LIQUID DOSAGE FORMS

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Liquid dosage forms

Dosage forms are essentially pharmaceutical products in the form which involves a mixture of active drug components and nondrug components (excipients). Liquid form of a dose of a drug used as a drug or medication intended for administration or consumption.

Liquid dosage forms are prepared:

a. By **dissolving** the active drug substance in an aqueous or non-aqueous (e.g. alcohol, ether, glycerin) solvent,

b. By **suspensing** the drug in appropriate medium, or

c. By **incorporating** the drug substance into an oil or water phases.

Advantages of LDF

Advantages:

a. Better for patients who have trouble swallowing expiration than other.

b. Faster absorption than solids.

c. More flexibility in achieving the proper dosage of medication.

d. Palatable.

e. Best choice for children and old age person.

Disadvantages of LDF

a. Shorter life than other dosage form,

b. Harder to measure accuracy,

c. Need special storage condition.

d. Less stable,

e. Easily affected by microorganisms,

f. Bulky to carry around.

g. Easy to loss by the breakage of the container.

h. Measuring dose is required.

Administration of LDF

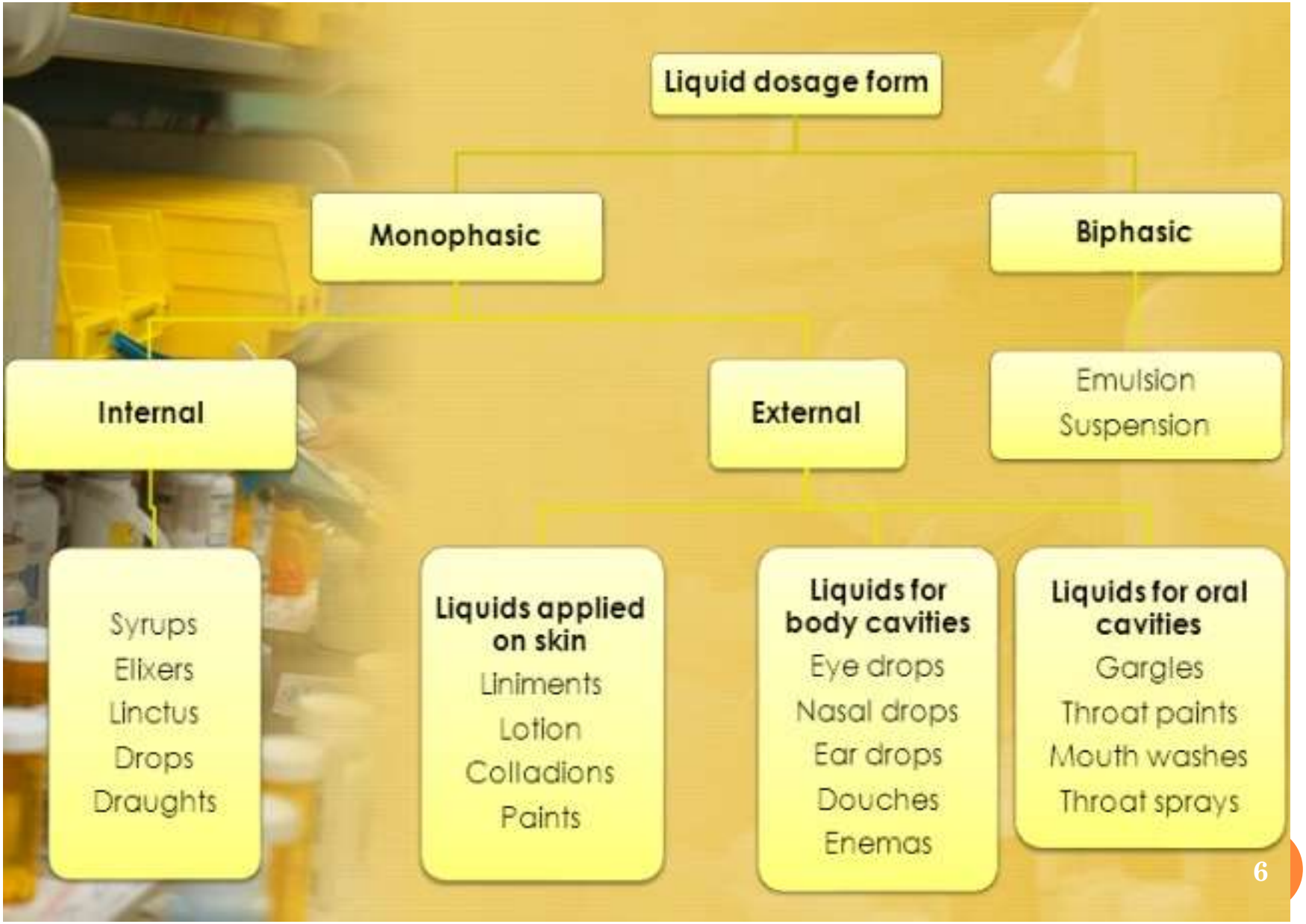
Liquid dosage forms can be administered:

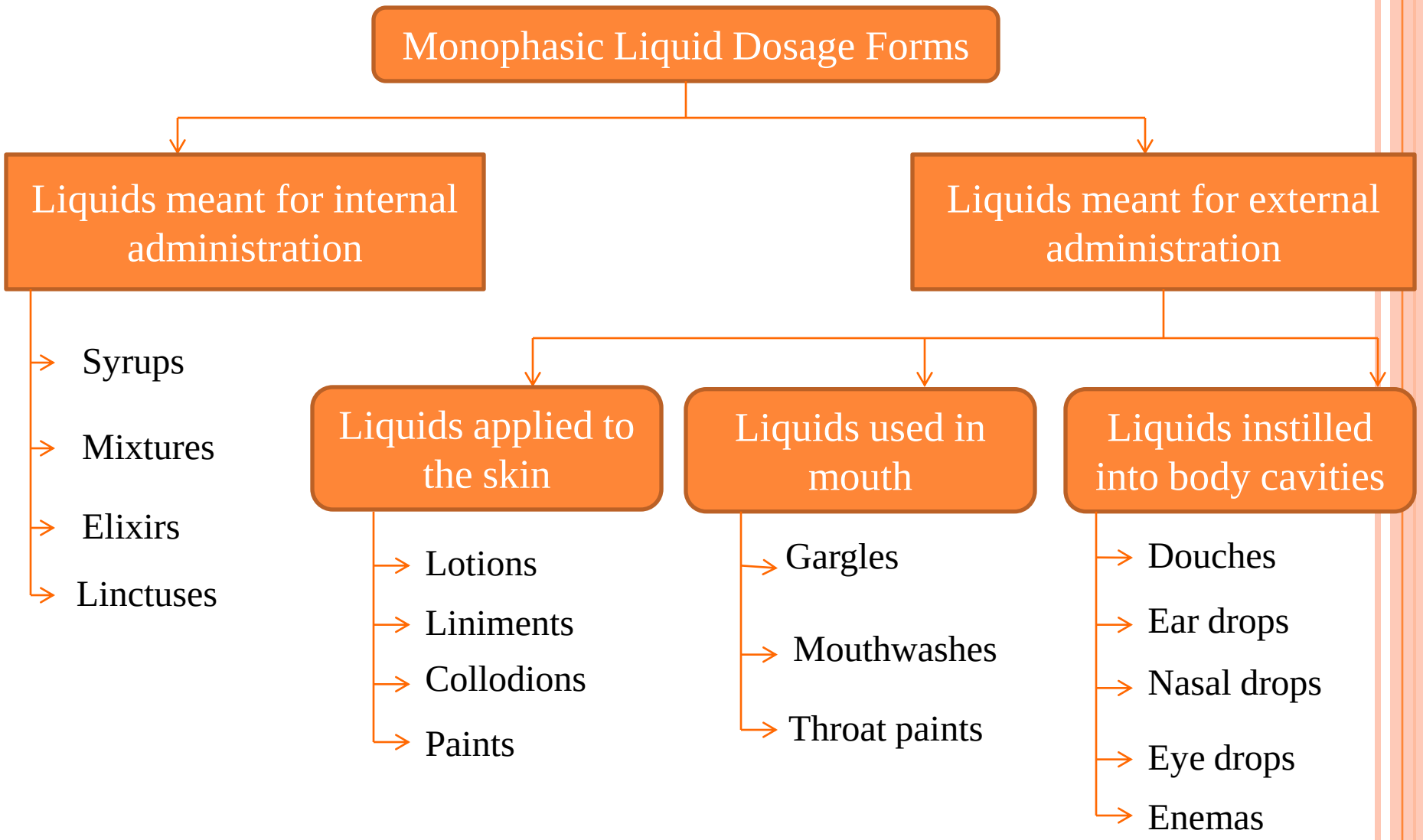
a. Topically - lotions or suspension applied to the skin, nasal drops, ear drops, eye solutions.

b. Orally (p.o.) – oral suspension, emulsion & solution.

c. Parenterally -

- subcutaneous injection (s.c.),
- intramuscular injection (i.m.)
- intravenous administration (i.v.)


Liquid dosage form
Monophasic
Biphasic
Internal
External
Emulsion
Suspension
Syrups
Elixers
Linctus
Drops
Draughts
Liquids applied on skin
Liniments
Lotion
Colladions
Paints
Liquids for body cavities
Eye drops
Nasal drops
Ear drops
Douches
Enemas
Liquids for oral cavities
Gargles
Throat paints
Mouth washes
Throat sprays


Monophasic Liquid Dosage Forms
Liquids meant for internal administration
Liquids meant for external administration
Syrups
Mixtures
Elixirs
Linctuses
Liquids applied to the skin
Liquids used in mouth
Liquids instilled into body cavities
Lotions
Liniments
Collodions
Paints
Gargles
Mouthwashes
Throat paints
Douches
Ear drops
Nasal drops
Eye drops
Enemas

Liquids meant for internal administrations

Syrup

Concentrated aqueous preparations of 60% to 85% sucrose with or without flavoring agents and medicinal substances.

e.g. Chlorpheniramine maleate syrup, Chloral hydrate syrup

Elixirs

Clear, aromatic, sweetened hydroalcoholic solutions with or without medicinal substances, intended for oral use.

eg:Dexamethasone elixir (Medicated)

Compound benzaldehyde elixir (Non-medicated)

Mixture

Liquid preparation meant for oral administration in which medicaments are dissolved in a suitable vehicle.

Eg: Orange peel infusion

Linctuses

Viscous, liquid and oral preparations that are generally prescribed for the relief of cough.

Eg: Codeine Linctus.

Liquids meant for external administrations

Gargles

Aqueous solutions containing antiseptics, antibiotics or anesthetics used to prevent or treat throat infections.

Available in concentrated form with direction for dilution with warm water before use.

Phenol gargle

Mouthwash

Aqueous solution with a pleasant taste and odor used to clean and deodorize the buccal cavity. Have antiseptic and astringent activity.

eg: Antiseptics-phenol derivatives

Astringents-Zinc chloride

a) Liquids used in the mouth

Throat paints

Viscous liquid preparation used for mouth and throat infections.

Eg:Phenol glycerine, Compound Iodine paint

Throat sprays

sprayed into the throat are intended to medicate the lungs

Liquids meant for external administrations

Douches
Medicated solution meant for rinsing a body cavity as eyes, ear or nasal cavities for cleaning or removing the foreign particles or discharge from them. Eg: isotonic sodium chloride solution

Enemas
Aqueous or oily solution that is introduced into the rectum and colon via the anus for cleansing, therapeutic or

b) Liquids instilled into body cavities

Nasaldrops
dministered through the nose to obtain a systemic or local effect. Used for symptoms such as nasal congestion caused by an allergy, or a related upper-respiratory problem.
Eg:Beclomethasone dipropionate nasal drops

Otic preparations
Applied to or in the ear to treat or prevent dermatitis of the ear, cerumen build up and ear infection.
soda glyceri

Eye drops
Sterile,aqueous/ oily solutions intended for instillation in eyeball.
Eg:Moxifloxacin eye

Liquids meant for external administrations

Collodions

Highly flammable syrupy solution of pyroxylin dissolved in ether and alcohol, which dries to a clear tenacious film
Used as a topical protectant to close small wounds, abrasions and cuts
hold surgical dressings

c) Liquids meant for external use (Skin)

Liniments

Alcoholic and oily liquid preparations
Intended for external application with rubbing to the affected area
Topically used to relieve pain and stiffness, such as from sore muscles or from arthritis

Paints

Solutions used to sterilize the skin.
Eg. Crystal violet , Magenta paint

Lotions

Either liquid or semi-liquid preparations that contain one or more active ingredients in an appropriate vehicle.
Topical preparation with a low to medium viscosity
Intended for application to unbroken skin without friction.
Calamine Lotio

Pharmaceutical Solutions

Aqueous

1. Douches
2. Enemas
3. Gargles
4. Mouthwashes
5. Nasal washes
6. Juices
7. Sprays
8. Otic solutions
9. Inhalations

Sweet &/or Viscid

1. Syrups
2. Honeys
3. Mucilages
4. Jellies

Nonaqueous

1. Elixirs
2. Spirits
3. Collodions
4. Glycerins
5. Liniments
6. Oleo Vitamin

Syrup


2 pack
Triaminic
Day Time
Cold
& Cough
Triaminic
Day Time
Cold & Cough

SYRUPS

Syrups are concentrated solutions of sucrose or other sugars to which medicaments or flavourings are often added. For example, **Codeine Phosphate Syrup** is used as a cough suppressant

Simple syrup: when water is used alone for making syrup.

Medicated syrup: when the aqueous preparation contains some added medicinal substance

Flavored syrup: which contains aromatic or pleasantly flavored substances and is intended to be used as a vehicle or flavor for prescription.

- Syrups can contain up to 85% of sugars
- Syrups often include sufficient of a polyhydric alcohol such as sorbitol, glycerol or propylene glycol in order to prevent crystallization and to maintain solubility of all ingredients.
- Syrups containing 65% by weight or more of sugars, are capable of resisting bacterial growth by virtue of their osmotic effect.
- Syrups often contain additional preservatives due to possibility of surface dilution of a syrup in a closed container.
- The crystallization of the sugar can be avoided by the addition of the polyhydric alcohols or by the inclusion of invert syrup, which is a mixture of glucose and fructose.

ORANGE and CHERRY SYRUPS

ADVANTAGES OF SYRUP

- Appropriate for any patient, whatever the age is
- The most natural and easiest route of administration
- Economical and safe to the patient
- No nursing is required, which means the patient can take it with no help
- The liquid dosage form is expected for certain types of products like cough medicines
- Suitable for water soluble stable drugs
- Self preservatives if having density 1.313

DISADVANTAGES OF SYRUP

- Delayed onset of action because absorption takes time
- Not suitable in emergency and for unconscious patients
- Not convenient for a patient with a gastrointestinal disorder such as diarrhea, constipation, ulceration, and hyperacidity in stomach
- Not suitable for diabetic patients
- Pleasant taste – children take more dose
- If sucrose content is not proper – prone to microbial growth
- Highly concentrated syrup get crystallized if other substances like glycerin, sorbitol not added.

COMPONENTS OF SYRUP

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

(a)Sweetening Agent- the sugar, usually sucrose, or sugar substitute used to provide sweetness and viscosity

*(b) A*ntimicrobial Preservatives

(c) Viscosity Modifier

(d) Flavorants

*(e) C*olorants

many types of syrups, especially those prepared commercially, contain special solvents, solubilizing agents, thickeners, or stabilizers.

PREPARATION OF SYRUP

There are four methods. Based on the physical and chemical properties on the ingredients, the choice of the method is selected-

I. **Solution with heat**
II. **Agitation without heat**
III. **Addition of sucrose to liquid medicament**
IV. **Percolation method**

1. Solution with heat-

temperature of purified water is increased to 80 to 85 C

↓

taken off from the heat source

↓

Then add sucrose and shake it thoroughly

↓

Those substances that are heat sensitive and volatile agents are added after the solution attain the room temperature

↓

during heating, the sucrose gets hydrolysed, results in the formation of dextrose and fructose

↓

these two sugars together called as invert sugar and the process is known as inversion

↓

The inversion leads to darkening of the solution

2.Agitation without heat-

vessel is taken generally made up of stainless steel or glass

⬇

The vessel should be larger than the desired volume of syrup required

⬇

Then the ingredients according to the formulation are added to water and mixed

⬇

It is better to dissolve solid ingredients in the water first and then to add them to syrup

⬇

This results in easy mixing as sugar solution generally retards mixing

3. Addition of sucrose to liquid medicament-

This method is generally used for fluid extracts.

But those substances which are soluble in alcohol will precipitate out as soon as the addition of water

An alternation is to first dissolve all the ingredients in water

Now after sometime all the precipitates formed are filtered out

Now add sucrose

But this method is of no use if the precipitates formed has active ingredients

3. Percolation

In this method, either sucrose maybe percolated to prepare the syrup or the sucrose of the medicinal component may be percolated to form an extractive to which sucrose or syrup may be added.

Procedure:

Purified water or aqueous solution of a medicating or flavoring liquid is allowed to pass slowly through a column of crystalline sucrose to dissolve it.

2. The percolate is collected and returned to the percolator as required until all of the sucrose has been dissolved.

3. Percolator with a pledget of cotton at the bottom is used

Example: Tolu Balsam syrup - flavor for cough syrup

4. Addition of Sucrose to a Medicated liquid or to a Flavored liquid

Occasionally, a medicated liquid, as a tincture of fluidextract is employed as the source of medication in the preparation of a syrup.

Many such tinctures and fluidextract contain alcohol-soluble constituents and are prepared with alcoholic vehicles.

Examples: Senna Syrup, NF and Cherry Syrup

Preservation of Syrups

- The USP suggests that syrups be kept at a temperature not above 25°C.
- Preservatives such as glycerin, methyl paraben, benzoic acid and sodium benzoate may be added to prevent bacterial and mold growth, particularly when the concentration of sucrose in the syrup is low.
- The concentration of preservative is proportional to the free water.
- The official syrups should be preserved in well dried bottles and stored in a cool dark place.

Dextrose-Based Syrups

- Dextrose may be used as a substitute for sucrose in syrups containing strong acids in order to eliminate the discoloration associated with inversion.
- Dextrose forms a saturated solution in water at 70% w/v, which is less viscous than simple syrup.
- It dissolves more slowly than sucrose and is less sweet Preservatives are required to improve the keeping qualities of such syrups. Glycerin is added in 30% to 45% v/v as preservative.

Artificial Syrups (Non-Nutritive Syrups)

- intended as substitutes for syrups and are to be administered to persons who must regulate their sugar and/or calorie intake accurately. e.g. persons suffering from diabetes mellitus.
- Some early formulae included glycerin, however, glycerin and propylene glycol are glycogenetic substances, i.e. they are materials which are converted into glucose in the body.
- An example of non–nutritive syrup is "Diabetic Simple Syrup". It contains compound sodium cyclamate (6% cyclamate sodium and 0.6% saccharin sodium)

However, the cyclamate studies showed that the sweetener could produce cancer in animals and, as a result, this substance was removed from a wide variety of products. Similar studies have been carried out on saccharin. Much research has been done to find a safe synthetic substitute for sucrose. As a result, aspartame which is about 200 times sweeter than sucrose, is being used now in many

Sorbitol-Based Syrups

- Sorbitol which is hexahydric alcohol made by hydrogenation of glucose has been used in the preparation of syrup.
- It is used mostly in the form of a 70% w/w aqueous solution.
- Sorbitol solution is not irritating to the membrane of the mouth and throat and does not contribute to the formation of dental carries.
- Sorbitol is metabolized and converted to glucose; however, it is not rapidly absorbed from the GlT as sugars. No significant hyperglycemia has been found (WHY?); it may be used as component of non-nutritive vehicles.
- Sorbitol solution does not support mold growth. Preservative should be used in solution containing less than 60% w/w sorbitol.
- It is chemically stable and inert with respect to drugs and other ingredients used in pharmaceutical perpetration.

HONEYS

Are thick liquid preparations. At one time, before sugar was available, honey was used as a base, instead of syrup.

There are few official preparations containing honey. e.g. Oxymel, or" acid honey "'is a mixture of acetic acid, water and honey

MUCILAGES

- The official mucilages are thick viscid, adhesive liquids, produced by dispersing gum (acacia or tragacanth) in water.
- Mucilages are used as suspending agents for insoluble substances in liquids; their colloidal character and viscosity prevent immediate sedimentation.
- Synthetic agents e.g. carboxymethylcellulose (CMC) or polyvinyl alcohol are nonglycogenetic and may be used for diabetic patients.

Jellys

- Preparations having a jelly-like consistency. They are prepared also from gums.
- Are used as lubricants for surgical gloves and catheters
- Lidocaine HCl Jelly USP is used as a topical anaethetic.

