method

2) Precipitation method

1. Dispersion method:

Method of preparation on laboratory scale:

- Dispersion method is used for preparing suspension containing diffusible, indiffusible drugs and drugs with good or poor wettability.

It involves the following steps;

a) Taring of container:

- A tared container in used because complete transfer of prepared suspension from a measuring cylinder is difficult.
- A quantity of water equivalent to a final volume of the preparation is measured using a measuring cylinder and transferred to a suitable container.

- The level of water is marked on the container and this marking is used for making up the final volume. This is known as Taring of container.

b) Size reduction:

- Particle size reduction is the first step in the preparation of any suspension. Particle size reduction is achieved by triturating the drug using a mortar and pestle. And subsequently sifting throw sieve no.80.
- The fine drug powder obtained is used for further processing.

c) Dispersion of drug into vehicle:

The powdered drug particles get uniformly dispersed in the vehicle. There are four possibilities;

The drug is diffusible, having good wettability.

The drug is indiffusible

The drug is poorly wettable.

The drug is a precipitate forming liquid.

2. Precipitation methods:

- These method is less widely used to prepare suspensions.
- The drug is suspended in a vehicle by precipitating it from its solution.
- The method is useful for drugs which are required to be sterile but are unstable on heating or irradiation.

This method is divided into three types;

- ✓ Precipitation with organic solvents
- ✓ Precipitation with pH change of media
- ✓ Precipitation with chemical reaction

Formulation of suspensions:

1. Drug:

- The drug should be insoluble in the vehicle with good chemical stability and wettability.
- It should have fine particle size and uniform particle size distribution.
- The drug should be present ion only one polymorphic form, because different polymorphic form have different solubility.

2. Wetting agents:

- Poorly wettable drug particles have air adsorbed on their surface which prevents their dispersion in the vehicle.
- To ensure adequate wetting, the adsorbed air should be displaced from the surface of the drug. this is achieved by use of wetting agents.

The most widely used wettings agents are;

1. Surface active agents
2. Hydrophilic colloids
3. Solvents

1. Surface active agents:

- Surfactants with HLB value between 7 and 9 would be suitable for use as wetting agents.
- Surfactants are capable of displacing the adsorbed air and occupying its place, thereby reducing the surface tension and this improves the wettability of drug particles.

Eg: tweens and spans.

2. Hydrophilic colloids:

- These act as protective colloids by coating the poorly wettable drug particles with a multimolecular layer.
- Eg: Acacia, bentonite.

3. Solvents:

- The solvent penetrates the loose agglomerates of powder and displaces the air from the pores. This enables wetting of the drug particles.
- Eg: Alcohol, glycerol.

3. Suspending agent/thickening agents or viscosity modifiers:

- A suspending agent is required to enhance viscosity of suspension and delay its sedimentation.
- A ideal suspension should be viscous during storage, so that suspended particles settle very slowly.
- At the same time, on moderate shaking, the viscosity should decrease sufficiently so that the product shall be poured easily form the container.
- The suspending agents can be classified into following types as shown below;

Natural polysaccharides:

1. Acacia:

- This is dried exudates from bark of Acacia Senegal and other species of acacia.
- It forms a protective coat around the dispersed particles and acts as protective colloid.
- It is sticky and not very effective, if used alone. Therefore it is combined with tragacanth, starch and sucrose in compound tragacanth powder.
- Acacia often has high microbial count. Therefore, preservative id necessary for suspensions containing acacia.

2. Tragacanth:

- Is a dried extract from Astragalus gummifer and other species of Astragalus.
- It forms a viscous solution or gel with water.
- It is used both for internal and external products as they are less sticky than acacia.
- It is susceptible to microbial growth and hence preservative is required.

3. Starch:

Is used in the form of 2.5% mucilage in water with other suspending agents because of high viscosity of mucilage.

4. Compound tragacanth powder:

- It is a mixture of Powdered acacia, tragacanth, starch and sucrose.
- Used in quantities of 2g per 100 ml of mixture.

5. Sodium alginate:

- It is sodium salt of alginic acid obtained from a seaweed laminaria.
- It forms a viscous colloidal solution with water, which must not be heated above 600C as this results in loss in viscosity.
- During preparation of the mucilage, sodium alginate should be wetted with alcohol to avoid lump formation and mixed with water using high speed mixer.

