**Pharmaceutical 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 non-medicated 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. Due to the inability of some children and elderly people to swallow solid dosage forms, it is fairly common today for a pharmacist to be asked to prepare an oral liquid dosage form of a medication available in the pharmacy only as tablets or capsules. In these instances, drug solubility, stability, and bioavailability must be considered case by case. The liquid dosage form selected for compounding may be a solution or a suspension, depending on the chemical and physical characteristics of the particular drug and its solid dosage form.

Medicated syrups are commercially prepared from the starting materials, that is, by combining each of the individual components of the syrup, such as sucrose, purified water, flavoring agents, coloring agents, the therapeutic agent, and other necessary and desirable ingredients. Naturally, medicated syrups are employed in therapeutics for the value of the medicinal agent present in the syrup.

Syrups provide a pleasant means of administering a liquid form of a disagreeable-tasting drug. They are particularly effective in the administration of drugs to youngsters, since their pleasant taste usually dissipates any reluctance on the part of the child to take the medicine. The fact that syrups contain little or no alcohol adds to their favor among parents. 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. Also, certain flavored syrups have an acidic medium, whereas others may be neutral or slightly basic, and the proper selection must be made to ensure the stability of any added medicinal agent. Perhaps the most frequently found types of medications
administered as medicated syrups are antitussive agents and antihistamines.

### 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; and (d) colorants. Also, many types of syrups, especially those prepared commercially, contain special

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**Table 13.6 EXAMPLES OF NONMEDICATED SYRUPS (VEHICLES)**

<table>
<thead>
<tr>
<th>SYRUP</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cherry syrup</td>
<td>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.</td>
</tr>
<tr>
<td>Cocoa syrup</td>
<td>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.</td>
</tr>
<tr>
<td>Orange syrup</td>
<td>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.</td>
</tr>
<tr>
<td>Ora-Sweet, Ora-Sweet SF</td>
<td>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.</td>
</tr>
<tr>
<td>OraBlend</td>
<td>A preblended combination of Ora-Sweet and Ora-Plus (1:1) and Ora-Sweet SF and Ora-Plus (1:1)</td>
</tr>
<tr>
<td>PCCA Accocia Syrup</td>
<td>A sweet, demulcent suspending vehicle with a mild vanilla flavor</td>
</tr>
<tr>
<td>PCCA-Plus Oral Suspending Vehicle</td>
<td>A preserved, buffered vehicle with demulcent qualities</td>
</tr>
<tr>
<td>PCCA Sweet SF</td>
<td>A sugar-free syrup containing sorbitol and can be used in diabetic patients as well as others</td>
</tr>
<tr>
<td>PCCA Syrup</td>
<td>A syrup vehicle with less sucrose than Syrup NF</td>
</tr>
<tr>
<td>Raspberry syrup</td>
<td>Sucrose-based syrup with raspberry juice about 48% by volume. Pleasant-flavored vehicle to disguise salty or sour taste of saline medicaments</td>
</tr>
<tr>
<td>SyrSpend™ SF Suspension Vehicle</td>
<td>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.</td>
</tr>
<tr>
<td>SyrSpend™ SF Alka</td>
<td>An alkaline suspension vehicle with a pH of about 7.0, when reconstituted as directed. It is low osmolality (&lt;50 mOsmol), pleasant-tasting, sugar-free, alkaline medium available in unflavored and cherry formulas</td>
</tr>
<tr>
<td>Syrup</td>
<td>85% sucrose in purified water. Simple syrup may be used as the basis for flavored or medicated syrups.</td>
</tr>
</tbody>
</table>
solvents (including alcohol), solubilizing agents, thickeners, or stabilizers.

**Sucrose- and Non-sucrose-Based Syrups**

*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 a sucrose syrup. The addition of one or more artificial sweeteners usually produces an excellent facsimile of a true syrup.

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. The resulting preparation generally requires no additional preservation if it is to be used soon; in the official syrup, preservatives are added if the syrup is to be stored. When properly prepared and maintained, the syrup is inherently stable and resistant to the growth of microorganisms. An examination of
this syrup reveals its concentrated nature and the relative absence of water for microbial growth. 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.

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.

**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 benzoic acid 0.1% to 0.2%, sodium benzoate 0.1% to 0.2%, and various combinations of methylparabens, propylparabens, and butylparabens totaling about 0.1%. 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%).

**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 (a) solution of the ingredients with the aid of heat, (b) solution of the ingredients by agitation without the use of heat or the simple admixture of liquid components, (c) addition of sucrose to a prepared medicated liquid or to a flavored liquid, and (d) percolation of either the source of the medicating substance or the sucrose.

**A. 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 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, 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. Sucrose, a disaccharide, may be hydrolyzed into monosaccharides, dextrose (glucose), and fructose (levulose). This hydrolytic reaction is inversion, and the combination of the two monosaccharide products is invert sugar. 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**

To avoid heat-induced inversion of sucrose, a syrup may be prepared without heat by agitation. 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. Huge glass-lined or stainless steel tanks with mechanical stirrers or agitators are employed in large-scale preparation of syrups. 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. 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.

**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 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. 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 a flavored syrup.

**Percolation**

In this process, purified water or an aqueous solution is allowed to pass through a bed of crystalline sucrose. A pledget of cotton is put in the neck of the percolator and purified water or aqueous solution is added in the percolator containing sucrose. The flow rate is controlled by the stopcock and maintained such that drops appear in rapid succession. If required, a small portion of liquid is re-passed through the percolator to dissolve the sugar completely in the liquid or aqueous solvent.