SHAMBHUNATH INSTITUTE OF PHARMACY, JHALWA, ALLAHABAD

LECTURE NOTES
ON

PHARMACEUTICS -I

UNIT –III

(BP-103T)

B. PHARM. 1st Year 1st Sem

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UNIT III

MONOPHASIC LIQUID DOSAGE FORMS

Liquid Dosage Forms are mainly of two main types:

a) Monophasic
b) Biphasic

Monophasic Liquid Dosage Forms are characterized by the presence of a single homogenous phase. E.g.Solution, waters, tinctures, etc….

DEFINITION AND METHOD OF PREPARATION OF CERTAIN MONPHASIC LIQUIDS:

GARGLES

Gargles are aqueous solutions used for the prevention or treatment of throat infections. Usually they are concentrated solutions and should be diluted with warm water before use. In using the gargles they are brought into intimate contact with the mucous membrane of the throat and are allowed to remain there for a few moments after which they are thrown out of the mouth.

Gargles should be dispensed in white fluted bottles.

e.g. aspirin gargle., Phenol Gargle

Method of Preparation

Phenol Gargle

Formula:

Phenol	16%w/v
Glycerin	75%w/v
Water	q.s. to produce 100ml

The Phenol is dissolved in glycerin and the required quantity of water is added to the mixture to make up the volume. The Formulation is diluted 5 times with potable water prior to use.

MOUTH WASHES

A mouthwash is an aqueous solution similar to a gargle but it is intended to wash the mouth. Mouthwashes are used for their deodorant action, refreshing action or antiseptic effect. They may also contain alcohol, glycerin, synthetic sweeteners, surfactants, flavoring and coloring agents.

Mouthwashes should be dispensed in white fluted bottles.

Eg. Zinc Sulphate and Zinc Chloride Mouthwash and Compound Sodium Chloride Mouthwash.

Method of Preparation

Formula:	
Potassium Bicarbonate	20 g
Sodium Borate	20 g
Thymol	0.5 g
Eucalyptol	1.0 ml
Alcohol	50 ml
Glycerin	100 ml
Purified Water, q.s.	
To make	1000 ml

Dissolve the potassium bicarbonate and sodium borate in 100ml purified water, add the glycerin when effervescence has ceased, add the mixture to 500ml purified water. Dissolve the other ingredients in the alcohol, and add the solution of salts to the alcoholic solution with agitation. Then add sufficient quantity of purified water to make the product measure 1000ml. Allow the mixture to stand, with occasional shaking during 24 hours. Filter using talc, if necessary to produce a clear solution.

THROAT PAINTS

Paints or Throat Paints are simple solutions of substances in a viscous solvent such as glycerin and liquid paraffin. A viscous solvent retains the medicament *in situ* for appreciable length of time after the preparation is applied. Throat paints are usually glycerin based as it possesses agreeable taste in addition to viscosity.

Egs. Iodine Throat Paint and Iodine Potassium Throat Paint, Mandl's Paint (Compound Iodine Paint).

Method of Preparation

Mandls Paint
Formula:
Potassium iodide 25g
Iodine 12.5g
Alcohol 90%v/v 40ml
Water 25ml
Peppermint oil 4ml
Glycerol up to 1000ml

Preparation:
(i) Potassium iodide is dissolved in water.
(ii) Iodine is added in the concentrated potassium iodide solution.
(iii) Peppermint oil is dissolved in alcohol 90%v/v and the alcoholic solution is added to the iodine solution.
(iv) Volume is made up with glycerin.

EAR DROPS

Ear drops are the solutions of drugs that are installed in to the ear with a droper. These are generally used for cleaning the ear, softeneing the wax and for treating the mild infection.

Ear drops are a form of medicine used to treat or prevent ear infections, especially infections of the outer ear and ear canal (otitis externa). Ear drops are solutions / suspensions of medicines in solvents like water, glycerol, diluted alcohol, or propylene glycol. These solutions can be instilled into the ear. For these ear drops to be effective sufficient contact time should be provided.

Method of Preparation

Sodium Bicarbonate Ear Drops B.P.
Formula:

Sodium bicarbonate	5g
Glycerol	30ml

Purified water (freshly boiled and cooled) q.s. to produce100 ml
Preparation:
Dissolve the sodium bicarbonate in about 60 ml of purified water; add the glycerol and sufficient Purified Water to produce 100 ml and mix.

