

LIQUID ORALS



BY ADMUND

DEFINITION:-

Liquid orals are the homogeneous liquid preparations containing one or more active ingredients with or without additives dissolved in a suitable vehicle, meant for oral administration.





TYPES OF LIQUID ORALS:-



- ➡ SUSPENSIONS

- ➡ EMULSIONS

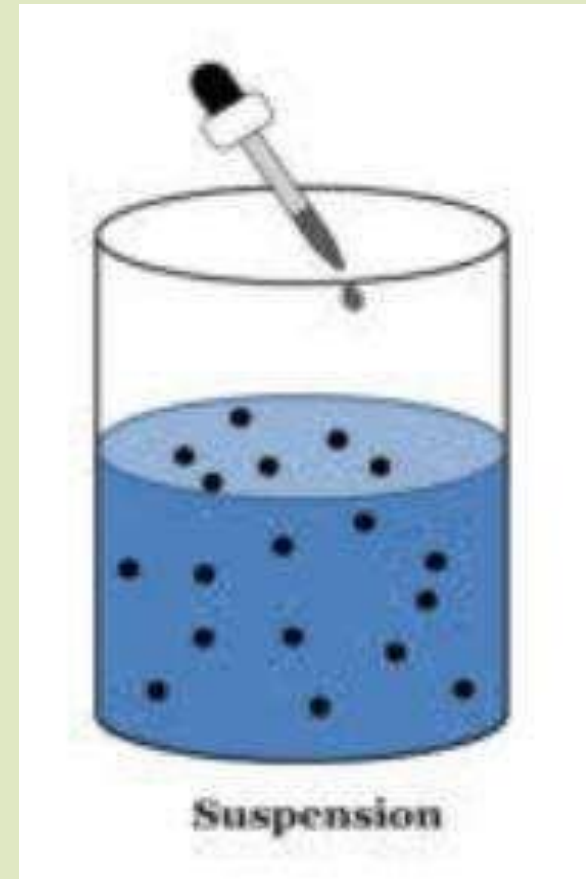
- ➡ SOLUTIONS

SUSPENSIONS



DEFINITION:-

Suspensions are the biphasic liquid dosage form of medicament in which the finely divided solid particles are suspended or dispersed in a liquid or semisolid vehicle with the help of suspending agent. The solid particle is the 'dispersed phase' or 'discontinuous phase' whereas the liquid vehicle is the 'continuous phase'.






ADVANTAGES:-

- Can improve chemical stability of certain drugs.
- Higher rate of bioavailability, as order of bioavailability is:-

Solution > Suspension > Capsules > Compressed tablets




DISADVANTAGES:-

- Physical stability, sedimentation and compaction.
 - Bulky, handling require care.
 - Uniform drug delivery cannot be achieved sometimes.
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IDEAL PROPERTIES OF SUSPENSIONS:-

1. The dispersed particles should not settle readily and the settled particles should redisperse immediately on shaking.
 2. The particles shouldn't form a cake on settling.
 3. The viscosity should be such that the preparation can be easily poured.
 4. It should be chemically stable.
 5. Suspensions for internal use must be palatable and suspension for external use must be free from gritty particles.
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TYPES OF SUSPENSIONS:-

Depending upon particle nature/dispersed particle nature the suspensions are of two types:-

1. Flocculated suspensions
2. Non-flocculated/deflocculated suspensions.

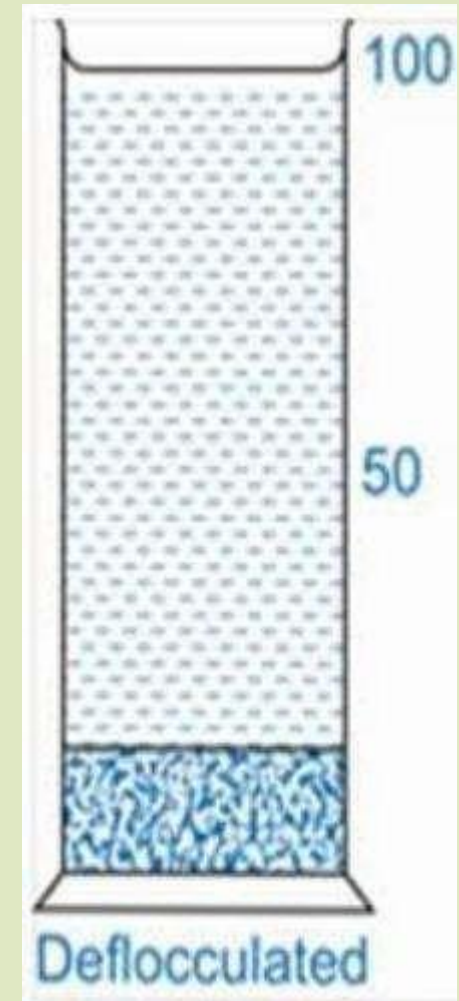
FLOCCULATED SUSPENSIONS:-

Suspension in which particles are weakly bonded, settle rapidly, do not form a cake and are easily resuspended with a minimum of agitation.



DEFLOCCULATED SUSPENSIONS:-

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




Differences between flocculated and deflocculated suspension

Flocculated	Non-flocculated
<ol style="list-style-type: none">1. Particles forms loose aggregates and form a network like structure2. Rate of sedimentation is high3. Sediment is rapidly formed4. Sediment is loosely packed and doesn't form a hard cake5. Sediment is easy to redisperse6. Suspension is not pleasing in appearance7. The floccules stick to the sides of the bottle	<ol style="list-style-type: none">1. Particles exist as separate entities2. Rate of sedimentation is slow3. Sediment is slowly formed4. Sediment is very closely packed and a hard cake is formed5. Sediment is difficult to redisperse6. Suspension is pleasing in appearance7. They don't stick to the sides of the bottle



FORMULATION OF SUSPENSIONS:-

- 
1. Flocculating agents.
 2. Suspending agents/thickening agents.
 3. Wetting agents.
 4. Dispersing agents.
 5. Preservatives.
 6. Organoleptic additives.



PREPARATION OF SUSPENSION

Step 1:

Suspensions are prepared by grinding the insoluble materials in the mortar To a smooth paste with a vehicle containing the wetting agent.




