

Pharmaceutical Technology I

Lecture-15

**Dextrose-based syrups
and
formulation of artificial syrups**

By

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Dextrose-Based Syrups

1. Dextrose may be used as a substitute for sucrose in syrups containing strong acids in order to eliminate the discoloration associated with caramelization.
2. Dextrose-based syrups do not turn brown in acid solutions, but they are subject to other difficulties.
3. Dextrose forms a saturated solution in water at 70% percent (w/v), which is less viscous than simple syrup.
4. Dextrose dissolves more slowly than sucrose, can be dissolved using agitation without use of heat.
5. It is less sweet than simple syrup.

6. The saturated solution of dextrose readily supports the growth of microorganisms, consequently, it is more easily fermented. So preservatives are required to improve the keeping qualities of such syrup.
- Glycerin may be added in 30 to 45% (v/v) to dextrose solution to
 1. Act as a preservative
 2. Increase the viscosity, and also,
 3. Give additional sweetness to the preparation.
 - However, syrups which contain glycerin and strong acid tend to develop a butyric odor on aging, so other types of preservatives and artificial sweetening agent are used instead of glycerin.

Formulation of Artificial Syrups

1. Non-nutritive syrups
 2. Sorbitol-based syrups
- Non-nutritive syrups: several formulas have been published for sugar-free vehicles which are intended as substitutes for syrups and are to be administered to person who must regulate their sugar and/ or caloric intake accurately.
 - For example, persons suffering from diabetes mellitus, which is characterized by hyperglycemia need such preparations.

- Some early formulas included glycerin in order to take advantage of its viscosity and sweetness.
- However, glycerin, as well as alcohol and propylene glycol (which is employed as substitute for glycerin in oral liquid medication), are glycogenetic substances i.e., they are materials which are converted into glucose in the body either directly or indirectly.
- Substance to be used as sugar substitutes should also be non glycogenetic e.g., sodium carboxy methylcellulose which is used in diabetic simple syrup as shown below

Diabetic simple syrup

Sodium carboxymethylcellulose	1.5%
(medium viscosity grad)	
Sweetening agent	q.s.
Preservative	q.s.
Purified water	q.s.

- The carboxy methylcellulose, a derived gum, function as viscosity builder.
- Using natural gum such as acacia and tragacanth for this purpose formed not colorless and tend to change their characteristics upon aging (especially tragacanth)
- Sodium alginate and methylcellulose also have been used as the base for sugar-free syrups. These substances are non glyco-genetic and produce clear, colorless product.
- Methylcellulose is nonionic, while sodium alginate and carboxy methylcellulose are anionic and incompatible with cationic drugs.

- Strong dehydrating agents cause coagulation of aqueous dispersions of both natural and derived gum. So, these syrups are incompatible with excessive amount of alcohol and electrolyte.
- Evidence of incompatibilities in viscosity:
 1. Simple increase or decrease in viscosity or,
 2. In extreme cases, gelation or precipitation.
- Solution of methylcellulose, unlike those of the other gums, gel when heated, since methylcellulose is less soluble at elevated temperatures owing to dehydration of the polymer.

- Preservatives must be included in the formulation, since aqueous solutions of gums readily support growth of microorganisms.
- Non-nutritive, synthetic sweetening agents are required in the formulation, these are
 1. Saccharin sodium rated 300 to 550 times as sweet as sucrose. It is used in concentration 0.1 to 0.2 percent, but it is characterized by a bitter aftertaste.
 2. Sodium cyclamate is 30 to 40 times as sweet as sucrose and has significantly less aftertaste than saccharin.

3. **Compound sodium cyclamate:** the combination of these two substances (1 and 2) is preferred to take advantage of the synergistic, sweetening effect that saccharin has on sodium cyclamate, with minimum aftertaste. But it was found that cyclamates has carcinogenic effects, **so its use have been stopped.**
4. Aspartyl phenylalanine methyl ester is new synthetic sweetening agent, or (aspartame), new low caloric sweetener, it is about 160 times sweeter than sucrose in aqueous solution.

