

MONOPHASIC LIQUID DOSAGE FORM



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Binapani Barik
Assistant Professor
School of Pharmacy and Life Sciences
Centurion University of Technology and Management

INTRODUCTION

- A solution is a liquid-preparation that contains one or more soluble chemical substances dissolved in a specified solvent.
- One phase system

Gargles

- They are aqueous solutions used in the prevention or treatment of throat infections.
- Usually they are prepared in a concentrated solution with directions for the patient to dilute with warm water before use.
- They brought in intimate contact with mucous membrane of throat and allowed to remain in contact with it for few seconds before thrown out of the mouth
- **Container**-clear, glass bottles with plastic screw cap. Colored bottles are required to be used if protection is required.
- **Labelling**- ‘for external use only” and proper dilution instruction should be written on label
- **Method of preparations**- They are usually prepared by dissolving all ingredients in solvents and then make up the volume as required.

Advantages and Disadvantages

Advantages-

1. Easy to use for the treatment of infection of pharynx just by gargling the solution using air from the lungs
2. Relieve Soreness In Mild Throat Infection
3. Supplied in conc. For so reduce container size
4. Suitable for variety of drugs like antibiotic, antiseptic etc

Disadvantages

1. Temporary effect of drugs
2. Not suitable for patients having respiratory problems
3. They might be swallowed

Formulation component of gargles

additives	ingredients	use
cosolvent	glycerine, propylene glycol etc	used to enhance solubility of drug
vehicle	Water, sometimes alcohol	To dissolve the excipients
Colouring agent	Amaranth, tartrazine solution or any FDA approved colour etc	Attractiveness
Flavouring agent	cardamom oils, cinnamon oils, menthols	To enhance acceptability
preservatives	Phenol, Chorocresol, Benzoic acid and its salts	To inhibit the growth of microorganism.
Medicament	<ol style="list-style-type: none"> 1. phenol, thymol 2. -potassium chlorate 3. volatile oil 4. potassium permanganate 	<ol style="list-style-type: none"> 1. Anti-infective- 2. Astringent 3. Antiseptic and deodorants- 4. Bactericidal-
antioxidant	Ascorbic acid , Sodium bisulfite, Sodium metabisulfite, thiourea	to prevent oxidative degradation of drugs

Mouthwashes

- These are non-sterile aqueous solution with pleasant taste and odour used for oral hygiene (clean and deodorize buccal cavity) and to treat infections of the mouth.
- **Container**-white fluted bottles
- **Labelling**-proper directions for mouthwash dilution must be mentioned
- “for external use only” provided in pH RANGE OF 5 TO 9.5
- “Not to be swallowed in large amount”

Advantages and disadvantages

- **Advantages-**

1. Utilized to remove Loosen debris and food from the mouth
2. Provide deodorant, refreshing, local analgesics or astringent effects
3. Sometimes used to treat the mouth infection by using antibacterial agent.

Disadvantage- If pH not monitored properly then may damage mouth tissues.

Classifications of mouthwashes

- Mouthwashes (mouthrinses) are generally classified as –
 1. cosmetic or
 2. therapeutic or
 3. Combination of the two.
- **1.Cosmetic rinses** are commercial products that remove oral debris before or after brushing, temporarily suppress bad breath, diminish bacteria in the mouth and refresh the mouth with a pleasant taste.
- **2.Therapeutic rinses** ALONG WITH benefits of their cosmetic counterparts, they also contain an added active ingredient, (for example fluoride or chlorhexidine), that help protect against some oral diseases.

