Pharmaceutical Technology
Lecture-10 and 11
Syrups

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Syrups

- Syrups are concentrated aqueous preparations of a sugar or sugar substitute with or without flavoring agents and medicinal substances.
- Syrups are sweet, viscous aqueous liquids
- Medicinaly, they are divided into two groups:

1. The flavoring syrups, which are used as vehicles, and
2. The medicated syrups which contain ingredients giving them therapeutic value.

- So, syrups containing flavoring agents but not medicinal substances are called non medicated or flavored vehicles (syrups).
- Some official, previously official, and commercially available non medicated syrups are presented in Table (13.6).
- These syrups are intended to serve
- as pleasant-tasting vehicles for medicinal substances
- to be added in the extemporaneous compounding of prescriptions or
- in the preparation of a standard formula for a medicated syrup, which is a syrup containing a therapeutic agent as mentioned above.

Table 13.6 EXAMPLES OF NONMEDICATED SYRUPS (VEHICLES)

SYRUP	COMMENTS
Cherry syrup	Sucrose-based syrup with cherry juice about 47% by volume. Tart fruit flavor is attractive to most patients, and acidic pH makes it useful as a vehicle for drugs requiring an acid medium.
Cocoa syrup	Suspension of cocoa powder in aqueous vehicle sweetened and thickened with sucrose, liquid glucose, glycerin; flavored with vanilla, sodium chloride. Particularly effective in administering bitter-tasting drugs to children
Orange syrup	Sucrose-based syrup uses sweet orange peel tincture, citric acid as the source of flavor and tartness. Resembles orange juice in taste; good vehicle for drugs stable in acidic medium
Ora-Sweet, Ora-Sweet SF	Commercial vehicles for extemporaneous compounding of (Paddock Laboratories) syrups. Both have a pH of 4–4.5 and are alcohol-free. Ora-Sweet SF is sugar-free.
Ora-Blend	A preblended combination of Ora-Sweet and Ora-Plus (1:1) and Ora-Sweet SF and Ora-Plus (1:1)
PCCA Acacia Syrup	A sweet, demulcent suspending vehicle with a mild vanilla flavor
PCCA-Plus Oral Suspending Vehicle	A preserved, buffered vehicle with demulcent qualities
PCCA Sweet SF	A sugar-free syrup containing sorbitol and can be used in diabetic patients as well as others
PCCA Syrup	A syrup vehicle with less sucrose than Syrup NF
Raspberry syrup	Sucrose-based syrup with raspberry juice about 48% by volume. Pleasant-flavored vehicle to disguise salty or sour taste of saline medicaments
SyrSpend™ SF Suspension Vehicle	A low osmolality suspending vehicle using modified starch technology. It is buffered at pH 4.2; it is sugar-free and paraben-free; it is available in unflavored, cherry, and grape formulations.
SyrSpend™ SF Alka	An alkaline suspension vehicle with a pH of about 7.0, when reconstituted as directed. It is low osmolality (<50 mOsmol), pleasant-tasting, sugar-free, alkaline medium available in unflavored and cherry formulas
Syrup	85% sucrose in purified water. Simple syrup may be used as the basis for flavored or medicated syrups.

- Perhaps the most frequently found types of medications administered as medicated syrups are antitussive agents and antihistamines.
- This is not to imply that other types of drugs are not formulated into syrups; a variety of medicinal substances can be found in syrup form and among the many commercial products. Examples of medicated syrups are presented in Table 13.7.

