Ministry of Higher Education and Scientific Research
Al- Rasheed University College/ Department of Pharmacy

Pharmaceutical Technology for 3rd year students

Lec # 3

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Oral Solutions and Preparations for oral Solution

- ✓ Liquid pharmaceuticals for oral administration are usually formulated such that the patient receives the usual **dose of the medication** in a conveniently administered volume, as 5, 10, or 15 mL.

- ✓ Examples of dry powder mixtures intended for reconstitution to oral solutions are the following:
- ➢ Cloxacillin Sodium for Oral Solution, USP(Teva), an anti-infective antibiotic.
- ➢ Penicillin V Potassium for Oral Solution, USP(Veetids, Geneva), an anti-infective antibiotic
- ➢ Potassium Chloride for Oral Solution, USP(K-LOR, Abbott), a potassium supplement

- ✓ the pharmacist should be sufficiently knowledgeable about the dispensed product to expertly advise the patient of the ***proper use, dosage, method of administration, and storage of the product.***

- ✓ Information regarding the solvents used in each commercial product appears on the product label and in the accompanying package insert.

✓ Oral Rehydration Solutions

Rapid fluid loss associated with diarrhea can lead to dehydration and ultimately death in some patients, particularly infants.

More than 5 million children younger than 4 years of age die of diarrhea each year world-wide.

Diarrhea is characterized by an increased frequency of loose, watery stools, and because of the rapid fluid loss, dehydration can be an outcome.

- ✓ The loss of fluid during diarrhea is accompanied by depletion of sodium, potassium, and bicarbonate ions; if severe, the loss can result in acidosis, hyperpnea, and vomiting as well as hypovolemic shock. If continuous, bouts of vomiting and diarrhea can cause malnutrition as well.

- ✓ The **goal** is to replace **lost fecal water** with an **oral rehydration** solution and use nutritional foods, such as soybean formula and bran.
- ✓ Oral rehydration solutions are usually effective in treatment of patients with mild volume depletion, 5% - 10% of body weight.

- ✓ Almost in domino fashion, sodium absorption promotes anion absorption, which in turn promotes water absorption to short-circuit dehydration.

- ✓To produce maximal absorption of sodium and water, studies have demonstrated that the optimal concentrations of glucose and sodium in an isotonic solution are 110 mM (2%) glucose and 60 mEq/L of sodium ion,

- ✓ A liter of typical oral rehydration solution contains;

  45 mEq Na^+,

  20 mEq K^+,

  35 mEq Cl^-,

  30 mEq citrate, and 25 g dextrose.

- ✓ Commercial ready-to-use oral electrolyte solutions to prevent dehydration or achieve rehydration include
- ✓ **Pedialyte Solution (Ross)**
- ✓ **Rehydralyte Solution (Ross.**
- ✓ **Infalyte Oral Solution**