Sorbitol-Based Syrups

- Sorbitol is a hexahydric alcohol ($C_6H_{14}O_6$).
- It is made by hydrogenation of glucose.
- It is used as a major component for syrup formulation.
- Crystalline sorbitol is a white, odorless and non-volatile solid.
- It is used most in the form of a 70% (w/w) aqueous solution.
 - Sorbitol solution is about 60% as sweet as sucrose and half as viscous as simple syrup.
 - It has excellent mouth feel qualities.
- Sorbitol solution is superior to simple syrup from both a physico-chemical and a physiologic stand point.

Advantages and Disadvantage of sorbitol

1. It is not irritating to membranes of the mouth and the throat.
2. Unlike sucrose; it is apparently does not contribute to the formation of dental caries.
3. Sorbitol is metabolized and converted to glucose; however, it is not absorbed from the gastrointestinal tract as rapidly as sugars. So no significant hyperglycemia has been found, and, consequently it may be used as a component of non-nutritive vehicles.

Disadvantage of sorbitol:

- The ingestion of excessive quantities of sorbitol may have a laxative effect.

Combination of sorbitol solution with sugar based syrup

- When sorbitol solution is included in sugar based formulation it improve flavor characteristic and reduced sweetness.
- It is also added to sucrose-based syrups to reduce the tendency of concentrated sugar solutions to crystallize.
- A blend of 30 percent sorbitol with 70 percent syrup USP show very little tendency toward crystallization. Consequently, sorbitol inhibits the sticking or locking of bottle caps which occurs with high concentrations of sucrose.

- Artificial syrup formulations based entirely on sorbitol may include saccharin sodium to intensify the mild sweetness of sorbitol which masks the aftertaste of the saccharin.
- While sorbitol solution does not ordinarily support mold growth, preservatives should be used in solutions containing less than 60 percent (w/w) of sorbitol.
- Sorbitol is chemically stable and practically inert with respect to drugs and other ingredients.
- Many drugs are more stable in sorbitol solutions than in sucrose syrups.

Application of syrups

- Syrups are intensely sweet vehicles which lack significant amount of alcohol and can function to
 1. Mask the taste of otherwise salty or bitter drugs, e.g.,
 - **Raspberry syrup** (a sucrose based syrup containing 48% by volume of raspberry juice. It is a pleasantly flavored vehicle used to disguise the salty or sour taste of saline medicaments.
 - While **cocoa syrup**, this syrup is a suspension of cocoa powder in an aqueous vehicle sweetened and thickened with sucrose, liquid glucose, and glycerin and flavored with vanilla and it is particularly effective in administering bitter tasting drugs to children.

- **Cocoa syrup** is effective because of its high viscosity; in effect it coats the tongue and thus it tends to inhibit diffusion of drug to the taste buds.
- Like cocoa syrup, **acacia syrup** also has a ‘blanketing’ effect to a lesser extent.

2. To provide acidic pH medium e.g.,
 - **Cherry syrup**: a sucrose based syrup containing 47% by volume of cherry juice. The syrup's tart and fruit flavor is attractive to most patients and the acidic pH of syrup makes it useful as a vehicle for drugs requiring an acid medium
 - **Orange syrup**: this sucrose based syrup utilize sweet orange peel tincture and citric acid as the source of flavor and tartness.
 - The syrup resembles orange juice in taste and is a good vehicle for drugs stable in an acidic medium.
 - weak acids are added for orange syrup for masking the salty tastes.

General discussion

1. 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.

2. An important advantage of syrups is their acceptability and wide variety of flavors and their high viscosity.
3. The flavors most frequently used in pharmaceuticals are cherry followed by orange, raspberry, chocolate and mint. Cherry was preferred for antibiotics, cough preparations and sulfa-antibiotics, chocolate for sulfonamides, and orange for vitamins.
4. Syrups as a vehicles most widely used for pediatric medication.

5. Antitussive preparations are a very important class of class of syrup products.
 - The cough suppressant action of syrup is due partially to their soothing effect on the mucous membranes of mouth and throat.
 - Studies have indicated that sorbitol solution has about the same antitussive effect as other commonly used syrup ingredient.

6. Syrup base serves as an effective vehicle for insoluble drugs, certain suspension products particularly those used for sulfonamides, employ syrup vehicles.
7. Another type of dosage form consists of solids which, on addition of an appropriate quantity of water, reconstitute into a syrup.
 - This type of product is designed for drugs such as antibiotics which deteriorate in aqueous solution but are stable in the solid state.