

Liquid dosage forms

Monophasic 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 **suspending** 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, drops, ear drops, eye solutions. nasal
- 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

- Syrups
- Mixtures
- Elixirs
- Linctuses

Liquids meant for external administration

Liquids applied to the skin

- Lotions
- Liniments
- Collodions
- Paints

Liquids used in mouth

- Gargles
- Mouthwashes
- Throat paints

Liquids instilled into body cavities

- Douches
- Ear drops
- Nasal drops
- Eye drops
- Enemas

Syrup

Concentrated aqueous preparations of 60% to 85% sucrose with or without flavoring agents and medicinal substances.
eg. Chlorpheniramine maleate syrup, Chloral hydrate syrup

Elixirs

Clear, sweetened hydroalcoholic solutions with or without medicinal substances intended for oral use.
eg. Dexamethasone elixir (Medicated)
Compound benzaldehyde elixir (Non-medicated)

Liquids meant for internal administration

ns

Mixture

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

Orange

Linctuses

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

Codeine Linct

Liquids meant for external administration

Gargles

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

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

Mouthwash

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

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

Eg: 1000

sodium chloride solution

Otic preparations

Applied to or in the ear to treat or

Enemas

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

b) Liquids instilled into body cavities

Eye drops

oily solutions
Sterile, aqueous/
intended for
instillation in
eyeball.

Eg: Moxifloxacin

Nasaldrops

Administered through the nose to obtain a systemic or local effect. Used for nasal congestion symptoms such as caused by an allergy, or a related upper-respiratory problem.

Eg: Beclomethasone
d

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

Liniments

Alcoholic and oily liquid preparations
Intended for external application with rubbing to the affected area
Typically used to relieve

Liquids meant for external use (Skin)

Paints

Solutions used to sterilize the skin.

Eg. Crystal

Lotions

Either liquid or semi-liquid preparations that contain one or more active ingredients in an appropriate vehicle.

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

Nonaqueou s

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

Syrup



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) Antimicrobial Preservatives

(c) *Viscosity Modifier*

(d) Flavorants

(e) Colorants

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



The inversion leads to darkening of the solution these two sugars together called as invert sugar and the process is known as inversion

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 may be 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 GIT as sugars. No significant hyperglycemia has been found (WHY?); it may be used as component of non-nutritive vehicles.
- ★ It is chemically stable and inert with respect to drugs and other ingredients used in pharmaceutical preparation. Preservative should be used in solution containing less than 60% w/w sorbitol.

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 anaesthetic.

Medicaments commonly used:

- Antibiotics – e.g. Lincomycin HCl
- Analgesics – E.g. – Meperidine HCl
- Adrenergic – e.g. – Pseudoephedrine HCl
- Antiemetics – e.g. – Chlorpromazine HCl
- Antihistaminics – e.g. Chlorpheniramine melete
- 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 Pharmaceuticals 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 Pharmaceuticals Ltd.	Dextromethorphan	Cough & Cold Remedies	Chronic dry cough/unproductive cough & acute dry cough which is interfering with normal function or sleep.
Tusca	Square Pharmaceuticals Ltd.	Guaiphenesin+ Pseudoephedrine +	Cough & Cold Remedies	Symptomatic relief of upper respiratory tract disorders accompanied by productive cough.
Duolax™	Square Pharmaceuticals	Trimepridine HCl Magnesium Hydroxide &	Laxative	Constipation, Hyperacidity with constipation, Anorectal disorder.

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 or 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

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°C)**

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

- The solid substances are dissolved in $3/4^{\text{th}}$ volume of the vehicle.
 - 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.
 - Liquid ingredients, if any, are added and mixed.
 - More vehicle is added to produce the final volume.
- Container.* Narrow mouthed, screw capped, colorless, plain bottle.
- The mixture is transferred to a bottle, capped tightly, polished and labeled. 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 through 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 amount 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.
Container: Narrow mouthed, screw capped, colorless, plain bottle.
Label: The mixture is transferred to the bottle, capped, polished and labeled. 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 precipitate 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



**THANK YOU FOR
YOUR PATIENCE**