Medicaments commonly used:

- Antibiotics – e.g. Lincomycin HCl
- Analgesics – E.g. – Meperidine HCl
- Adrenergic – e.g. – Pseudoehedrine HCl
- Antiemetics – e.g. – Chlorpromozine HCl
- Antihistaminics – e.g. Chlorpheniramine meleate
- Antitussive – e.g. – Dextromethorphan HBr
- Iron supplement – e.g. – Ferrous sulphate

SOME IMPORTANT FORMULATIONS:

- **Simple syrup I.P.**

Sucrose ------ 667g

Purified water to ----- 1000g

- **Ferrous sulphate syrup U.S.P.**

Ferrous sulphate ------- 40g

Citric acid,hydrous ----- 2.1g

Peppermint spirit ----- 2.0ml

Sucrose ----- 825g

Purified water to ----- 1000ml

SOME SYRUPS PRESENT IN MARKET

Brand Name	Company	Active Ingredient	Therapeutic Class	Use
Ambrox	Square Pharmaceutical Ltd.	Ambroxol Hydrochloride	Cough & Cold Remedies	Productive cough, Acute and chronic inflammatory disorders of upper and lower respiratory tracts associated with viscid mucus including acute and chronic bronchitis
Brofex	Square Pharmaceutical Ltd.	Dextromethorphan	Cough & Cold Remedies	Chronic dry cough/unproductive cough & acute dry cough which is interfering with normal function or sleep.
Tusca	Square Pharmaceutical Ltd.	Guaiphenesin+ Pseudoephedrine + Triprolidine HCl	Cough & Cold Remedies	Symptomatic relief of upper respiratory tract disorders accompanied by productive cough.
Duolax™	Square	Magnesium	Laxative	Constipation, Hyperacidity with

Elixir


PHARMACY MEDICINE
Children's
Panadol
1-5 YEARS
Elixir
tutti frutti flavour


Ferrol
CHILDREN'S
ELIXIR
For nasal congestion, runny nose, sneezing and hay fever.
ALCOHOL FREE
STRAWBERRY
FLAVOURED LIQUID
Manufactured by:
GPC
Ferrol
CHILDREN'S ELIXIR

ELIXIRS

Are clear, sweetened, hydroalcoholic solutions intended for oral use, and are usually flavored for palatability.

Its Alcohol Content may vary from as low as 5% to as high as 40%.

Advantages of Elixirs:

a. Better able to maintain both water-soluble and alcohol-soluble components in solution.

b. Has stable characteristics.

c. Easily prepared by simple solution.

d. Used as vehicles for wide variety of potent on nauseous medicaments.

e. Less viscous than syrups, thus do not create difficulty in filtration operation

f. Provide flexibility and ease of dosage administration.

g. Containing over 10 to 12% alcohol are self preservative and do not require the addition of preservative.

Disadvantages of Elixirs:

a. Less effective than syrups in masking taste of medicated substances.

b. Contains alcohol, accentuates saline taste of bromides

c. Less sweet and less viscous since they contain less proportion of sugar.

d. Having high percentage of alcohol require sweetening agent then sucrose since sucrose is slightly soluble in alcohol. Saccharine used in preparation which has bad after taste.

e. Costlier than syrups and require many legal processing with excise department.

2 TYPES OF ELIXIRS

1. **HIGH ALCOHOLIC ELIXIR (HAE)** –
   75% to 78% alcohol

2. **LOW ALCOHOLIC ELIXIR (LAE)** –
   8% to 10 % alcohol

NOTE: Elixirs containing at least 10% to 12% alcohol are already "self-preserving"

COMPONENTS OF ELIXIR FORMULATION

- Alcohol and Water – primary solvents
- Glycerin and Propylene Glycol- adjuncts

  (viscosity builders and stabilizers)
- Sweeteners
- Flavorants and Colorants
- Medicinal substances

- Some important formulations:

Piperazine citrate elixir I.P. 1966

Piperazine citrate ---- 18g

Chloroform spirit ---- 0.5 ml

Glycerin ---- 10 ml

Orange oil ---- 0.025ml

Syrup ---- 50 ml

Purified water to -- 100 ml

Advantages and Disadvantages of Syrups as Dosage Form

- Maintain both water-soluble and alcohol-soluble components in solution
- Stable
- Easy to prepare (by simple solution method)
- Less effective in masking the taste of drugs because elixirs are less sweet and less viscous
- Not recommended for children due to their alcohol content

CLASSES OF ELIXIRS

I. NON-MEDICATED ELIXIRS

- Employed as vehicles

- Examples:

  Aromatic Elixir, NF

  Isoalcoholic Elixir

CLASSES OF ELIXIRS

II. MEDICATED ELIXIRS

Examples:

Diphenhydramine Elixir

Phenobarbital Elixir

Digoxin Elixir

Clip slide

Preparation of Elixirs

- By simple solution method
- By admixture of two or more liquids

STORAGE and PRESERVATION of ELIXIRS

Stored in a tightly closed, light-resistant containers

Protected from excessive heat (do not store above 40^0C)

Mixture

- A mixture is a liquid preparation intended for oral administration in which drugs may be dissolved, suspended or dispersed in a suitable vehicle. Generally several doses are contained in a bottle.

Classification: Mixtures may be classified as follows:

- 1. Simple mixtures
- 2. Mixtures containing diffusible solids
- 3. Mixtures containing indiffusible solids
- 4. Mixture containing precipitate forming liquids

1. Simple mixture

- A simple mixture is one that contains only soluble ingredients.

Method of dispensing

(a) The solid substances are dissolved in 3/4th volume of the vehicle.

(b) The solution is examined against light for any foreign particle. If foreign particles are present then the solution is passed through cotton wool. Little vehicle is poured through the cotton wool to wash down any drug present in the wool.

(c) Liquid ingredients, if any, are added and mixed.

(d) More vehicle is added to produce the final volume.

(e) The mixture is transferred to a bottle, capped tightly, polished and labeled.

Container: Narrow mouthed, screw capped, colorless, plain bottle.

Label: The ink used in the label *Black.*

Special instructions: *None*

2. Mixture containing diffusible solids

- Diffusible solids are those, which are not soluble in water, but on shaking they can be mixed with it and remain evenly distributed throughout the liquid for a sufficiently long time. So dose transfer is uniform.
- However, on standing the insoluble solids settle at the bottom. Whenever a dose is taken the bottle should be shaken to redisperse the solid.
- *Examples of diffusible solids*: Bismuth carbonate, light kaolin, magnesium oxide, magnesium carbonate, magnesium trisilicate etc.

Method of dispensing

(a) All the solid ingredients are powdered in a mortar and mixed thoroughly.

(b) Small amount of vehicle is added to the powder and triturated to form a smooth paste.

(c) More volume of the vehicle is added.

(d) If foreign particles are present then the mixture is strained though a muslin cloth.

(e) Liquid ingredient, if any, is added and the volume is produced with the vehicle.

(f) The mixture is transferred to the bottle.

Container: Narrow mouthed, screw capped, colorless, plain bottle.

Label: The ink used in the label *Black*.

Special instruction: SHAKE WELL BEFORE USE

3. Mixture containing indiffusible solids

- Indiffusible solids are those substances, which are not soluble in water and they do not uniformly distribute throughout the vehicle. Even after shaking they settle quickly, therefore it becomes difficult to measure the dose accurately. In this type of mixture a suspending agent is used that increases the viscosity of the vehicle and thus reduces the rate of settling of the particles.
- *Examples of indiffusible solids*: Chalk powder, acetyl salicylic acid etc.
- *Examples of suspending agents*: Compound tragacanth powder, Tragacanth mucilage, tragacanth powder.
-

- ***Method of dispensing***

(a) Indiffusible, diffusible powders and calculated amount of suspending agent are triturated in a mortar.

(b) Small mount of vehicle is added to the powder and triturated to make a smooth paste.

(c) More amount of the vehicle is added. Strained through a muslin cloth if any foreign particle is present.

(d) Liquid ingredient, if any, is added. Volume is made up with the rest of the vehicle.

(e) The mixture is transferred to the bottle, capped, polished and labeled.

Container: Narrow mouthed, screw capped, colorless, plain bottle.

Label: The ink used in the label *Black*.

Special instruction(s): SHAKE WELL BEFORE USE

4. Mixture containing precipitate forming liquid

- Some liquid preparations contain resinous matter that is precipitated on addition of water. This precipitates sticks to the container and forms clots.
- To disperse this type of liquid first a protective colloid is dispersed in vehicle and then the precipitate forming liquid is added with constant stirring. The resinous particles are coated with the protective colloid.

***Examples of precipitate forming liquids*:**

- Compound benzoin tincture
- Benzoin Tincture
- Lobelia ethereal tincture
- Myrrh tincture
- Tolu Tincture
- *Examples of suspending agents*: Compound tragacanth powder, Tragacanth mucilage

Method of dispensing by using Compound tragacanth powder

- (a) Any insoluble solid is powdered in a mortar and mixed with compound tragacanth powder. Small amount of the vehicle is added to form a smooth paste. The volume is produced to 50% of the final volume with the vehicle.
- (b) The precipitate forming liquid is taken in a dry measuring cylinder and is added to the suspension slowly, while the suspension is stirred rapidly. The gum particles coat the resinous particles and give a hydrophilic property to the resin particles.

Method of dispensing by using Tragacanth mucilage

- (a) Mucilage is taken and added with equal volume of vehicle in a beaker.
- (b) The precipitate forming liquid is measured in a dry measuring cylinder and added into the center of the mucilage with constant stirring.
- (c) If electrolyte is present, it is diluted with vehicle and then mixed with the mucilage.
- (d) The mixture is strained, if required, and the volume is produced with vehicle.
- (e) The mixture is transferred to the bottle, capped, polished and labeled.

- (c) If any electrolytes are there it should be added only after the resin particles are completely coated with gum, otherwise heavy clotting will take place.
- (d) Strained it necessary and volume is made up with vehicle.
- (e) The mixture is transferred to the bottle, capped, polished and labeled.

- *Container*: Narrow mouthed, screw capped, colorless, plain bottle.
- *Label*: The ink used in the label *Black*.

Special instruction(s): SHAKE WELL BEFORE USE

Liquids used for Oral Cavity

Mouthwash


NEW
Colgate
Kids


Coolmint
LISTERINE
ANTIBACTERIAL MOUTHWASH


Mouthwash
Freshburst

Definition of Mouthwash

A medicated liquid used for cleaning the oral cavity and treating mucous membranes of the mouth. may contribute to surface softening and increased wear of dental resins and composite materials.

Types of Mouthwash

Fluoride mouthwashes contain sodium fluoride which helps to strengthen the teeth as well as adding extra protection against tooth decay.

cosmetic mouthwashes do not offer the same protection as other types and are used more as a means of disguising bad breath (halitosis).

Antiseptic mouthwashes contain chlorhexidine gluconate - a chemical which stops the growth of bacteria and is suitable for people with a mouth infection.

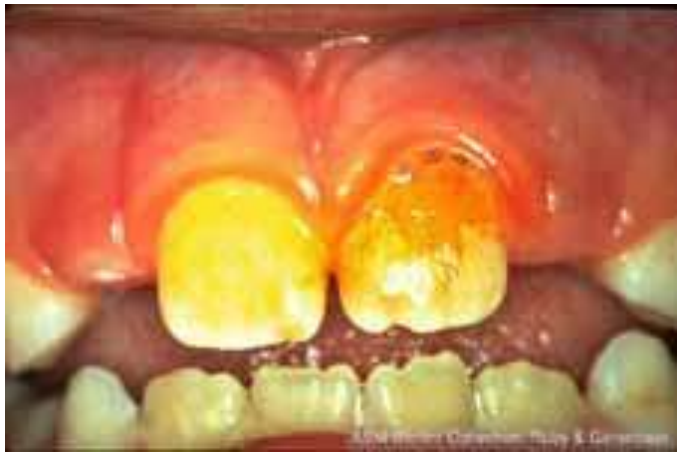
Natural mouthwashes are alcohol-free (and contain no fluoride) and work in much the same way as conventional mouthwashes.
They can also treat a mouth infection or injury.

Total care mouthwashes contain anti-bacterial ingredients which help to reduce the build up of plaque and prevent gum disease.

Advantages of Mouthwash:

- can boost your oral health.
- may prevent plaque from building up
- Rinses with fluoride can help prevent cavities.

- Fluoride protects against tooth deca (cavities).
- Mouthwash can help you target plaque.
- Prevents dry mouth.

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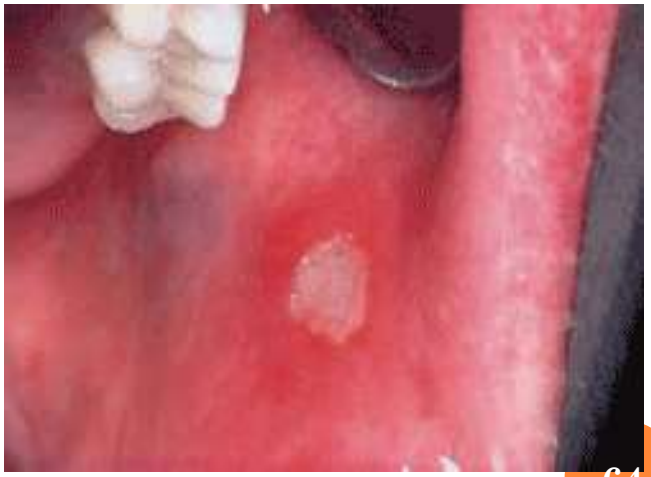
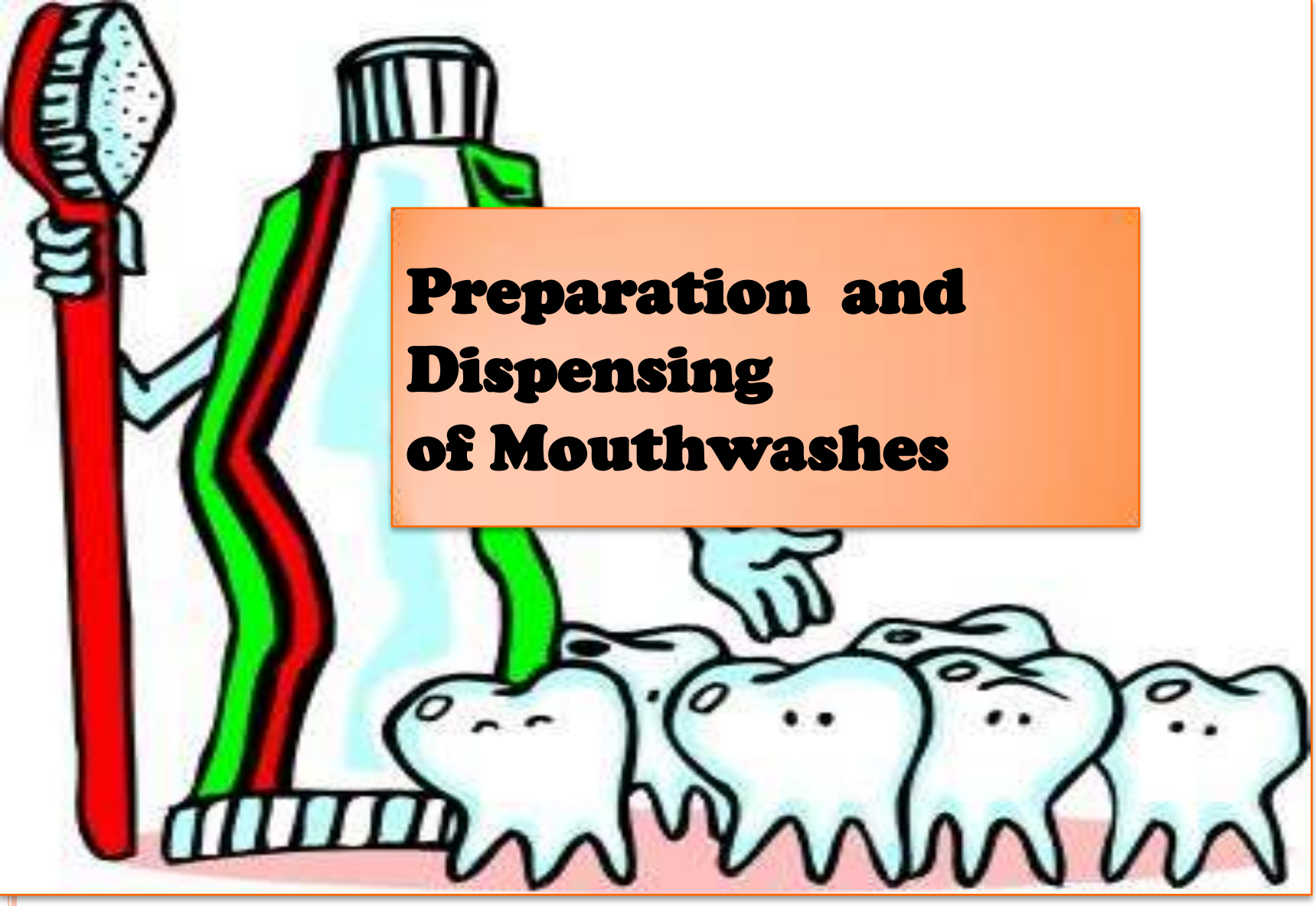


Disadvantages of Mouthwash:

- Some mouth rinses contain high levels of alcohol—ranging from 18 to 26 percent. This may produce a burning sensation in the cheeks, teeth, and gums.



Preparation and Dispensing of Mouthwashes

Preparation of Mouthwashes

- To prepare mouthwash following ingredients are added:
- Flavoring - such as eucalyptol or menthol
- Preservative- sodium benzoate.
- Vehicle - Water
- Sweeteners - sodium saccharine and sucralose.
- Colorants
- Antiseptic agent - fluoride
- Detergent

PREPARATION OF SODIUM CHLORIDE MOTHWASH

Sodiun Bicarbonate..10g

Sodium Chloride…….15g

Chloroform……..500ml

Pepprmintoil……..25ml

Water…….qty to prepare 1000ml

- Dissolve Na bicarbonate $ Nacl in 10 ml
- Add chloroform & peppermint oil
- Makeup the volume
- Dispense the solution

Packaging & Storage

Containers:

- **fluted**
- **plastic screw caps**
- **Colorless bottles are used unless protection from light is necessary.**
- **narrow mouthed**

Storage:

- **Store at room temperature**
- **Away from sunlight**
- **Keep out of reach of children**

LABELING

- Product information
- Active ingredients
- Uses
- Warnings
- Direction
- Storage
- Inactive ingredients

Direction to use

- Before using a mouth rinse, brush and floss teeth.
- Measure the proper amount of rinse
- Dilute it before use
- Thirty seconds is the suggested rinsing time.
- Do not rinse, eat, or smoke for thirty minutes after using a mouthwash.

EXAMPLES OF MOUTH WASHES

- **Antisceptic:** Listerene or Phenolic mouthwash
- **Analgesic:** lidocaine hydrochloride
- **Bactericidal (Cosmetic):** Fluoride mouthwash
- **Anticavity:** Floride rinse


GARGLES

Definition :

Gargles are aqueous and hydro alcoholic solution which is used to treat or prevent throat infection.

DIRECTIONS:

- They are dispensed in concentrated form with directions for dilution with warm water.

- They are brought into intimate contact with the mucous membrane of the throat and allow to remain for few moments

Uses:

- Deodorant effect
- Anti-bacterial
- Astringent
- Mild anesthetic actions

STORAGE

- Store at room temperature

- Keep out of the reach of children.

- Store away from direct sunlight, heat and moisture.

Labelling

- **The label should include:**

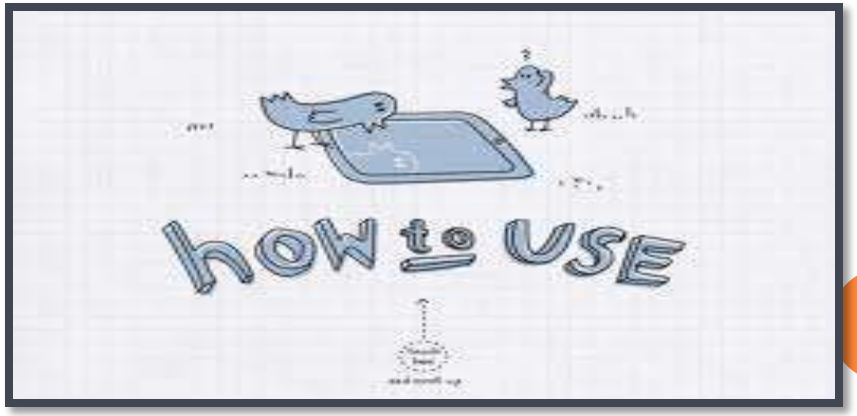
(1) the name of the pharmaceutical product;
(2) the name(s) of the active ingredients
(3) the amount of active ingredient in a suitable dose-volume;
(4) the name and concentration of any antimicrobial preservative and the name of any other excipient;
(5) the batch (lot) number assigned by the manufacturer;
(6) the expiry date and, when required, the date of manufacture;
(7) any special storage conditions or handling precautions that may be necessary;
(8) directions for use, warnings, and precautions that may be necessary;
(9) the name and address of the manufacturer or the person responsible for placing the product on the market.

Warnings

- Always read the label.
- Use only as directed.
- Avoid contact with the eyes.
- NOT TO BE SWALLOWED

Usage

- Dilute 1ml to 20ml with water gargle for 30 seconds, repeat 3 to 4 hourly.



CONTAINER

- The containers should be made of material that will not adversely affect the quality of the preparation
- containers should be made from material that is sufficiently transparent to permit the visual inspection of the contents
- preparation contains volatile ingredients, it should be kept in a tightly closed container

PACKAGING

- Small flip top bottles

- Strong damp-proof, water-proof packing

Topic:
THROAT PAINT

THROAT PAINTS

"**Throat Paints** are solutions or dispersions of one or more active ingredients intended for application to the mucosa of the throat or mouth."