NASAL DROPS

Nasal drops and liquid nasal sprays are solutions, emulsions or suspensions intended for instillation or spraying into the nasal cavities. Nasal drops are the solutions of drugs that are instilled in to the nose with a dropper. These are usually aqueous and not oily drops since the latter inhibits the movements of cilia in the nasal mucosa and if used for the long periods may reach the lungs and cause lipoid pneumonia. Nasal drops or sprays are used as local treatments for conditions such as nasal congestion and allergic rhinitis. In some situations, the nasal delivery route is preferred because it provides an agreeable alternative to injection or pills. Substances can be assimilated extremely quickly and directly through the nose. Many pharmaceutical drugs exist as nasal sprays for systemic administration (e.g. treatments for pain, migraine, osteoporosis and nausea). Other applications include hormone replacement therapy, treatment of Alzheimer's disease and Parkinson's disease. Nasal sprays are seen as a more efficient way of transporting drugs with potential use in crossing the blood–brain barrier.

Method of Preparation

Ephedrine Nasal Drops B.P.C.

Formula:

Ephedrine Hydrochloride	0.5 g
Chlorbutol	0.5 g
Sodium Chloride	0.5 g
Purified water	q.s. to produce100 ml

Preparation:

About 40 ml of water is heated and then the chlorbutol powder is added and triturated in a mortar and pestle. The solution is cooled and then the Sodium Chloride and Ephedrine powder in required quantity are added into the solution and triturated to ensure complete dissolution. The Solution prepared is filtered and then the volume is made up.

ENEMA

Enema is a fluid injected into the lower bowel by way of the rectum. The most frequent use of an enema is to relieve constipation or for bowel cleansing before a medical examination or "procedure". An enema may also be employed to check diarrhea, as a vehicle for the administration of food, water or medicine, as a stimulant to the general system, as a local application and, more rarely, as a means of reducing temperature.

Method of Preparation

Sodium Butyrate Enema

Formula:

Sodium Acetate	8.16 gm
Sodium Propionate	4.8 g
Sodium Butyrate	2.8 gm
Sodium Chloride	2.5 gm
Purified water	q.s. to produce1000 ml

Preparation:

Sodium Propionate, Sodium Butyrate and Sodium Acetate are taken together and then triturated in a mortar and pestle. Water in sufficient quantity is added to bring about solution. The Sodium Chloride is then added and the resulting solution is filtered and the volume made up with purified water.

SYRUPS

- *Syrups* are concentrated, aqueous preparations of a sugar or sugar-substitute with or without added flavoring agents and medicinal substances.
- Syrups containing flavoring agents but not medicinal substances are called *flavored vehicles* (syrups).e..g Cherry Syrup, Cocoa Syrup, Orange syrup, Raspberry Syrup.
- Syrups containing medicinal agents are called *medicated syrups*. e.g. Chlorpheniramine maleate syrup, Ipecac syrup, Chloral hydrate syrup etc.

Components of syrups

Most syrups contain the following components in addition to the purified water and any medicinal agents present:

1. the sugar, usually sucrose, or sugar substitutes used to provide sweetness and viscosity,
2. antimicrobial preservatives,
3. flavorants, and
4. colorants.

Sucrose and non-sucrose based syrup

Sucrose is most frequently employed in syrups. In special circumstances it may be replaced by sugars, such as, *dextrose*, or non-sugars as *sorbitol, glycerin* and *propylene glycol*.

Methyl cellulose or hydroxyethyl cellulose –these two materials are not hydrolyzed and absorbed into the blood stream, and their use results in an excellent syrup-like vehicle.

Taste masking by syrup

The syrup imparts a characteristics "body" (viscosity) and together with the sweetness and the flavorants results in a type of pharmaceutical preparation that is quite effective in making the taste of added medicinal agents. When the syrup is swallowed, only a portion of dissolved drug actually makes contact with the taste buds, the remainder of the drug being carried past them and down the throat in the containment of the viscous syrup.

In the case of antitussive syrups (e.g. linctus) the thick sweet syrup has a soothing effect on the irritated tissues of the throat as it passes over them.

Simple syrup USP-NF contains 85% w/v sucrose (64.74%w/w). At this concentration the syrup is resistant to microbial growth, due to unavailability of the water required for the growth of micro-organisms. Syrup IP is a solution containing 66.7% w/w Sucrose.

Only a very slight excess of water (46.3 – 42.5 = 3.8 ml per 100 ml of syrup) is employed in the preparation of syrup. The sight excess of water permits the syrup to remain physically stable under conditions of varying temperature.