Table 13.7 EXAMPLES OF MEDICATED SYRUPS BY CATEGORY

SYRUP	REPRESENTATIVE COMMERCIAL PRODUCTS	CONCENTRATION OF COMMERCIAL PRODUCT*	COMMENTS
Analgesic			
Meperidine HCl	Demerol Syrup (Sanofi-Synthelabo)	50 mg/5 mL	Opioid analgesic for the relief of moderate to severe pain, adjunct to general anesthesia
Anticholinergics			
Dicyclomine HCl	Bentyl (Axcan Scandipharm)	10 mg/5 mL	Adjunctive therapy in the treatment of peptic ulcer
Oxybutynin chloride	Various	5 mg/5 mL	Relief of symptoms with voiding in patients with uninhibited neurogenic and reflex neurogenic bladder
Antiemetics			
Chlorpromazine HCl	Thorazine Syrup (GlaxoSmithKline)	10 mg HCl/5 mL	Control of nausea and vomiting
Dimenhydrinate	Children's Dramamine Liquid (Pharmacia)	12.5 mg/5 mL	Control of nausea, vomiting, motion sickness
Prochlorperazine edisylate	Various	5 mg/5 mL	Control of nausea and vomiting
Promethazine HCl	Various	6.25, 25 mg/5 mL	Control of nausea, vomiting, motion sickness, allergic reactions
Anticonvulsant			
Sodium valproate	Depakene Syrup (Abbott)	250 mg as sodium salt/5 mL	Sole or adjunctive therapy in simple (petit mal), complex absence seizure disorders
Antihistamines			
Chlorpheniramine maleate	Chlor-Trimeton Allergy Syrup (Schering-Plough)	2 mg/5 mL	For prevention, treatment of allergic reactions
Desloratadine	Clarinex Syrup (Schering)	0.5 mg/1 mL	For relief of nasal and nonnasal symptoms of allergic rhinitis and urticaria
Hydroxyzine HCl	Atarax Syrup (Roerig)	10 mg/5 mL	
Antipsychotic			
Citalopram hydrobromide	Celexa (Forest)	10 mg/5 mL	For depression
Lithium citrate	Various	8 mEq/5 mL	Management of psychotic disorders
Risperidone	Risperdal (Janssen)	1 mg/mL	For treatment of schizophrenia
Antitussives			
Dextromethorphan	Benylin Adult Cough Formula (Warner-Lambert)	15 mg/5 mL	For relief of cough
Diphenhydramine	Benadryl Allergy Liquid Medication (McNeil)	12.5 mg/5 mL	For control of coughs due to colds or allergy
Antiviral			
Amantadine HCl	Symmetrel Syrup (Endo)	50 mg/5 mL	Prevention of respiratory infections caused by A2 (Asian) viral strains. Treatment of idiopathic Parkinson disease

(Continued)

Table 13.7 EXAMPLES OF MEDICATED SYRUPS BY CATEGORY (Continued)

SYRUP	REPRESENTATIVE COMMERCIAL PRODUCTS	CONCENTRATION OF COMMERCIAL PRODUCT[a]	COMMENTS
Lamivudine	Epivir Oral Solution (GlaxoSmithKline)	10 mg/mL	Treatment of HIV
Ritonavir	Norvir (Abbott)	80 mg/mL	Treatment of HIV
Bronchodilators			
Albuterol sulfate	Proventil Syrup (Schering) Ventolin Syrup (Schering)	2 mg/5 mL	Relief of bronchospasm of obstructive airway disease: prevention of exercise-induced bronchospasm
Metaproterenol sulfate	Alupent Syrup (Boehringer Ingelheim)	10 mg/5 mL	
Cathartic			
Lactulose	Chronulac Syrup (Hoechst)	10 g/15 mL	15–30 mL qd as laxative
Cholinergic			
Pyridostigmine bromide	Mestinon Syrup (ICN Pharmaceuticals)	60 mg/5 mL	Treatment of myasthenia gravis
Decongestant			
Pseudoephedrine hydrochloride	Sudafed Children's Nondrowsy (Pfizer Consumer)	15 mg/5 mL	Temporary relief of nasal congestion of common cold, hay fever, upper respiratory allergies, sinusitis
Emetic			
Ipecac	Various	21 mg ether-soluble alkaloids of Ipecac/15 mL	To induce vomiting in poisoning. Dose of 15 mL may be repeated in 20 min if vomiting does not occur. If after the second dose vomiting does not occur, the stomach should be emptied by gastric lavage.
Expectorant			
Guaifenesin	Guaifenesin Syrup (Roxane)	100 mg/5 mL	For symptomatic relief of respiratory conditions associated with cough and bronchial congestion
Fecal softener			
Docusate sodium	Colace Syrup (Purdue)	20 mg/5 mL	Stool softener by surface action
Gastrointestinal stimulant			
Metoclopramide	Various	5 mg/5 mL	Relief of symptoms of diabetic gastroparesis (gastric stasis) and gastroesophageal reflux
H2 receptor antagonist ranitidine HCl	Zantac Syrup (GlaxoSmithKline)	15 mg/mL	Treatment of duodenal ulcers and GERD
Hemostatic			
Aminocaproic acid	Amicar Syrup (Xanodyne)	1.25 g/5 mL	Treatment of excessive bleeding from systemic hyperfibrinolysis, urinary fibrinolysis
Hypnotic Sedative			
Chloral hydrate	Chloral Hydrate Syrup (Pharmaceutical Associates)	250 mg/5 mL	Sedative at 250 mg; hypnotic to induce sleep at 500 mg. Alcoholic beverages should be avoided. Usually diluted with water or some other beverage

[a]A usual single dose unless otherwise stated.