Semisynthetic polysaccharides:

1. Methylcellulose:

- Methylcellulose is soluble in cold water, but insoluble in hot water.
- It is available in different viscosity grades based on its molecular weight. High viscosity grades such as MC 2500 and 4500 are used as suspending and thickening agents.
- It is susceptible to bacterial growth.
- It is used in both internal and external preparations.

2. Sodium carboxymethyl cellulose:

- It is soluble in both cold and hot water.
- It is available in various viscosity grades, depending upon the degree of polymerization.
- It is susceptible to microbial growth. Therefore, preservatives should be added.
- It is often used in 0.25-1% concentration as suspending agent.

3. Microcrystalline cellulose (MCC):

- MCC is prepared form wood cellulose by addition of acid and mechanical action.
- At low concentration it disperses in water forming a colloidal dispersion, while in high concentration it produces a thixotropic gel.

Inorganic agents:

Clays:

These are naturally occurring materials which hydrate readily, absorbing many times their own volume of water.

a) Bentonite:

- It is very fine cream coloured natural colloidal hydrated aluminium silicate. It hydrates readily and absorbs large amount of water and swells upto about 12 times its original volume.
- Its 2 % dispersion is generally used as suspending agent.

b) hectorite:

- It is white powder and it absorbs about 14 times its own volume of water.
- In industry it is used as suspending agent for external use suspension.

c) Veegum:

- It is a creamy white odorless and tasteless powder used as thickening agent in both internal and external use preparation alone or in combination with other suspending agents.
- Chemically it is colloidal aluminium magnesium silicate.

Aluminum hydroxide

- It is used as wetting agent for substances not readily miscible with water.
- It is used as suspending agent for barium sulphate, calamine.

Synthetic suspending agents:

1. Carbopols (carbomers):

- Is a synthetic copolymer of acrylic acid and allyl sucrose available in several viscosity grades.
- It is widely used in industry for internal and external preparations.
- It gels in water at concentration of less than 1%.
- It forms acidic, low viscosity solutions in water.
- Carbopol gels are prepared by adding it to water in small amounts with continuous stirring using a high speed stirrer. The pH is adjusted above 6 using triethanolamine and stirred slowly taking care not to incorporate air bubbles.
- It is resistant to microbial growth.

2. Colloidal silicone dioxide (Aerosil):

- It is white, nongritty light powder.
- When suspended in a liquid, the particles associate due to hydrogen bonding, producing a network that obstructs sedimentation.
- A concentration of 1.5-4% in water is enough to stabilize suspensions.

4. Flocculating agent:

- A controlled flocculation is required to produce suspensions having adequate redispersibility and high viscosity to minimize sedimentation rate. To achieve this, flocculating agents are added.

a) Electrolytes

b) Surfactants

c) Hydrophilic polymers

a) Electrolytes:

- These are widely used flocculating agents.
- Formation of flocculated suspensions requires addition of appropriate concentration of electrolyte.

Eg: Sodium acetate, sodium citrate.

b) Surfactants:

- Nonionic surfactants form a loose flocculated structure.

c) Hydrophilic polymers:

- Starch, glycerin, cellulose derivatives, tragacanth and carbomer can be used to control flocculation.
- Their linear branched chain molecules form a gel like network and get adsorbed onto the surface of dispersed particles.

5. Vehicle:

- Suspension is formulated because a drug is insoluble in water.
- Aqueous suspensions utilize water as a vehicle of choice.
- Syrup, or viscosity building agent, or glycerin may be added to enhance the viscosity of the aqueous phase.

6. Preservative:

- A suitable preservative should be included in a suspension, to prevent the growth of microorganism.
- The preservative used should be nontoxic and effective at a low concentration against a broad spectrum of organisms.
- It should be chemically stable over a wide range of pH and temperature.
- It should be soluble in required concentration.
- It should be odorless, colorless and tasteless.
- It should not get adsorbed/absorbed on the surface of dispersed particles or should not react with containers and closures.

Eg: Benzoic acid, cholrbutanol, sodium benzoate.

7. Coloring and flavoring agents:

- Natural or synthetic coloring agents are added to impart colour to the preparation, or to improve patient acceptance.
- Flavoring agents are added to improve the patient acceptance.
- Children tend to prefer sweet, fruity flavors.

8. Sweetening agent:

- Sweetening agent are added to improve palatability of preparation.
- Sucrose, sorbitol and mannitol are often used as sweeteners.
- Saccharine and aspartame are official sweeteners.
- It should be colorless, odorless and tasteless.
- It should be chemically stable at room temperature.
- Synthetic sweeteners such as sodium saccharine can affect the degree of flocculation.