If the syrup were completely saturated with sucrose, under cool storage conditions some sucrose might crystallize from solution and, by acting as nuclei, initiate a type of chain reaction that would result in the separation of an amount of sucrose disproportionate to its solubility at the storage temperature. The syrup would then be very much unsaturated and probably suitable for

microbial growth. However, the syrup NF is stable and resistant to crystallization as well as to microbial growth.

Preparation of Syrups

Syrups are frequently prepared by one of four general methods; depending upon the physical and chemical characteristics of the ingredients.

1. Solution of the ingredients with the aid of heat
2. Solution of the ingredients by agitation without the use of heat
3. Addition of sucrose to a prepared medicated liquid or to a flavored liquid and
4. by percolation of either the source of the medicating substance or of the sucrose.

Solution with the aid of heat

The sugar is generally added to the purified water, and heat is applied until solution is effected. Then other required heat-stable components are added to the hot syrup, the mixture is allowed to cool, and its volume is adjusted to the proper level by the addition of Purified Water.

The use of heat facilitates the rapid solution of the sugar as well as certain other components of syrups.

If excessive heating occurs then sucrose may be hydrolyzed into dextrose (D-glucose), and fructose (levulose). This hydrolytic reaction is referred to as *inversion*, and the combination of the two monosaccharides is *invert sugar*. When heat is applied in the preparation of a sucrose syrup, some inversion of the sucrose is almost certain. The speed of inversion is greatly increased by the presence of acids, the hydrogen ion acting as a catalyst to reaction.

Solution by agitation without heat

Sucrose and other formulation agents may be dissolved in purified water by placing the ingredients in a vessel of greater capacity than the volume of syrup to be prepared, thus permitting the thorough agitation of the mixture.

Addition of sucrose to a medicated liquid or to a flavored liquid

Medicated liquid such as tincture or fluid extract is employed as the active ingredient in the preparation of syrup.

If the extract contains alcohol soluble ingredients and the alcohol amount is high then sucrose is added directly and stirred.

If alcohol content is low and all the ingredients are water soluble then the liquid extract is directly mixed with prepared syrup.

Preparation of syrup by percolation

In this method purified water or an aqueous solution is passed slowly through a bed of crystalline sucrose, thus dissolving it and forming the syrup. If required a poriton of the percolate is recycled.

ELIXIRS

Elixirs are clear, liquid, oral preparations of potent or nauseous drugs. They are pleasantly flavoured and usually attractively coloured and are very stable.

- Elixirs usually contains *potent drugs*, such as antibiotics, antihistamines and sedatives.
- *Vehicles* used in elixirs are alcohol, glycerol and propylene glycol.
  They are used

  (i) for the production of clear solution. Essential oils from flavoring agents may produce faint opalescence, hence alcohol 10 – 20% is useful for keeping oils in solution.

  (ii) When potent medicaments of low solubility is required to be dispensed, a mixture of solvents that will give complete solution is used.

  e.g. Phenobarbitone is virtually insoluble in water but a clear product can be made by dissolving it in alcohol and then diluting with glycerol and water.

  e.g. One part of paracetamol is soluble in 70 parts of water, 7 parts of alcohol, 9 parts of propylene glycol or 40 parts of glycerol. In paracetamol elixir a mixture of alcohol, propylene glycol and glycerol is used as vehicle.

Other adjuncts used are:

(i) *Chemical stabilizers*

e.g. Neomycin Elixir B.P.C. is adjusted to pH 4 to 5 with citric acid to minimize the darkening that occurs on storage.

e.g. Disodium edetate should be incorporated to sequester heavy metals that catalyse decomposition of antibiotic.

(ii) *Colouring agents*

e.g. Amaranth	Magenta red
Tartrazine	Saffron
Green S	Green

(iii) *Sweetening agents*

e.g. Sucrose syrups, glycerol, sorbitol solution, invert syrup and saccharin sodium are used.

(iv) *Flavours*

e.g. Blackcurrant Syrup in Chloral Elixir

Concentrated Raspberry Juice with invert syrup

Lemon spirit with syrup and invert syrup.
Compound Orange Syrup

(v) *Preservatives*

- 20% alcohol, propylene glycol or glycerol are preservative
- Syrup is self-preservative due to high osmotic pressure
- The most common additional preservative in chloroform; it is used in the form of double strength water.
- Sometimes the preparations contain benzoic acid and methyl parahydroxy benzoate.

Method of Preparation:
Aromatic Elixir USP

Formula:

Compound Orange Spirit	10 ml
Syrup	375 ml
Talc	30 g
Alcohol	240ml
Purified Water, each q.s.	
To make	1000ml

Preparation:
Add to the Compound Orange Spirit sufficient quantity of alcohol to make 250ml, add to this the syrup in several portions, agitating vigorously after each addition and then add in the same manner the required quantity of purified water. Mix the talc with the liquid and filter through a filter wetted with diluted alcohol, returning the filtrate until a clear liquid is obtained.