Step 2:

All soluble ingredients are dissolved in same portion of the vehicle and added to the smooth paste to step 1 to get slurry.



Step 3:

The slurry is transferred to a graduated cylinder, the mortar is rinsed with successive portion of the vehicle.



Step 4: Decide whether the solids are

- Suspended in a structured vehicle
- Flocculated
- Flocculated and then suspended

Add the vehicle containing the suspending agent (or) flocculating agent




Step-5:

Make up the dispersion to the final volume .

Thus suspension is prepared.



STABILITY OF SUSPENSIONS:-




A stable suspension can be redispersed homogenously throughout its shelf life. The more stable pharmaceutical suspensions are flocculated i.e., the suspended particles are bonded together physically to form a loose cake.



EVALUATION OF SUSPENSION STABILITY:-

The following are commonly used for evaluating the physical stability of suspensions:-

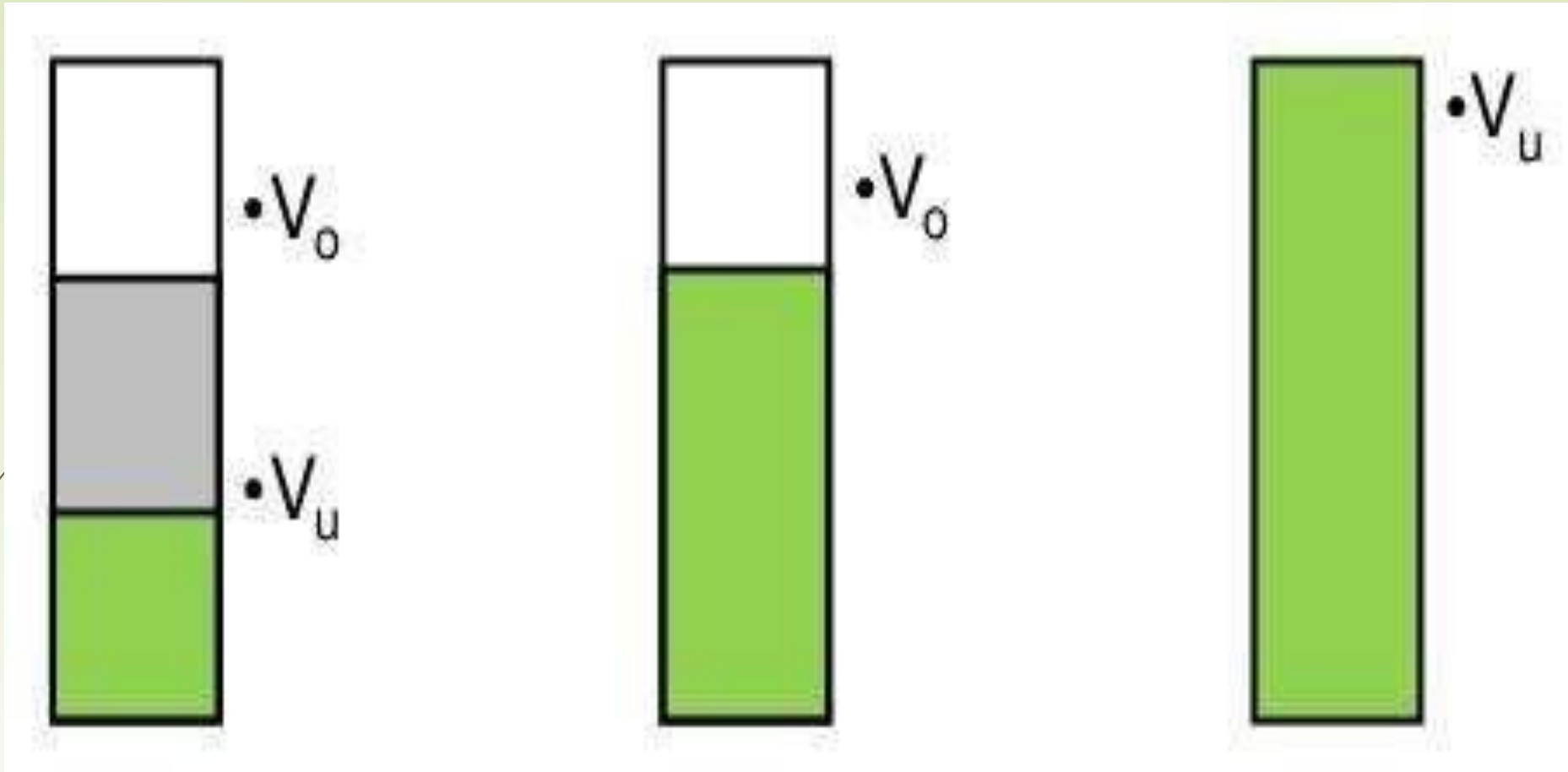
1. Sedimentation method.
 2. Rheological method.
 3. Electrokinetic method.
 4. Micromeritic method.
- 

1.SEDIMENTATION METHOD:-

It is determined by keeping a measured volume of suspension in a graduated cylinder in an undisturbed position for a definite period of time, the ultimate volume (V_0) and the initial volume (V_u) of the sediment is to be noted.

Sedimentation volume is a ratio of the ultimate volume of sediment (V_0) to the original volume of the sediment (V_u) before settling.