Stability of suspensions

A physically stable suspension

- Should settle slowly and should be readily redispersed on moderate shaking of the container.
- The particle size of the dispersed substance should remain fairly constant throughout the shelf life of suspension.
- Should be poured readily and evenly from its container.

The physical stability of suspension depends on the ;

- Nature of the dispersed phase.
- The dispersion medium or vehicle.
- The additives included in suspension.
- The rate of settling of particles as described by Stoke's law.

- Stoke's law and its equation was derived for an ideal situation in which uniform perfectly spherical particles settle without turbulence.
- Therefore, the stokes equation does not apply precisely to the usual pharmaceutical suspensions in which the dispersed solid is irregularly shaped.

Stokes law is given by the equation;

$$V \text{ or } dx/dt = d\,(\rho s - \rho p)g/\,18\eta$$

Where,

V or dx/dt = velocity or rate of settling

d = diameter of the particles

ρs = density of the particle

ρp = density of the medium.

g= acceleration due to gravity

η = Viscosity of the medium.

From the equation it is clear that,

- The rate of settling is directly proportional to the diameter of the particle.
- The rate of settling will increase if density of the particles is increased.
- The rate of settling is inversely proportional to the viscosity of the medium.

Factors affecting stability of suspension:

Based on stokes law there are 3 main factors affecting stability of suspension;

- Diameter of dispersed particles
- Difference between density of dispersed particle and dispersion medium
- Viscosity of dispersion medium

1. Diameter of dispersed particles:

- The rate of settling is directly proportional to diameter of dispersed particle.
- Larger the particle, faster would be the rate of settling.

2. Difference between density of dispersed particles and dispersion medium:

- The rate of settling is directly proportional to difference.
- Hence reduction in difference between the density of particle and density of dispersion medium reduces the rate of settling.

3. Viscosity of dispersion medium:

- The rate of settling is inversely proportional to viscosity of dispersion medium. If viscosity of the medium is increased, the rate of settling of particles is slower and a good dispersion is achieved.

Emulsion

- Emulsion is defined as biphasic liquid dosage form , consisting of two immiscible liquids, one of which is dispersed throughout the other.
- The system being stabilized by the presence of third substance, the emulsifying agent.

Ideal characteristics of emulsion:

- The dispersed phase of an emulsion should have fine droplet size.
- There should be very slow aggregation and creaming of the droplets of the internal phase.
- The emulsion should easily redispersed on shaking.

Adv:

- Unpalatable oils and oil soluble drugs can be administered in palatable form by preparing oil in water emulsions where oil shall be the internal phase.
- The rate of absorption is increased as the drug dissolved in the internal phase is distributed as fine droplets.
- It is possible to incorporate two incompatible ingredients, one in each phase.

Dis:

- Liquid emulsions are less stable than solutions and suspension.
- Storage conditions may affect stability.
- Being a liquid dosage form, emulsions are bulky, difficult to transport and prone to container breakages.

Classification:

1. Depending on the type of dispersed phase:

1. Simple emulsion

a) Oil in water (o/w) emulsion:

Are the emulsions in which oily liquid is the dispersed phase and an aqueous liquid is the continuous phase. The emulsions that are administered orally are usually o/w emulsions.

b) Water in oil emulsion (w/o):

Are the emulsions in which an aqueous liquid is the dispersed phase and oily liquid is the continuous phase. These are mainly used for external applications.

2. Multiple emulsion:

a) o/w/o emulsion: are the emulsions where the aqueous phase is enclosed between two oily phases.

b) w/o/w: are the emulsions in which the oily phase is enclosed between two aqueous phases.

2. Depending on the size of droplets:

a)Microemulsions: these are also called as micellar emulsions and are translucent and transparent having droplet diameter in the size range of 10-200nm. They contain droplets of oil dispersed in water or vice versa.

b)Macroemulsions: depending on the droplet size these are classified as fine and coarse emulsions and are milky in appearance. Fine emulsions have a droplet diameter in the size range of 0.1 and 5 micron.