LINIMENTS

Liniments are liquid, semi-liquid or occasionally semi-solid preparations intended for application on the skin. Liniments must be applied **by rubbing with friction**.
They may be alcoholic or oily solutions or emulsions.
Most are massaged onto the skin e.g. counter-irritant type.
Some are applied on warm dressing or with a brush. e.g. analgesic and soothing type.
Liniments must not be applied to broken skin because they would be very irritating.

e.g. Soap Liniment BPC
Camphor Liniment BP
Methyl salicylate liniment BPC

Alcohol is the main *vehicle*. In increases the penetration of counter-irritant molecules through skin.

Method of Preparation

Camphor Liniment

Formula:

Camphor	200 g
Cottonseed Oil	800 g
To make	1000 g

Preparation

Place the cottonseed oil into a suitable dry flask or bottle, heat on a steam bath, add camphor and stopper the container securely. Agitate to dissolve the camphor without further heating.

LOTIONS

Lotions are liquid preparations for external application **without friction**.
They are either dabbed on the skin or applied on a suitable dressing and covered with water proof material to reduce evaporation.

e.g. Zinc sulfate and salicylic acid for ulcer
Salicylic acid lotion for dandruff
Salicylic acid and mercuric chloride lotion for follicular infection

N.B. Copper and Zinc sulfate have astringent action.
Salicylic acid has keratolytic action.

Method of Preparation:

Calamine Lotion

Formula:

Calamine	150g
Zinc Oxide	50g
Glycerin	50ml
Bentonite	30gm
Sodium Citrate	5gm
Liquified Phenol	5ml
Rose Water	q.s. (To make 1000ml)

Preparation:

Dissolve the Sodium citrate in a small volume of rose water. Mix the powders (Calamine, Zinc Oxide and Bentonite) intimately with the above solution by triturating. Required quantity of liquefied phenol and glycerin are added to the above mixture and the the final volume is made up by using rose water.

BIPHASIC LIQUID DOSAGE FORMS

Biphasic systems consist of two distinct phases:

- the substance that is dispersed known as the dispersed (or) internal phase,
- and a continuous (or) external phase.

SUSPENSION

Suspension are the biphasic liquid dosage form of medicament in which the finely divided insoluble solid material suspended in a liquid medium. The average size of suspended particles ranges from 0.5 μm to 5.0 μm in most of the pharmaceutical suspension.

Reasons for the formulation of a pharmaceutical suspension:

– The drug is insoluble in the delivery vehicle.
– To mask the bitter taste of the drug.
– To increase drug stability.
– To achieve controlled/sustained drug release.

Classification:

Based On General Classes

1. Oral suspension- eg: Paracetamol suspension antacids, Tetracycline HCl.
2. Externally applied suspension- eg :Calamine lotion.
3. Parenteral suspension- eg: Procaine penicillin G, Insulin Zinc Suspension

Based on Proportion of Solid Particles

1. Dilute suspension (2 to10%w/v solid)- eg: cortisone acetate, predinisolone acetate
2. Concentrated suspension (50%w/v solid)- eg: zinc oxide suspension

Based on Electrokinetic Nature of Solid Particles

1. Flocculated suspension
2. Deflocculated suspension

Summary of flocculated and deflocculated suspension

Flocculated Suspension	Deflocculated Suspension
1. Particles are loose aggregates.	1. Individuals particles exists as separate entity.
2. The rate of sediment is high.	2. The rate of sediment is slow.
3. Supernatant is clear.	3. Supernatant is cloudy.
4. Particle experience attractive forces.	4. Particle experience repulsive forces.
5. Sediment is easy to redisperse.	5. Sediment is difficult to redisperse.
6. Does not form a hard cake.	6. Hard cake is formed.
7. Sediment is rapidly formed.	7. Sediment is slowly formed.
8. Sediment is loosely packed.	8. Sediment is very closely packed.

9. Suspension is not pleasing in appearance.	9. Suspension is pleasing in appearance.

Features Desired In Pharmaceutical Suspensions:

- The suspended particles should not settle rapidly and sediment produced, must **be easily re-suspended** by the use of moderate amount of **shaking**.
- It should be easy to pour yet **not watery** and **no grittiness.**
- It should have **pleasing odour** , **colour and palatability**.
- Good **syringeability**.
- It should be **physically, chemically and microbiologically stable**.
- Parenteral /Ophthalmic suspension should be sterilizable.