$$\text{Sedimentation volume } F = V_0/V_u$$



Sedimentation rate of a suspension

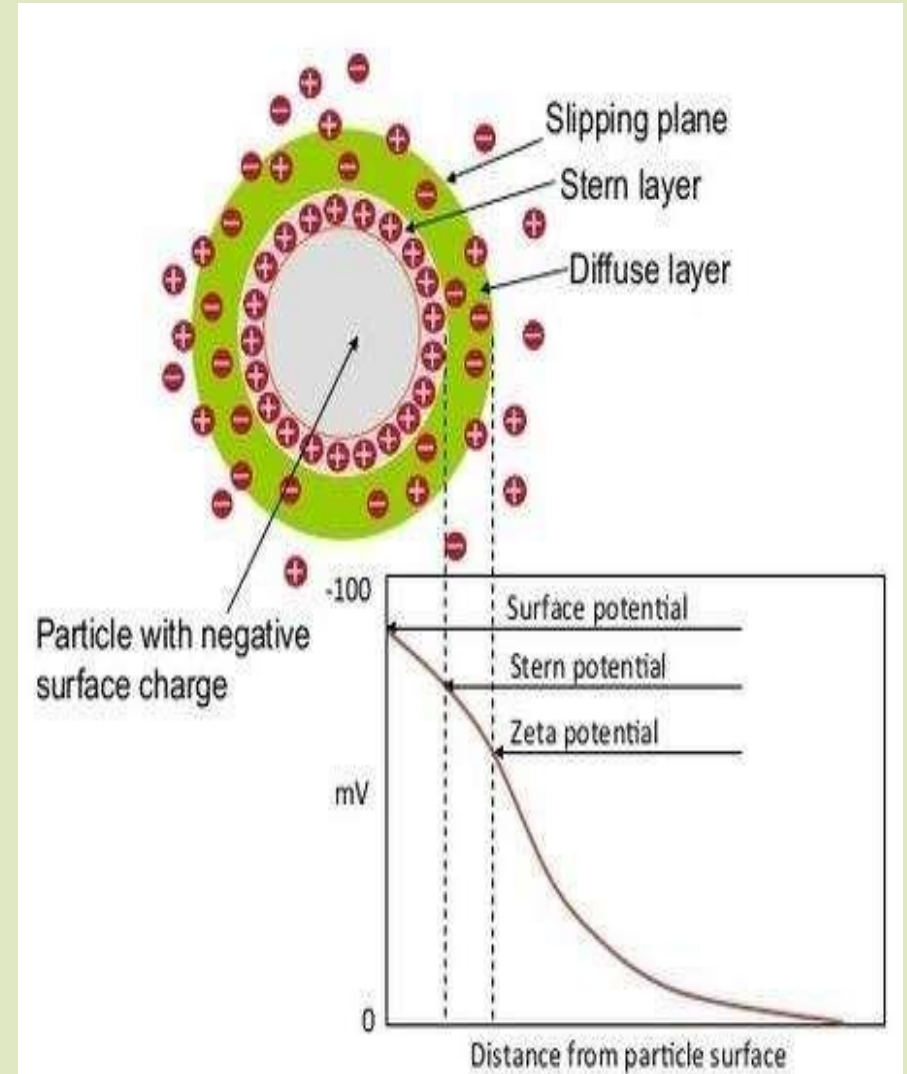
2.RHEOLOGICAL METHOD:-

- It provides information about settling behaviour.
- The arrangement of the vehicle and the particle structural features.
- Brookfield viscometer is used to study the viscosity of the suspension.If viscosity of the suspension increases,the stability of the suspension increases.




3.ELECTROKINETIC METHOD:-

The determination of surface electric charge or zeta potential is helpful to find out the stability of suspension. Zeta potential can be calculated from the migration of particle measured by the electrophoretic method.





4.MICROMERITIC METHOD:-



The stability of suspension depends on the particle size of the disperse phase. The size of the particle in a suspension may grow and ultimately leads to the formation of clumps or caking. So, any change in particle size distribution with reference to time gives a stable suspension. The particle size can be studied by microscopy or coulter-counter method.

EMULSIONS



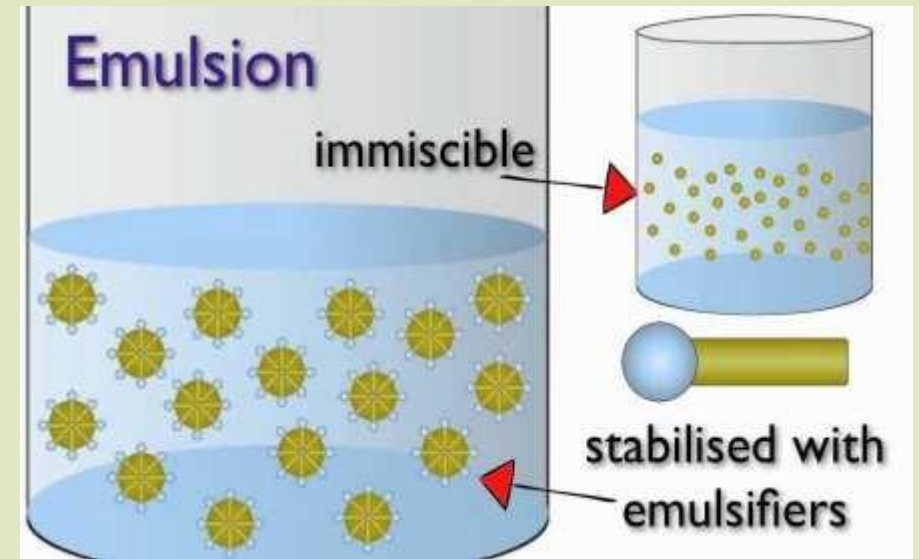
Cream: Oil-in-Water



Butter: Water-in-Oil

DEFINITION:-


An emulsion is defined as a dibasic or heterogenous liquid preparation immiscible liquids which is dispersed as a minute globules in another liquid by adding emulsifying agent.






CLASSIFICATION OF EMULSIONS:-

Emulsions can be classified into the following types:-

1. Oil in water (o/w) type of emulsion.
 2. Water in oil (w/o) type of emulsion.
 3. Microemulsions
 4. Multiple/double emulsion.
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ADVANTAGES:-

- ➡ Mask the unpleasant taste.
 - ➡ Sustained release medication.
 - ➡ Inert and chemically non-reactive.
 - ➡ Reasonably odourless & cost effective.
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DISADVANTAGES:-

- Packing, handling & storage is difficult.
 - Thermodynamically unstable & have short shelf-life.
 - Leads to creaming & cracking.
 - Leads to phase inversion.
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FORMULATION OF EMULSIONS:-

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1. Selection of phases.
 2. Phase volume ratio.
 3. Choice of emulgent.
 4. Antimicrobial agents.
 5. Anti-oxidants.
 6. Viscosifiers/consistency agents.
 7. Colouring agents.
 8. Sweetening agents.
 9. Flavouring agents.
 10. Emulsifying agents.