Throat paints are viscous due to a high contact of glycerin, which being sticky, adhere to the affected site and prolong the action of the medicaments.

EXAMPLES

1. **Compound Iodine Paint** (Mandl's Paint) – used for pharyngitis or tonsillitis. Iodine throat paint is designed to kill germs. It can be used on sore throats and ulcers to ease them
2. **Crystal Violet Paint** – used for thrush.

Preparation of Throat Paint

e.g. <u>Mandl's Throat Paint</u>

Formula:

- *Potassium iodide 25g*
- *Iodine 12.5g*
- *Alcohol 90%v/v 40ml*
- *Water 25ml*
- *Peppermint oil 4ml*
- *Glycerol up to 1000ml*

Method of preparation

(i) Potassium iodide is dissolved in water.

(ii) Iodine is added in the concentrated potassium iodide solutions to form KI3 (or higher iodides).

(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.

ACTION: ANTISEPTIC

USES: Tonsillitis, Pharyngitis

ROLE OF INGREDIENT

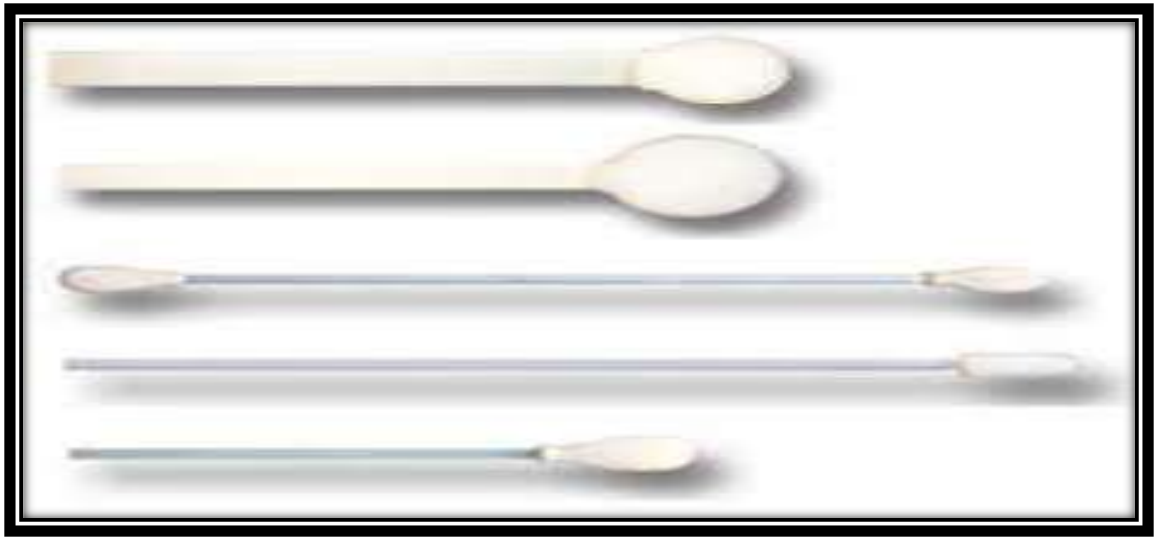
- **Potassium Iodide**: To make soluble iodine in water
- **Iodine**: Antiseptic, Penetrate inn pores and have germicidal effect, treat small abrasion and wounds in Skin
- **Alcohol**: Preservative
- **Water**: Solvent
- **Peppermint Oil**: Flavoring agent
- **Glycerin**: Vehicle, Viscous, sticky, adhere to affected site and prolong effect of medicament

PACKAGING

- A wide mouthed, fluted, light resistant, screw-capped, glass-jar is used.
- Dispense in amboured colored bottle
- A wax card liner is used for screw caps (because iodine attacks other materials).
- Since glycerin is hygroscopic solvent, it must be stored in tightly close container.
- A small quantity of Sodium Citrate or acetate is added as preservative for longer time

DIRECTION

- Apply with the help of soft brush or a cotton swab.
- Food and water before and after application of throat paint, should be avoided for 1 hour



LABELING

- ***For local application***
- ***Store in a cool place.***
- ***Shake the bottle before use.***
- ***Not to be swallowed in large amount.***
- ***<u>Date:</u> 01.01.03***
- **<u>Advice to the patient:</u>**

Pharmacist should demonstrate the use of throat brush to the patient.

LIQUIDS INSTILLED INTO BODY CAVITIES

Douches

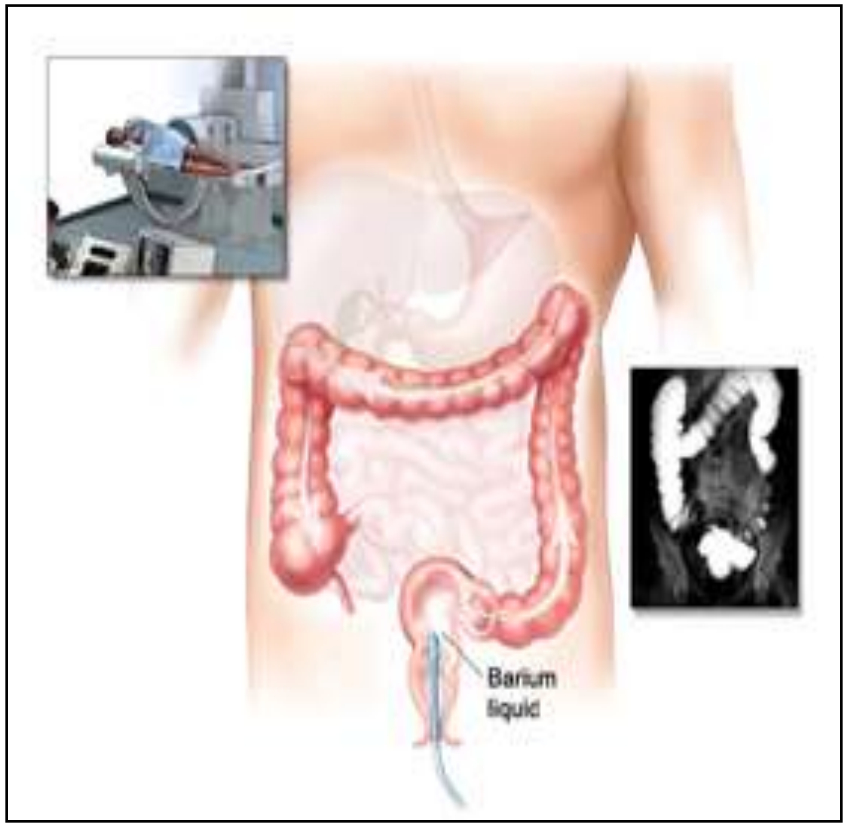
- Douche is an aqueous solution, which is directed against a part or into a cavity of the body.
- It functions as a cleansing or antiseptic agent.
- Eye douches are used to remove foreign particles and discharges from the eyes. It is directed gently at an oblique angle and is allowed to run from the **inner** to the **outer** corner of the eye.
- Pharyngeal douches are used to prepare the interior of the throat for an operation and to cleanse it in supportive conditions.
- Similarly, there are nasal and vaginal douches.
- Douches most frequently dispensed in the form of a powder with directions for dissolving in a specified quantity of water.

Rx
Boric Acid Douche

Boric Acid	**20gm**
Purified water to	**1000 ml**

Enemas

- These preparations are rectal injections employed to:
  - evacuate the bowel (evacuation enemas),
  - influence the general system by absorption (retention enemas) e.g. nutritive, sedative or stimulating properties
  - affect locally the site of disease (e.g. anthelmintic property)
  - they may contain radiopaque substances for roentgenographic examination of the lower bowel.
- Retention enemas are used in small quantities (about 30ml) and are thus called retention microenema.
- Starch enema may be used either by itself or as a vehicle for other forms of medication

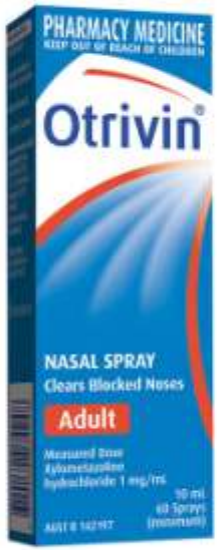


Rx-1		Rx-2	
Enema of Glycerin		Soft Soap Enema	
Glycerin	50 ml	Soft Soap	50 gm
Purified water	100 ml	Purified water	100 ml

Nasal Solutions

Nasal solutions are usually aqueous solutions designed to be administered to the nasal passages in drops or sprays.

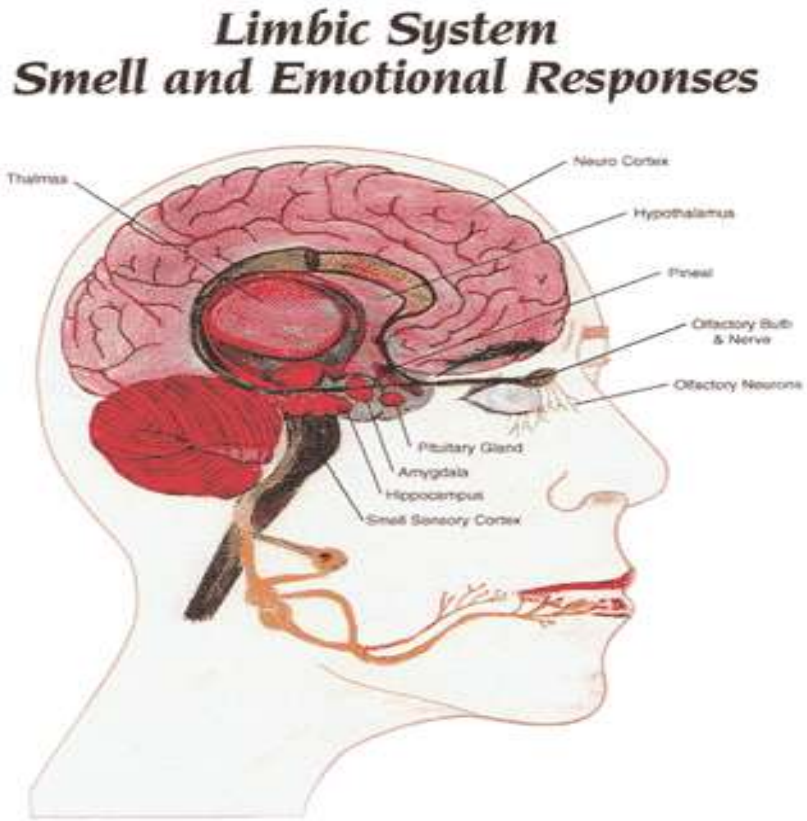
- **Ephedrine Sulfate or Naphaxoline Hydrochloride Nasal Solution USP** are administered for their **local** effect to reduce nasal congestion
- **Lypressin Nasal Solution USP** for its **systemic** effect for the treatment of diabetes insipidus

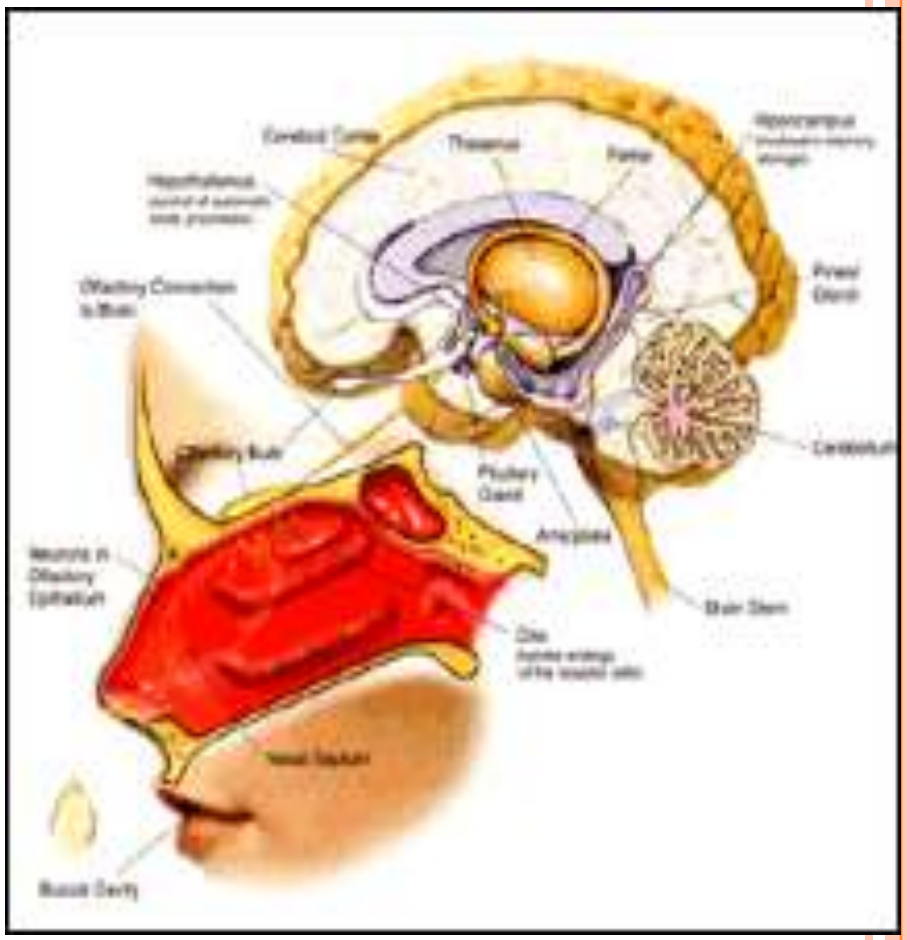


- The current route of administration of peptides and proteins is limited to parental injection because of inactivation within the GIT. As a result there is considerable research on intranasal delivery of these drugs such as insulin.

- Intranasal drug administration offers rapid absorption to the systemic circulation. This route is safe and acceptable alternative to the parental administration

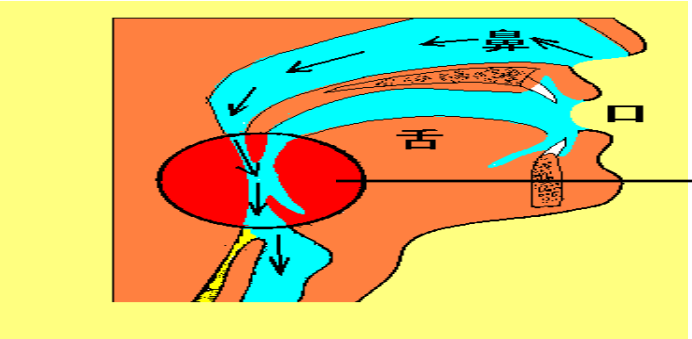
There is a direct route of transport from the olfactory region to the central nervous system (CNS) without prior absorption to the circulating blood. **The olfactory receptor cells are in contact with the nasal cavity and the CNS** and they provide a rout of entry to the brain that circumvents the blood brain barrier





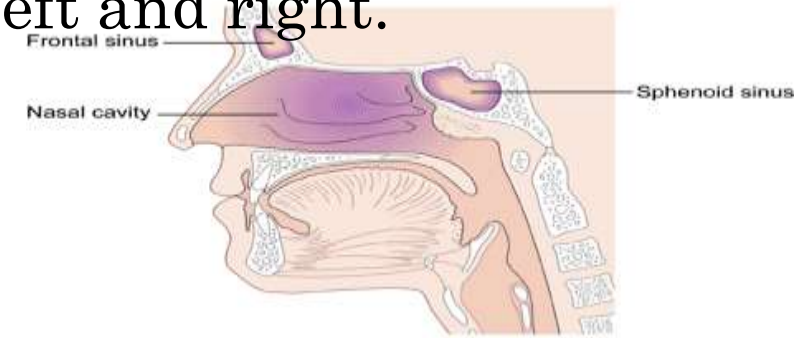
- Commercial nasal preparations include antibiotics, antihistamines and drugs for asthma prophylaxis.

- Current studies indicate that nasal sprays are deposited in the pharynx with the patient in an upright position.

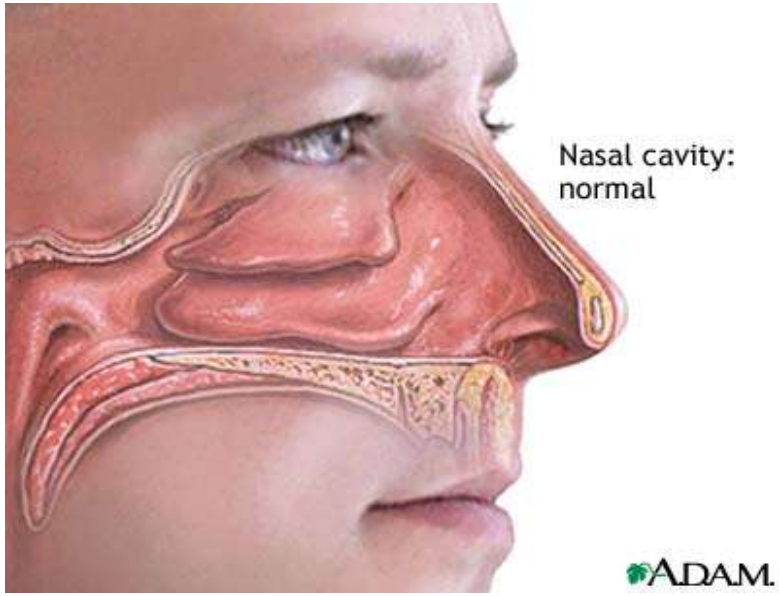


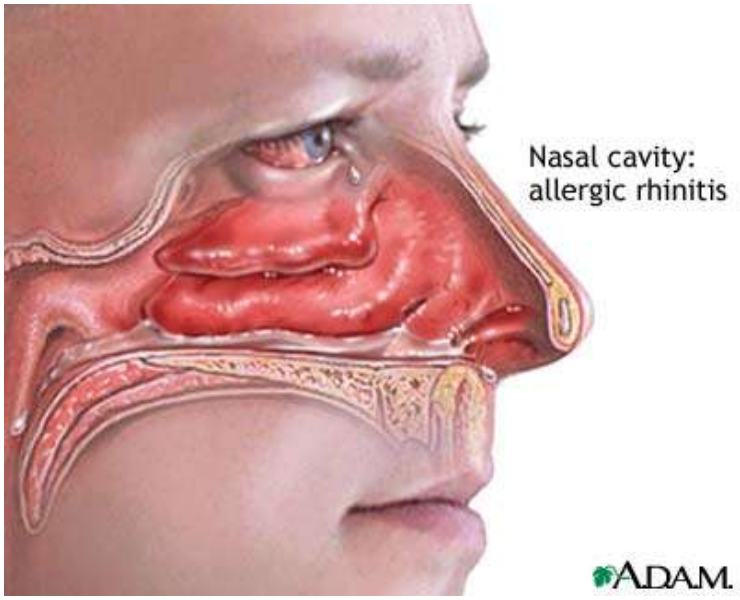
Pharynx

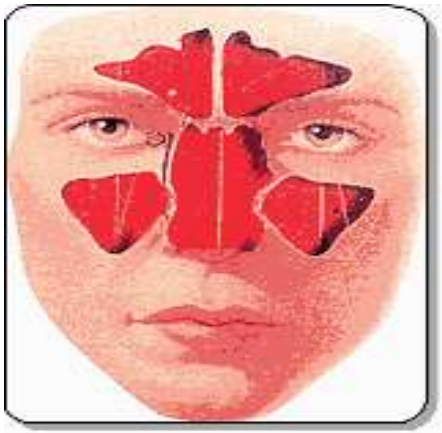
- Drops spread more extensively than the spray and three drops cover most of the walls of the nasal cavity, with the patient in a supine position and head tilted back and turned left and right.



- Nasal decongestant solutions are employed in the treatment of **rhinitis** of the common cold and for allergic rhinitis (hay fever) and for **sinusitis**.