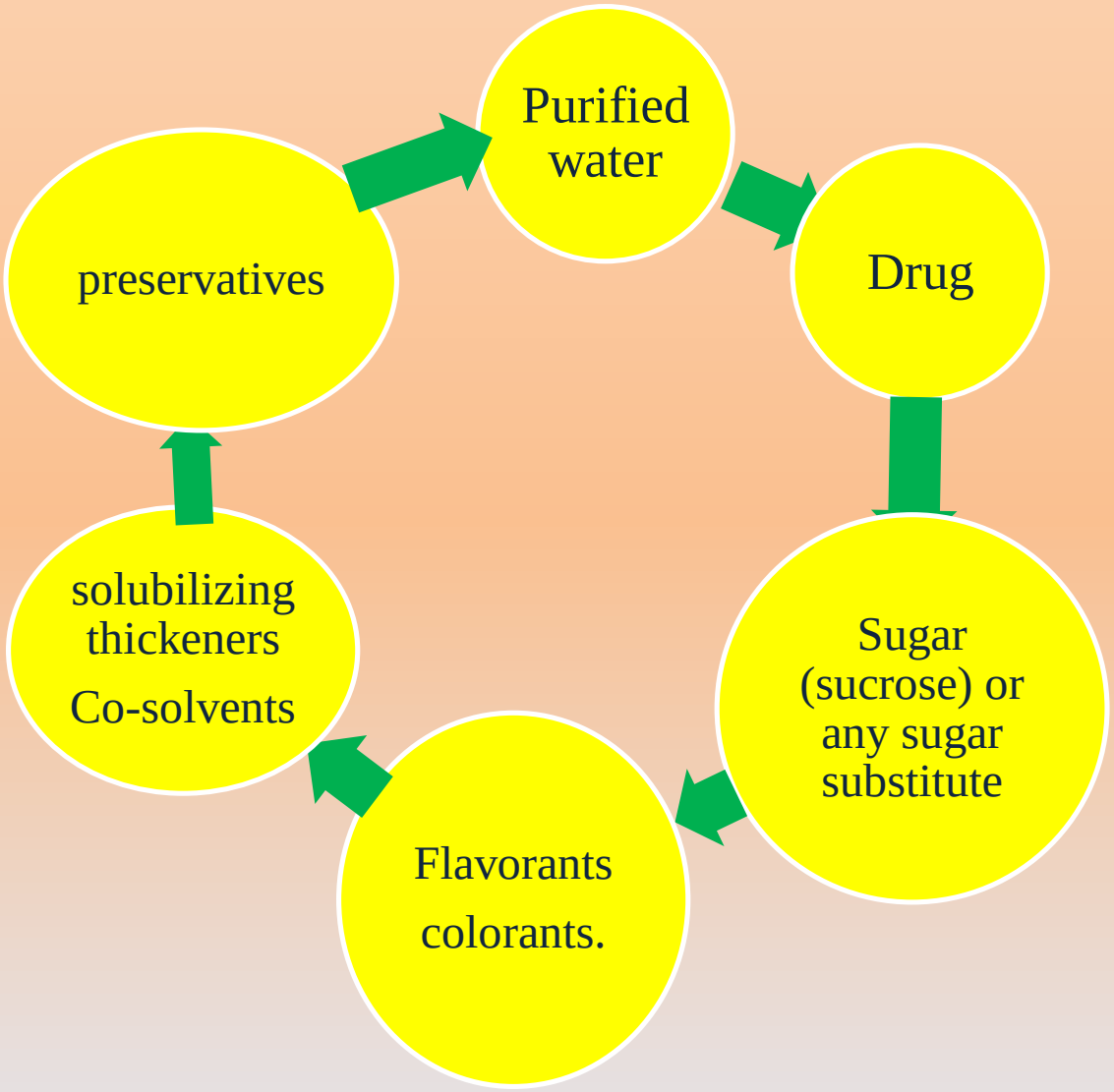
Syrups

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.

Syrups Components



Sucrose

- ✓ Sucrose is the sugar most frequently employed in syrups.
- ✓ other sugars or substances such as ***sorbitol, glycerin, and propylene glycol***.
- ✓ In some instances, all ***glycogenetic*** are replaced by ***nonglycogenetic*** substances, such as ***methylcellulose or hydroxyethylcellulose***.

- ✓The aqueous sugar medium of dilute sucrose solutions is an efficient nutrient medium for the growth of microorganisms, whereas concentrated sugar solutions are quite resistant because of the unavailability of the water required for the growth.

- ✓ If the syrup were completely **saturated** with sucrose, in cool storage, some sucrose might **crystallize** from solution

- ✓ Most syrups contain a high proportion of sucrose, usually 60%-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.

- ***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.

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, etc.) is used.

Antimicrobial Preservatives

1- the proportion of water available for growth,

2-the nature and inherent preservative activity of some formulative materials (e.g., many flavoring oils that are inherently sterile and possess antimicrobial activity),

3- the capability of the preservative itself.

1- benzoic acid 0.1-0.2%,

2-sodium benzoate 0.1-0.2%,

3-various combinations of methylparabens, propylparabens, and butylparabens totaling about 0.1%.

take advantage of their potentiating effect

- ✓ Frequently, alcohol is used in syrups in small amounts. Its not sufficient to have preservative effect. it concentrate in vapors above the syrup & thus prevents the growth of surface molds. but normally it is not present in the final product in amounts that would be considered to be adequate for preservation (15% -20%).

✓ ***Syrups can be preserved*** by

(a) storage at low temperature

(b) adding preservatives such as glycerin, benzoic acid, sodium benzoate, methyl paraben, or alcohol.

(c) by the maintenance of a high concentration of sucrose as a part of the formulation.