IDENTIFICATION TESTS:-

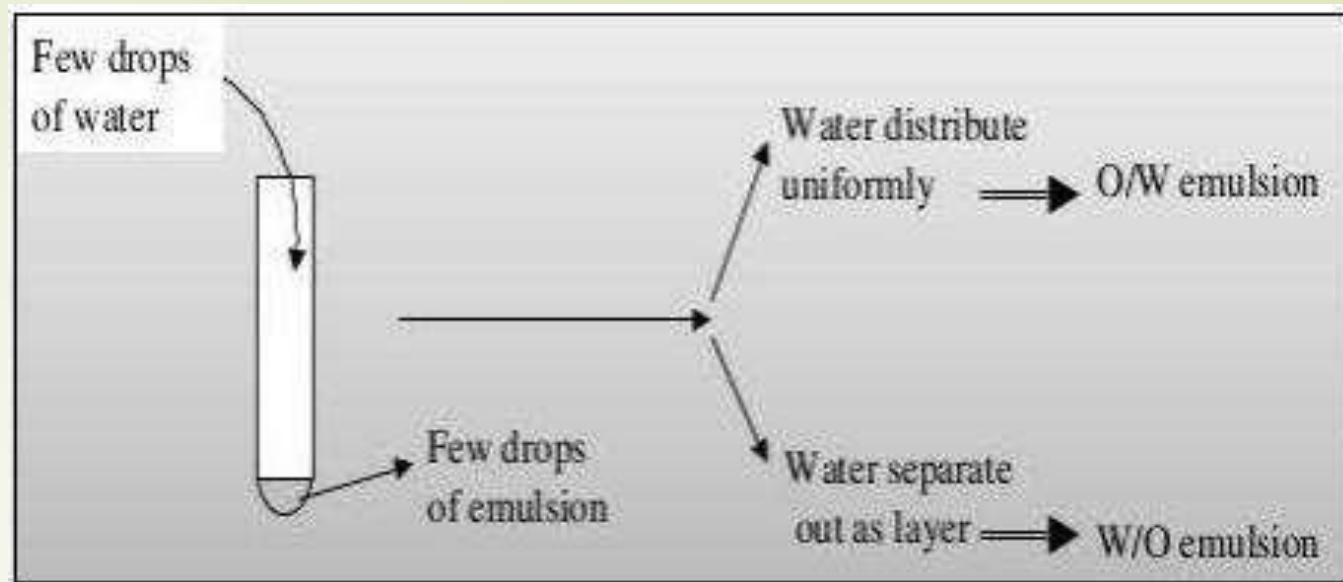
The type of emulsion can be determined by the following tests:-

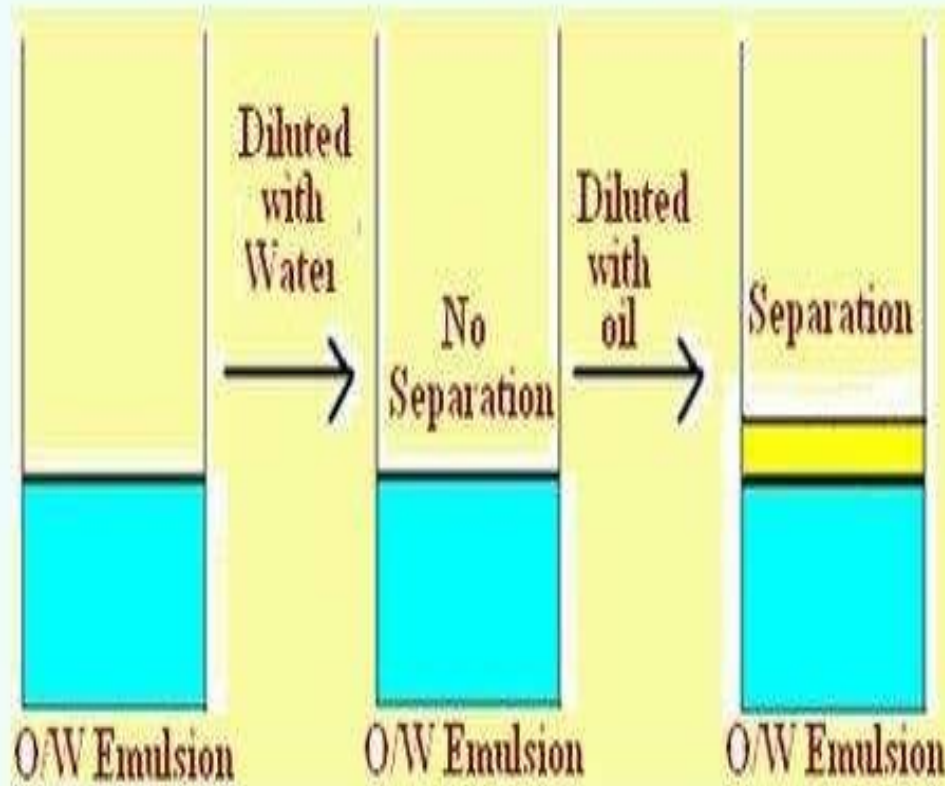
1. Dilution test.
2. Conductivity test.
3. Dye test.
4. Fluorescence test.
5. Cobalt chloride test (CoCl_2).