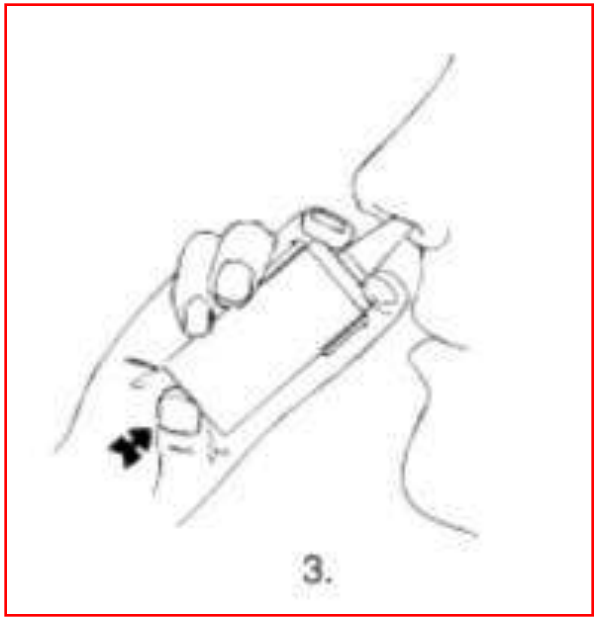
Sinuses are air-containing cavities in certain bones of the skull

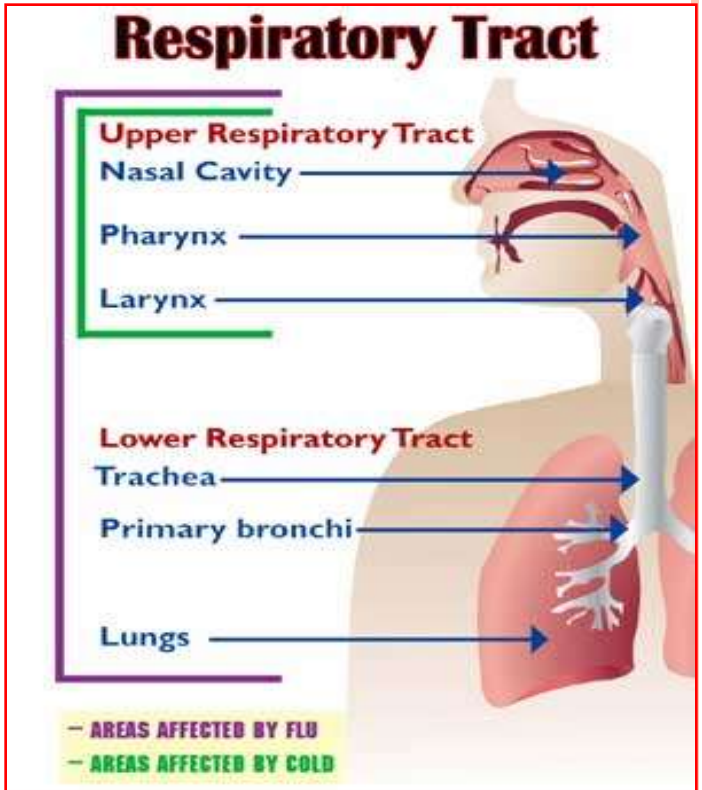
- Their frequent use or their use for prolonged periods may lead to chronic edema of the nasal mucosa, i.e. **rhinitis medicainentosa**, aggravating the symptom that they are intended to relieve. Thus, they are best used for short periods of time used for short periods of time (no longer than 3 to 5 days).

- Nasal solutions are prepared so that they are similar in many respects to nasal secretions, so that normal ciliary action is maintained thus aqueous nasal solutions usually are isotonic and slightly buffered to maintain a pH of 5.5 to 6.5.

Sprays

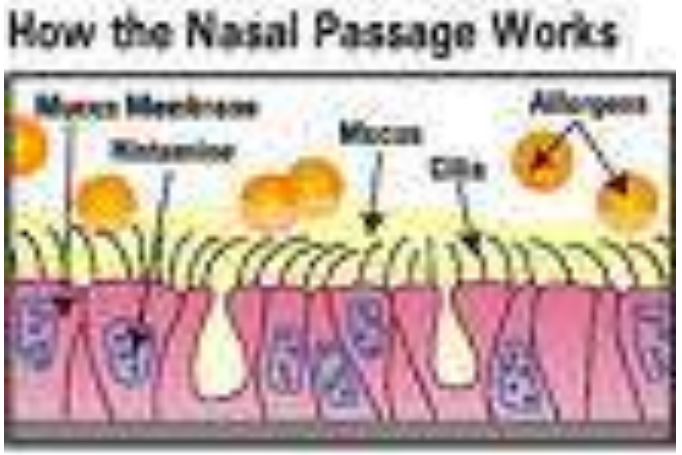
- Sprays are solutions of drugs in aqueous vehicles and are applied to the mucous membrane of the nose and throat by means of an atomizer nebulizer.
- The spray device should produce relatively **coarse droplets** if the action of the drug is to be restricted to the **upper respiratory tract**. Fine droplets tend to penetrate further into the respiratory tract than is desirable.





★**Many of the older sprays were prepared by dissolving drug in light liquid petrolatum**. This vehicle may retard the normal ciliary action of the nasal mucosa and if drops of oil enter the trachea, can cause lipoid pneumonia. **Therefore** aqueous sprays, which are isotonic with nasal secretions and of approximately the same pH are to be preferred. Such sprays may contain antibiotics, antihistamines, vasoconstrictors, alcohol, and suitable solubilizing and wetting agents.

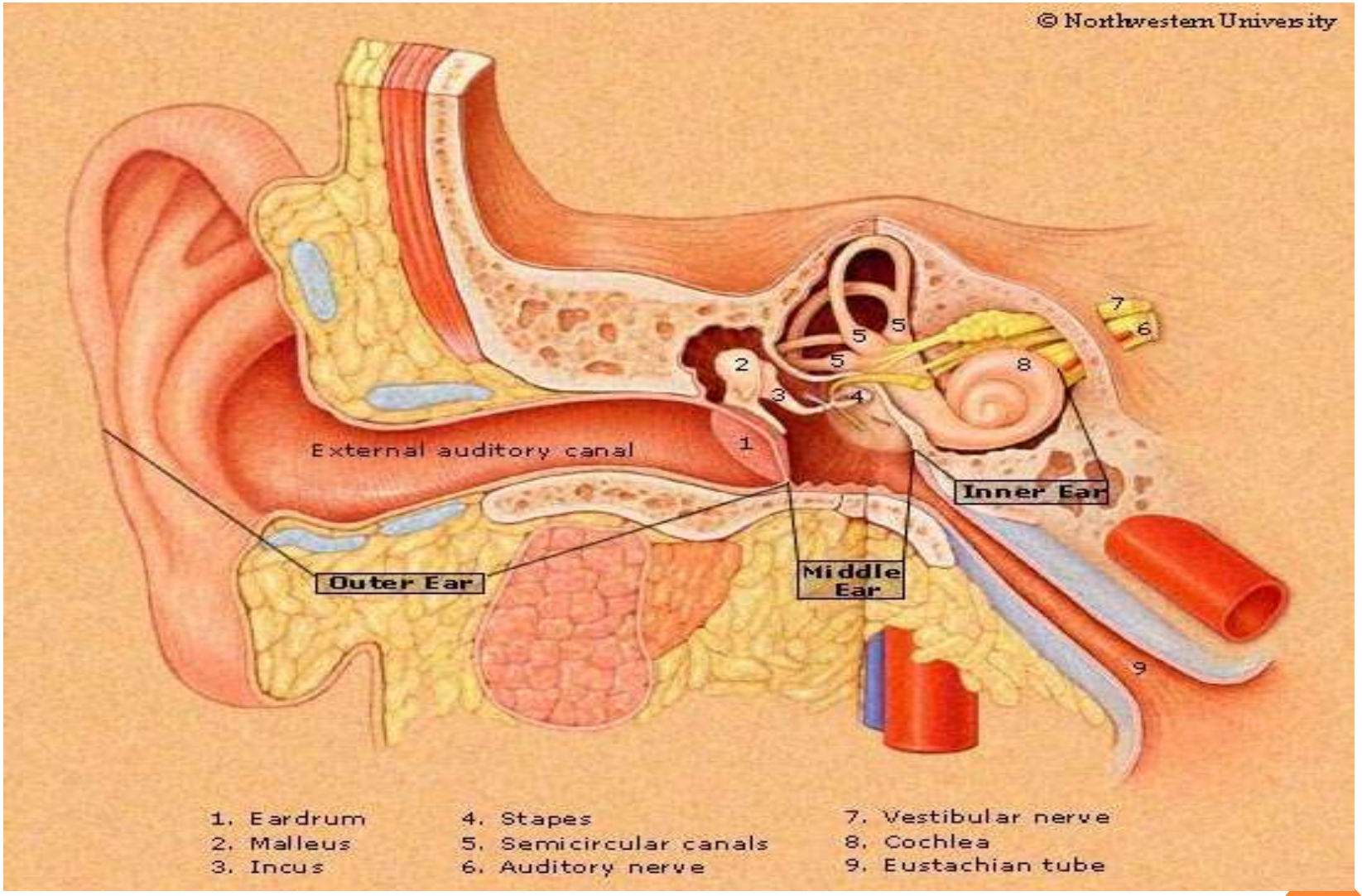
★They are used for the treatment of allergy and/or vasodilatation (congestion) that occur with common cold.



Otic Solutions

- The main classes of drugs used for topical administration to the ear include local anesthetics, e.g.: benzocaine; antibiotics e.g.; neomycin; and anti-inflammatory agents, e.g.; cortisone.
- These preparations include the main types of solvents used, namely glycerin or water.
- The viscous glycerin vehicle permits the drug to remain in the ear for a long time.

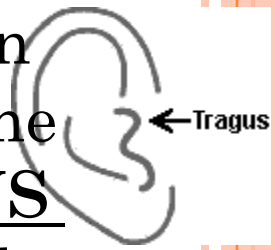
- Anhydrous glycerin, being hygroscopic, tends to remove moisture from surrounding tissues, thus reducing swelling.
- Viscous liquids like glycerin or propylene glycol either are used alone or in combination with a surfactant to aid in the removal of cerumen (ear wax).
- In order to provide sufficient time for aqueous preparations to act, it is necessary for the patient to remain on his side for a few minutes so the drops do not run out of the ear.


© Northwestern University
External auditory canal
Outer Ear
Middle Ear
Inner Ear
1. Eardrum
2. Malleus
3. Incus
4. Stapes
5. Semicircular canals
6. Auditory nerve
7. Vestibular nerve
8. Cochlea
9. Eustachian tube


CELSUS
7.5 mL
Ciprofloxacin
Dexamethasone
Anti-infective/Anti-inflammatory
FOR
EXTERNAL
USE ONLY
Rx

auditory
canal
therapeutic
formulation
infected
region

For a Middle Ear Infection:



While the person receiving Otic solution lies on his/her side, the person giving the drops should gently press the (**TRAGUS**)4 times in a pumping motion. This will allow the drops to pass through the hole or tube in the eardrum and into the middle ear.

For an Ear Canal Infection

While the person receiving the medication lies on his/her side, the person giving the drops should gently pull the outer ear upward and backward. This will allow the ear drops to flow down into the ear canal.

Ophthalmic Preparations

Introduction

The human eye is an amazing organ and the ability to see is one of our most treasure possessions. Thus the highest standards are necessary in the compounding of ophthalmic preparation and the greatest care is required in their used. It is necessary that all ophthalmic preparation are sterile and essentially free from foreign particles.

THE OPHTHALMIC PREPARATION MAY BE CATEGORIZED AS FOLLOWS :

1. **Eye drops** including solution and suspension of active medicament for instillation into the conjunctival sac.
2. **Eye lotions** for irrigation and cleaning the eye surface.
3. **Eye ointment**, **creams, and gels** containing active ingredient(s) for application to the lid margins and/or conjunctival sac.
4. **Contect lens solution** to facilitate the wearing and care of contect lenses.
5. **Parenteral product for** intracorneal, intravitreous or retrobulbar injection.
6. **Solid dosage forms placed in the conjunctival sac** and designed to release active ingredient over a prolong period.

MEDICAMENTS CONTAINED IN OPHTHALMIC PRODUCTS INCLUDING :

- Anesthetics used topically in surgical procedure.
- Anti-infective such as antibacterial, antifungal, and antiviral.
- Anti-inflammatory such as corticosteroid and antihistamine.
- Antiglucoma agent to reduce intraocular pressure, such as beta-blocker.
- Astringents such as zinc sulphate.

MEDICAMENTS CONTAINED IN OPHTHALMIC PRODUCTS INCLUDING : (CONT…)

- Diagnostic agents such as fluorescein which highlight damage to the epithelial tissue.
- Miotics such as pilocarpine which constrict the pupil and contract ciliary muscle increasing drainage from the anterior chamber.
- Mydriatics and cycloplegics such as atropine which dilate the pupil and paralysis the ciliary muscle and thus facilitate the examination of the interior of the eye.

Eye Drops


NDC 0065-8533-02
Rx Only
CIPRODEX
(ciprofloxacin 0.3% and
dexamethasone 0.1%)
STERILE
TIC SUSPENSION
5 mL
Alcon
CIPRODEX
STERILE OTIC SUSPENSION
7.5 mL

Formulation of The Eye Drops

- **Active ingredient**(s) to produce desired therapeutics effect.
- Vehicle, usually aqueous but occasionally may be oil e.g. tetracycline hydrochloride.
- **Antimicrobial preservative.**
- Adjuvant to adjust tonicity, viscosity or pH in order to increase the comfort in use and to increase the stability of the active ingredient(s).
- Suitable container for administration of eye drops which maintains the preparation in a stable form and protects from contamination during preparation, storage and use.

Antimicrobial Preservatives

- Antimicrobial preservative to eliminate any microbial contamination during use and thus maintain sterility.
- **It is essential for multiple dose of eye drops.**
- Normal healthy eyes are quite efficient at preventing penetration by microorganisms. Eye that have damaged epithelia have their defenses compromised and may be colonized by microorganism.
- The lack of vascularity of cornea and certain internal structures of the eye make it very susceptible and difficult to treat once infection has been establish.

Antimicrobial Preservatives (Cont …)

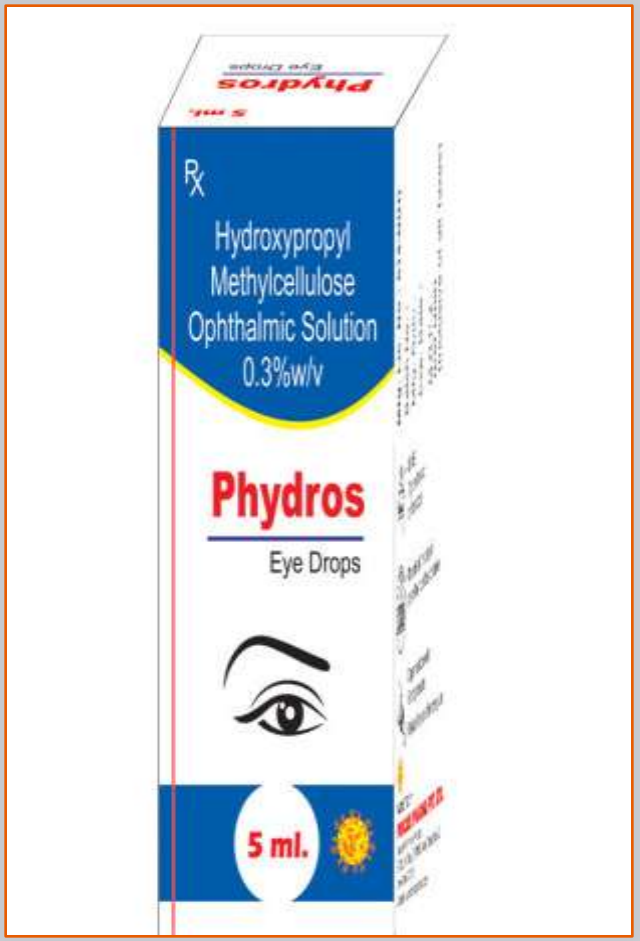
- No single substance is entirely satisfactory for use as a preservative for ophthalmic solution. The system that have been used.
- The eye drops supplied for use during intraocular surgery should not contain a preservative because of the risk of damage to the internal surface of the eye.
- Preservative suitable eye drops such as Benzalkonium chloride 0.1% w/v, chlorhexidine acetate 0.01 % w/v, chlorbutol 0.5 % w/v, phenylmercuric salts 0.001-0.04 % w/v, thiomersal 0.005-0.01 % w/v.

TONICITY

- may possible eye drops are made isotonic with lachrymal fluid (approximately equivalent to 0.9 % w/v sodium chloride solution).
- The eye will tolerate small volumes of eye drops having tonicities in the range equivalent 0.7 – 1.5 % w/v sodium chloride.
- The tonicity of hypotonic eye drops by addition of the tonicity of the lachrymal fluid.

Viscosity Enhancers

- There is general assumption that increase the viscosity of an eye drop increase the residence time of the drop in the eye and results in increase penetration and therapeutic action of the drug.
- Viscosity enhancers including polyvinyl alcohol 1.4 % w/v & methylcellulose derivative such as hypromellose " hydroxypropyl derivative of methylcellulose" 0.5 – 2 % w/v.



pH Adjustment

- the best compromise is required after considering the following factors:
  - the pH offering best stability during preparation and storage.
  - The pH offering the best therapeutic activity.
  - the comfort of the patient.

pH Adjustment (Cont …)

- Most active ingredient are salts of weak bases and are **most stable at an acid pH** but most active at a slightly alkaline pH.
- The lachrymal fluid has **a pH of 7.2 – 7.4 and** also possesses considerable buffering capacity. Thus a **50 mcl eye drop** which is weakly buffered will be rapidly neutralized by lachrymal fluid. Where possible very acidic solution, such as adrenalin acid tartrate or pilocarpine hydrochloride are buffered to reduce stinging instillation.
- Suitable buffers for eye drops including **Borate buffer, Phosphate buffer, Citrate buffer.**

Antioxidants

- Reducing agent are preferentially oxidizing and are added to eye drops in order to protect the active ingredient from oxidation.
- Active ingredient requiring protection including adrenalin, sulphacetamide, phenylephedrine…etc.

Chelating Agent

- Traces of heavy metals can catalyse breakdown of active ingredient by oxidation and other mechanism. Therefore chelating agent such as **disodium edetate** may be including to chelating the metal ions and thus enhance stability.
- disodium edetate is a very useful adjuvant to ophthalmic preparations at concentration of up to **0.1 % w/v** to enhance antimicrobial activity & chemical stability.

Container of Eye Drops

- Container should be regarded as part of the total formulation.
- They should protect the eye drops from microbial contamination, moisture and air.
- Container materials **should not be shed or leached** into solution neither should any of the eye drop formulation be sorbed by the container.
- If the product is to sterilized in the final container all parts of the container must withstand the sterilization method.
- Container may be **made of glass or plastic** and may be single or multiple dose. The latter should not contain more than **10 ml.**

EYE LOTIONS


COLLAGEN
moistfull
firming
eye cream


OLAY
TOTAL effects
7
IN ONE
EN UN
anti-aging EYE TREATMENT
SOIN anti-âge POUR LES YEUX
Eye cream with vitamins brightens the eye area and fights 7 signs of aging around your eyes
Cette crème pour les yeux, enrichie de vitamines, illumine la région des yeux et combat 7 signes de l'âge autour des yeux
NET WT/POIDS NET 14 g (0.5 OZ)
13 mL (0.4 FL OZ)

EYE LOTIONS ARE STERILE AQUEOUS SOLUTIONS INTENDED FOR USE IN **WASHING OR BATHING THE EYE OR FOR IMPREGNATING EYE DRESSINGS**.

Eye lotions may contain excipients, for example to adjust the tonicity or the viscosity of the preparation or to adjust or stabilise the pH.

These substances do not adversely affect the intended action or, at the concentrations used, cause undue local irritation.

EYE LOTIONS SUPPLIED IN MULTI-DOSE CONTAINERS CONTAIN A SUITABLE ANTIMICROBIAL PRESERVATIVE IN APPROPRIATE CONCENTRATION EXCEPT WHEN THE PREPARATION ITSELF HAS ADEQUATE ANTIMICROBIAL PROPERTIES.

The antimicrobial preservative chosen is compatible with the other ingredients of the preparation and remains effective throughout the period of time during which the eye lotions are in use.

If eye lotions are prescribed **without an antimicrobial** preservative, they are supplied in **single-dose** containers.

Eye lotions intended for use in surgical procedures or in **first-aid treatment do not contain an antimicrobial** preservative and are supplied in single-dose containers.

Eye lotions examined under suitable conditions of visibility, are practically clear and practically free from particles.

The containers for multidose preparations do not contain more than **200 ml of eye lotion**, unless otherwise justified and authorised.

Characteristics of an eye lotion :

- **Sterile and usually containing no preservative**
- **Isotonic with lachrymal fluid**
- **Neutral pH**
- **Large volume but not greater than 200 mL**
- **Non-irritant to ocular tissue**

Labelling

1. Title identifying the product and concentration of contents
2. ‘Sterile until opened’
3. ‘Not to be taken’
4. ‘Use once and discard remaining solution’
5. Expiry date

Preserved eye lotion would need the additional labelling:

'Avoid contamination of contents during use'

'Discard remaining solutions not more than 4 weeks after first opening'

<u>The lotions should be supplied in coloured fluted bottles and sealed to exclude microorganisms.</u>

Eye ointments, creams or gels

SEMI-SOLID EYE PREPARATIONS ARE STERILE OINTMENTS, CREAMS OR GELS INTENDED FOR APPLICATION TO THE CONJUNCTIVA.
THEY CONTAIN ONE OR MORE ACTIVE SUBSTANCES DISSOLVED OR DISPERSED IN A SUITABLE BASIS.
THEY HAVE A HOMOGENEOUS APPEARANCE.

Semi-solid eye preparations comply with the requirements of the monograph on *Semi-solid preparations for cutaneous application*.

The basis is non-irritant to the conjunctiva.

SEMI-SOLID EYE PREPARATIONS ARE PACKED IN SMALL, STERILISED COLLAPSIBLE TUBES FITTED OR PROVIDED WITH A CANNULA AND HAVING A CONTENT OF NOT MORE THAN 5 G OF THE PREPARATION.

The tubes must be well-closed to prevent microbial contamination.

Semi-solid eye preparations may also be packed in suitably designed single-dose containers.

The containers, or **the nozzles of tubes**, are of such a shape as to facilitate administration without contamination.

Tubes are tamper-proof.

Ointments have the disadvantage **of temporarily interfering with vision,** but have the advantage over liquids of providing greater total drug bioavailability.

However, ointments take a longer time to reach peak absorption.

Requirements to the semi-solid eye drugs

1. Sterility
2. The absence of irritating
3. Stability
4. A good distribution of MS
5. Softness consistency
6. Good contact with eye
7. Rapid formation of thinnest film on the eyeball
8. Lack of adhesion for ever
9. There should be soft, and at 15-50 ° C have a stable viscosity.