PREPARATION

The formulation of a suspension depends on whether the suspension is flocculated or deflocculated.

Three approaches are commonly involved

1. Use of structured vehicle
2. Use of controlled flocculation
3. Combination of both of the methods

1. Structured vehicle

- Structured vehicles are also called as **thickening** or **suspending agents**.
- They are aqueous solutions of natural and synthetic gums.
- These are used to **increase** the **viscosity** of the suspension.
- It is applicable only to deflocculated suspensions.
  e.g. methyl cellulose, sodium carboxy methyl cellulose, acacia, gelatin and tragacanth.
- These structured vehicles entrapped the particle and reduces the sedimentation of particles.
- Thus, the use of deflocculated particles in a structure vehicle may form solid hard cake upon long storage.
- Too high viscosity is not desirable as:
  a) It causes difficulty in pouring and administration.
  b) It may affect drug absorption since they **adsorb on the surface of particle and suppress the dissolution rate.**
- Structured vehicle is not useful for **Parenteral suspension** because they may create problem in **syringeability** due to high viscosity.

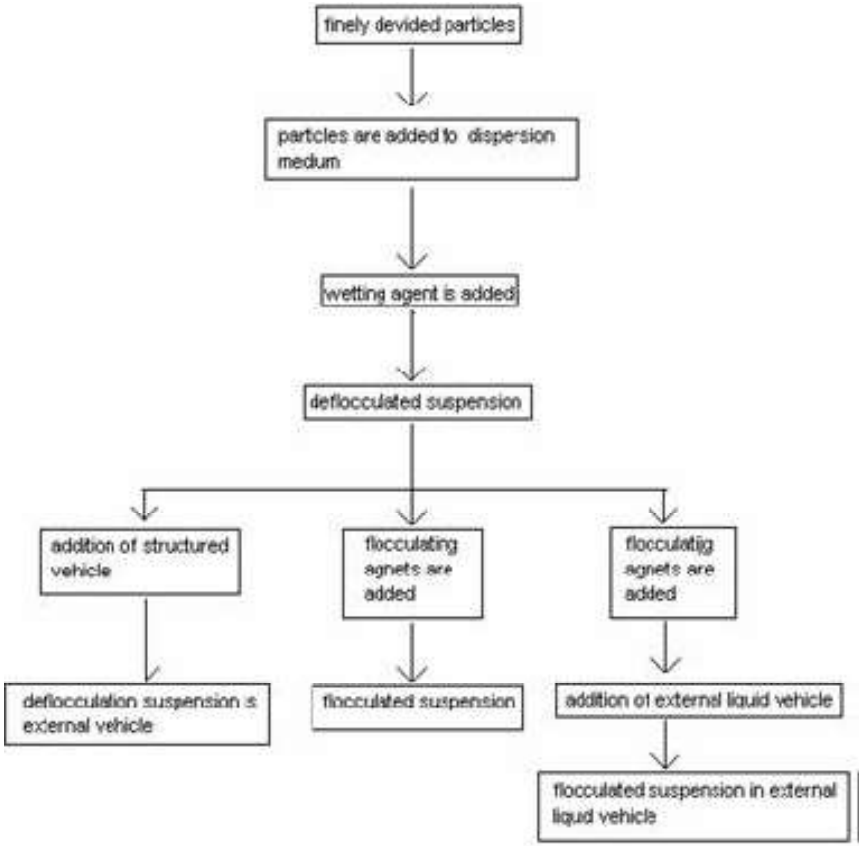
2. Controlled flocculation

- Controlled flocculation of particles is obtained by adding flocculating agents, which are:
  (1) electrolytes
  (2) surfactants
  (3) polymers

3. Flocculation in structured vehicles

- Sometimes suspending agents can be added to flocculated suspension to retard sedimentation.
- Examples of these agents are:
  Carboxymethylcellulose (CMC),
  Carbopol 934,
  Veegum, and bentonite

Flow chart of formulation of suspension



INGREDIENTS FOR FORMULATION OF SUSPENSIONS:

VEHICLE:

- Vehicles, in pharmaceutical formulations, are the liquid bases that carry drugs and other excipients in dissolved or dispersed state.
- Pharmaceutical vehicles can be classified as under;
  Aqueous vehicles: Water, hydro-alcoholic, polyhydric alcohols and buffers.
  These may be thin liquids, thick syrupy liquids, mucillages or hydrocolloidal bases.
  Oily vehicles: Vegetable oils, mineral oils, organic oily bases or emulsified bases.
- The most commonly used solvents are alcohol, glycerin, polyethylene glycol and polypropylene glycol.
- The mechanism by which they provide wetting is that they are miscible with water and reduce liquid air interfacial tension.
- Liquid penetrates in individual particle and facilitates wetting.