1.DILUTION TEST:-

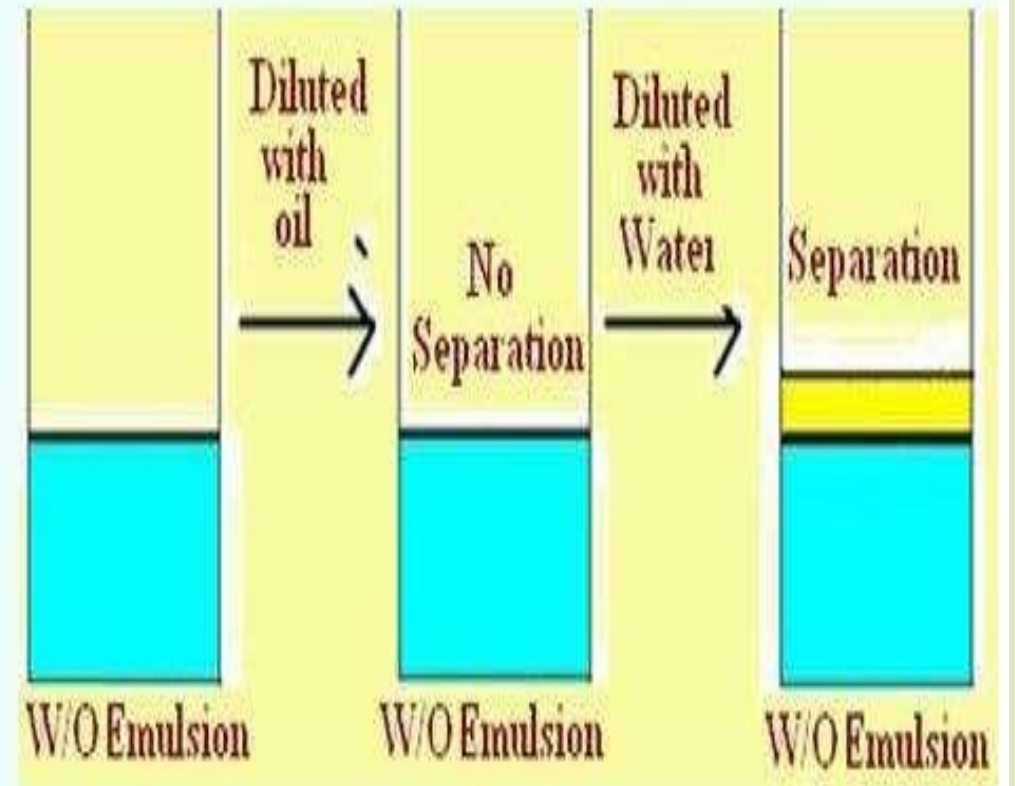
This test is based on the solubility of external phase of emulsion.

- ➡ o/w emulsion can be diluted with water.
- ➡ w/o emulsion can be diluted with oil.





Dilution Test for oil in water emulsion

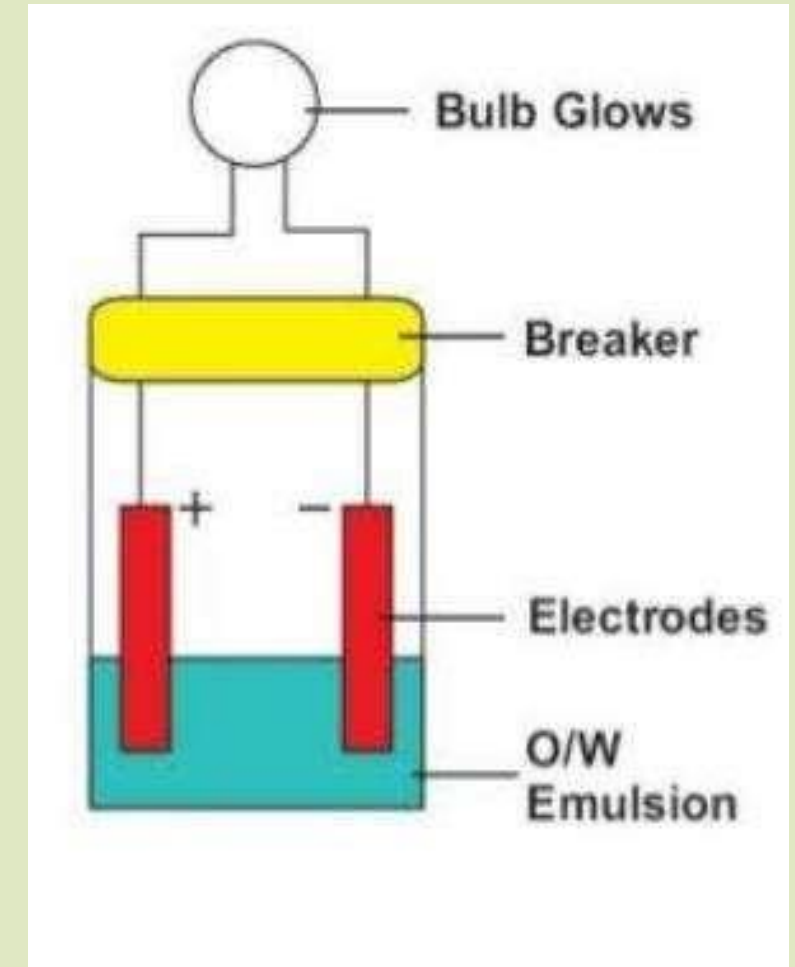


Dilution test for water in oil emulsion

2.CONDUCTIVITY TEST:-

The basic principle of this test is that water is a good conductor of electricity. Therefore in case of o/w emulsion this test will be +ve as water is the external phase.

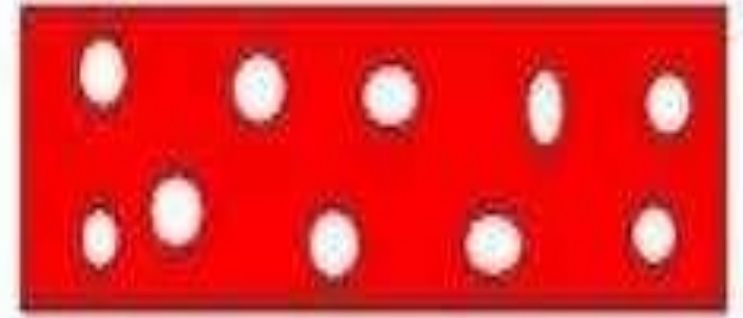
In this test,an assembly is used in which a pair of electrodes connected to an electric bulb is dipped into an emulsion.If the emulsion is o/w type,the electric bulb glows.



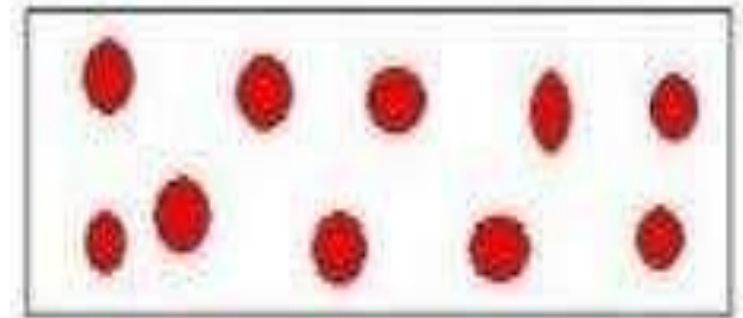
3.DYE TEST:-

When an emulsion is mixed with a water soluble dye such as amaranth and observed under the microscope.