- Pharmaceutically, syrups are classified best according to their basic formulas:

1. **Sugar based syrups**: which are concentrated solution of sugar
2. **Artificial syrups**: which are formulated with artificial sweetening agents and viscosity builders.

- Although there are many different sugars, sucrose and dextrose have been the only one used in the preparation of syrups.
- Sucrose is obtained from sugar cane, sugar beet, or less commonly, sugar maple.

- In past honey was used as a base for thick liquid preparations known as Honey or Mels.
- Oxymels (sour or acid honeys), are preparations containing acetic acid and honey.
- Liquid glucose, prepared by incompletely hydrolyzing starch, may also be used as a component of syrups.
- Sucrose is the preferred carbohydrate for syrups because of its purity, degree of sweetness, lack of color and ease of handling.

Components of Syrups

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

1. The sugar, usually sucrose, or sugar substitute used to provide sweetness and viscosity;
2. Antimicrobial preservatives;
3. Flavorants; and
4. Colorants

- Also, many types of syrups, especially those prepared commercially, contain special solvents (including alcohol), solubilizing agents, thickeners, or stabilizers.

Sucrose- and Nonsucrose-Based Syrups

- Sucrose is one of the purest of commercially available substances and is the preferred carbohydrate for syrup because of purity, degree of sweetness, lack of color & ease of handling.
- Sucrose is the sugar most frequently employed in syrups, although in special circumstances, it may be replaced in whole or in part by other sugars or substances such as sorbitol, glycerin, and propylene glycol.

- In some instances, all glycogenetic substances (materials converted to glucose in the body), including the agents mentioned earlier, are replaced by nonglycogenetic substances, such as methylcellulose or hydroxyethylcellulose.
- These two materials are not hydrolyzed and absorbed into the blood stream, and their use results in an excellent syrup-like vehicle for medications intended for use by diabetic patients and others whose diet must be controlled and restricted to nonglycogenetic substances.
- The viscosity resulting from the use of these cellulose derivatives is much like that of sucrose syrup. The addition of one or more artificial sweeteners usually produces an excellent facsimile of a true syrup.

- The characteristic body that the sucrose and alternative agents seek to impart to the syrup is essentially the result of attaining the proper viscosity.
- This quality, together with the sweetness and flavorants, results in a type of pharmaceutical preparation that masks the taste of added medicinal agents.
- When the syrup is swallowed, only a portion of the dissolved drug actually makes contact with the taste buds, the remainder of the drug being carried past them and down the throat in the viscous syrup.
- This type of physical concealment of the taste is not possible for a solution of a drug in an unthickened, mobile aqueous preparation.
- In the case of antitussive syrups, the thick, sweet syrup has a soothing effect on the irritated tissues of the throat as it passes over them.

- **Formulation of sugar based syrups**
- In order to formulate syrup properly, one must consider the properties of the basic vehicle, particularly its stability, sucrose is subjected to two degradative pathways in aqueous solution:

1. fermentation and
2. hydrolysis.

- Most syrup contain a high proportion of sucrose, usually 60% to 80%, not only because of the desirable sweetness and viscosity of such solutions but also because of their inherent stability in contrast to the unstable character of dilute sucrose solutions.

- As a carbohydrate, sucrose in dilute aqueous solution provides a nutrient medium for the growth of microorganisms, particularly yeasts and molds. The consequences of this growth include turbidity, fermentation and changes in taste.
- On the other hand, concentrated sugar solutions are quite resistant to microbial growth because of the unavailability of the water required for the growth of microorganisms.
- Nearly saturated solutions of sucrose, if stored properly, are self-preserving. Such solutions contain no “free water”, thus behave as an anhydrous medium with respect to growth of microorganisms.