Technology of the eye ointments

1. Preparing of the ointments base
2. Production of the ointments base
3. Filtering of the ointments base
4. Introducing MS in the ointments base
5. Homogeny of the ointment
6. Packaging, labeling.

Eye ointments are normally prepared using aseptic techniques to incorporate the finely powdered active ingredient or a sterilized concentrated solution of the medicament into the sterile eye ointment basis.

Immediately after preparation the eye ointment is filled into the sterile containers which are then sealed so as to exclude microorganisms.

The screw cap should be covered with a readily breakable seal.

All apparatus used in the preparation of eye ointments must be scrupulously clean and sterile.

Certain commercial eye ointments may be sterilized in their final containers using ionising radiation.

Preparation of eye ointment basis

The paraffins and the wool fat are heated together and filtered, while molten, through a coarse filter paper in a heated funnel into a container which can withstand **dry heat sterilization temperatures**.

The container is closed to exclude microorganisms and together with contents is maintained at 160°C for 2 hours.

CONTAINERS FOR EYE OINTMENTS

Eye ointments should be supplied in **small sterilized collapsible tubes** made of metal or in a suitable plastic.

The tube should not contain more **than 5g of** preparation and must be fitted or **provided with a nozzle** of a suitable shape to facilitate application to the eye and surrounds without allowing contamination of the contents.

The tubes must be suitably sealed to prevent microbial contamination.

Eye ointment may also be packed in suitably **designed single-dose containers.**

LABELLING

- The **names and percentages** of the active ingredients.
- The **date after** which the eye ointment **is not intended** to be used.
- The conditions under which the eye ointment should be stored – normally at a temperature not exceeding 25°C..
- The name and concentration of **any antimicrobial** preservative or other substance added to the preparation
- **A statement to the effect that the contents are sterile providing the container has not been opened.**

OPHTHALMIC INSERTS

OPHTHALMIC INSERTS – IS STERILE DRUGS ARE INTENDED FOR INSERTING IN THE CONJUNCTIVE SAC. THEY CONSIST OF MATRIX, WHICH INCLUDES MS IN THE MEMBRANE CONTROLLING RATE OF THE MEDICINES SUBSTANCES RELEASE.

Ophthalmic inserts are solid or semi-solid preparations of suitable size and shape, designed to be inserted in the conjunctival sac, to produce an ocular effect.

Advantages of ophthalmic inserts:

1. Accuracy of dosing.
2. Convenience of using.
3. Prolonged action.
4. Absence of the allergic reaction.
5. Shorter time of the coarse treatment in 2-3 time.

Classification of the eye inserts:

- ***Soluble***
- ***Insoluble***
- ***Soluble in the biological liquid*** **– is matrices with homogenous dispersible MS, which is included (or not) in the hydrophobic layer. Layer isn't penetrated for active substances.**

SOLUBLE OPHTHALMIC INSERTS:

1. Natural polymers (collagen) are base of the inserts.
2. Artificial (man-made) polymers (methylcellulose) are base of the inserts.

Disadvantages:

- High rate of penetration of tear fluid.
- Blurred vision.

CLASSIFICATION OF INSOLUBLE OPHTHALMIC INSERTS:

a) Diffuse system, consisting of a central reservoir with drugs in it.

b) Osmotic system, consisting of the central part surrounded by the peripheral part.

The central part has as simple reservoir and two different departments.

In the reservoir there is MS and auxiliary substances to create osmotic pressure.

c) Hydrophilic contact lenses is a coherent system that consists of a polymer that allows you to keep aqueous solutions of the MS or solid components.

Classification of the contact lenses

1. Rigid
2. Semi-rigid
3. Elastomeric
4. Soft hydrophilic
5. Biopolymeric

Characterization of the contact lenses:

Advantage of the lenses – they are able to correct refractive defects of vision and improves visual acuity.

Disadvantage

- Permanent contact with hands.
- Required frequent washing, which causes the risk of contamination and loss of drugs
- High price.

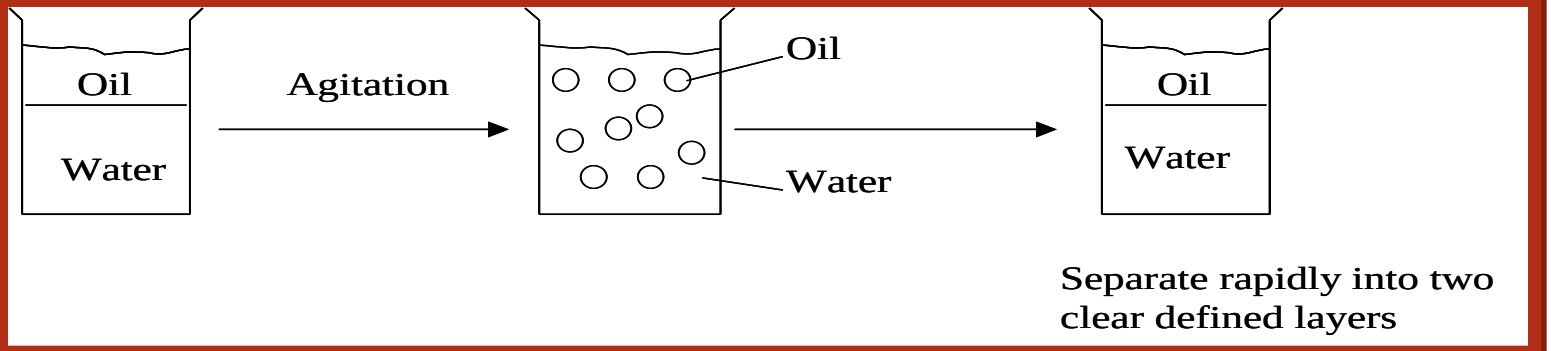
EMULSIONS

Emulsions

1) Definition.
2) Types of Emulsions.
3) Advantages/ Disadvantages.
4) Test of Identifications.
5) Emulsifying Agents.
6) Types of Emulsifying Agents.
7) Theories of Emulsification.
8) Preparation of Emulsions.
9) Stability of Emulsions.

Definition

- An Emulsion is a mixture of two or more liquids that are normally Immiscible.

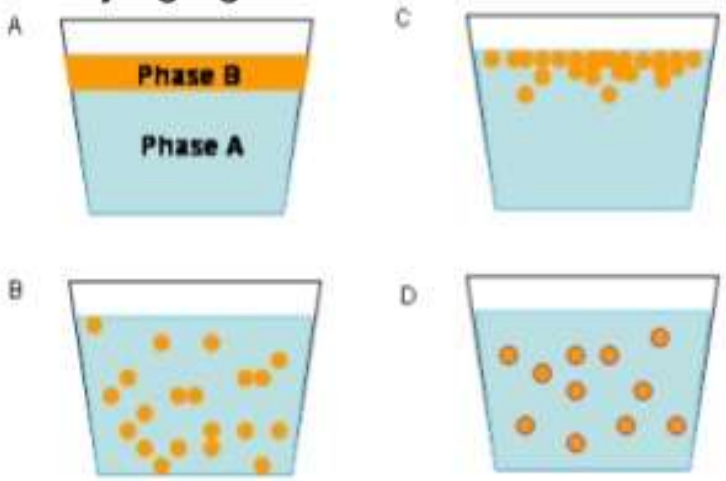


OR

- Emulsion, is a mixture of two or more liquids in which one is present as droplets, of microscopic or ultramicroscopic size, distributed throughout the other.

Emulsion

An emulsion is a thermodynamically unstable system consisting of at least two immiscible liquid phases, one of which is dispersed as globules in the other liquid phase, stabilized by the presence of an emulsifying agent.



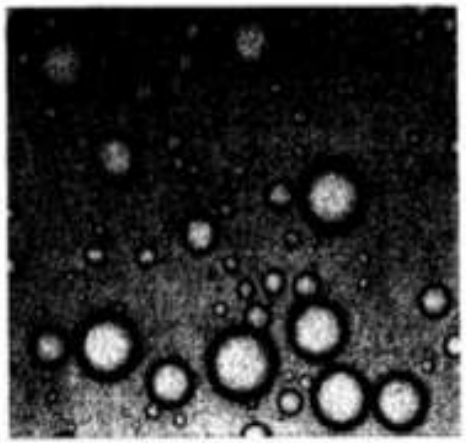


Fig. 13.8 *Mineral oil in water emulsion. The largest oil globule in the photograph measures approximately 0.04 mm. (Courtesy of James C. Price, Ph.D., College of Pharmacy, The University of Georgia.)*

A'. Two immisicble liquids, not emulsified; B'. An emulsion of Phase B dispersed in Phase A; C'. The unstable emulsion progressively separates; D'. The (purple) surfactant positions itself on the interfaces between Phase A and Phase B, stabilizing the emulsion

Internal Phase or External Phase in Emulsions:

- The dispersed liquid is known as the **Internal or Discontinuous phase.**
- whereas the dispersion medium is known as the **External or Continuous phase.**

Types 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.
- Water in Oil in water (W/O/W): Water in Oil emulsion dispersed in water – multiple emulsion.

Based on size of liquid droplets:

- 0.2 – 50 mm Macroemulsions
- 0.01 – 0.2 mm Microemulsions

Advantages of Emulsions:

- Mask the unpleasant taste O/W is convenient means of oral administration of water-insoluble liquids.
- Oil-soluble drugs can be given parentrally in form of oil-in water emulsion. (e.g Taxol).
- Emulsion can be used for external application in cosmetic and therapeutic Application because of Better and faster absorption.
- Sustained release medication.
- Nutritional supplement.
- Inert and chemically non-reactive.
- Reasonably odorless and cost Effective.

- Radiopague agents for diagnostic purposes.
- Intravenous Nutrition (maintenanceof debilitated patients)- Intralipid, Nutralipid).
- Fluorocarbon Emulsions- fluorocarbons have high capacities for dissolving gases like O_2 and CO_2 and serve as blood substitutes for a short period of time.

DISADVANTAGES OF EMULSIONS:

- Emulsions are thermodynamically unstable and have short shelf-life.
- Improper formulation of emulsions leads to creaming and cracking of emulsion.
- Improper selection of emulsifying agent leads to phase inversion and some times it may also lead to cracking.

Identification test for Emulsions:

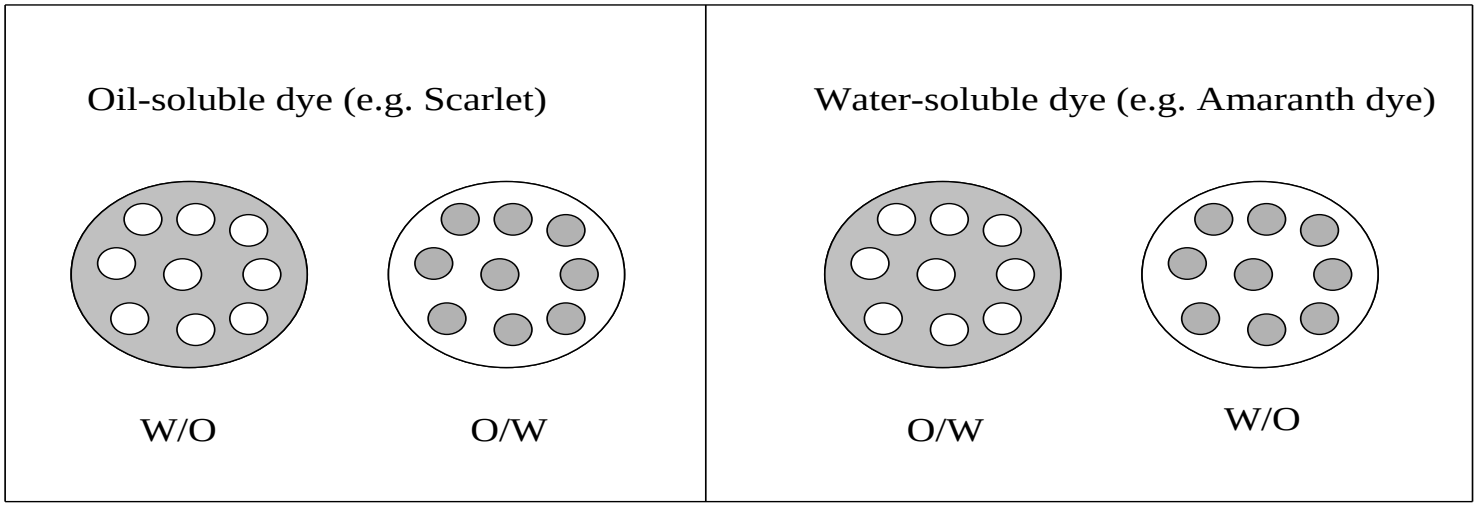
By using Naked eye, it is very difficult to differentiate between o/w or w/o emulsions. Thus, the following methods have been used to identify the type of emulsions.

1) Dye Test
2) Dilution Test
3) Electrical conductivity Test
4) Fluorescence Test.
5) Cobalt Chloride Test.

1) DYE TEST:

- Water-soluble dye will dissolve in the aqueous phase.
- Oil-soluble dye will dissolve in the oil phase.

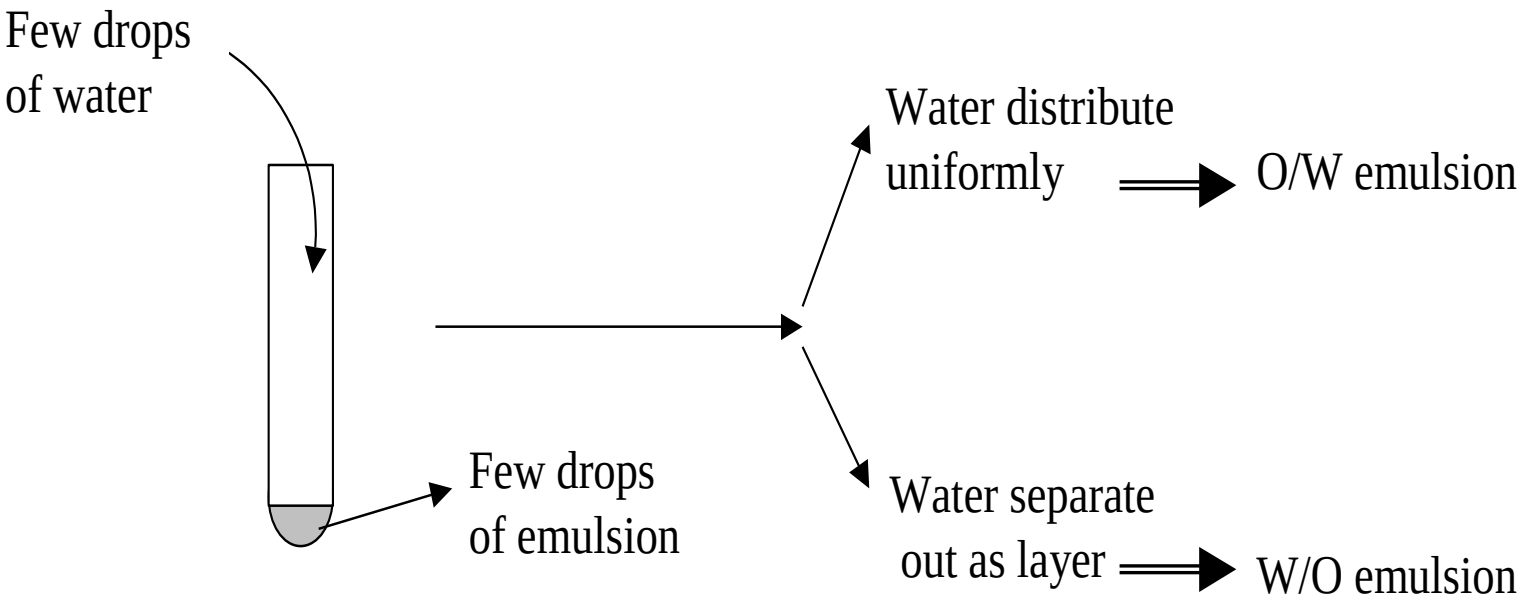
Microscopic View



2) Dilution test:

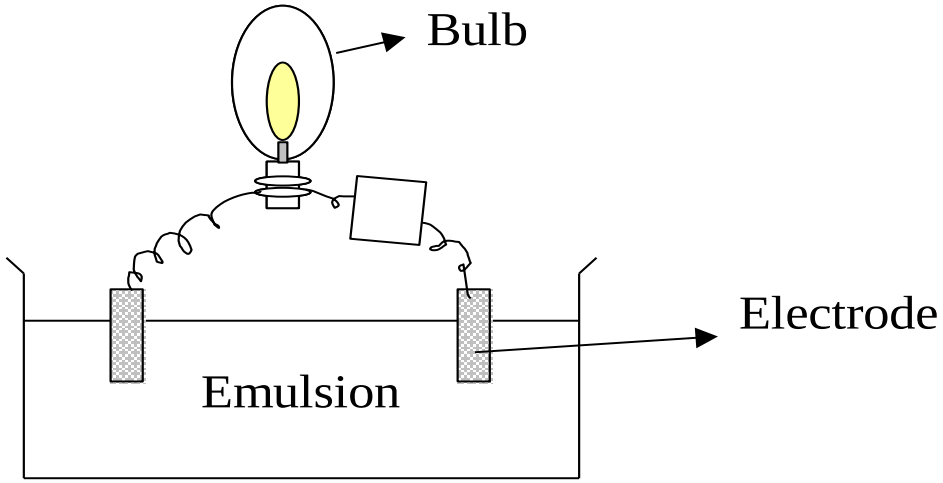
Based on the solubility of external phase of emulsion.

- ✓ O/W emulsion can be diluted with water.
- ✓ W/O emulsion can be diluted with oil.



3) Electrical Conductivity test:

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



- Bulb glows with O/W
- Bulb doesn't glow with W/O

3) Fluorescence test:

- Oils give fluorescence under UV light, while water doesn't.
- Therefore, O/W emulsion shows spotty pattern when observed under UV.
- while W/O emulsion fluoresces.

4) Cobalt Chloride test:

- Principle:
- Cobalt Chloride solution is used for identification of Emulsion. It is water soluble so it changes colour when encountered by O/W emulsion.

Procedure:

Filter paper is Dipped in Emulsion.

Filter paper changes its color from blue to Pink

- Result:

Emulsion is O/W otherwise not.

Emulsifying Agent:

- Definition: Emulsions are stabilized by adding an emulsifying agent. These agents have both a hydrophilic and a Lipophilic part in their chemical structure. All emulsifying agents get adsorbed onto the Oil : water interface to provide a protective barrier around the dispersed droplets. In addition to this protective barrier, emulsifiers stabilize the emulsion by reducing the interfacial tension of the system.

Classification Of Emulsifying Agents:

- Emulsifying agents can be classified according to:
  1) chemical structure:
- Synthetic Emulsifying Agents
- Natural Emulsifying Agents
- Finely Dispersed Solids
- Auxilary Agents

2) Mechanism of action:

- ✓ Monomolecular
- ✓ Multi-molecular
- ✓ Solid particle films.

Synthetic Emulsifying Agents

1) Anionic: (pH > 8)

- ✓ Sodium stearate
- ✓ Potassium laurate
- ✓ Sodium dodecyl sulfate
- ✓ Sodium sulfosuccinate.
- ✓ Sodium or potassium oleate
- ✓ Triethanolamine stearate
- ✓ sodium lauryl sulfate.

2) Cationic: (pH 3-7)

- ✓ Benzalkonium chloride,
- ✓ Benzethonium chloride
- ✓ Quaternary ammonium salts.

3) Non Ionic (pH 3-10)

- Polyglycol,
- Fatty acid esters,
- Lecithin.
- Sorbitan esters (Spans).
- Polyoxyethylene derivatives of sorbitan esters (Tweens),
- Glyceryl esters.

* * * Cationic and Anionic surfactants are generally limited to use in topical, o/w emulsions * * *

Natural Emulsifying Agents

Derived from Plants and Animals:

Vegetable derivatives:

- ✓ Acacia
- ✓ Tragacanth
- ✓ Agar
- ✓ Pectin
- ✓ Carrageenan
- ✓ Lecithin

Animal derivatives:

- ✓ Gelatin
- ✓ Lanolin
- ✓ Cholesterol

Finely Divided or Finely Dispersed Solid Particle Emulsifiers

- These agents form a particulate layer around dispersed particles. Most will swell in the dispersion medium to increase viscosity and reduce the interaction between dispersed droplets. Most commonly they support the formation of o/w emulsions, but some may support w/o emulsions. For Instance,,
- Bentonite
- Veegum,
- Hectorite,
- Magnesium Hydroxide,
- Aluminum Hydroxide
- Magnesium Tri silicate.

Auxiliary Emulsifying Agents

- A variety of fatty acids (e.g., stearic acid), fatty alcohols (e.g., stearyl or cetyl alcohol), and fatty esters (e.g., glyceryl monostearate) serve to stabilize emulsions through their ability to thicken the emulsion..
- A system was developed to assist in making systemic decisions about the amounts and types of surfactants needed in stable products. The system is called the HLB (hydrophile-lipophile balance) system and has an arbitrary scale of 1 - 18. HLB numbers are experimentally determined for the different emulsifiers. .

