Solutions

They are liquid preparations that contain one or more chemical substances dissolved in a suitable solvent or mixture of mutually miscible solvents.

Classification:

-According to use: oral, otic, ophthalmic, or topical.

-According to composition :

a. Aqueous solutions containing a sugar are classified as syrups (even though some syrups may contain some alcohol).

b. Sweetened hydroalcoholic (combinations of water and ethanol) solutions are termed elixirs

c. Solutions of aromatic materials are termed spirits if the solvent is alcoholic or aromatic waters if the solvent is aqueous.

d. Solutions prepared by extracting active constituents from crude drugs are termed tinctures or fluidextracts, depending on their method of preparation and concentration.

Oral solutions, syrups, elixirs, spirits, and tinctures are prepared and used for the specific effects of the medicinal agents they carry. Additional substances may present, these additional agents are frequently included to provide color, flavor, sweetness, or stability.

In formulating or compounding a pharmaceutical solution, the pharmacist must use information on the solubility and stability of each solute with regard to the solvent or solvent system.

Solubility:

Solubility can be defined in two ways:

- Quantitative term as the concentration of solute in concentrated solution at certain temperature.
- Qualitative term as spontaneous interactions of two or more substances to form a homogenous molecular dispersion.

The solubility of an agent in a particular solvent indicates the maximum concentration to which a solution may be prepared with that agent and that solvent.

When molecules interact, attractive and repulsive forces are in effect. The attractive forces cause the molecules to cohere, whereas the repulsive forces prevent molecular interpenetration and destruction. When the attractive and repulsive forces are equal, the potential energy between two molecules is minimal and the system is most stable.

When a solute dissolves, the substance's intermolecular forces of attraction must be overcome by forces of attraction between the solute and the solvent molecules. This entails breaking the solute-solute forces and the solvent–solvent forces to achieve the solute–solvent attraction. When a solvent at a given temperature has dissolved all of the solute possible, it is said to be saturated.

The solubility expressed as grams of solute dissolving in milliliters of solvent. These terms are defined in the USP and presented in this table:

DESCRIPTIVE TERM	PARTS OF SOLVENT REQUIRED FOR 1 PART OF SOLUTE
Very soluble	<1
Freely soluble	1–10
Soluble	10–30
Sparingly soluble	30–100
Slightly soluble	100–1,000
Very slightly soluble	1,000–10,000
Practically insoluble or insoluble	>10,000

Organic compounds may be water soluble if they contain polar groups capable of forming hydrogen bonds with water. In fact, the greater the number of polar groups present, the greater will likely be the organic compound's solubility in water.
The introduction of halogen atoms into a molecule tends to decrease water solubility because of an increase in the molecular weight of the compound without a proportionate increase in polarity.

Solubility enhancement techniques:

- Using of a different solubilizing agent or different chemical salt form of the medicinal agent.
- Alteration pH of the solution.
- Substitution in part or in whole of the solvent.
- Reduction of particle size of drug.
- Complexation.

Factors affecting solubility:

- Nature of solute and solvent:When two substances are similar they can dissolve each other (like dissolve like). Polar solutes dissolve in polar solvent and vice versa.
- Temperature: Most chemicals absorb heat when they are dissolved and are said to have a positive heat of solution, resulting in increased solubility with an increase in temperature. A few chemicals have a negative heat of solution and exhibit a decrease in solubility with a rise in temperature.
- Particle size of the solute
- Agitation.

Syrups

Syrups are concentrated aqueous preparations of a sugar or sugar substitute with or without flavoring agents and medicinal substances.

Syrups containing flavoring agents but not medicinal substances are called nonmedicated or flavored vehicles (syrups).

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.

Any water-soluble drug that is stable in aqueous solution may be added to a flavored syrup. However, care must be exercised to ensure compatibility between the drug substance and the other formulative components of the syrup.

Components of syrups:

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

(*a*) The sugar usually sucrose, or sugar substitute used to provide sweetness and viscosity

(b) Antimicrobial preservatives.

(c) Flavorants.

(d) Colorants.

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

Sucrose and non sucrose based syrups:

Sucrose is the most frequently used sugar employed in syrups, 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 nonglycogenetic substances.

The viscosity resulting from the use of these cellulose derivatives is much like that of a sucrose syrup.

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 enhancement 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.

Most syrups 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. The aqueous sugar medium of dilute sucrose solutions is an efficient nutrient medium for the growth of microorganisms, particularly yeasts and molds. 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.

This aspect of syrups is best demonstrated by the simplest of all syrups, 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.

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, therefore preservatives must be used.

Antimicrobial preservatives:

The amount of a preservative required to protect a syrup against microbial growth depend on:

- The proportion of water available for growth.
- The nature and inherent preservative activity of some formulative materials(e.g many flavoring oils are inherently sterile and possess antimicrobial activity).
- The capability of preservative itself.

Examples of preservative used and their concentration:

- Benzoic acid 0.1-0.2%.
- Sodium benzoate 0.1-0.2%.
- Combinations of methylparaben, propylparaben and butylparaben 0.1%.

Flavorants:

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 be water soluble.

Colorants:

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.

Colorants must be:

- Water soluble.
- Non reactive with other syrup components.
- Stable at the pH range and under intensity of light.

Preparation of syrups:

We have four general methods for preparation:

a. Solution of the ingredients with aid of the heat.

b. Solutions of ingredients by agitation without aid of heat.

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

d. Percolation.

The selection of the method depends on the physical and chemical characteristics of the ingredients.

a. Solution of the ingredients with aid of heat:

We use this method in case of :

- Desirability to prepare the syrup as quickly as possible.
- The syrup's components are not damaged or volatilized by heat.

In this method:

- Sugar is added to the purified water, and heat is applied until the sugar is dissolved.
- Other heat-stable components are added to the hot syrup, the mixture is allowed to cool.
- Volume is adjusted to the proper level by the addition of purified water.
- If heat labile 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.

Sucrose, a disaccharide, may be hydrolyzed into monosaccharides, dextrose (glucose), and fructose (levulose). 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.

Invert sugar is sweeter than sucrose and darker than sucrose 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.

b. Solution by agitation without use of Heat

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.

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 a 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.

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

A medicated liquid, such as a tincture or fluidextract, is employed as the source of medication in the preparation of a 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.
- If the alcohol-soluble components are undesirable, 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.

d. 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 contains the medicinally active alkaloids emetine, cephaline, and psychotrine. These alkaloids are extracted from the powdered ipecac by percolation with a hydroalcoholic solvent.