- If the concentration of sucrose is significantly less than that of syrup, USP that is less than 85% (w/v) of sucrose, preservative should be added.
- Syrup, NF, also called simple syrup. It is prepared by dissolving 85 g of sucrose in enough purified water to make 100 mL of syrup.
- The resulting preparation generally requires no additional preservation if it is to be used soon; in the official syrup, preservatives are added if the sucrose concentration is less than 85% or syrup is to be stored. When properly prepared and maintained, the syrup is inherently stable and resistant to the growth of microorganisms

- Syrup has a specific gravity of about 1.313, which means that each 100 mL of syrup weighs 131.3 g.
- Because 85 g of sucrose is present, the difference between 85 and 131.3 g, or 46.3 g, represents the weight of the purified water.
- Thus, 46.3 g, or mL, of purified water is used to dissolve 85 g of sucrose.
- The solubility of sucrose in water is 1 g in 0.5 mL of water; therefore, to dissolve 85 g of sucrose, about 42.5 mL of water would be required. Thus, only a very slight excess of water (about 3.8 mL per 100 mL of syrup) is employed in the preparation of syrup.

- Although not enough to be particularly amenable to the growth of microorganisms, the slight excess of water permits the syrup to remain physically stable in varying temperatures.
- If the syrup were completely saturated with sucrose, in cool storage, some sucrose might crystallize from solution and, by acting as nuclei, initiate a type of chain reaction that would result in separation of an amount of sucrose disproportionate to its solubility at the storage temperature. The syrup would then be very much unsaturated and probably suitable for microbial growth.
- Note: Simple syrup is a saturated solution at 4°C, so no crystallization should be observed unless the temperature drops below 4°C or super saturated.

- As formulated, the official syrup is stable and resistant to crystallization and microbial growth.
- However, many of the other official syrups and a host of commercial syrups are not intended to be as nearly saturated as Syrup, NF, and therefore must employ added preservative agents to prevent microbial growth and to ensure their stability during their period of use and storage.
- As noted earlier, sucrose-based syrup may be substituted in whole or in part by other agents in the preparation of medicated syrups.
- A solution of a polyol, such as sorbitol, or a mixture of polyols, such as sorbitol and glycerin, is commonly used.
- Sorbitol Solution, USP, which contains 64% by weight of the polyhydric alcohol sorbitol, is employed as shown in the following example formulations for medicated syrups:

Antihistamine Syrup

Chlorpheniramine maleate 0.4 g
Glycerin 25.0 mL
Syrup 83.0 mL
Sorbitol solution 282.0 mL
Sodium benzoate 1.0 g
Alcohol 60.0 mL
Color and flavor qs
Purified water, to make 1,000.0 mL

Ferrous Sulfate Syrup

Ferrous sulfate 135.0 g
Citric acid 12.0 g
Sorbitol solution 350.0 mL
Glycerin 50.0 mL
Sodium benzoate 1.0 g
Flavor qs
Purified water, to make 1,000.0 mL

Acetaminophen Syrup

Acetaminophen 24.0 g
Benzoic acid 1.0 g
Disodium calcium EDTA 1.0 g
Propylene glycol 150.0 mL
Alcohol 150.0 mL
Saccharin sodium 1.8 g
Purified water 200.0 mL
Flavor qs
Sorbitol solution, to make 1,000.0 mL

Cough and Cold Syrup
Dextromethorphan Hydrobromide 2.0 g
Guaifenesin 10.0 g
Chlorpheniramine maleate 0.2 g
Phenylephrine hydrochloride 1.0 g
Sodium benzoate 1.0 g
Saccharin sodium 1.9 g
Citric acid 1.0 g
Sodium chloride 5.2 g
Alcohol 50.0 mL
Sorbitol solution 324.0 mL
Syrup 132.0 mL
Liquid glucose 44.0 mL
Glycerin 50.0 mL
Color qs Flavor qs
Purified water, to make 1,000.0 mL

• All materials used in the extemporaneous compounding and manufacturing of pharmaceuticals should be of USP–NF quality and obtained from FDA-approved sources.