- Low HLB Indicates ?
- ✓ Low number of hydrophilic groups on the Molecule thus imparting Lipophilic character:

- ✓ Spans have low HLB numbers, Because of their oil soluble character, Spans will cause the oil phase to predominate and form an w/o emulsion.
- High HLB indicates ?
- Emulsifier has a large number of hydrophilic groups on the molecule thus imparting hydrophilic Character.
- Tweens have higher HLB numbers, Because of their water soluble character, Tweens will cause the water phase to predominate and form an o/w emulsion.

HLB VALUE & APPLICATION

1 ~ 3	Anti-foaming agent.
3 ~ 6	W/o emulsifying agents.
7 ~ 9	Wetting agents.
8 ~ 18	O/w emulsifying agents.
13 ~15	Detergents.
15 ~18	Solubilizing Agents.

How to Calculate HLB ????

- Combinations of emulsifiers can produce more stable emulsions than using a single emulsifier with the same HLB number. The HLB value of a combination of emulsifiers can be calculated as follows:

$$HLB = \frac{(Quantity\ of\ surfactant\ 1)(HLB\ surfactant\ 1) + (quantity\ of\ surfactant\ 2)(HLB\ surfactant\ 2)}{quantity\ of\ surfactant\ 1 + quantity\ of\ surfactant\ 2}$$

Numerical 1:

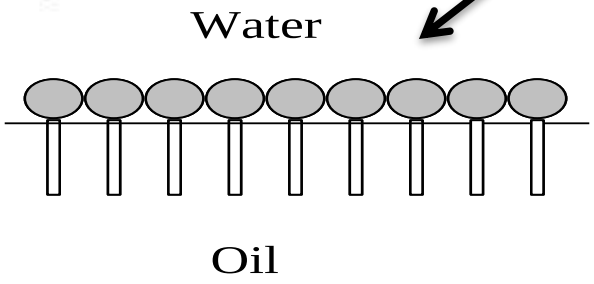
- *What is the HLB value of a surfactant system composed of 20 g Span 20 (HLB = 8.6) and 5 g Tween 21 (HLB = 13.3)?*

$$HLB = \frac{(\text{Quantity of surfactant 1})(\text{HLB surfactant 1}) + (\text{quantity of surfactant 2})(\text{HLB surfactant 2})}{\text{quantity of surfactant 1} + \text{quantity of surfactant 2}}$$

$$HLB = \frac{(20\ g)(8.6) + (5\ g)(13.3)}{(20\ g + 5\ g)} = 9.54$$

Classification of emulsifying agents

- Surface active agents (monomolecular film)
- Hydrophilic colloids (multimolecular film)
- Finely divided solid particles (Particulate film)



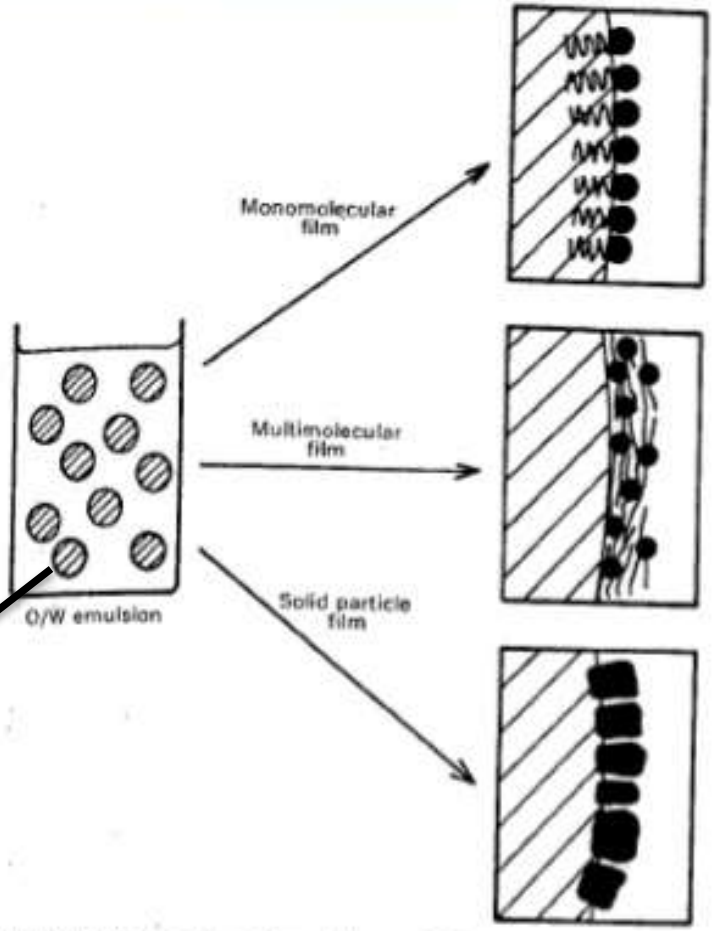


Figure 22-6. Types of films formed by emulsifying agents at the oil–water interface. Orientations are shown for O/W emulsions. ▩: oil. □: water.

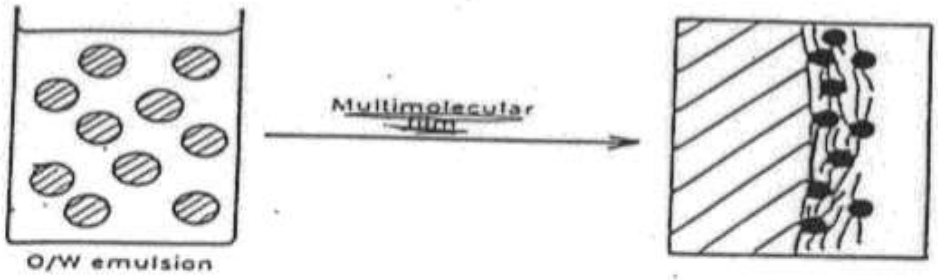
Classification of Emulsions Based on Mechanism of Action:

1) Monomolecular film: To reduce the interfacial tension Oil droplets are surrounded by a coherent monolayer of the surfactant which prevents coalescence. If the emulsifier is ionized, the presence of strong charge may lead to repulsion in droplets and hence increasing stability. Adsorbed at oil/water interface to form

2) Multimolecular film or Hydrophillic Colloids

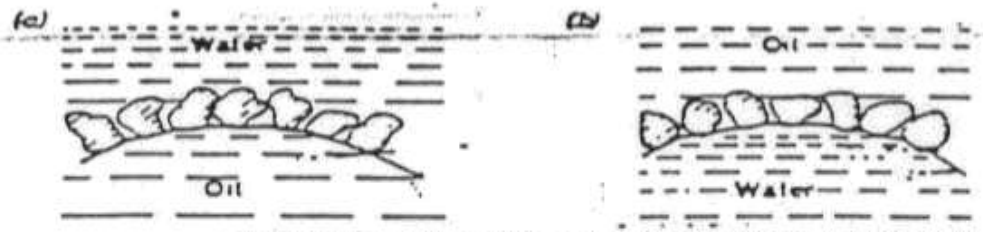
3) Finely divided solid particles: They are adsorbed at the interface between two immiscible liquid phases to form Particulate film.

2. ***Hydrophilic Colloids*** – form multimolecular films



- promote O/W
- form strong films
- may be charge
- do not cause appreciable lowering of surface tension
- increase in viscosity of dispersion medium

3. ***Finely divided solid particles*** – form solid particle films



. Stabilisation of emulsions by finely divided solids: (a) preferential wetting by water leading to an O/W emulsion; (b) preferential wetting by oil leading to a W/O emulsion

- particles are smaller than droplet
- particles are wetted by both oil and water
- O/W and W/O emulsion can be formed depending on preferential wetting by oil or water.

Theories of Emulsification:

Many theories have been advanced to account for the way or means by which the emulsion is stabilized by the emulsifier. At the present time no theory has been postulated that seems to apply universally to all emulsions.

1) Electric Double Layer Theory.
2) Phase Volume Theory.
3) Hydration Theory of Emulsions
4) Oriented wedge theory.
5) Adsorbed Film and Interfacial tension Theory

1) Electric Double Layer Theory:

The oil globules in a pure oil and pure water emulsion carry a negative charge. The water ionizes so that both hydrogen and hydroxyl ions are present. The negative charge on the oil may come from adsorption of the OH ions. These adsorbed hydroxyl ions form a layer around the oil globules. A second layer of oppositely charged ions forms a layer in the liquid outside the layer of negative ions. These two layers of oppositely charged ions are known as the Helmholtz double layer. They are not confined to emulsions but accompany all boundary phenomena. The electric charge is a factor in all emulsions, even those stabilized with emulsifying agents

2) Phase Volume Theory:

If spheres of the same diameter are packed as closely as possible, one sphere will touch 12 others and the volume the spheres occupy is about 74 per cent of the total volume. Thus if the spheres or drops of the dispersed phase remain rigid it is possible to disperse 74 parts of the dispersed phase in the continuous phase; but if the dispersed phase is increased to more than 74 parts of the total volume, a reversal of the emulsion will occur. However, the dispersed phase does not remain rigid in shape but the drops flatten out where they come in contact with each other, nor are all the dispersed particles the same, so that it is possible for the dispersed phase to consist of from 1 to 99 per cent of the emulsion.

3) Hydration Theory of Emulsions:

- Fischer and Hooker state that hydrated colloids make the best emulsifiers. Fischer states the emulsifying agent, by which a permanent emulsion is obtained, invariably "proves to be a hydrophilic colloid when water and oil emulsions are concerned (a lyophilic colloid of some sort when other than aqueous mixtures are under consideration). Put another way, oil cannot permanently be beaten into water, but only into a colloid hydrate."
- Fischer and Hooker have found albumin, casein, and gelatin to be good emulsifying agents.

4) Oriented wedge theory:

- This theory deals with formation of monomolecular layers of emulsifying agent curved around a droplet of the internal phase of the emulsion.

Example:

- In a system containing 2 immiscible liquids, emulsifying agent would be preferentially soluble in one of the phases and would be embedded in that phase.

- Hence an emulsifying agent having a greater hydrophilic character will promote o/w emulsion and vice-versa.

- Sodium oleate is dispersed in water and not oil. It forms a film which is wetted by water than by oil. This leads the film to curve so that it encloses globules of oil in water.

- Sodium Oleate Zinc Oleate

5) Adsorbed film and interfacial tension theory:

- Lowering interfacial tension is one way to decrease the free surface energy associated with the formation of droplets. Assuming the droplets are spherical,

- $\Delta F = \frac{6 \gamma V}{D}$
- V= volume of the dispersed phase in ml, d is the mean diameter of the particles.
- γ = interfacial tension

- It is desirable that:
- The surface tension be reduced below 10dynes/cm by the emulsifier and Be absorbed quickly.

6) Surface Tension Theory:

- A drop of liquid forms a spherical shape which gives it the smallest surface area per unit volume
- When 2 drops come together to form a bigger drop- gives lesser surface area. Also called surface tension at air-liquid interface
- Surface Tension- Force that has to be applied parallel to the surface of liquid to counterbalance exactly the internal inward forces that tend to pull the molecule together.
- When there are two immiscible liquids-it is called interfacial tension.

Methods of Preparation Of Emulsions:

- Commercially, emulsions are prepared in large volume mixing tanks and refined and stabilized by passage through a colloid mill or homogenizer. Extemporaneous production is more concerned with small scale methods.

- ✓ 1) Dry Gum Methods
- ✓ 2) Wet Gum Methods
- ✓ 3) Bottle Method
- ✓ 4) Beaker Method.
- ✓ 5) In situ Soap Method.

DRY GUM METHOD FOR PREPARATION OF EMULSIONS:

- Dry gum method is used to prepare the initial or primary emulsion from oil, water, and a hydrocolloid or "gum" type emulsifier.

Dry Gum Methodology

(4 parts oil, 2 parts water, and 1 part Emulsifier).

- Procedure: Take mortar, 1 part gum is levigated with the 4 parts oil until the powder is thoroughly wetted; then the 2 parts water are added all at once, and the mixture is vigorously triturated until the primary emulsion formed is creamy white and produces a "crackling" sound as it is triturated.

- Active ingredients, preservatives, color, flavors are added as a solution to the primary emulsion.

- When all agents have been incorporated, the emulsion should be transferred to a calibrated vessel, brought to final volume with water.

Preparing emulsion by dry gum method

- Cod liver oil 50 mL
- Acacia 12.5 g
- Syrup 10 mL
- Flavor oil 0.4 mL
- Purified water, qs ad 100 mL

- Accurately weigh or measure each ingredient
- Place cod liver oil in dry mortar
- Add acacia and give it a very quick mix
- Add **25 mL** of water and immediately triturate to form the thick, white, homogenous primary emulsion
- Add the flavor and mix
- Add syrup and mix
- Add sufficient water to total 100 mL

Wet Gum Method

Methodology

(Oil 4 parts + Water 2 parts + Emulsifier 1 parts)

Procedure: In this method, the proportions of oil, water, and emulsifier are the same (4:2:1), but the order and techniques of mixing are different. The 1 part gum is triturated with 2 parts water to form a mucilage; then the 4 parts oil is added slowly, in portions, while triturating. After all the oil is added, the mixture is triturated for several minutes to form the primary emulsion. Then other ingredients may be added as in the continental method. Generally speaking, the English method is more difficult to perform successfully, especially with more viscous oils, but may result in a more stable emulsion.

Bottle Method

- This method may be used to prepare emulsions of volatile oils, Oleaginous substances of very low viscosities.
- This method is a variation of the dry gum method.
- One part powdered acacia (or other gum) is placed in a dry bottle and four parts oil are added. The bottle is capped and thoroughly shaken. To this, the required volume of water is added all at once, and the mixture is shaken thoroughly until the primary emulsion forms.
- Reference: http://pharmlabs.unc.edu/labs/emulsions/beaker.htm

Beaker Method

- The most appropriate method.
- Dividing components into water soluble and oil soluble components.
- All oil soluble components are dissolved in the oily phase in one beaker and all water soluble components are dissolved in the water in a separate beaker.
- Oleaginous components are melted and both phases are heated to approximately 70°C over a water bath. The internal phase is then added to the external phase with stirring until the product reaches room temperature.

In situ Soap Method:

- Two types of Soaps developed by this Methods:

1) Calcium Soaps

2) Soft Soaps

1) Calcium Soaps: W/O type Emulsions. E.g. Oleic acid + Lime water. Prepared by simple mixing of equal volumes of Oil and Lime water.

✓ Emulsifying agent used is Calcium salt of free fatty acids. E.g. Olive Oil + Oleic acid (FAA) = calcium Oleate.

Advantage: O/W is external Phase used frequently on dry skin and sun burned skin.

Calamine LinimentPreparation:

- Calamine…….
- Zinc Oxide……. 80g
- Olive Oil…….
- Calcium Hydro Oxide sol. 1000ml

Stability Issues:

1. Emulsions are, by nature, physically unstable; that is, they tend to separate into two distinct phases or layers over time.
2. **Creaming** occurs when dispersed oil droplets merge and rise to the top of an o/w emulsion or settle to the bottom in w/o emulsions. In both cases, the emulsion can be easily redispersed by shaking.
3. **Coalescence (breaking or cracking)** is the complete and irreversible separation and fusion of the dispersed phase.
4. **Phase inversion** or a change from w/o to o/w (or vice versa) may occur. This is considered a type of instability by some.

- Addition of Electrolyte: Addition of $Cacl_2$ into O/W emulsion formed by sodium stearate will be inverted into W/O.

PHARMACEUTICAL SUSPENSIONS

CONTENTS

- Definition.
- Classification.
- Advantages & disadvantages.
- Applications.
- Theoretic consideration of suspensions.
  - Sedimentation
  - Brownian movement
  - Electrokinetic properties

- Formulation of suspensions
- Packing of suspensions
- Storage requirement & labelling
- Evaluation of suspension
- Dissolution study of suspensions
- Innovation of suspensions

WHAT ARE SUSPENSIONS

WHY WE ARE USING SUSPENSIONS?

DISPERSE SYSTEM

- The term "**Disperse System**" refers to a system in which one substance (**The Dispersed Phase**) is distributed, in discrete units, throughout a second substance (**the continuous Phase**).
- Each phase can exist in **solid, liquid**, or **gaseous state** .
- *Suspensions are heterogenous system consisting of 2 phases.*

A solid in liquid dispersion in which the particles are of colloidal size.

DISPERSE SYSTEM

DISPERSED MEDIUM

- **Aqueous oily liquid**

DISPERSED PHASE

- **Insoluble solid**

Definition

- A Pharmaceutical suspension is a coarse dispersion in which internal phase (**therapeutically active ingredient**)is dispersed uniformly throughout the external phase.

- The **internal phase** consisting of insoluble solid particles having a range of size(**0.5 to 5 microns**) which is maintained uniformly through out the suspending vehicle with aid of **single or combination of suspending agent.**

- The external phase (**suspending medium**) is generally aqueous in some instance, may be an organic or oily liquid for non oral use.

The reasons for the formulation of a pharmaceutical suspension:

-- when 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.

SOME PHARMACEUTICAL SUSPENSIONS

- 1. Antacid oral suspensions
- 2. Antibacterial oral suspension
- 3. Dry powders for oral suspension (antibiotic)
- 4. Analgesic oral suspension
- 5. Anthelmentic oral suspension
- 6. Anticonvulsant oral suspension
- 7. Antifungal oral suspension

Classification

Based On General Classes

- Oral suspension
  eg: Paracetamol suspension
  antacids, Tetracycline HCl.

- Externally applied suspension
  eg :Calamine lotion.

- Parenteral suspension
  eg: Procaine penicillin G
  Insulin Zinc Suspension

Based on Proportion of Solid Particles

- Dilute suspension (2 to10%w/v solid)

Eg: cortisone acetate, predinisolone acetate

- Concentrated suspension (50%w/v solid)

Eg: zinc oxide suspension

Based on Electrokinetic Nature of Solid Particles

- Flocculated suspension
- Deflocculated suspension

Based on Size of Solid Particles

- **Colloidal suspensions (< 1 micron)**

  -Suspensions having particle sizes of suspended solid less than about 1micron in size are called as colloidal suspensions.

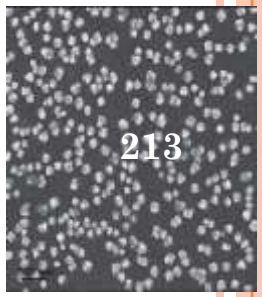
Coarse suspensions (>1 micron)

- Suspensions having particle sizes of greater than about 1micron in diameter are called as coarse suspensions.

Coarse dispersion
Barium sulphate

Nano suspensions (10 ng)

- Suspensions are the biphasic colloidal dispersions of nanosized drug particles stabilized by surfactants.
- Size of the drug particles is less than 1mm.



Advantages And Disadvantages

Advantages

.Suspension can improve chemical stability of certain drug.
E.g. Procaine penicillin G.

➢Drug in suspension exhibits higher rate of bioavailability than other dosage forms.

Solution > Suspension > Capsule > Compressed Tablet > Coated tablet

➢Duration and onset of action can be controlled.
E.g. Protamine Zinc-Insulin suspension.

➢Suspension can mask the unpleasant/ bitter taste of drug.
E.g. Chloramphenicol

Disadvantages

- Physical stability , sedimentation and compaction can causes problems.
- It is bulky sufficient care must be taken during **handling and transport.**
- **Uniform and accurate dose can not be achieved** unless suspension are **packed in unit dosage form.**

Applications

- Suspension is usually applicable for drug which **is insoluble (or) poorly soluble.**
  E.g. Prednisolone suspension

- To prevent **degradation** of drug or to **improve stability of drug.**
  E.g. Oxy tetracycline suspension

- To mask the taste **of bitter of unpleasant drug**.
  E.g. Chloramphenicol palmitate suspension

- Suspension of drug can be formulated for **topical application**
  e.g. Calamine lotion

- Suspension can be formulated for parentral application in order to **control rate of drug absorption**. E.g. penicillin procaine

- **Vaccines as a immunizing agent** are often formulated as suspension. E.g. Cholera vaccine

- **X-ray contrast agent** are also formulated as suspension .
eg: Barium sulphate for examination of alimentary tract.

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.

THEORITIC CONSIDERATION OF SUSPENSIONS

A knowledge of the theoretic considerations pertaining to suspension s technology ultimately help formulator to select ingredients that are

- Appropriate for suspension preparation
- That available for milling
- Mixing equipment

- **Some theoretic considerations are :**
  - **Particle size control.**
  - **Wetting**
  - **Sedimentation**
  - **Brownian movement**
  - **Electokinetic**
  - **Aggregation**

Particle size control:

- Particle size of any **suspension is critical and must be reduced within the range .**

-Too large or too small particles should be avoided.

Larger particles will:

- settle faster at the bottom of the container
- particles > 5 um impart a gritty texture to the product and also cause irritation if injected or instilled to the eye
- particles > 25 um may block the needle

-Too fine particles will easily form hard cake at the bottom of the container.

Wetting of the particles

- Hydrophilic materials (talc, ZnO, Mg_2CO_3) are easily wetted by water while hydrophobic materials (sulphur , charcoal) are not due to the layer of adsorbed air on the surface.

- Thus, the particles, even high density, float on the surface of the liquid until the layer of air is displaced completely.

- The use of wetting agent allows removing this air from the surface and to easy penetration of the vehicle into the pores.

- However hydrophobic materials are easily wetted by non-polar liquids.

THEORY OF SEDIMENTATION

SEDIMENTATION:

Sedimentation means settling of particle (or) floccules occur under gravitational force in liquid dosage form.