SUSPENDING AGENTS:

- Suspending agents are also known **as hydrophilic colloids** which form colloidal dispersion with water and increase the viscosity of the continous phase.
- Suspending agent form film around particle and decrease interparticle attraction.
- Most suspending agents perform two functions i.e. besides **acting as a suspending agent** they also **imparts viscosity to the solution,** and thus retard particle sedimentation.
- The selection of an appropriate suspending agent is crucial in formulating a pharmaceutical suspension.
- Suspending agents can be classified into cellulose derivatives, clays, natural gums, and synthetic gums.

Stability pH range and concentrations of most commonly used suspending agents.

Suspending agents	**Stability pH range**	**Concentrations used as suspending agent**
Sodium alginate	4-10	1–5 %
Methylcellulose	3-11	1–2 %
Hydroxyethyl cellulose	2-12	1-2%
Hydroxypropyl cellulose	6-8	1-2%
Hydroxypropyl methylcellulose	3-11	1-2%
CMC	7-9	1-2%
Colloidal silicon dioxide	0-7.5	2-4 %

WETTING AGENTS:

- *Wetting agents* – are used in liquid dosage forms to create a homogenous dispersion of solid particles in a liquid vehicle.
- Wetting agents are Surfactants (HLB Value 7 to 9) that when dissolved in water, lower the contact angle and aid in spreadability of water on the particles surface to displace the air layer at the surface and help in wetting and solubilization
- Hydrophilic materials are easily wetted by water while hydrophobic materials are not.
- However hydrophobic materials are easily wetted by non-polar liquids.
- The extent of wetting by water is dependent on the hydrophillicity of the materials.
- If the material is more hydrophilic - less difficulty in wetting by water.
- The concentration used is less than 0.5 %.
- Eg. Tweens, spans, poloxamers.

EVALUATION OF SUSPENSIONS:

- Sedimentation method
- Rheological method
- Electro kinetic method
- Micromeritic method
- pH measurement
- Visual inspection

Sedimentation method:

Two parameters are studied for determination of sedimentation.

1. Sedimentation volume,
2. Degree of flocculation.

1. Sedimentation volume:

- Sedimentation volume is a ratio of the ultimate volume of sediment (Vu) to the original volume of sediment (Vo) before settling.

$$\mathbf{F = V\,u\,/\,Vo}$$

Where, Vu = final or ultimate volume of sediment

VO = original volume of suspension before settling

- F has values ranging from less than one to greater than one.
- When F < 1 ⟶ Vu < Vo
- When F =1 ⟶ Vu = Vo
  The system is in flocculated equilibrium and show no clear supernatant on standing
- When F > 1 Vu > Vo
  Sediment volume is greater than the original volume due to the network of flocs formed in the suspension and so loose and fluffy sediment

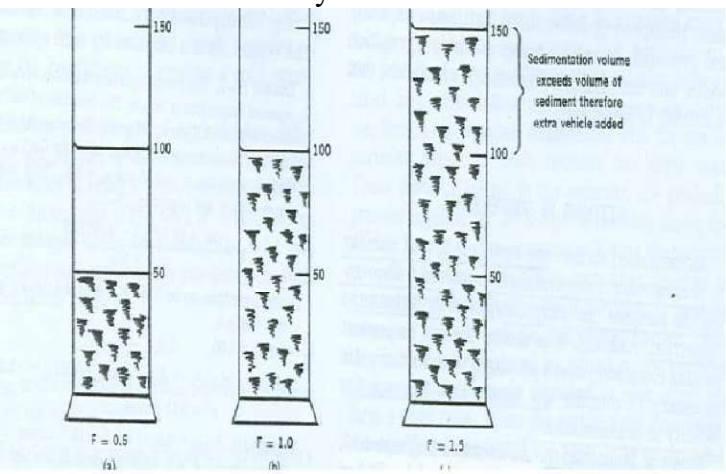


Fig: Suspensions quantified by sedimentation volume (f)

- The suspension formulation (50mL) was poured separately into 100 mL measuring cylinder and sedimentation volume was read after 1, 2, 3 and 7 days and thereafter at weekly intervals for 12 weeks.
- Triplicate results were obtained for each formulation.
- Sedimentation volume was calculated according to the equation:

$$\mathbf{F = Vu/Vo}$$

Where, F = sedimentation volume, Vu = ultimate height of sediment and Vo=initial height of total suspension

2. Degree of flocculation (β):

- It is the ratio of the sedimentation volume of the flocculated suspension ,F , to the sedimentation volume of the deflocculated suspension, F∞

$$ß = F / F\infty$$

$$ß = \frac{\text{(Vu/Vo) flocculated}}{\text{(Vu/Vo) deflocculated}}$$

- The minimum value of ß is 1,when flocculated suspension sedimentation volume is equal to the sedimentation volume of deflocculated suspension.