Formulation component of gargles

additives	ingredients	use
cosolvent	glycerine, propylene glycol etc	used to enhance solubility of drug
vehicle	Water, sometimes alcohol	To dissolve the excipients
Colouring agent	Amaranth, tartrazine solution or any FDA approved colour etc	Attractiveness
Flavouring agent	spearmint, peppermint, eucalyptus and menthol	They get rid of the unpleasant smell and taste of the other raw materials and give a cold, refreshing taste.
preservatives	Phenol,Chorocresol,Benzoic acid and its salts like sodium benzoate	To inhibit the growth of microorganism.
Medicament	<ol style="list-style-type: none"> 1. phenol,thymol 2. zinc sulphate, zinc chloride 3. volatile oil 4. potassium permangnate 	<ol style="list-style-type: none"> 1. Anti-infective- 2. Astringent 3. Antiseptic and deodorants- 4. Bactericidal-

Formulation component of gargles

additives	ingredients	use
Deoderant	sodium chloride and sodium bicarbonate as a hypertonic solution	To deodourize the mouth cavity
Sweetening agent	sodium saccharin, sorbitol, glycerol, Xylitol	improve the taste
alcohol	The amount of alcohol is usually ranging from 18 - 26 % .	preservative and a semi-active ingredient.
Abrasives-	e.g.calcium carbonate, calcium phosphate, aluminium hydroxide, sodium bocarbonate	Abrasives are the substances that are used for abrading, grinding or polishing. They remove substances adhering to the surface of the teeth without scratching it and bring out their natural luster
<i>Anti-halistsosis agents</i>	zinc ion	the anaerobic, Gram-negative bacteria use sulphurcontaining amino acids as substrates in their production of volatile sulphur-containing compounds (VSC) which gives unpleasant smell in mouth . This agent stops this

Method of preparation-

- **Solution method** where most of the ingredients are dissolved in solvent or co-solvent mixture to form clear solution

THROAT PAINT

- Viscous liquid preparation Used for mouth and throat infection
- Paints can be applied onto skin and mucous membranes. But all paints cannot be used for application onto mucous membrane
- **Container**-airtight, coloured fluted bottle
- **LABELING**-'for external use only", it should also contain auxillary label like: Throat paints usually contain volatile oils as flavouring agents. Therefore to prevent their volatalisation at higher temperature,
- NOT TO BE SWALLOWED IN LARGE QUANTITIES KEEP THE CONTAINER TIGHTLY CLOSED.
- **Storage**-dispensed in air tight container and stored in cool place
- **Direction:** Throat paints should contain the direction to the patients as, Apply with camel brush, as directed.

Advantages and disadvantages

Advantages-

1. Used for treatment of throat infection and mouth infection
2. Highly viscous solution so retain to the applied place for longer period of time
3. Glycerine used as a solvent which provides viscosity and turns liquid sweet.

Disadvantages-

1. Applied with the help of brush or small cotton piece
2. They initiate salivation, hence patient has to spit

Formulations-

1. **SOLVENT**- Viscous solvent must be used so as to retain the formulation at the site of action for longer time e.g. glycerin, liquid paraffine
2. **Medicament**-
Antiseptic-e.g Iodine, crystal violet
Astringent-tannic acid, boric acid
Anti-infective-phenol, thymol
3. **Flavoring agent**-They get rid of the unpleasant smell and taste of the other raw materials and give a cold, refreshing taste. E.g. water-insoluble essential oils, such as spearmint, peppermint, eucalyptus and menthol are often used as flavouring agent dissolved with the help of cosolvents
- 4.. **Colouring agent**- an attractive appearance e.g. FD&C Colours
5. **Sweetening agent**- improve the taste e.g. sodium saccharin, sorbitol, glycerol, Xylitol
6. **Preservatives**- prevent the growth of micro-organisms in mouthwashes. E.g. sodium benzoate, methyl paraben and ethyl paraben

Method of preparation

- Simple solution method with the aid of heat

Syrup

- It is a concentrated aqueous solution of a sugar, usually sucrose with or without medicinal and flavoring agent.
- Flavored syrups are a convenient form of masking disagreeable tastes.
- **Advantages-**
 1. Act as, antioxidant by retarding the oxidation, as sugar is hydrolyzed in to laevulose and dextrose.
 2. Act as preservative by retarding the growth of bacteria, fungi and mould because of high osmotic pressure.
 3. Good patient compliance especially pediatric patients as syrups are sweet in test.
 4. Pleasant means of administering liquid dosage form of a disagreeable taste
 5. Much like by children and adults
 6. Suitable for water soluble drugs.