Antimicrobial Preservative

- The amount of a preservative required to protect a syrup against microbial growth varies with the proportion of water available for growth, the nature and inherent preservative activity of some formulative materials (e.g., many flavoring oils that are inherently sterile and possess antimicrobial activity), and the capability of the preservative itself.
- Among the preservatives commonly used in syrups with the usually effective concentrations are

1. benzoic acid 0.1% to 0.2%,
2. sodium benzoate 0.1% to 0.2%, and
3. various combinations of methylparabens, propylparabens, and butylparabens totaling about 0.1%.
4. Frequently, alcohol is used in syrups to assist in dissolving the alcohol-soluble ingredients, but normally, it is not present in the final product in amounts that would be considered to be adequate for preservation (15% to 20%).
5. Glycerin (45-50%)
6. Sorbic acid (0.1%)

- Notes

1. The benzoates, the parabens and sorbic acid are most effective in acid solutions; they are ineffective in alkaline solutions.
2. Mixtures of parabens are frequently employed to take advantage of their potentiating effect.
3. Small amounts of alcohol used as a solvent although is not sufficient to have a preservative effect, the alcohol concentrates in vapors above the syrup and thus prevents the growth of surface molds.
4. In sealed containers, vaporization of water from syrup and its subsequent condensation on the syrup result in the formation of a dilute solution of sucrose on the surface and this can support mold growth.

Preservation of Syrups

- Syrups can be preserved by (a) storage at low temperature; (b) adding preservatives such as glycerin, benzoic acid, sodium benzoate, methylparaben, or alcohol in the formulation; or (c) the maintenance of a high concentration of sucrose as a part of the formulation.
- High sucrose concentrations will usually protect an oral liquid dosage form from growth of most microorganisms.
- A problem arises, however, when pharmacists must add other ingredients to syrups that can result in a decrease in the sucrose concentration. This may cause a loss of the preservative effectiveness of the sucrose. This can be overcome, however, by calculating the quantity of a preservative (such as alcohol) to add to the formula to maintain the preservative effectiveness of the final product.

Example

- Calculate the amount of benzoic acid required to preserve 100 mL 65% (w/v) sucrose solution.
- If 0.1% of preservative is required then 100 mL of 65% sucrose solution equivalent to:

  65%/x = 85%/100

  x = 76.5 mL of solution is free from free water

  100 – 76.5 = 23.5 mL free water need preservation.

  23.5 x 0.1 / 100 = 0.0235 g = 24.5 mg benzoic acid should be used
- The more free water, the more preservative required in the product.
- If the formula contains glycerin and alcohol, the amount of preservative used will decrease.
- For example, if we have 5 mL glycerin; this 5 ml will preserve 5 mL of free water, then
- 23.5 – (5 + 5) = 13.5 mL is free water require preservation.
- 13.5 x 0.1/100 = 0.0135 g = 13.5 mg benzoic acid should be used

Example

Rx active drug 5 mL volume occupied

Other drug solids 3 mL volume occupied

Glycerin 15 mL

Sucrose 25 g

Ethanol 95% qs

Purified water q.s. 100 mL

- How much alcohol would be required to preserve this prescription? We will use the free-water method to calculate the quantity of alcohol required.
- Simple syrup contains 85 g sucrose per 100 mL of solution, which weighs 131.3 g (specific gravity, 1.313). It takes 46.3 mL of water to prepare the solution (131.3 – 85 = 46.3), and the sucrose occupies a volume of (100 – 46.3 = 53.7) 53.7 mL.

1. Because this solution is preserved, 85 g of sucrose preserves 46.3 mL of water, and 1 g of sucrose preserves 0.54 mL of water. With 25 g of sucrose present, the amount of water preserved is 25 x 0.54 = 13.5 mL
2. Because 85 g of sucrose occupies a volume of 53.7 mL, 1 g of sucrose will occupy a volume of 0.63 mL. The volume occupied by the sucrose in this prescription is 25 x 0.63 = 15.75 mL
3. The active drug and other solids occupy 8 mL (5 + 3) volume.
4. Each mL of glycerin can preserve an equivalent quantity of volume (2 × 15 = 30), so 30 mL would be preserved.
5. The volume taken care of so far is 13.5 + 15.75 + 8 + 30 = 67.25 mL.

The quantity of free water remaining is

100- 67.25= 32.75mL

6. Because it requires about 18% alcohol to preserve the water,

0.18 x 32.75 = 5.9 mL of alcohol (100%) would be required.