Rheological method:

- It provides information about settling behavior.
- The arrangement of the vehicle and the particle structural features.
- Brookfield viscometer is used to study the viscosity of the suspension
- It is mounted on heli path stand and using T-bar spindle.
- T-bar spindle is made to descend slowly into the suspension and the dial reading on the viscometer is then a measure of the resistance the spindle meets at various levels.
- This technique also indicates at **which level of the suspension the structure is greater owing to particle agglomeration.**
- The dial reading is plotted against the number of turns of the spindle.
- The better suspension show a lesser rate of increase of dial reading with spindle turns, i.e. the curve is horizontal for long period.

Electro kinetic method

- Measurement of Zeta-potential using Micro electrophoresis apparatus & ZetaPlus (Brookhaven Instruments Corporation, USA)
- It shows the stability of a disperse system.

Zeta potential

- The zeta potential of the formulated suspensions was determined using a ZetaPlus (Brookhaven Instruments Corporation, USA).
- Approximately 1mL of suspension was transferred into a plastic Cuvette using a pipette and diluted with distilled water.
- The Brookhaven zeta potential software was used for the measurement.
- Parameters set to a temperature of 25^0 C and refractive index(1.33)
- The zeta potential of the formulations was determined on day 0, 7, 14, 21 and day 28 post formulation.

Micromeritic method:

- The stability of suspension depends on the **particle size of the dispersed phase.**
- Change in the 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 studied by –
  -microscopy
  -coulter counter method

pH measurement:

- The measurement and maintenance of pH is also very important step in the Quality control testing
- Generally there are 2 different types of methods used in the measurement of pH.

Methods for pH measurement:

- The simplest and cheapest is to dip a piece of pH paper into the sample.
- The paper is impregnated with chemicals that change color and the color may be compared to a chart supplied with the paper to give the pH of the sample.
- If greater accuracy is required a pH meter should be used.
- A typical pH meter consists of a special measuring glass electrode connected to an electronic meter that measures and displays the pH reading.

Visual inspection:

- With visual inspection, the ingredients and the final products are carefully examined **for purity and for appearance.**
- Physical appearance of products for patient adherence and compliance is critical so it should be: -Good looking
  -Elegance in appearance.

EMULSIONS

- An emulsion is a biphasic system in which one phase is intimately dispersed in the other phase in the form of minute droplets ranging in diameter from **0.1 µm to 100 µm.**
- It is **thermodynamically unstable** system, which can be stabilized by the presence of an emulsifying agent.
- The **dispersed phase** is also known as **internal phase** or the **discontinuous phase**
- The **outer phase** is called **dispersion medium, external phase** or **continuous phase.**
- **Emulsifying agent** is also known as **intermediate** or **interphase**.

Classification of emulsions:

- Based on **dispersed phase**:

  Oil in Water (O/W): Oil droplets dispersed in water

  Water in Oil (W/O): Water droplets dispersed in oil

- Based on **size of liquid droplets:**

  0.2 –50 mm **Macroemulsions** (Kinetically Stable)

0.01 –0.2 mm **Microemulsions** (Thermodynamically Stable)

TEST FOR 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. Oil in water emulsion can easily be diluted with an aqueous solvent whereas water in oil emulsion can be diluted with a oily liquid.

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 positive 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.

(a) o/w type emulsion (b) w/o type emulsion

3. **Dye Solubility Test**:

In this test an emulsion is mixed with a water soluble dye (amaranth) and observed under the microscope. If the continuous phase appears red, it means that the emulsion is o/w type as water is in the external phase and the dye will dissolve in it to give color. If the scattered globules appear red and continuous phase colorless, then it is w/o type. Similarly if an oil soluble dye (Scarlet red C or Sudan III) is added to an emulsion and the continuous phase appears red, then it is w/o emulsion.