- ➡ If the continuous phase appears red, then it means that the emulsion is o/w type as water is the external phase.
- ➡ If the scattered globules appear red and continuous phase is colourless, then it is w/o type.



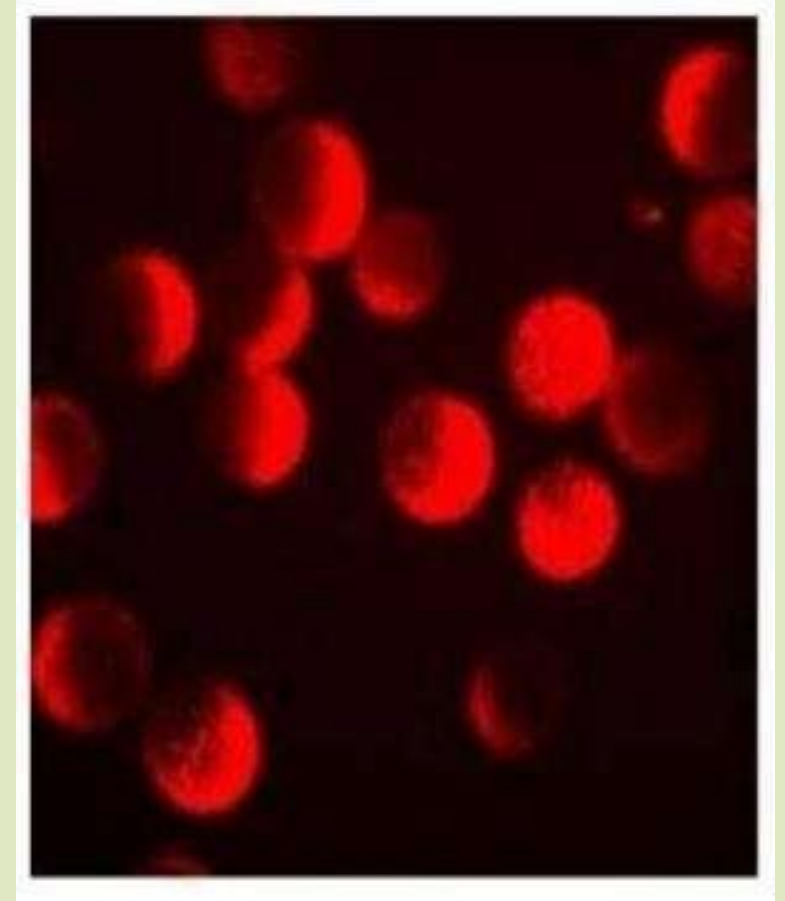
O/W Emulsion



W/O Emulsion

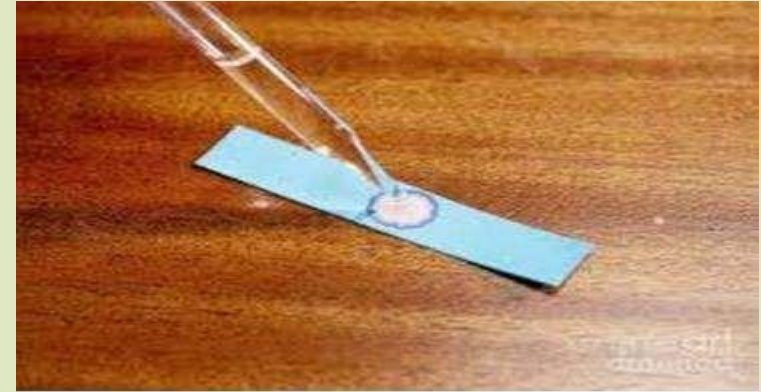
4.FLUORESCENCE TEST:-

Oil gives fluorescence under UV light, while water doesn't. Therefore, o/w emulsion shows spotty pattern when observed under UV, while w/o emulsion fluoresces.



5. COBALT CHLORIDE TEST:-

When a filter paper soaked in cobalt chloride solution is dipped into an emulsion and dried, it turns from blue to pink, indicating that the emulsion is o/w type.




Blue cobalt-chloride paper turning pink in the presence of water






PREPARATION OF EMULSIONS:-

The emulsions are prepared by two methods:-

1. Small scale method
 - a) Dry gum method
 - b) Wet gum method
 - c) Bottle method.
 2. Large scale method.
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EVALUATION OF EMULSIONS:-

1. Size distribution analysis.
 2. Rate of phase separation.
 3. Viscosity & rheological study.
 4. Measurement of dielectric constant.
 5. Conductivity measurement.
 6. Influence of temperature.
 7. Microwave radiation.
 8. Microelectrophoretic measurement.
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STABILITY OF EMULSIONS:-

The following three changes usually occurs during the storage of emulsion:-

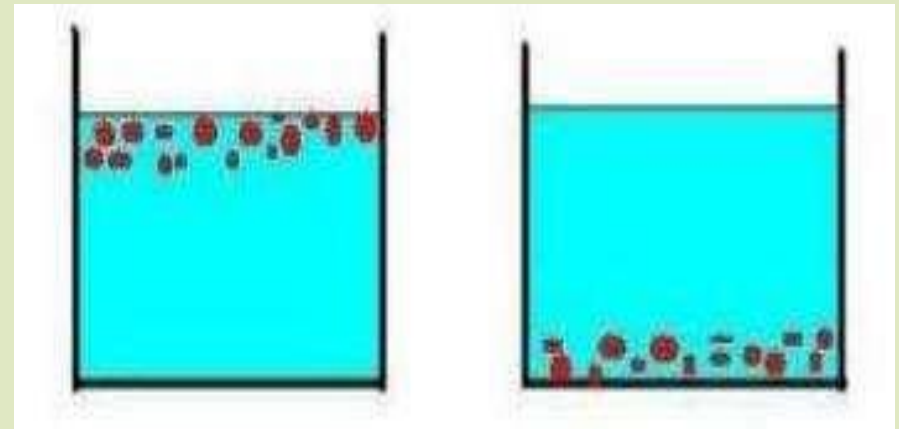
1. Creaming.
 2. Cracking.
 3. Phase inversion.
- 

1.CREAMING:-

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

The creaming depends on "Stokes law", the rate of creaming depends on the various factors.