3. Depending on the physical state:

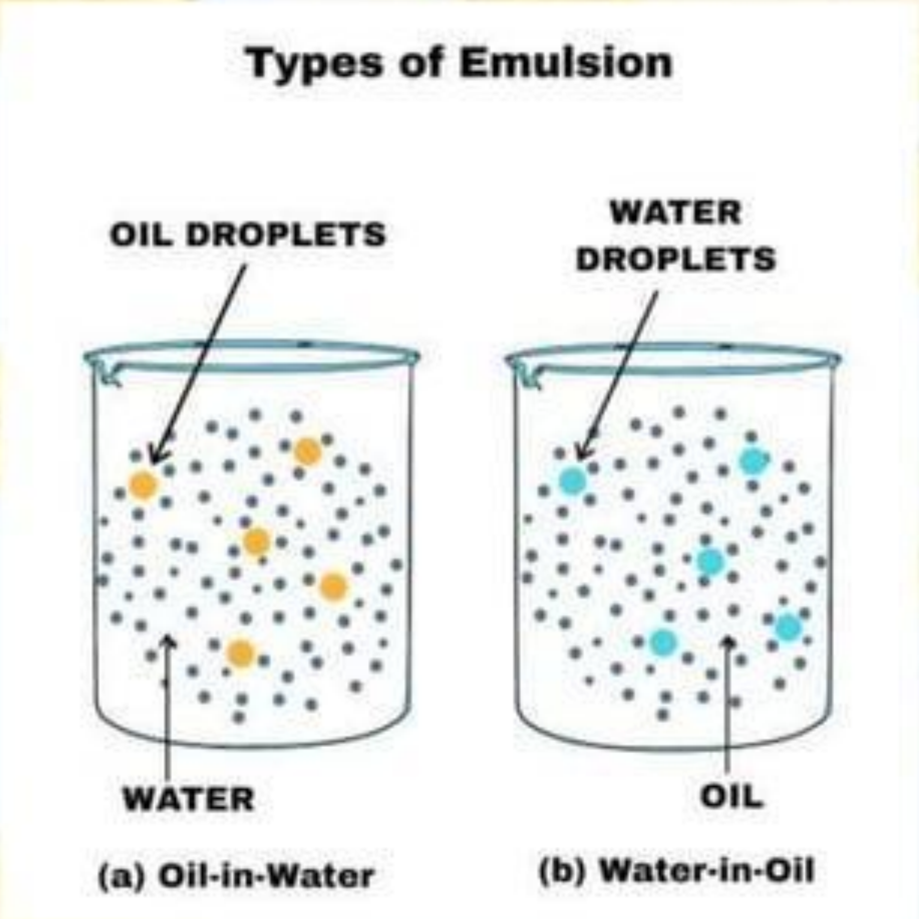
a)Liquid emulsions: these are used orally, parenterally or externally. Oral emulsions are usually o/w type. Dispersed phase must be very finely subdivided in emulsion for parenteral use and the emulsifying agents must be nontoxic.

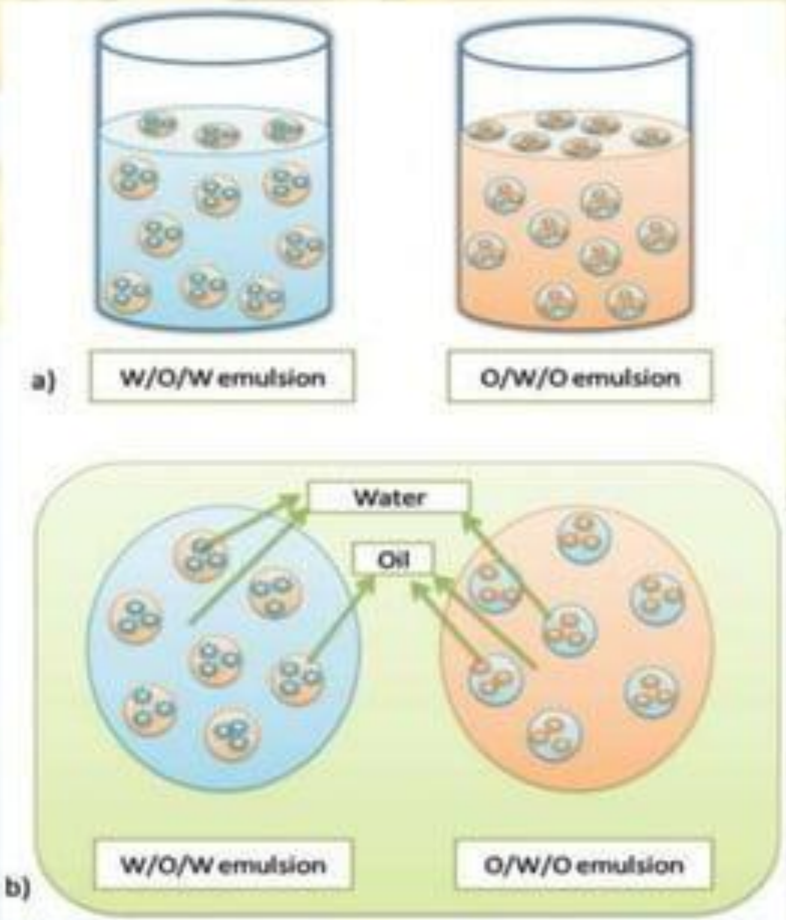
b)Semisolids or creams: these are external preparations and may be of o/w or w/o type.