7. If 95% ethanol is used, 5.9/0.95 = 6.21 mL would be required.

To prepare the prescription, about 6.21 mL of 95% ethanol can be added with sufficient purified water to make 100 mL of the final solution.

- **Incompatibilities**

1. If a preparation containing high concentration of alcohol sucrose will crystallize, simple syrup can tolerate 10% alcohol without crystallization.
2. When solution containing pectin are mixed with sucrose syrup gellation is observed, since sucrose partially dehydrates pectin.
3. When syrup are diluted with aqueous solutions, the necessity for additional preservative should be considered.

- **Flavorant**
- Most syrups are flavored with synthetic flavorants or with naturally occurring materials, such as volatile oils (e.g., orange oil), vanillin, and others, to render the syrup pleasant tasting.
- Because syrups are aqueous preparations, these flavorants must posses sufficient water-solublility. However, sometimes a small amount of alcohol is added to a syrup to ensure the continued solution of a poorly water-soluble flavorant.
- Commercial flavoring systems (FLAVORx) may also be considered and used.
- **Colorant**
- To enhance the appeal of the syrup, a coloring agent that correlates with the flavorant employed (i.e., green with mint, brown with chocolate) is used. Generally, the colorant is water soluble, nonreactive with the other syrup components, and color stable at the pH range and under the intensity of light that the syrup is likely to encounter during its shelf life.

- Hydrolysis: sucrose is a disaccharide and consequently can be hydrolyzed to give the monosaccharides dextrose (glucose) and levulose(fructose or fruit sugar)

$$C_{12}H_{22}O_{11} + H_2O \longrightarrow C_6H_{12}O_6 + C_6H_{12}O_6$$

(+) Sucrose (+) Dextrose (-) levulose

- Note:

1. Dextrose and levulose have the same formula but have different structures
2. The hydrolytic reaction is specific-acid, i.e., hydrogen-ion catalyzed.
3. This reaction is also called inversion because a solution of sucrose rotates polarized light to the right (dextrorotatory), while the same solution after hydrolysis is levorotatory.
4. The solution of invert sugar are fermented more easily than are solution of sucrose.
5. The invert sugar is sweeter than sucrose since

   Dextrose 74 < Sucrose 100 < Fructose 173.

   The numbers refer to degree of sweetness.
6. Degradation of levulose is responsible for the brown discoloration which develops in some of the colorless syrup. This change is called caramelization. It takes place particularly in syrups containing strong acids.

Preparation of Syrups

- Syrups are most frequently prepared by one of four general methods, depending on the physical and chemical characteristics of the ingredients. Broadly stated, these methods are
  1. solution of the ingredients with the aid of heat, or so-called hot process,
  2. solution of the ingredients by agitation without the use of heat or the simple admixture of liquid components,
  3. addition of sucrose to a prepared medicated liquid or to a flavored liquid, and
  4. percolation of either the source of the medicating substance or the sucrose. Sometimes a syrup is prepared by more than one of these methods, and the selection may simply be a matter of preference on the part of the pharmacist. Many of the official syrups have no officially designated method of preparation.

Solution with the Aid of Heat

- Syrups are prepared by this method when it is desired to prepare the syrup as quickly as possible and when the syrup's components are not damaged or volatilized by heat.
- In this method, the sugar is generally added to the purified water, and heat is applied until the sugar is dissolved. Then, other heat-stable components are added to the hot syrup, the mixture is allowed to cool, and its volume is adjusted to the proper level by the addition of purified water.
- If heatlabile agents or volatile substances, such as volatile flavoring oils and alcohol, are to be added, they are generally added to the syrup after the sugar is dissolved by heat, and the solution is rapidly cooled to room temperature.

- The use of heat facilitates rapid solution of the sugar and certain other components of syrups; however, caution must be exercised against becoming impatient and using excessive heat.
- When heat is applied in the preparation of a sucrose syrup, some inversion of the sucrose is almost certain. The speed of inversion is greatly increased by the presence of acids, the hydrogen ion acting as a catalyst to the reaction.
- Should inversion occur, the sweetness of the syrup is altered because invert sugar is sweeter than sucrose, and the normally colorless syrup darkens because of the effect of heat on the levulose portion of the invert sugar.