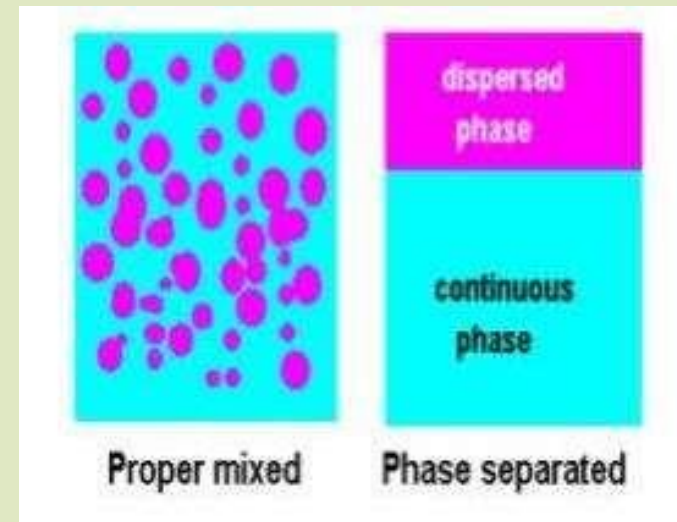
$$V = \frac{2r^2(d_1 - d_2)g}{9\eta}$$



2.CRACKING:-

Cracking means the separation of two layers of dispersed phase and continuous phase due to coalescence of dispersed phase globules. Cracking may be due to the following reasons:-

- a) By addition of emulsifying agent of opposite type.
- b) By decomposition of emulsifying agent.
- c) By addition of common solvent.
- d) By micro organisms.
- e) Changes in temperature.

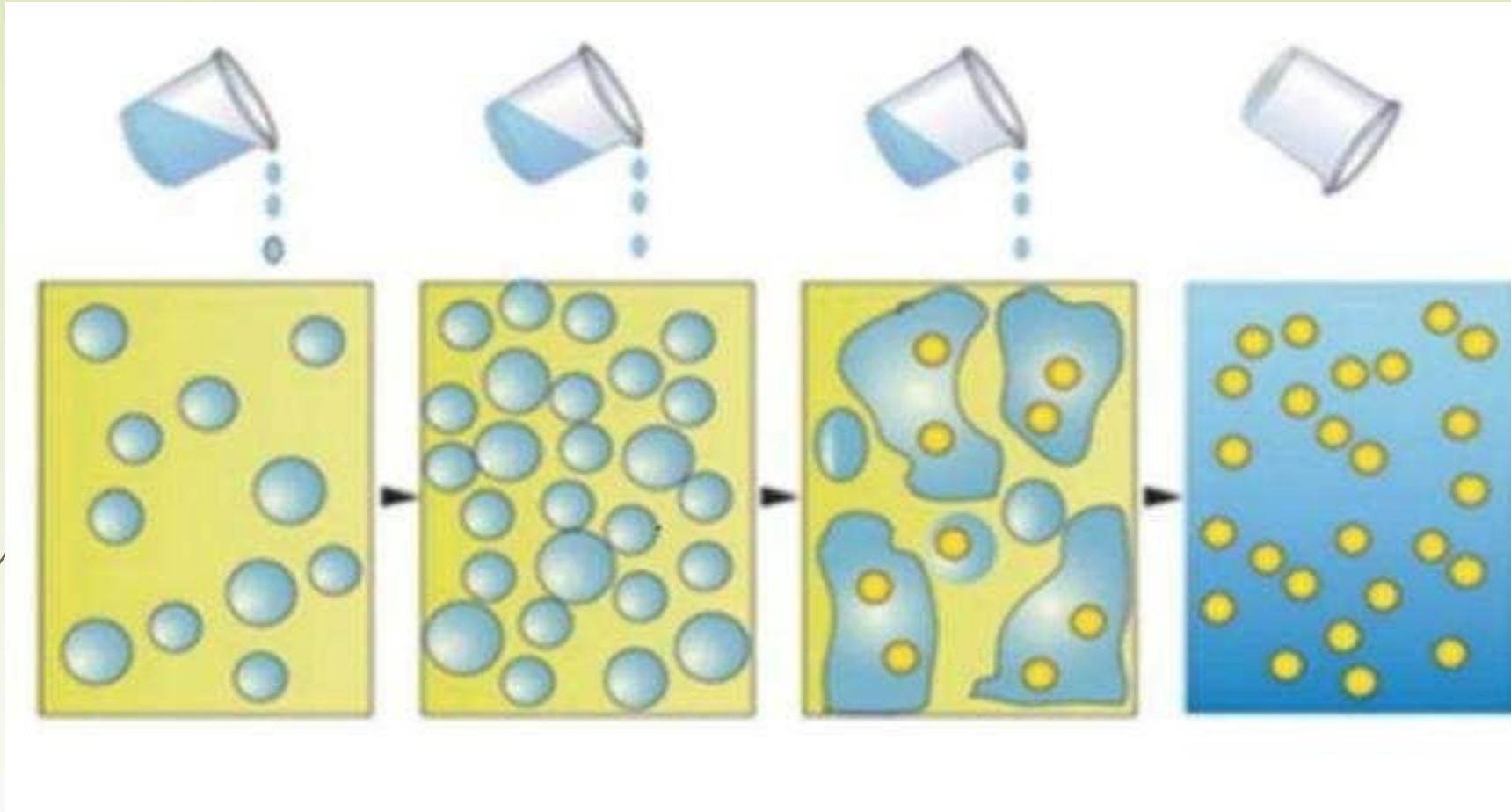




3.PHASE INVERSION:-

Phase inversion means change of one type of emulsion into the other type i.e., o/w emulsion changes into w/o type and vice versa.It may be due to following reasons:-

- a)By the addition of an electrolyte.
- b)By changing the phase volume ratio.
- c)By temperature change.
- d)By changing the emulsifying agent.