4. Depending on the route of administration :

a) Internal: these are mainly o/w type of emulsions.

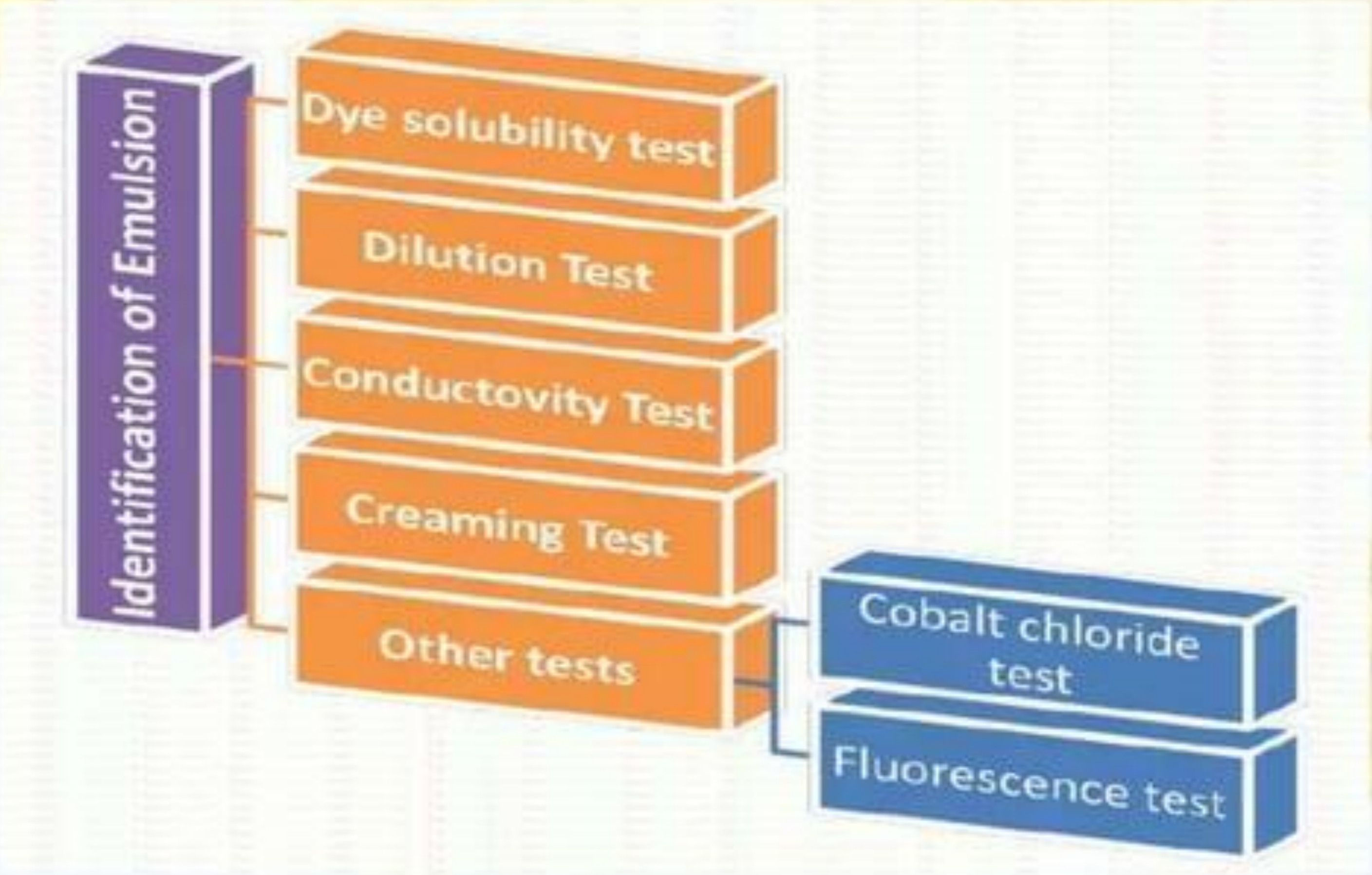
b)External: liniments, lotions and creams are o/w or w/o type.