- When the syrup is greatly overheated, it becomes amber colored as the sucrose caramelizes. Syrups so decomposed are more susceptible to fermentation and to microbial growth than the stable, undecomposed syrups.
- Because of the prospect of decomposition by heat, syrups cannot be sterilized by autoclaving. The use of boiled purified water in the preparation of a syrup can enhance its permanency, and the addition of preservative agents, when permitted, can protect it during its shelf life. Storage in a tight container is a requirement for all syrups.

- **Solution by Agitation Without the Aid of Heat**

1. To avoid heat-induced inversion of sucrose, syrup may be prepared without heat by agitation. Syrup made without heat is practically colorless
- On a small scale, sucrose and other formulative agents may be dissolved in purified water by placing the ingredients in a vessel larger than the volume of syrup to be prepared, permitting thorough agitation of the mixture.
- This process is more time consuming than the use of heat, but the product has maximum stability

2. Sometimes, simple syrup or some other non medicated syrup, rather than sucrose, is employed as the sweetening agent and vehicle. In that case, other liquids that are soluble in the syrup or miscible with it may be added and thoroughly mixed to form a uniform product. Example: glycyrrhiza syrup (Licorice syrup)

- When solid agents are to be added to a syrup, it is best to dissolve them in minimal amount of purified water and incorporate the resulting solution into the syrup.
- When solid substances are added directly to syrup, they dissolve slowly because the viscous nature of the syrup does not permit the solid substance to distribute readily throughout the syrup to the available solvent and also because a limited amount of available water is present in concentrated syrups.

- **Addition of Sucrose to a Medicated Liquid or to a Flavored Liquid**
- Occasionally, a medicated liquid, such as a tincture or fluidextract, is employed as the source of medication in the preparation of syrup. Many such tinctures and fluidextracts contain alcohol-soluble constituents and are prepared with alcoholic or hydroalcoholic vehicles.
- If the alcohol-soluble components are desired medicinal agents, some means of rendering them water soluble is employed.
- However, if the alcohol-soluble components are undesirable or unnecessary components of the corresponding syrup, they are generally removed by mixing the tincture or fluidextract with water, allowing the mixture to stand until separation of the water-insoluble agents is complete, and filtering them from the mixture.

- The filtrate is the medicated liquid to which the sucrose is added in preparation of the syrup. If the tincture or fluidextract is miscible with aqueous preparations, it may be added directly to simple syrup or to flavored syrup.
- Examples of syrups prepared by this method:

1. Cherry syrup
2. Roseberry syrup
3. Orange syrup and
4. Tolue Balsam syrup

- **Percolation**
- In the percolation method, either sucrose may be percolated to prepare the syrup or the source of the medicinal component may be percolated to form an extractive to which sucrose or syrup may be added.
- This latter method really is two separate procedures: first the preparation of the extractive of the drug and then the preparation of the syrup.
- An example of a syrup prepared by percolation is ipecac syrup, which is prepared by adding glycerin and syrup to an extractive of powdered ipecac obtained by percolation.

- The drug ipecac, which consists of the dried rhizome and roots of Cephaëlis ipecacuanha, contains the medicinally active alkaloids emetine, cephaline, and psychotrine.
- These alkaloids are extracted from the powdered ipecac by percolation with a hydroalcoholic solvent. The syrup is categorized as an emetic with a usual dose of 15 mL.
- This amount of syrup is commonly used in the management of poisoning in children when evacuation of the stomach contents is desirable. About 80% of children given this dose will vomit within half an hour.
- For a household emetic in the event of poisoning, 1-oz bottles of the syrup are sold without a prescription. Ipecac syrup also has some application as a nauseant expectorant in doses smaller than the emetic dose.

- Syrup is made by dissolving sucrose in boiling water or preferably without heat by percolation with purified water about 465 mL total. Cotton is packed loosely in the neck of the percolator to remove mechanical impurities such as lint.
- The cotton is moistened after packing and before the sucrose is placed in the percolator, so that the first concentrated syrup will pass through satisfactory.
- In making small quantities, it is always necessary to pass the percolate through the percolator several times before all the sucrose is dissolved and get syrup has sp.gr. 1.313.
- Advantage: this process has the advantage of requiring little attention and it is well suited to manufacture of large quantities of syrup.