- ✓ Using, the free–water method to calculate the quantity of alcohol required.

- How to calculate the amount of preservative?? The amount of added preservative may be estimated from a knowledge of the **calculated free water.**

E.g. –

Rx

Active drug	5 mL volume occupied
Other drug solids	3 mL volume occupied
Glycerin	15 mL
Sucrose	25 g
Ethanol	95% q.s.
Purified water q.s.	100 mL

Preparation of Syrups
1- Solution with the Aid of Heat:

If heat–labile substances, such as volatile flavoring oils and alcohol, are to be added, they are added to the syrup after the sugar is dissolved by heat, and the solution is rapidly cooled to room temperature.

Advantages:

- ✓ The invert sugar formed on hydrolysis has several interesting properties;

1- Solutions on invert sugar are fermented more easily than solutions of sugar. In which the first step in fermentation is inversion.

2- invert sugar is sweeter than sucrose, in regard to sweetness, sucrose is rated 100, dextrose rated 74 while levulose 173.

3- degradation of levulose formed by inversion seems to be responsible for the brown discoloration which develops in some colorless syrups. This change is called caramelization & it takes place particularly in syrups containing strong acids.

2- Solution by Agitation (Without the Aid of Heat) ;

✓Syrup may be prepared without heat by agitation.

✓ On a small scale, sucrose & 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.

✓Advantages;

Despite the process is more time consuming than the use of heat, but the product has maximum stability.

3- Addition of Sucrose to a Medicated Liquid or to a Flavored Liquid:

Frequently Medicated liquids such as tinctures & fluidextracts are used in the preparation of medicated syrups.

4- Percolation

Non- sucrose based Sryp or Sugar Fee Syrup (Diabetic Simple Syrup, Artificial Syrup & Non nutritive Syrup)

- Types of agents used for preparation of non-Sucrose based syrups;

1- ***Glycerin, propylene glycol***

- ***Methylcellulose, hydroxyethylcellulose & Sodium alginate***
- ***Carboxymethylcellulose***, a bodying agent (viscosity builder).

- ✓ 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.

Preservative? Why??

- ✓ Syrups made of natural or derived gums are incompatible with excessive amounts of alcohol or electrolytes & the evidence is the increment or decrement in the syrup viscosity.

- ✓ 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.

- ✓ 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.

- ✓ As noted earlier, sucrose-based syrup may be substituted in whole or in part by other agents in the preparation of 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

- ***Sorbitol-based Syrup;***

its hexahydric alcohol made by hydrogenation of glucose. Its Chemically stable, inert with respect to drugs and other ingredients. It Characterized by;

70% (w/w) aqueous solution U.S.P., trade mark Sorbo®.

Sorbitol based solution have extended shelf lives required in proprietary products. ????

Its compatible with other polyols & simple syrup & as much as 10% (v/v) of alcohol can be added before crystallization is observed. Why??

- ✓ Preservatives should be used in solutions containing less than 60% (w/w) of sorbitol ????

- ***Saccharine sodium;***

- ***Aspartylphenylalanine methyl ester***,

- ✓ The overall taste of the diabetic simple syrup is described as being (slick & demulscent, but not offending).

- ✓ Mouth feel characteristic of sucrose syrup is not the same as that produced from Non-nutritive syrup formulas intended as substitutes for official sucrose-based syrups.


QUESTIONS

Al-Rasheed University College, Department of Pharmacy

Pharmaceutical Technology for 3rd year students; ; Lec 4,

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Solution using mixed solvent Systems; Spirits, Elixirs and Extracted Products

- Products for Internal use may contain ethanol, glycerol, propylene glycol (PG), & certain oils.

- Solvents such as acetone, benzene and petroleum ether are not used internally.


elixir

Elixirs

✓Elixirs are clear, sweetened hydroalcoholic solutions intended for oral use & are usually flavored to enhance their palatability.

✓Its one of the official & most widely used liquid preparations for oral administration. Their popularity is due to?

✓Each elixir requires a specific blend of alcohol and water to maintain all of the components in solution.

✓The proportion of alcohol in elixirs varies widely because the individual components of the elixirs have different water and alcohol solubility characteristics.

✓In addition to alcohol & water, other solvents, such as glycerin & PG, are employed as adjunctive solvents.