Disadvantages of syrup

1. Not suitable for diabetic patients
2. Children may mistakenly taken extra dose as pleasant taste
3. Concentration if not appropriate result in microbial growth
4. If kept in cold place , sucrose crystallizes and is warm place occur fermentation.

Types of syrup

- **1. simple syrup-** when water is used alone for the preparation of sucrose solution.

E.g. simple syrup IP. Consist of 66.7 % w/w of sucrose in water

- **2. medicated syrups-**when syrup contains medicinal substances used for therapeutic purpose

E.g. codeine phosphate syrup,ferrous sulphate syrup

- **3.Flavoured syrups-**when syrup contains aromatic or flavouring agents

E.g. orange syrup,lemon syrup

Formulation component of syrup

additives	ingredients	use
Main ingredients	Sucrose or other sugar substituent	Sweetener, preservative
vehicle	Water, glycerin	As a solvent for dissolving ingredients
Chemical stabilizers	Glycerin, sorbital, propylene glycol	To prevent crystallization of sucrose
Colouring agent	Amaranth, tartrazine solution etc	Attractiveness
Flavouring agent	Raspberry juice, lemon juice, vanilla flavour etc	To enhance acceptability
preservatives	Benzoic acid, sodium benzoate, methyl paraben	To inhibit the growth of microorganism
medicament	Lincomycin Analgesic antiemetic	Antibiotic Meperidine Hydrochloride Chlorpromazine HCL

Method of preparations

- Three methods-

- 1. Solution with the aid of heat**-sugar is added to purified water and heat is applied until solution forms. Then solution allowed to cool and volume is adjusted.
- 2. Solution with agitation**-sugar and ingredients are dissolved in purified water by placing in container and allowed to agitate the mixture for long time till whole of the sugar dissolves and then make up the volume
- 3. Percolation method**-sucrose is percolated with purified water as solvent by slowly passing the solvent through column of crystallization of sucrose to dissolve it. The percolate is collected. This process is repeated until the whole sugars dissolves.

- **DISPENSING**-in well dried, well stoppered bottles, narrow mouthed, amber coloured bottles with plastic screw cap
- **Storage**-store in cool place
- **Label**-store in fairly cool temperature, not exceeding 25 °C in dark place.



ELIXIRS

Defination:

- **Elixirs** as clear, sweetened hydroalcohol liquids intended for oral use containing flavoring substances or active medicinal agents.

Their primary solvents are alcohol and water, with glycerin, sorbitol and syrup sometimes as an additional solvent and/or sweetening agents.

Alcohol concentration 4-40%

Advantages of presence of alcohol

1. Enhances the solubility of insoluble drugs in water
2. If more than 20 % alcohol present, no requirement of preservative as alcohol acts as a preservative

Types of elixir

- **1. non-medicated elixir-** do not contain medicament, but contain flavoured substances to make it acceptable
- **2. medicated elixir-**when elixir contains medicinal substances used for therapeutic purpose like antibiotic, antihistaminics, antitussive etc

E.g. piperazine citrate elixir, paracetamol elixir

Formulation component of elixir

additives	ingredients	use
vehicle	Water, glycerin, alcohol	As a solvent for dissolving ingredients
Colouring agent	Amaranth, tartrazine solution etc	Attractiveness
Flavouring agent	Raspberry juice, lemon juice, vanilla flavour, orange oil, tincture of lemon etc	To enhance acceptability of the product
preservatives	Benzoic acid, sodium benzoate, methyl paraben, chloroform spirit, methyl ester of p- hydroxy benzoic acid.	To inhibit the growth of microorganism
medicament	Antibiotic, antihistaminics, sedative	Therapeutic purpose
Sweetening agent	Sucrose, saccharine, syrups, glycerine	To enhance the taste
stabilizer	EDTA, Citric acid	To stabilize the product by minimize the darkening that occurs on storage. Disodium edetate should be used to sequester heavy metals that catalyse decomposition of the antibiotics.