Velocity of sedimentation expressed by Stoke's equation

Where,

$$v_{sed.} = \frac{d^2(\rho_s - \rho_o)g}{18\eta_o} = \frac{2r^2(\rho_s - \rho_o)g}{9\eta_o}$$

d = Diameterof particle

r = radius of particle

$v_{sed.}$ = sedimentation velocity in cm / sec

ρ_s = density of disperse phase

ρ_o = density of disperse media

g = acceleration due to gravity

η_o = viscosity of disperse medium in poise

Limitation Of Stoke's Equation ·

Stoke's equation applies only to:

- Spherical particles in a **very dilute suspension** (0.5 to 2 gm per 100 ml)
- Particles which **freely settle without collision** .
- Particles with **no physical or chemical attraction.**

Sedimentation Parameters

Sedimentation volume (F) or height (H) for flocculated suspensions:

Definition:

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

$$F = V_u / VO$$

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

The sedimentation volume gives only a qualitative account of flocculation.

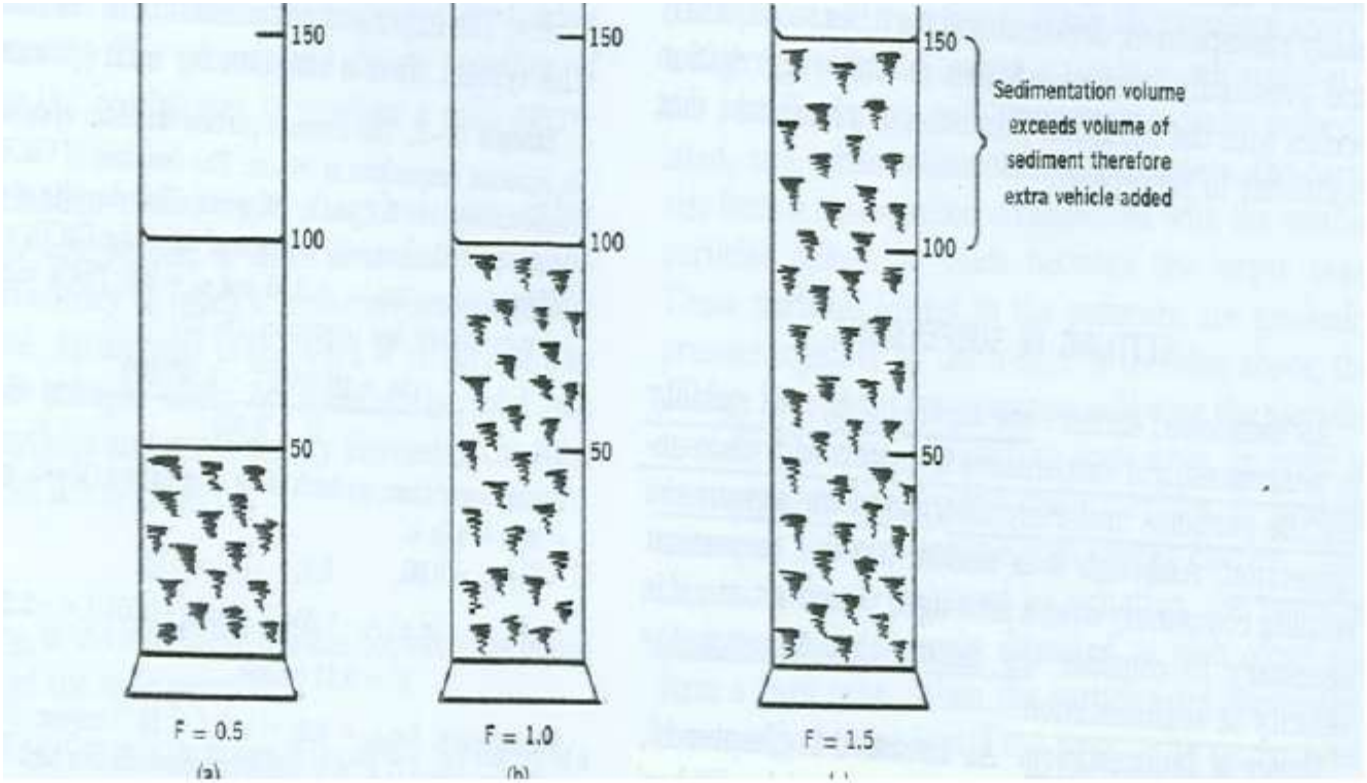


Fig : Suspensions quantified by sedimentation volume (f)

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∞

$$ß = F / F\infty$$

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

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

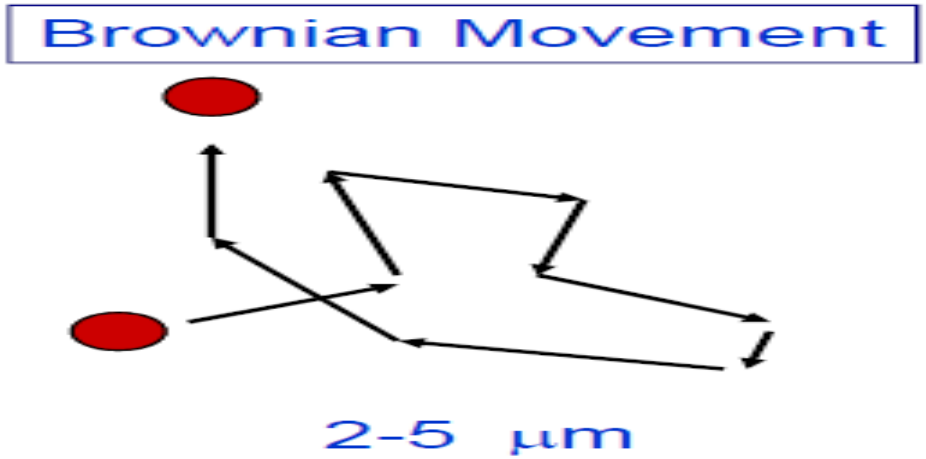
2.Brownian Movement (Drunken walk)

- Brownian movement of particle prevents sedimentation by keeping the dispersed material in random motion.

- Brownian movement depends on the **density of dispersed phase** and **the density and viscosity of the disperse medium**.

- The kinetic bombardment of the particles by the molecules of the suspending medium will keep the particles suspending, provided that their size is below critical radius (r).

- **Brownian movement can be observed,**
  - If particle size is about 2 to 5mm,
  - When the density of particle & viscosity of medium are favorable.



Brownian motion is given by equation:

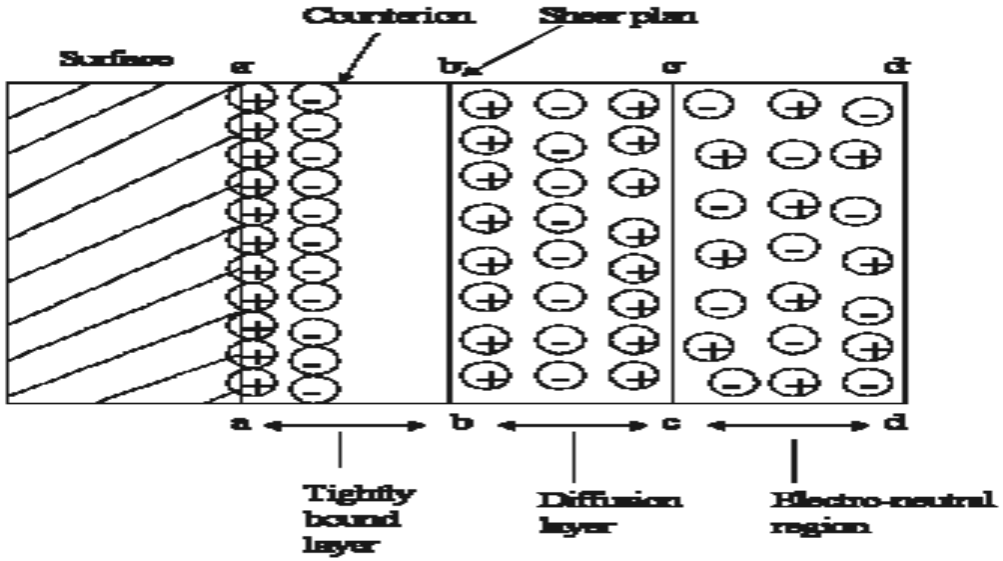
$$Di^2 = \frac{RTt}{N_3 \pi \eta r}$$

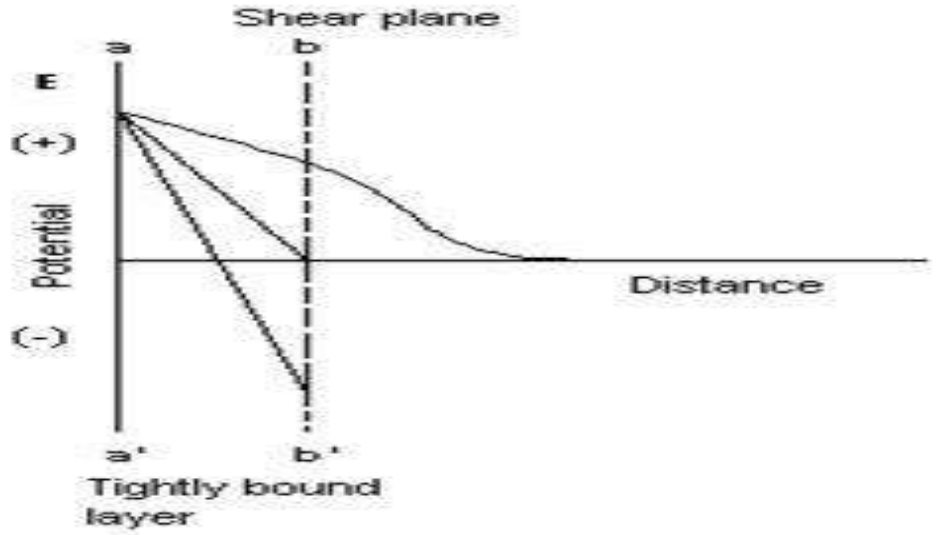
Where, R = gas constant
T = temp. in degree Kelvin
N = Avogadro's number
η = viscosity of medium
t = time
r = radius of the particle

3.Electro kinetic Properties

Zeta Potential

The zeta potential is defined as the difference in potential between the surface of the tightly bound layer (shear plane) and electro-neutral region of the solution.





- As the potential drops off rapidly at first, followed more gradual decrease as the distance from the surface increases.

- This is because the counter ions close to the surface acts as a screen that reduce the electrostatic attraction between the charged surface and those counter ions further away from the surface.

- Zeta potential has practical application in **stability of systems** containing dispersed particles .

- Since this potential, rather than the Nernst potential, governs the degree of repulsion between the adjacent, similarly charged, dispersed particles.

- If the zeta potential is reduced below a certain value , the attractive forces exceed the repulsive forces, and the particles come together.

- This phenomenon is known as flocculation.

- The flocculated suspension is one in which zeta potential of particle is -20 to +20 mV.

- **Thus the phenomenon of flocculation and de flocculation depends on zeta potential carried by particles**.

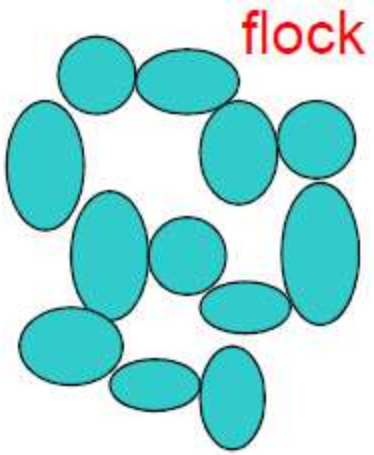
Deflocculation and flocculation

Flocculated Suspensions

➢ In flocculated suspension, **formed flocs (loose aggregates**) will cause increase in sedimentation rate due to increase in size of sedimenting particles.

➢ Hence, flocculated suspensions sediment more rapidly.

➢Here, the sedimentation depends **not only on the size** of the flocs but also on the porosity of flocs.

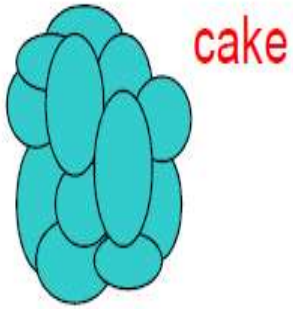


Deflocculated suspensions

- In deflocculated suspension, individual particles are settling.

- Rate of sedimentation is slow , which prevents entrapping of liquid medium which makes it difficult to re-disperse by agitation.

- This phenomenon called ‘caking’ or ‘claying’.



- In deflocculated suspension larger particles settle fast and smaller remain in supernatant liquid so supernatant appears cloudy.

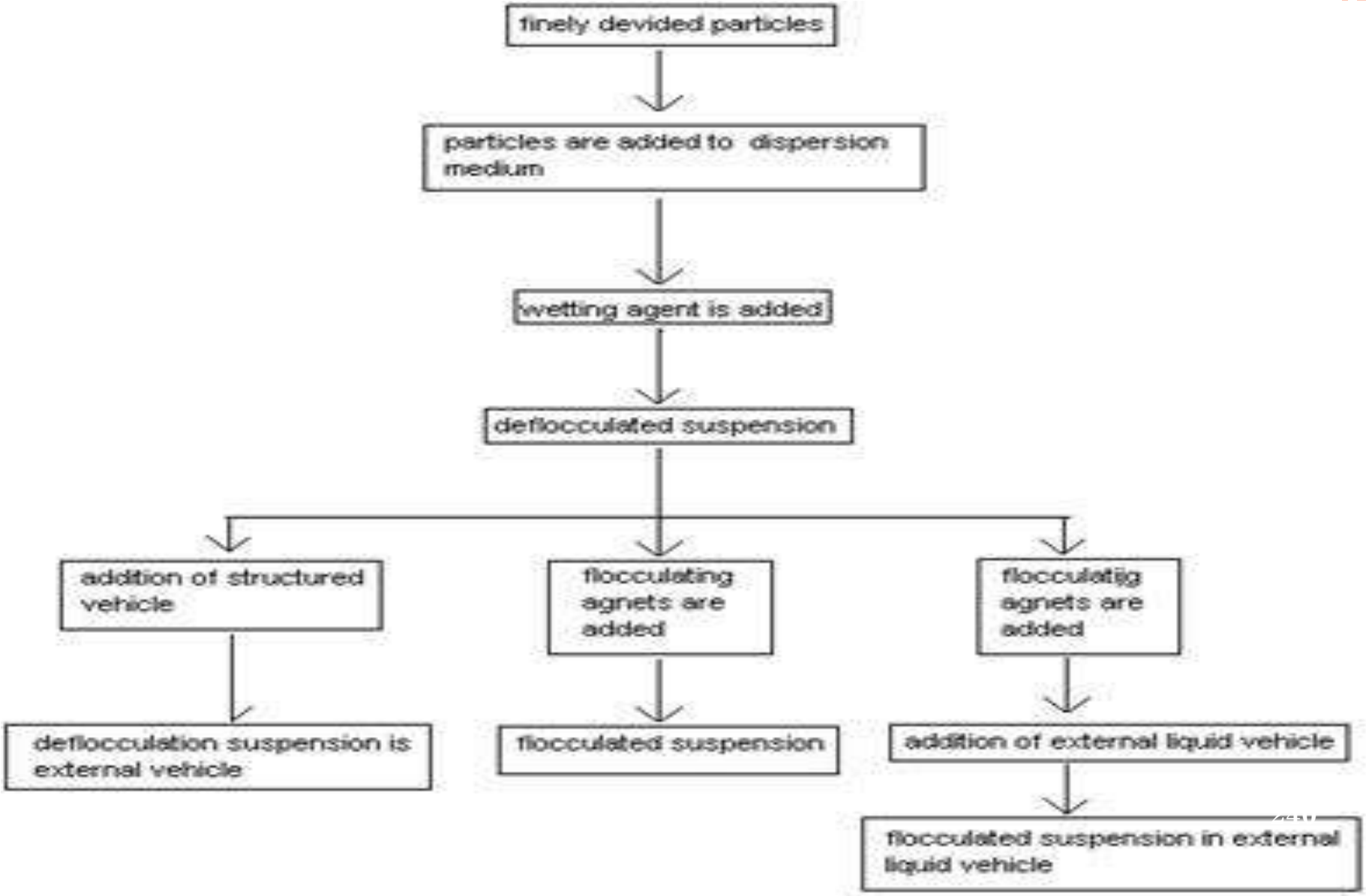
FORMULATION OF SUSPENSIONS

- 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

Flow chart of formulation of suspension



Structured vehicle

- Structured vehicles called also **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.

Controlled flocculation

- Controlled flocculation of particles is obtained by adding flocculating agents, which are:

(1) electrolytes

(2) surfactants

(3) polymers

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

INGREDIENTS FOR

FORMULATION OF SUSPENSIONS

Wetting agents	They are added to disperse solids in continuous liquid phase.
Flocculating agents	They are added to floc the drug particles
Thickeners	They are added to increase the viscosity of suspension.
Buffers and pH adjusting agents	They are added to stabilize the suspension to a desired pH range.
Osmotic agents	They are added to adjust osmotic pressure comparable to biological fluid.
Coloring agents	They are added to impart desired color to suspension and improve elegance.
Preservatives	They are added to prevent microbial growth.
External liquid vehicle	They are added to construct structure of the final suspension.

Suspending agents

- Suspending agent 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.**

- Preferred suspending agents are those that give **thixotropy** to the media such as

Xanthan gum,
Carageenan,
Na CMC/MC mixers,
Avicel RC 591
Avicel RC 581 and
Avicel CL 611.

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 %

List of Suspending Agents

Alginates

- Methylcellulose
- Hydroxyethylcellulose
- Carboxymethylcellulose
- Sodium Carboxymethylcellulose
- Microcrystalline cellulose
- Acacia
- Tragacanth
- Xantham gum
- Bentonite
- Carbomer
- Carrageen
- Powdered cellulose
- Gelatin

Alginates

- Alginate salts have about same **suspending action to that of Tragacanth.**

- Alginate solution looses its viscosity when heated above 60ºC **due to polymerization.**

- Maximum viscosity is observed at a **pH range of 5-9** of alginate.

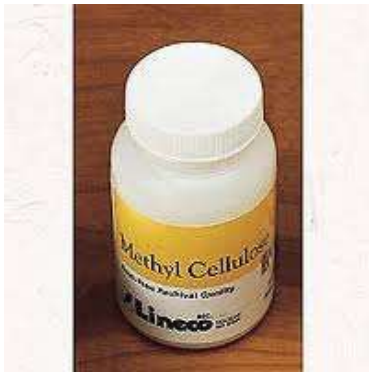
- Chemically alginates are polymers composed of **mannuronic acid** and **glucuronic acid monomers**.

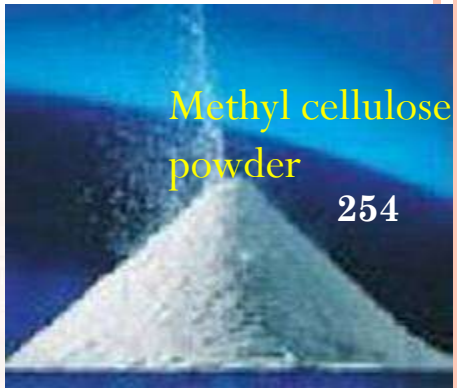
- In practice, alginate is used at concentration **less than 10 % w/w, particularly at 5 % w/w.**

Methylcellulose

- Methylcellulose is available in several viscosity grades.
- The difference in viscosity is due to **difference in methylation and polymer chain length.**
- Methylcellulose is more soluble in cold water than hot water.
- Methylcellulose is stable at **pH range of 3-11.**

Methyl cellulose —(on heating)→ Gel form —(on cooling)→ **Solution form**





➢ Hydroxy ethylcellulose:

- Hydroxyethylcellulose (HEC) is another good suspending agent having somewhat similar characteristics to methylcellulose.

- In HEC **hydroxyethyl group is attached to cellulose chain**.

- Unlike methylcellulose, HEC is soluble in both hot and cold water and **do not form gel on heating**.

Carboxy methylcellulose (CMC)

- Carboxy methylcellulose is available at different viscosity grades.
- **Low, medium and high viscosity grades are commercially available.**
- In case **of HV-CMC, the viscosity** significantly decreases when temperature **rises to 40 ºC from 25 ºC**.
- Therefore, to improve viscosity and stability of suspension MV-CMC is widely accepted.

Microcrystalline Cellulose (MCC; Tradename-Avicel)

- It is **not soluble in water**, but it readily disperses in water to give thixotropic gels.

- It is used in combination with Na-CMC, MC or HPMC, because they facilitate dispersion of MCC.

The advantages of MCC:

- **Alginate complex compositions** are that they provide excellent **stability.**

- Formulation of dry powder suspensions with MCC;

  Alginate complexes produce an excellent dry readily hydratable and dispersible formulation for reconstitution.

Wetting Agents

- 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 %.

Surfactants

- Surfactants decrease the interfacial tension between drug particles and liquid thus liquid is penetrated in the pores of drug particle displacing air from them and thus ensures wetting.

- Generally, we use **non-ionic surfactants** but ionic surfactants can also be used depending upon certain conditions.

- **Polysorbate 80** is most widely used due to its following advantages

  - It is non-ionic so no change in pH of medium
  - No toxicity. Safe for internal use.