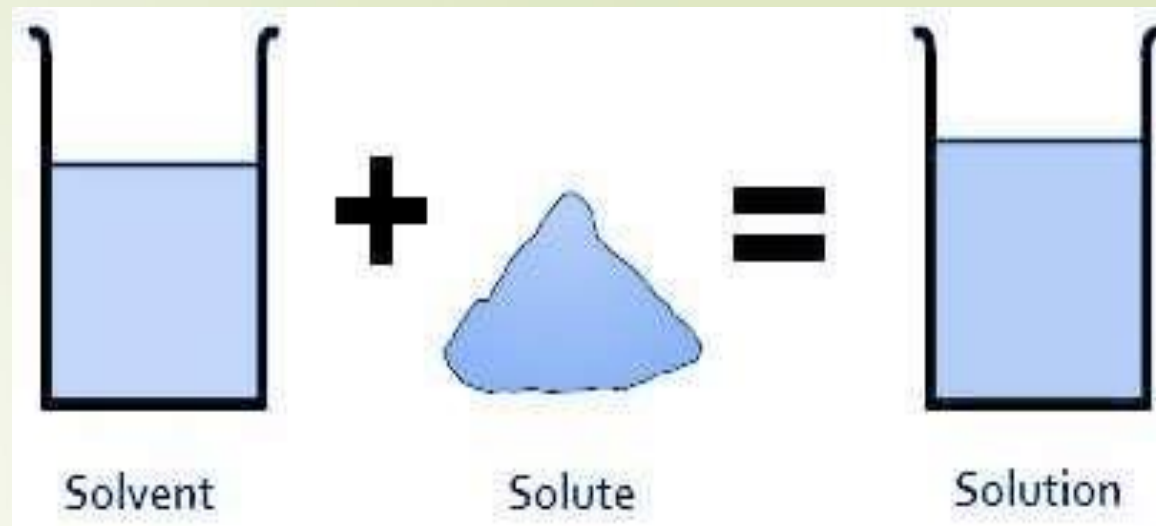
Phase inversion

SOLUTIONS



DEFINITION:-

In pharmaceutical terms, solutions are liquid preparations that contain one or more chemical substances dissolved in a suitable solvent or mixture of mutually miscible solvents.





ADVANTAGES:-

1. Drug available immediately for absorption i.e., bioavailability of solutions is greater than that of oral solid dosage forms.
2. Flexible dosing.
3. Designed for oral route of administration.
4. No need to shake container.
5. Facilitates swallowing in difficult cases.




DISADVANTAGES:-

1. Drug stability reduced in solutions.
2. Bulky,difficult to transport and prone to container breakages.
3. Technical accuracy needed to measure dose on administration.
4. Measuring device is needed for administration.
5. Some drugs are poorly soluble.



CLASSIFICATION OF SOLUTIONS:-

- Oral solutions
 - Oral syrups
 - Oral elixirs
 - Linctus
 - Mouth washes/gargles
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1. ORAL SOLUTIONS:-

- Oral solutions are administered to the GIT to provide absorption of the therapeutic agent.
- Oral solutions formulated over a broad p^H range due to the flexibility of GI environment.
- The usual p^H of oral solutions is about 7.0, unless there are issues regarding the solubility or stability of drugs.



2. ORAL SYRUPS:-

Syrups are highly concentrated aqueous solutions of sugar or a sugar substitute that contain a flavouring agent.

Eg:-Cherry syrup, orange syrup, raspberry syrup.



3. ORAL ELIXIRS:-

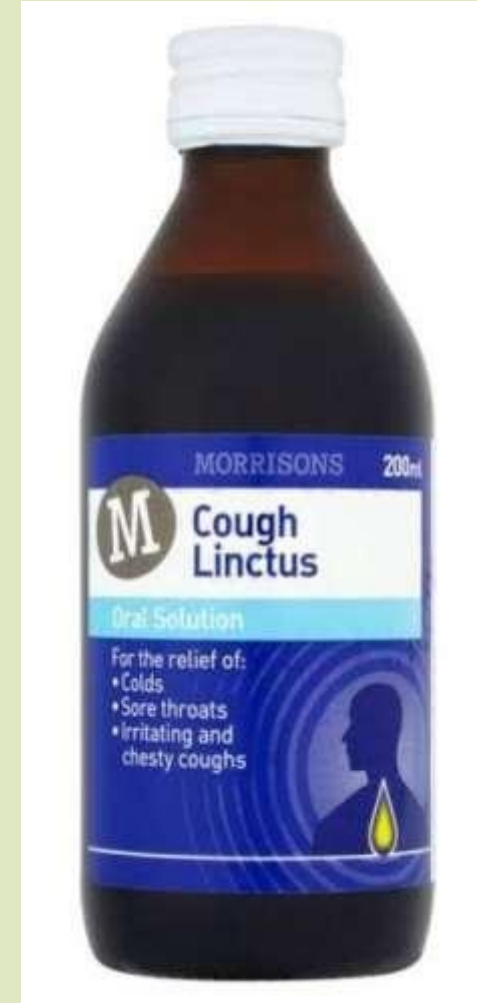
Elixir is a clear, hydroalcoholic solution formulated for oral use. The presence of alcohol in elixirs causes a problem in paediatric formulations and for adults who wish to avoid alcohol. It usually contains:-

- ➡ Purified water
- ➡ Alcohol
- ➡ Polyol cosolvents



4.LINCTUS:-

- A liquid oral preparation used for a demulcent, expectorant or sedative effect in treatment of cough.
- Linctuses are viscous preparations that contain the therapeutic agent dissolved in a vehicle composed of a high percentage of sucrose or other sweetening agents.
- Primarily employed for the treatment of cough, due to their soothing actions on the inflamed mucous membranes.



5.MOUTH WASHES/GARGLES:-

- These are designed for the treatment of infections and inflammation of the oral cavity.
- Formulations designed for this purpose employ water as the vehicle, although a cosolvent (alcohol) may be employed to solubilize the active agent.
- They include preservatives, colouring and flavouring agents and sweetening agents.





STABILITY OF SOLUTIONS:-

Both the chemical and physical stability of solution in their container are important. A solution must retain its initial clarity, colour, odour, taste and viscosity over its allocated shelf life.

Major signs of instability are:-

1. Colour change
2. Precipitation
3. Microbial growth
4. Chemical gas formation.



Thank
you