Method of preparation:

- Dissolve the water-soluble ingredients in part of the water, add and dissolve the sucrose in it.
- Dissolve the other ingredients in the alcohol. (Concentration of alcohol should be 5- 40% to make clear solution)
- The aqueous solution is then added to the alcoholic solution with constant stirring and make up the volume with the solvent or vehicle specified in the formulation. Elixirs should be brilliantly clear and therefore strained or Filtered, if necessary
- A high alcoholic content is maintained during preparation by adding aqueous phase to the alcoholic solution.

Storage

- ❑ It should be dispensed in narrow mouthed, screw capped, colorless plain bottle.
- ❑ In cool place , to prevent volatilization of alcohol at high temperature

Advantages over syrups

- ❑ less sweet than syrups
- Elixirs are more fluid than syrups.
- It often is desirable, it is more effective in masking such tastes.
- More stable than syrups
- Elixirs are more readily prepared and manufactured than syrups.
- An Elixir may contain both water and alcohol soluble ingredients.

Disadvantage of elixirs

- Alcohol is not good for children.
- Because they contain volatile materials, it must be stored in a watertight screw-top jar and away from sources of ignition.

Label-

All necessary requirements of liquid dosage form meant for internal use. Amount of alcohol content must be mentioned

Eardrops

Solutions of drugs intended to be instilled into the ear with a dropper.

- **Container-** coloured , fluted glass bottle with dropper in the cap
- **Labelling-** 'FOR EXTERNAL USE ONLY'
- **Storage-**'store in cool place'

Advantages and disadvantages

Advantages-

1. Use for the removal of ear wax
2. Used in treatment of ear infection, inflammation and pain

Disadvantages-

1. Due to liquid nature, patient has to tilt the head at 45°C For about 10-15 minutes
2. Aqueous solutions are not suitable as they do not get mixed with fatty serum

FORMULATIONS

- **1. Solvent**-Unhydrous Glycerine and propylene glycol used mainly for two purpose-
 - A. To soften the ear wax As they are miscible with fatty ear wax and make maximum contact between medication and ear tissue.
 - B. Hygroscopicity of vehicle draw moisture from tissue thus reduce inflammation and prevent growth of microorganism
- 2.Preservative**- to prevent growth of microorganism
e.g. chlorbutanol (0.5%), thiomersal (0.01%)
- 3.Antioxident**- to prevent oxidation of active medicament
e.g. sodium biosulphate
- 4. medicament**-
 - Antiinfective- chloramphenicol
 - Wax softner-hydrogen peroxide,sodium bicarbonate
 - Antiseptic-phenol, boric acid
 - Astringent-aluminium acetate
 - Anti-inflammatory agent-hydrocortisone,dexamethasone

METHOD OF PREPARATION

- SIMPLE SOLUTION METHOD

Nasal drops

- Aqueous solution that are instilled into the nose with dropper
- **Container-** coloured fluted bottles fitted with dropper or in suitable plastic container
- **Labelling-** 'FOR EXTERNAL USE ONLY'
- **Storage-** stored in cool place

Advantages and disadvantages

- **Advantages-**

1. Used to reduce swelling of the nasal mucosa
2. Used to reduce nasal congestion

Disadvantages-

1. They may induce nasal congestion if not used as per direction given
2. Aqueous solution donot prolong the action

Requirement for nasal vehicle

1. pH Must be between 5.5 to 7.5.
2. Have mild buffer capacity
3. Compatible with nasal tissue
4. Compatible with other active ingredients
5. Must contain preservatives
6. Stable
7. Have a proper viscosity