Hydrophilic Colloids

- Hydrophilic colloids coat hydrophobic drug particles in one or more than one layer.

- This will provide hydrophillicity to drug particles **and facilitate wetting.**

- They cause deflocculation of suspension because force of attraction is declined. e.g**. acacia, tragacanth, alginates, guar gum.**

Solvents

- The most commonly used solvents used 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.

Buffers

Buffers are the materials which when dissolved in a solvent will **resist any change in pH when an acid or base is added.**

- To encounter stability problems all liquid formulation should be formulated to an optimum pH.

- Rheology, viscosity and other property are also dependent on the pH of the system.

➢. Generally pH of suspension preferably at **7.4-8.4.**

➢ Most commonly used buffers are salts of weak acids such as

carbonates,
citrates,
gluconates,
phosphate and tartrates.

Osmotic Agents

- They are added to produce **osmotic pressure comparable to biological fluids** when suspension is to be intended for ophthalmic or injectable preparation.

- Most commonly used osmotic agents are

  - dextrose,
  - mannitol
  - sorbitol.
  - sodium chloride,
  - sodium sulfate
  - glycerol.

Preservatives

- Naturally occurring suspending agents such as tragacanth, acacia, xanthan gum are susceptible to microbial contamination.

- This leads to:

  - loss in suspending activity of suspending agents,
  - loss of color, flavor and odor,
  - change in elegance etc.

Name of preservatives	Concentration range
Propylene glycol	5-10%
Disodium EDTA	**0.1%**
Benzalkonium chloride	**0.01-0.02%**
Benzoic acid	0.1%
Butyl paraben	0.006-0.05% oral suspension 0.02-0.4% topical formulation

Disodium EDTA


benzalkanonium

Flavoring And Coloring Agents

- They are added to increase patient acceptance.

- Only **sweetening agent** are not capable of complete taste masking of unpleasant drugs therefore, a **flavoring agents are incorporated**.

Eg:

Acacia	Ginger	Sarsaparilla syrup
Anise oil	Glucose	Spearmint oil
Benzaldehyde	Glycerin	Thyme oil

Coloring agents

- Colors are obtained from natural or synthetic sources.
- Plant colors are most widely used for oral suspension.
- The **synthetic dyes should be used within range of(0.0005 % to 0.001%)**
  - **Color aids in identification of the product.**
  - **The color used should be acceptable by the particular country.**

Most widely used colors are as follows.

- ·
- · Brilliant blue (blue)
- · Indigo carmine(blue)
- · Amaranth (red)
- **· Tartarazine (yellow)**
  - **Annatto seeds(yellow to orange)**

Sweetening Agents

They are used for taste masking of bitter drug particles.

Bulk sweeteners

- Sugars such as **xylose, ribose, glucose, mannose.**
- Sugar alcohols such as **sorbitol, xylitol, mannitol**

A bulk sweeteners is used at **concentration of 15-70 %**

Artificial sweetening agents

- Sodium cyclamate
- Sodium saccharin
- Aspartame

Humectants

- Humectants absorb moisture and prevent degradation of API by moisture.

- Examples of humectants most commonly used in suspensions are
  - propylene glycol
  - glycerol.

- Total quantity of humectants should be **between 0-10 % w/w.**

Antioxidant

- Ascorbic acid derivatives such as **ascorbic acid, erythorbic acid,**
- Thiol derivatives such as **thio glycerol, cytosine, acetylcysteine**,
- Tocopherols
- Butylated hydroxy anisole(BHA)
- Butylated hydroxytoluene (BHT)
- Sodium bi sulfite,
- Sodium sulfateacetone

PREPARATION OF SUSPENSIONS

Following consideration are important for manufacturing pharmacist

- **Selection of right material that go into the manufacture.**
- **The step involved and their sequence in the manufacture.**
- **Preservation and storage of the product.**

Small scale preparation of suspensions:

Step 1:

Suspensions are prepared by grinding (or) levigating 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 step1 to get slurry.

Step 3:

The slurry is transformed 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.

Packaging of Suspensions

Introduction

- Pharmaceutical suspensions for oral use are generally packed in **wide mouth container** having adequate space above the **liquid to ensure proper mixing.**

- Parenteral suspensions are packed in either glass ampoules or vials.

Ideal Requirements of Packaging Material

- It should be inert.
- It should effectively preserve the product from light, air, and other contamination through shelf life.
- It should be cheap.
- It should effectively deliver the product without any difficulty.

Materials Used For Packaging

Generally glass and various grades of plastics are used in packaging of suspension.

Glass

Generally **soda lime** and **borosilicate glass** are used in preparation of non sterile suspensions.

- Amber glass doesn't allow U.V light to pass through.

- Amber characteristics can be developed in the glass by addition of various types of additives.

Type of glass	**Additive giving amber color**
Soda lime	FeO + sulfur (in presence of reducing agent)
Borosilicate	$FeO+TiO_2$

Disadvantages of Glass Materials:

- They are **fragile**.
- They are **very heavy as compared to plastic so handling and transport is difficult.**
- Most important disadvantage of glass that **glass constituents get extracted into the product.**

Plastic

Due to the negative aspects of glass, plastic material significantly use of plastic as packaging material for sterile as well as non-sterile pharmaceutical suspension increased.

Advantages Of Plastic Material:

- Non breakability.
- Light weight.
- Flexibility.

Materials used: -

Polyethylene, PVC, polystyrene, polycarbonate etc

Closure And Liners

With an exception of ampoules all containers required elastomeric closure.

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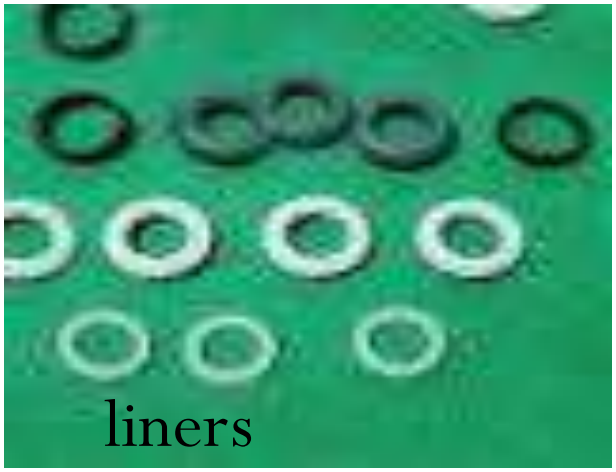


Factors affecting in selecting closure:

- Compatibility with product.
- Seal integrity.
- It should be stable throughout the shelf life.

Factors affecting in selecting liner:

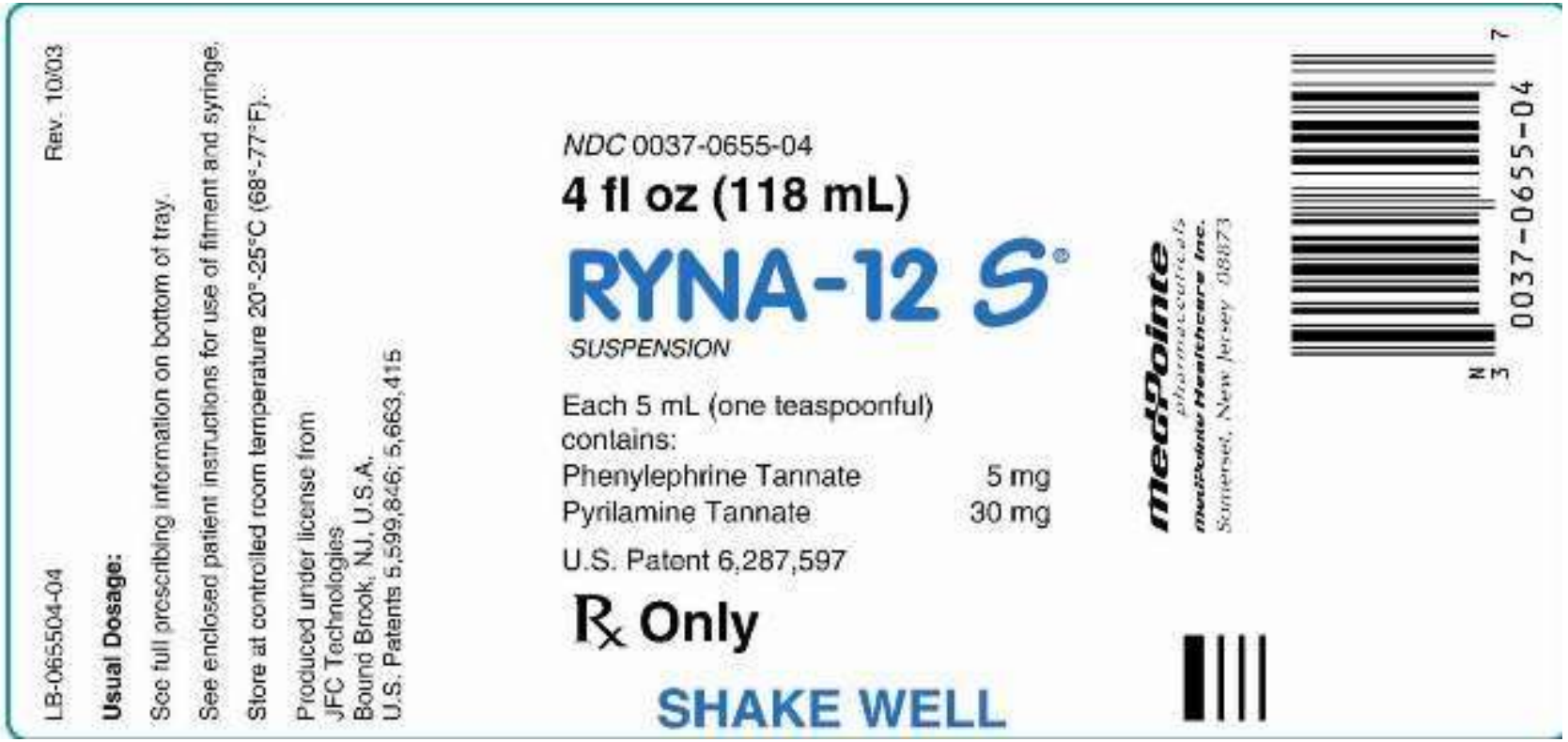
- Chemical resistance.
- Appearance
- Gas and vapor transmission.
- Removal torque.
- Heat resistance.
- Shelf life.
- Economical factors

STORAGE REQUIREMENTS & LABELLING

Labelling:

- **Shake well before use**
- **Do not freeze**
- **Protect from direct light(for light sensitive drugs)**
- **In case of dry suspensions powder the specified amount of vehicle to be mixed may indicated clearly on label.**

Label:


LB-065504-04
Rev. 10/03
Usual Dosage:
See full prescribing information on bottom of tray.
See enclosed patient instructions for use of fitment and syringe.
Store at controlled room temperature 20°-25°C (68°-77°F).
Produced under license from
JFC Technologies
Bound Brook, NJ, U.S.A.
U.S. Patents 5,599,846; 5,663,415
NDC 0037-0655-04
4 fl oz (118 mL)
RYNA-12 S®
SUSPENSION
Each 5 mL (one teaspoonful) contains:
Phenylephrine Tannate 5 mg
Pyrilamine Tannate 30 mg
U.S. Patent 6,287,597
℞ Only
SHAKE WELL
medPointe
pharmaceuticals
medPointe Healthcare Inc.
Somerset, New Jersey 08873
0037-0655-04

STORAGE :

- Suspensions should be stored in cool place but should not be kept in a refrigerator

- Freezing at very low temperatures should be avoided which may lead to aggregation Of suspended particles

Stored at controlled temperature from **20-25 ^{0}c**

Evaluation of Suspensions

Evaluation of Suspensions

- Sedimentation method
- Rheological method
- Electro kinetic method
- Micromeritic method

Sedimentation method :

Two parameters are studied for determination of sedimentation.

1. Sedimentation volume,

2. Degree of flocculation.

,

Sedimentation volume

- The suspension formulation (50 mL) was poured separately into 100 mL measuring cylinders 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:

$$F = V_u / V_o$$

- Where, F = sedimentation volume, V_u = ultimate height of sediment and V_o = initial height of total suspension

➢Rheological method

➢ It provide 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 .
➢ 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 level.

- 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 1 mL 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 25^0C 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

PHOTOMICROSCOPIC TECHNIQUE

- The microscope can be used estimate and detect changes in **particle size distribution** and **crystal form.**

- Rapid processing of photo micrographs is enhanced by attaching Polaroid camera to the piece of monomolecular microscope

- By using this photo micrographs we can determine the changes in **physical properties** and stability of suspensions.

FREEZE- THAW TEST

- Freeze-Thaw test conducted by placing the sample in a freezer for 18 hours followed by thawing at room temperature for 4 to 6 hours.

- Repeat the Freeze-Thaw cycle **for up to 10 times.**

- This test is conducted to determine the tendency to crystallize or cloud

Freeze-thaw testing freezer

pH MEASUREMENT

- The measurement and maintenance 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 .

DISSOLUTION STUDY OF SUSPENSIONS

Introduction:

The drug release from suspensions is mainly through dissolution.

- Suspensions share many physico-chemical characteristics of tablet & capsules with respect to the process of dissolution.
- As tablets & capsules disintegrate into powder and form suspensions in the biological fluids.
- So dissolution is carried as follows

Dissolution Testing

Official Method (Conventional Method):

- It is known as paddle method.

- The apparatus consists of a cylindrical **1000- ml round bottom** flask in a multiple – spindle dissolution drive apparatus and immersed in a controlled **temp bath maintained**

- Dissolution profile of the 500 mg sample suspension is
  - **determined at 37°C in 900 ml of**
  - **pH 7.2 phosphate buffer using**
  - **the FDA paddle method at 25 RPM.**

- The paddle should position to extend to **exactly 2.5 cm** above the flask bottom.

- The suspension is to be introduced carefully into the flask at the bottom using a **10- ml glass syringe** with an attachment **19-cm needle**.

- Withdraw **5 ml of dissolution medium** (and replace with an equal volume of drug –free buffer) in a 5 ml glass syringe.

- Immediately filter through **a 0.2 µm membrane** and analyze.

INNOVATIONS OF SUSPENSIONS

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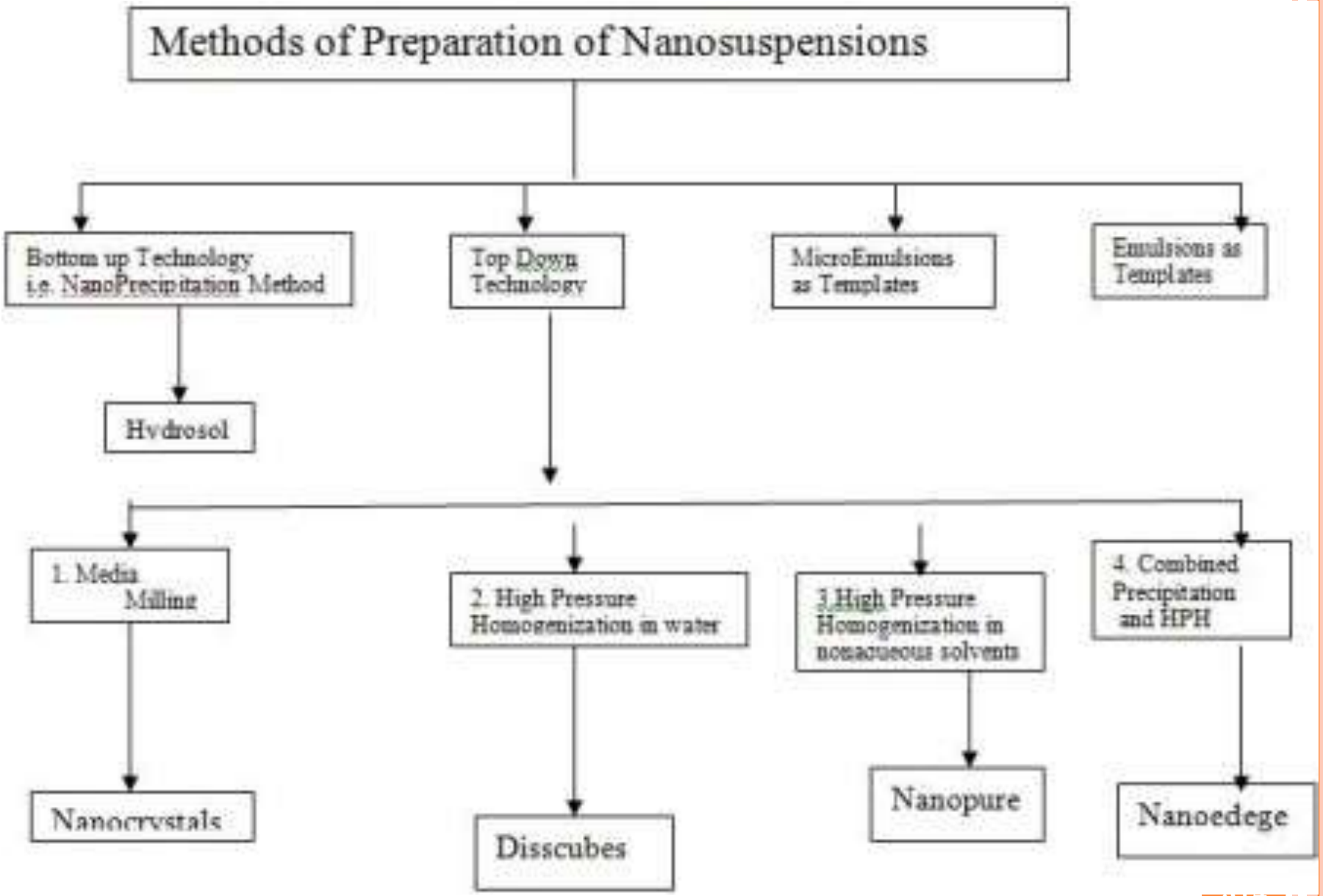
1. Nano suspensions
2. Taste masked pharmaceutical suspensions
3. Sustained release suspensions

1. Nano suspensions:

- Nano suspensions are the **biphasic colloidal dispersions of nano sized drug particles stabilised by surfactants without the matrix materials.**

- They can also be defined as a biphasic system consisting of pure drug particles dispersed in an aqueous vehicle in which the diameter of the suspended particle is **less than 1 µm in** size.


Methods of Preparation of Nanosuspensions
Bottom up Technology i.e. NanoPrecipitation Method
Top Down Technology
MicroEmulsions as Templates
Emulsions as Templates
Hydrosol
1. Media Milling
2. High Pressure Homogenization in water
3.High Pressure Homogenization in nonaqueous solvents
4. Combined Precipitation and HPH
Nanocrystals
Disscubes
Nanopure
Nanoedege

2.Taste Masked Pharmaceutical Suspensions

- Un-palatability due to bad taste is a major concern in most of the dosage forms containing bitter drugs.

- In case of suspensions also taste masking is being applied to mask bitterness of drugs formulated.

The taste masking approaches for suspensions are:

a. **Polymer coating of drugs.**

b. **Encapsulation with basic drugs.**

c. **Polymer coating with basic substances.**

d. **Coating and pH control**.

a. Polymer Coating of Drugs

The polymer coat allows the **time for all of the particles to be swallowed before the threshold concentration** is reached in the mouth and the taste is perceived.

The polymers used for coating are

- Ethyl cellulose
- Eudragit RS 100
- Eudragit RL 100
- Eudragit RS 30 D
- Eudragit RL 30 D

b. Encapsulation with a Basic Substance

- Here a basic substance is mixed with a bitter tasting drug which is insoluble at high pH.

- The mixer is then encapsulated with a polymer (cellulose derivative, vinyl derivative or an acid soluble polymer
  Eg: **copolymer of dimethyl ammonium methyl methacrylate).**

- The drug after encapsulation are suspended, **dispersed or emulsified in suspending medium to give the final dosage form**.

c. Coating and pH Control

- Those drugs which are soluble at high pH are preferably be maintained in a suspension at a low pH where the drug exhibit maximum insolubility.

- Similarly drugs which are soluble at low pH are preferably maintained in suspension at a high pH where the drug is insoluble.

- Also applying polymeric coating to the drug substance avoids solubilization of drug when administered providing taste masking.

Some Examples of Taste Masked Suspensions

Sr.No	Name of the drug	Taste masking approach
1	RISPERIDONE	pH control and polymer coating (with Eudragit RS)
2	DICLOFENAC	Polymer coating with Eudragit RS 100
3	LEVOFLOXACIN	Polymer coating (Eudragit &cellulose acetate,)

Sustained Release Suspensions

- Sustained release is a method to **increase only the duration of action of drug being formulated without affecting onset of action**.

- In suspension sustained release affected by coating the drug to be formulated as suspension by **insoluble polymer coating**.

- The polymer coating **provides sustained release** and also masks the **taste of the bitter drug.**

- The polymer used for sustained release in suspension is as follows as
  - **Ethyl cellulose,**
  - **Eudragit,**
  - **Cellulose acetate, etc.**

- **The main advantage of sustained release suspension is decrease in dosing frequency.**

Approaches used in formulation of sustained release oral suspensions

1. Ion exchange resin.
2. Microencapsulation technique
3. Saturated drug suspension as a suspending medium.
4. Using non aqueous vehicle.
5. Reconstitution.
6. Protective coating.

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Thank you.

THANK YOU FOR YOUR PATIENCE