4. **Cobalt Chloride Test**:

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

5. **Fluorescence Test**:

If an emulsion on exposure to ultra-violet radiations shows continuous fluorescence under microscope, then it is w/o type and if it shows only spotty fluorescence, then it is o/w type.

Emulsifying Agents:

- It is a substance which stabilizes an emulsion.
- Pharmaceutically acceptable emulsifiers must also:

- be stable
- be compatible with other ingredients
- be non –toxic
- possess little odor , taste , or color .

It should not interfere with the stability of efficacy of the active agent .

Types of Emulsifying Agents:

1) Hydrophilic colloids: -Acacia, Tragacanth, Agar, Pectin.

2) Protein Substances: -Gelatin, Egg yolk, Caesin

3) High Molecular Weight Alcohols: -Stearyl Alcohol, Cetyl Alcohol, Glyceryl Mono stearate

4) Surfactats: - Spans and tweens

5) Finely divided solids: - Bentonite, Magnesium Hydroxide, Aluminum Hydroxide

MANUFACTURING:

Proportions of Oil, Water and Gum required for formation of primary emulsion

Type of oil	Example	Proportions of		
		Oil	Water	Gum
Fixed	Almond oil A rachis oil Castor oil Cod-liver	4	2	1
Mineral	Liquid paraffin	3	2	1
Volatile	Turpentine oil Cinnamon oil Peppermint oil	2	2	1
Oleo-resin	Male fern extract Balsam of peru	1	2	1

Dry Gum Method

Pestle mortar
↓
Oil
↓
Gum acacia
↓
Dispersion by trituration only one direction
↓
Water (all at once)
↓
Stir at one side (direction) until thick paste (white colour)
↓
Stir vigorously (clicking sound are appear)
↓
Primary emulsion
↓
Add more of water to produce required volume

Wet Gum Method

Pestle mortar
↓
Water
↓
Gum acacia
↓
Homogenous mucilage form
↓
Oil (all at once)
↓
Stir at one side (direction) until thick paste (white colour)
↓
Stir vigorously (clicking sound are appear)
↓
Primary emulsion
↓
Add more of water to produce required volume

Bottle or Forbes Bottle Method

- useful for extemporaneous preparation of emulsion from volatile oils or oleaginous substance of low viscosity.

powdered acacia

\+ Dry bottle

2 parts of oil

- This method is not suitable for viscous oils (i.e. high viscosity oil).

Stability of Emulsion:

A. Flocculation and Creaming
B. Cracking
C. Miscellaneous Instability
D. Phase Inversion

A. Flocculation and Creaming:

- Flocculation consists of the joining together of globules to form large clumps or floccules which rise or settle in the emulsion more rapidly then the individual globules to give a concentrated layer is known as creaming.
- Separation of cream from milk is a good example of creaming of emulsions.
- Creaming is a temporary phase and it is redistributed by mild shaking or stirring to get again homogeneous emulsion.
- Creaming is not aggregation process.

- The velocity of creaming is governed by stokes law process of creaming is explained by stokes law.

$$V = \frac{2r2\,(d_1-d_2)\,g}{9\,\eta}$$

Where, V - velocity of creaming
d_1 - density of disperse phase
d_2 - density of dispersion medium
g - gravitational consta
r - radius of globules
η - viscosity of continuous phase
Directly proportional to the density difference between the oil and water phases
Directly proportional to the square of the radius of globules
Inversely proportional to the viscosity of dispersion medium

Factors affecting the rate of creaming and sedimentation:

i. Globule size: Globule of small size have less tendency to cream
ii. Viscosity: Higher the viscosity of continuous phase less creaming
iii. Density: Less difference in density of two phase means more stability of emulsion
iv. Temperature: Lower temperature is more suitable for the better stability of emulsion

B. Cracking:

- Separation of two layers of disperse and continuous phase.
- Due to the coalescence of dispersed phase which is difficult to redisperse by shaking.
- a cracked emulsion cannot be corrected.
- cracking represents permanent instability.
- cracking of the emulsion may be due to:
  -addition of an emulgent of opposite nature.
  -decomposition or precipitation of emulgent.
  -addition of a common solvent in which both oily and aqueous phases are miscible.
  -extremes of temperature.
  -microorganism.

C. Miscellaneous Instability:

Emulsions may deteriorate if stored under extremely high or low temperature or in presence of light. Hence emulsions are usually packed in air tight containers and stored at moderate temperature.

D. Phase Inversion:

- It is the change in the type of emulsion from oil in water to water in oil and vice versa.
- It is the physical process.
- Phase inversion may be brought about by varying the phase volume ratio, addition of electrolytes and temperature changes.