✓Naturally, for elixirs containing agents with poor water solubility, the proportion of alcohol required is greater than for elixirs prepared from components having good water solubility.

✓Although many elixirs are sweetened with sucrose or with a sucrose syrup, some use sorbitol, glycerin, and/or artificial sweeteners.

✓All elixirs contain flavorings agents? & most of them have coloring agents?

✓Elixirs containing more than 10%-12% of alcohol are usually self preserving & do not require the addition of an antimicrobial agent.

- ✓ One advantage of elixirs over their counterpart drugs in solid dosage forms is the flexibility and ease of dosage administration to patients who have difficulty swallowing solid forms.

- ✓ A disadvantage of elixirs for children and for adults why”??

- The proportion of alcohol in elixirs varies widely because the individual components of the elixirs have different water and alcohol solubility characteristics.

- In official elixirs, the alcohol contents varies from 4-40%.

Types of Elixirs

- **Non-medicated elixirs**
- They are used as solvents or vehicles for the preparation of medicated elixirs: aromatic elixirs (USP), isoalcoholic elixirs (NF), or compound benzaldehyde elixirs (NF). Active ingredient dissolved in a solution that contains 15 to 50% by volume of ethyl alcohol

- **Medicated elixirs**
- Antihistaminic elixirs: used against allergy: chlorampheniramine maleate elixirs (USP), diphenhydramine HCl elixirs.
- Sedative and hypnotic elixirs: sedatives induce drowsiness, and hypnotics induce sleep: pediatric chloral hydrate elixirs.
- Expectorant: used to facilitate productive cough (cough with sputum): Terpin hydrate elixirs.
- Miscellaneous: acetaminophen (paracetamol) elixirs, which are used as analgesics.

➢ Elixirs Classification

A/ Medicated; are employed for the therapeutic benefit of the medicinal agent. Most official and commercial elixirs contain a single therapeutic agent ???

1- Antihistaminics (chlorpheniramine maleate Elixir U.S.P.)

2- Sedative &hypnotics (Phenobarbital Elixir,U.S.P.)

3- Expectorants (Terpine Hydrate & Codeine Elixir,N.F.)

4- Miscellaneous (Dexamethasone Elixir, N.F.

B-Non-medicated elixirs

ex. Aromatic Elixir N.F., Benzaldehyde Elixir N.F.

Nonmedicated elixirs may be useful to the pharmacist in the immediately filling of prescriptions involving;

- ✓If a hydroalcoholic vehicle is selected, the proportion of alcohol should be only slightly above the amount needed to effect and maintain the drug's solution.

- ✓When a pharmacist is called on to dilute an existing medicated elixir, the nonmedicated elixir he or she selects as the diluent should have approximately the same alcoholic concentration as the elixir being diluted.

- ✓ Also, the flavor and color characteristics of the diluent should not be in conflict with those of the medicated elixir, and all components should be chemically and physically compatible.
- ✓ In years past, when pharmacists were called on more frequently than today to compound prescriptions, the three most commonly used nonmedicated elixirs were aromatic elixir, compound benzaldehyde elixir, and isoalcoholic elixir.