Identification of type of emulsion:

Several tests are available to identify the type of emulsion.



Identification of type of emulsion:

1. Miscibility test:

Principle: dilution of emulsion with external phase maintains physical stability of emulsion.

Method:

Dilute the test emulsion with water, if emulsion not shows separation of water phase, it indicates oil in water emulsion.

2. Fluorescence test:

Principle: many oils fluorescence when exposed to UV light.

Method: emulsion is observed against UV light under microscope. Fluorescence of entire field indicates oil as external phase and spotty fluorescence is observed when water is external phase.

3. Color test:

Principle: Water phase or oil phase shows coloration when an emulsion is triturated with water or oil soluble coloring agent.

Method:

- Triturate emulsion with oil soluble dye and observe under microscope. If internal phase (globules) appears colored against colorless background; indicates oil-in-water type of emulsion.
- If droplets remain colorless, it indicates w/o emulsion.

4. Conductivity test:

Principle: water as continuous phase is good conductor of electrical current.

Method:

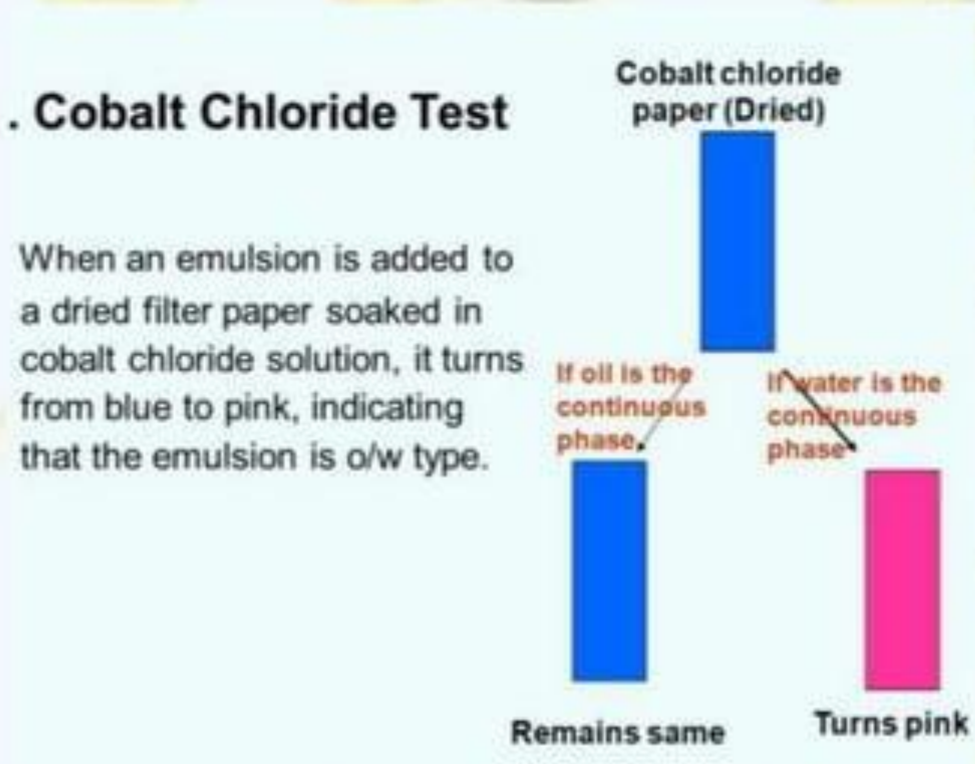
- Immerse a pair of electrodes in an emulsion and circuit them to lamp and electric potential.
- Under the applied current, if lamp glow, it indicates water as continuous phase.

5. Cobalt paper test:

Principle: Anhydrous cobalt is blue and hydrated cobalt is red.

Method:

Treat filter paper with cobalt chloride solution and dry. Deep the paper in an emulsion. The color change from blue to pink-red indicates oil-in water emulsion.



Formulation of emulsion:

1. Drug:

- In most of the emulsions oil itself acts as drug.