Formulation ingredients

- 1. **Vehicle**- water and preparation must be isotonic
- 2. **preservatives**- prevent growth of microorganism in product
- E.g. chlorbutanol(0.5%), BKC (0.01-0.05%)
- **3.Tonicity adjusting material**- to adjust tonicity of nasal drops
- E.g. sodium chloride, dextrose
- 4. **Buffer**- to adjust the pH of product
- E.g. phosphate buffer pH 6.5
- 5. **Medicament**-
- Ephedrine hydrochloride, corticosteroid etc

Method of preparations

- Simple solution method if required heating can be done

Enemas

- Enemas are aqueous or oily solutions or suspensions or o/w type emulsions, which are intended to introduce into rectum for cleansing, therapeutic or diagnostic purposes.
- They are also used to cause evacuation and for local or systemic or therapeutic action of the medicaments
- **DISPENSING** Enemas are dispensed in coloured, fluted glass bottle along with rectal nozzle.
- Now-a-days enemas are supplied in single use, squeeze plastic bottles or disposable polyethylene or polyvinyl chloride bags sealed with rectal nozzle, which should be lubricated before administration

- **DIRECTION:** Warm up to the body temperature(37 o C),before use(only for large volume enemas) and administer as directed .
- **STORAGE:** Enemas should be stored in a cool and dark place .
- **LABEL :** Label should bear all necessary requirements of liquid dosage forms,except dose.
- **Auxillary label**-FOR RECTAL USE ONLY.
- LUBRICATE THE NOZZLE BEFORE USE.
- WARM TO THE BODY TEMPERATURE BEFORE USE.- (ONLY FOR LARGE VOLUME ENEMAS)
- STORE IN A COOL AND DARK PLACE.
- USE WITH IN TWO DAYS AFTER ISSUE OR DISCARD THE REMAINING PORTION AFTER TWO DAYS OF ISSUING.
- KEEP AWAY FROM THE REACH OF CHI LDREN.

ADVANTAGES AND DISADVANTAGES

- **Advantages-**

1. Suitable for local and systemic effect also
2. The drugs which are not given by oral or parenteral routes preferred by this route
3. Administered in large volume
4. Used for study of lower GIT, if contain x ray contrast medium

- **Disadvantages-**

1. Patient uncomfortable
2. Require assistant or nurse for administration

Types of enema

- There are three types of enemas-
- 1)Cleansing enemas
- 2)Therapeutic enemas
- 3)Diagnostic enemas
- **1.Cleansing enemas** These are also called Evacuating enemas . They are used to evacuate faeces in constipation and before any surgery of the gut.
- Volume of enema is depending upon the age and condition of the patient.
- The large volume enemas should be warmed to body temperature(37 o C),before administration to prevent cold shock. (warm water stimulate intestinal mucosa and cold water produce cramping

Type of enema

- **2.Therapeutic enemas** These are Medicated enemas .These are used to produce medicated effects in the bowel or in lower part of the colon in children and comatose patients.
- This action may be obtained by its local action(as in the case of piles, ulcerative colitis and inflammatory bowel disease) or systemic(therapeutic) action
- They contain therapeutic agents like, Sedatives :Chloral hydrate,Paraldehyde Anthelmintics :Quassia(for thread worms) Anti-inflammatory agents :Corticosteroids(for ulcerative colitis) Nutrients :Vitamins,Minerals
- **3.Diagnostic enemas** They contain radio opaque substances,which are used for X-ray examination of lower bowel or colon part. Eg: Barium sulphate suspension

Formulations of enema

- **1. medicament-**
- Laxative-e.g. glycerine, soft soap
- Sedative-e.g. chloral hydrate
- Anthelmintics-e.g. quasia

Drug must be soluble in suitable solvents

Method of preparations-simple solution method

Liniments

- Alcoholic or oily clear solutions intended for applications to the skin with friction or massage and should not be applied to broken skin.
- They are rubbed onto the affected area; because of this, they were once called embrocation.
- They are applied with friction and rubbing of the skin, the oil or soap base providing for ease of application and massage.