EXAMPLES OF MEDICATED ELIXIRS BY CATEGORY

ELIXIR	REPRESENTATIVE COMMERCIAL PRODUCTS	USUAL ADULT DOSE/VOLUME OF COMMERCIAL ELIXIR	COMMENTS
Adrenocortical Steroid			
Dexamethasone	Dexamethasone Elixir	500 mg/5 mL	Synthetic analog of hydrocortisone, about 30 times more potent. Commercial elixir is packaged with a calibrated dropper for accurate measurement of small doses; intended primarily for children; also has utility for adults with trouble swallowing tablets. Used for many indications: rheumatoid arthritis, skin diseases, allergies, inflammatory conditions. Commercial product contains 5% alcohol.
Analgesic, Antipyretic			
Acetaminophen	Children's Tylenol Elixir (McNeil)	160 mg/5 mL	Reduction of pain and lowering of fever particularly in patients sensitive to or unable to take aspirin. Elixir is especially useful for pediatric patients and is alcohol-free.
Anticholinergic, Antispasmodic			
Hyoscyamine sulfate	Alaven	0.125 mg/5 mL	Used to control gastric secretion, visceral spasm, hypermotility, abdominal cramps. Commercial product contains 20% alcohol.
Antihistamine			
Diphenhydramine HCl	Diphenhydramine HCl Elixir	12.5 mg/5 mL	Antihistamines are used for a variety of allergic reactions, for example, perennial and seasonal allergic rhinitis, vasomotor rhinitis, allergic skin manifestations of urticaria, reactions to insect bites. Commercial product contains 5.6% alcohol.
Antipsychotic			
Fluphenazine HCl	Fluphenazine HCl Elixir (Pharmaceutical Associates)	2.5 mg/5 mL	Management of psychotic disorders
Cardiotonic			
Digoxin	Various	50 mg/mL	Among other effects, increases the force of myocardial contraction. Used in congestive heart failure, atrial fibrillation, other cardiac conditions. Commercial product contains 10% alcohol.
Sedatives, Hypnotics			
Butabarbital sodium	Butisol Sodium Elixir (Medpointe)	30 mg/5 mL	In low dosage, sedatives; in higher dosage, hypnotics. Butabarbital sodium elixir contains 7% alcohol; phenobarbital elixir contains 14% alcohol.
Phenobarbital	Various	20 mg/5 mL	

Preparation of Elixirs

1. Simple solution with agitation &/or
2. By the admixture of two or more liquid ingredients.

- Although most elixirs can be prepared by simple procedure, their small scale manufacture is usually time consuming.

- Frequently, the final mixture will be cloudy???? **because of separation of some of the flavoring oils by the reduced alcoholic concentration.**

- If this occurs, the elixir is usually permitted to stand for a prescribed number of hours???? **to ensure saturation of the hydroalcoholic solvent & to permit the oil globules to coalesce so that they may be more easily removed by filtration.**

- Talc, a frequent filter aid in the preparation of elixirs, absorbs the excessive amounts of oils & therefore assists in their removal from the solution.

- Despite the presence of glycerin, syrup, sorbitol, & PG in elixirs generally contributes to the solvent effect of the hydroalcoholic vehicle, assists in the dissolution of the solute, & enhances the stability of the preparation. But, the presence of these materials amy slow the rate of filtration???.

❑ Phenobarbital Elixir

Phenobarbital	4.0 g
Orange oil	0.25 mL
Propylene glycol	100.0 mL
Alcohol	200.0 mL??
Sorbitol solution	600.0 mL
Color	q.s.

Purified water, to make 1000mL

- The U.S. Food and Drug Administration (FDA) has proposed that insofar as possible manufacturers of over-the-counter (**OTC**) oral drug products restrict the use of alcohol and include appropriate warnings in the labeling.

➢ *Storage conditions*

elixirs should be stored in tight, light–resistant containers & protected from excessive heat due to their content of volatile oils & alcohol.

Elixirs are, sweetened, flavored, hydro-alcoholic solutions intended for oral use.

Types of elixirs:

1. Non-medicated elixir → employed as vehicle.
2. Medicated elixir → employed for therapeutic effect of the drug they contain.

Syrup	Elixir
……..	Less sweet
……..	Less viscose
……..	Lower sucrose content
Lower dissolving capacity	Higher dissolving capacity
……..	Simple manufacturing
……..	More stable


Spirits

Spirits (Essence)

✓Are alcoholic or hydroalcoholic solutions of volatile substances.

✓Generally, the alcoholic concentration in spirits is rather high, usually more than 60 %.

✓For medicinal purposes, spirits may be taken orally, applied externally, or used by inhalation. When taken orally, they are generally mixed with a portion of water to reduce the pungency of the spirit.

METHOD OF PREPARATION OF SPIRITS

1- Simple Solution

Majority of spirits are prepared by dissolving the solute in alcohol by agitation. Filtration is generally desirable to obtain a sparking clear product.

2- Solution with Maceration

Macerate the vegetable materials in a suitable solvent to remove the undesired constituents or to extract one which is desired.

Ex., Peppermint Spirit

- When mixed with water or with an aqueous preparation, the volatile substances present in spirits generally separate from the solution & form a milky preparation.

- ***Uses of Spirits;***

- ***Storage Condition;***

Spirits should be stored in tight, light-resistant containers and in a cool place.

Thanks a lot for your Attention

Dr.Esraa Ghazy ...