2. Oil phase:

- Apart form the therapeutic benefits it can also be used to dissolve oil soluble drugs.
- They provide emollient effect especially in external preparations.
- The oil phase also aids in in-situ soap formation.

3. Aqueous phase:

- Water is generally used as an aqueous phase.
- However in some emulsion, cinnamon water have been used as aqueous phase.
- The water soluble drugs if present, are first dissolved in the aqueous phase then mixed with the oily phase.

4. Emulsifying agents:

Can be classified into various types;

1. Polysaccharides

a) Natural:

- These hydrocolloids form o/w emulsions.
- They form a multimolecular interfacial film around each oil drop.
- They increase the viscosity of water phase.
- Acacia is most frequently used natural polysaccharides for oral emulsion, however. Due to its sticky nature, acacia emulsions are not suitable for external use.

- Emulsion stabilizers such as tragacanth, sodium alginate or agar are used in combination with acacia to increase the viscosity of aqueous phase.

b) Semisynthetic polysaccharides:

- These are used as o/w emulsifying agents and stabilizers.
- Low viscosity grades of methyl cellulose are suitable as emulsifying agents.

Eg: Sodium CMC, methylcellulose.

2. Surfactants:

- Surfactants are typically amphiphilic molecules that contain both hydrophilic and lipophilic groups.
- The surfactant molecule lowers the surface tension between the oil and water phases forming a stable emulsion.

1. Anionic:

- In aqueous solution, they dissociate to form a large anion which is responsible for its emulsifying activity.
- They are cheap. Due to their toxicity, they are used for external emulsion.

b) Alkali metal and ammonium soap:

These are sodium, potassium or ammonium salts of long chain fatty acids and they form o/w emulsion.

Eg: Sodium stearate.

c) Divalent metal soaps:

- Calcium salts of fatty acids are commonly used and they produce w/o emulsions.
- They are incompatible with monovalent emulsifying agents.

Eg: Calcium oleate.

d) Amine soaps:

- Triethanolamine salts of fatty acid are used and they produce o/w emulsion.
- They are not used internally and are unstable in presence of acids and electrolytes.

Eg: Triethanolamine stearate

2. Cationic:

- In aqueous solution, these ionize into large cation responsible for their emulsifying ability.
- They produce o/w emulsion, are unstable at high pH and incompatible with anionic surfactants.
- They are used as disinfectants and preservatives.

Eg: Cetrimide.

3. nonionic:

- In aqueous solutions, they do not ionize.
- They are nontoxic or nonirritant, therefore can be used orally or parenterally.

Eg: Span, Tween, Glyceryl monostearate.

4. Finely divided solids:

They act as emulsifying agents by forming thick impenetrable particulate film.

Clays are mainly used as emulsion stabilizers in lotions and creams.

Eg: Bentonite, Hectorite.

5. Antioxidants:

- An antioxidant used in formulation should be compatible with drug and excipients used.

Eg: BHA, BHT, Ascorbic acid, tocopherol.

6. Preservative:

- Microbial growth may produce physical changes in an emulsion such as breaking of emulsion, discoloration, gas and changes in viscosity.

7. Organoleptic additives:

- Flavoring agents may be incorporated in the emulsions in order to mask the unpalatable taste of oil.
- Coloring agents are not added to emulsions as they are milky in appearance.

Eg: Peppermint oil.

8. Buffers:

- Buffers may be necessary to maintain the chemical stability of the drug or to control tonicity or to ensure physiological compatibility.

9. Density modifiers:

- From stokes law, it can be seen that if the disperse phase and dispersion medium both have same densities, then creaming will not occur.
- Eg: Glycerol, sucrose.

Preparation of emulsion:

Emulsions are prepared by several methods and equipments.

Equipments:

1. Porcelain mortar and a flat head pestle:

- These are used on a laboratory scale.
- Porcelain mortar has got a rough rather than smooth surface, which ensures proper grinding action and reduction of globule size.
- A glass mortar is too smooth to produce the proper reduction of the internal phase.

2. Mechanical stirrers:

- Am emulsion may be stirred by various impellers mounted on shafts, which are placed directly on the system to be emulsified.

- Entrapment of air is the limitation.
- Hand homogenizers are used to produce more fine globules and emulsions of improved quality.

3. Homogenizers:

- In homogenizers the dispersion of two liquids is achieved by forcing the mixture through several small orifices.
- The speed of homogenizer and the duration of operation can be varied depending on the droplet size required.