General uses of Liniments

- Antipruritic - used to relieve itching
- Astringents - causes biological tissue to contract
- Emollients - products that soften skin or treat dry skin
- Analgesics-reduce pain
- Rubefacient-Substance that causes redness (Rubar)
- Counterirritant- an agent applied locally to produce superficial inflammation with the object of reducing inflammation in deeper adjacent structures.

Advantages and disadvantages

- **Advantages-**

1. Used as rubefacient, counter-irritant and penetrating action in skin

Disadvantages-

1. Liniments required rubbing so patient may be uncomfortable
2. Alcoholic or hydroalcoholic solutions may produce irritation to skin

Formulation component of liniment

additives	ingredients	use
vehicle	Alcohol, oils like peanut oil, sesame oil, cotton seed oil etc	Solvent select based on action whether massage or deep penetration into skin needed
Flavouring agent	Rose oil, jasmine oil, lemon oil etc	To enhance acceptability of the product by pleasant smelling
medicaments	Counter irritant-camphor Analgesics- methyl salicylate	Therapeutic purpose

How Liniments are prepared

- The vehicle should be selected for the type of action desired (rubefacient, counterirritant, massage) and also on the solubility of the desired components in the various solvents
- Prepared in the same manner as solutions

There are two types of Liniments

ALCOHOLIC LINIMENTS

1. used generally for their rubefacient, counterirritant, astringent, penetrating effects mildly and
2. penetrate the skin more readily than do those with an oil base.
3. Alcohol used as solvent
4. E.g. soap liniment

OLEAGINOUS LINIMENTS

1. Milder in their action but is more useful when massage is required
2. less irritating to the skin, depending on their ingredients
3. may function solely as protective coatings.
4. Oil used as solvent
5. E.g. camphor liniment

Liniments:

- Liniments should **NOT** be applied to skin that is bruised/Broken because excessive irritation might occur. This application should be marked for “**external use only**”
- Dermatologist prescribe products of this type but only those containing the rubefaciants are advertised extensively and used by consumers for treating minor muscular aches and pains.

- **Dispensing**-amber coloured container, narrow mouthed bottle, tightly closed with coloured plastic screw cap
- Label-
 1. for external use only
 2. Not to be applied on broken skin
 3. Shake well before use

Storage-Store in cool and dark place, away from the flame

Lotions

- Clear solutions aqueous or oily, suspensions or emulsions intended for applications to skin without friction.

Advantages and disadvantages

- **Advantages-**

1. They are soothing and applied gently by dapping
2. Comfortably spread without rubbing
3. Alcoholic lotions provide cooling effect on applications

- **Disadvantages-**

1. Alcoholic or hydroalcoholic lotions gets dried easily, hence not suitable for prolonged action

Formulation component of lotions

additives	ingredients	use
vehicle	Alcohol, isopropyl alcohol, water, liquid paraffine isopropyl myristate etc	For making the content soluble
Cosolvent	Glycols, glycerine, propylene glycol, PEG 400, 600	FOR INCREASING THE SOLUBILITY OF DRUGS IN SOLVENTS
Flavouring agent and colouring agent	Colours for FD&C Cherry, raspberry, apple, rose	To enhance acceptability
medicaments	Astringent-copper, zinc shipmates Keratolytics, fungicidal, bacteriostatics	Therapeutic purpose
Preservatives	Chlorbutanol Benzyl alcohol B-phenylethyl alcohol etc	In order to prevent microbial growth

Methods of preparations

- Simple solution method

- **Dispensing**-coloured fluted bottles
- **Labelling**
 1. For external use only
 2. Shake well before use
- **Storage**-well closed , air tight container cool place

Thank you