4. Colloid mills:

- They operate on principle of high shear which is normally generated between rotor and stator of the mill.
- Colloid mill consists of fixed stator plate and a rotating rotator plate. Material pumped through an adjustable gap between the rotor and stator is homogenized .

Ultrasonifiers:

- Ultrasonic energy is used to produce pharmaceutical emulsions.
- They are useful for laboratory preparation of emulsions of moderate viscosity and extremely low particle size.

Methods of emulsion preparation:

- ✓ Dry gum method
- ✓ Wet gum method
- ✓ Bottle method
- ✓ Auxillary method
- ✓ In situ soap method

1. Dry gum method:

- In this method, acacia is used as emulsifying agent. However, it is a weak emulsifying agent. Therefore, tragacanth is also included in the formulation to form a stable emulsion.
- A dry porcelain mortar with rough inner surface is used to prepare emulsion with fine globule size.
- In this method, the emulsifying agent is mixed with the oil before addition of water. It is also called as 4:2:1 method.
- For every 4 parts of oil, 2 parts of water and 1 part of emulsifying agent or gum is added in preparing the primary emulsion. Further dilution is made with water.

A **general procedure** is given below;

- One part of acacia is mixed with four parts of oil in a porcelain mortar.
- Two parts of water are added all at once and the mixture is triturated immediately, rapidly and continuously until a creamy-white primary emulsion if formed.
- About three minutes of mixing is required to produce a primary emulsion.
- Other liquid ingredients, which are miscible with the external aqueous phase are added to the primary emulsion.
- Solid ingredients like preservatives, coloring and flavoring agents are dissolved in sufficient quantity of water and added to the emulsion in the mortar.
- The emulsion is then transferred to a measuring cylinder.
- The mortar is rinsed with water and the rinsing are transferred to the measuring cylinder.
- The final volume is made up with water.

Example: Castor oil emulsion

Castor oil	37.5ml
Acacia Powder	10gm
Cinnamon water q.s.	100ml

Method:

- Weigh accurately the required quantities of castor oil and acacia and transfer to a mortar.
- Triturate the ingredients
- Add two parts of cinnamon water all at ones and triturate the mixture.
- Dilute the primary emulsion with cinnamon water and then make up the volume with water.

2. Wet gum method:

- The proportion of oil, water and emulsifier are the same as in dry gum method but the order and technique of mixing is different.

- The gum is triturated first with small amount of water miscible wetting agent such as glycerin.
- The wetted gum is then triturated with twice its weight of water to form mucilage.
- The oil is then slowly added in portions, with constant, rapid and light trituration.
- If the emulsion shows a tendency to break, few drops of water are added and trituration continues until the emulsion reforms.
- After all the oil has been added the mixture is triturated to form a primary emulsion.
- The emulsion is transferred to a measuring cylinder and volume is made up with water.

3. Bottle method:

- It is used for extemporaneous preparation of emulsions containing volatile oils or oleaginous substances of low viscosity.
- Two parts of oil phase and powdered acacia are added in dry bottle of doubled capacity and the mixture is thoroughly shaken in capped container.
- A volume of water approximately equal to that of the oil phase is added in portions and the bottle is shaken vigorously after each addition to produce a primary emulsion.
- Any other water soluble ingredients, if present are added as aqueous solutions and the final volume is made up with water.

Example of emulsion prepared using bottle method:

Benzyl benzoate application B.P.

Formula:

Benzyl benzoate	25gm
Emulsifying wax	2gm
Purified water	100ml

Method:

- Warm the required quantity of benzyl benzoate into a porcelain dish. Melt the emulsifying wax in another porcelain dish. Add the benzyl benzoate into melted emulsifying wax, mix and allow the mixture to cool to about 600C.
- Transfer the oily mixture to the bottle and add water upto the mark.

4. Auxiliary method:

- An emulsion prepared by other methods can also be improved by passing it through a hand homogenizer, which forces the emulsion through a very small orifice, reducing the dispersed droplet size to about 5 micron or less.
- The hand homogenizer is less efficient in reducing the particle size of very thick emulsions.

5. In situ soap method:

- In this method emulsifying agent (soap) is not externally added but it is formed while preparing the emulsion.
- The two types of soaps formed are soft soap and calcium soaps.
- If the soap formed is monovalent the emulsion is o/w, while divalent soaps form w/o emulsion.

Thank you…!