Pharmaceutical Technology

Lecture 17
Elixirs
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Elixirs

- Elixirs are clear, sweetened, hydroalcoholic solutions for oral use, and are usually flavored to enhance their palatability.
- Non-medicated elixirs are employed as vehicles and medicated elixirs for the therapeutic effect of the medicinal substances they contain.

What are the differences between elixirs and syrups?

- Compared with syrups, elixirs are usually

1. Less sweet and less viscous because they contain a lower proportion of sugar and consequently are less effective in masking the taste of medicinal substances.

- However, because of their hydroalcoholic character,

2. elixirs are better able than aqueous syrups to maintain both water-soluble and alcohol-soluble components in solution.
3. Also because of their stable characteristics and ease which are prepared (by simple solution), from a manufacturing standpoint, elixirs are preferred over syrups

Component of Elixirs

- The proportion of alcohol in elixirs varies widely because the individual components of the elixirs have different water and alcohol solubility characteristics.
- Each elixir requires a specific blend of alcohol and water to maintain all of the components in solution.
- 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.

- In the official elixirs, the alcohol content varies from 4 to 40 percent. Generally, there is just enough alcohol to keep volatile oil or the medicinal substances in solution.
- In addition to alcohol and water, other solvents, such as glycerin and propylene glycol are frequently employed in elixirs as adjunctive solvents.

- Although many elixirs are sweetened with sucrose or with a sucrose syrup, some utilise sorbitol, glycerin and/ or artificial sweeteners.
- Elixirs having a high alcohol content usually utilise an artificial sweeteners, such as saccharin, which is required only in small amounts, rather than sucrose which is only slightly soluble in alcohol and requires greater quantities for equivalent sweetness.

- Elixirs containing over 10 to 12% of alcohol are usually self preserving and do not require the addition of an antimicrobial agent or their preservation.
- All elixirs contain flavoring materials to increase their palatability and most have coloring agent to enhance their appearance.

- Although the USP monographs for medicated elixirs provide standards, they do not generally provide official formulas. Formulations are left up to the individual manufacturers.
- Example formulations for some medicated elixirs are as follows

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	1,000.0 mL

Theophylline Elixir

Theophylline	5.3 g
Citric acid	10.0 g
Liquid glucose	44.0 g
Syrup	132.0 mL
Glycerin	50.0 mL
Sorbitol solution	324.0 mL
Alcohol	200.0 mL
Saccharin sodium	5.0 g
Lemon oil	0.5 g
FD&C Yellow No. 5	0.1 g
Purified water, to make	1,000.0 mL

- Medicated elixirs are formulated so that a patient receives the usual adult dose of the drug in a convenient measure of elixir.
- For most elixirs, one or two teaspoonfuls (5 or 10 mL) provides the usual adult dose of the drug.
- 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.

- **Disadvantage of elixirs**

  A disadvantage of elixirs for children and for adult who choose to avoid alcohol is their alcohol content.

- **Storage of elixir**

  Because of their usual content of volatile oils and alcohol, elixirs should be stored in tight, light resistant containers and protect from excessive heat.

Preparation of elixirs

- Elixirs are usually prepared by simple solution with agitation and/ or by the admixture of two or more liquid ingredients.
- Alcohol-soluble and water-soluble component are generally dissolved separately in alcohol and in purified water, respectively.
- Then the aqueous solution is added to the alcoholic solution, rather than the reverse, in order to maintain the highest possible strength at all times so that minimal separation of the alcohol-soluble components occurs.

- When the two solutions are completely mixed the mixture is made to volume with the specific solvent or vehicle.
- Frequently the final mixture will not be clear, but cloudy, due principally to the separation of some of the flavoring oils by the reduced alcoholic concentration.
- If this occurs, the elixir is usually permitted to stand for prescribed number of hours, to ensure the saturation of the hydroalcoholic solvent and 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, has the ability to absorb the excessive amounts of oils and therefore assist in their removal from the solution.
- The presence of glycerin, syrup, sorbitol and propylene glycol in elixirs generally contributes to the solvent effect of the hydroalcoholic vehicle, assists in the dissolution of the solute, and enhances the stability of the preparation. However, the presence of these materials adds to the viscosity of the elixir and slows the rate of their filtration.

Non medicated elixirs

- Nonmedicated elixirs may be useful to the pharmacist in the extemporaneous filling of prescriptions involving

  (a) the addition of a therapeutic agent to a pleasant-tasting vehicle and

  (b) dilution of an existing medicated elixir.
- In selecting a liquid vehicle for a drug substance, the pharmacist should be concerned with the solubility and stability of the drug substance in water and alcohol.

- 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 non-medicated 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.

Examples of non medicated elixirs

- In years past, when pharmacists were called on more frequently than today to compound prescriptions,the three most commonly used non medicated elixirs were:

1. Aromatic elixir
2. Compound benzaldehyde elixir
3. Iso-alcohoic elixir

Aromatic elixir, USP

- It is the most widely used non medicated elixir
- It consists of compound orange spirit, syrup, alcohol, water, and talc.
- It is a rather simple preparation. Yet it is a difficult to prepare it in small quantities.

- The difficulty arises from

1. the loss in volume resulting from repeated filtration about 10-20% of volume loss due to this step.
2. the slowness in filtration result from the syrups being added before preparation is filtered. This ingredient, plus the talc, make it nearly impossible to get a good rate of filtration.

Suggestions

- Dissolving the sugar in the filtrate to increase the rate of filtration
- The use of terpene-less oils (water-soluble) to avoid the difficulty occur (cloudiness) which is due to the insolubility in water of the oils present in compound orange spirit.
- Both of these suggestions make it possible for elixir to be made more rapidly.

Content of sugar and alcohol in Aromatic elixir

- The sugar content of aromatic elixir is about 31 percent, or less than half that of syrup.
- The alcohol content is from 21 to 23percent by volume.

- **Compound benzaldehyde elixir, NF**
- Is prepared by simple solution and is used when a bitter almond-like flavor is desired

Iso-Alcoholic Elixir, NF

- It is composed of two separate parts, low alcoholic elixir with an alcohol content of from 8 to 10 percent, and high alcoholic elixir with an alcohol content of from 73 to 78 percent.
- By mixing two solutions, the final product may be obtained which has an alcoholic content within the ranges required for elixirs.

Medicated Elixir

- As noted previously, medicated elixirs are employed for the therapeutic benefit of the medicinal agent. Most official and commercial elixirs contain a single therapeutic agent.
- The main advantage of having only a single therapeutic agent is that the dosage of that single drug may be increased or decreased by simply taking more or less of the elixir, whereas when two or more therapeutic agents are present in the same preparation, it is impossible to increase or decrease the dose of one without an automatic and corresponding adjustment in the dose of the other, which may not be desired.

- Medicated elixirs which have therapeutic action, some times used as the vehicle for other drug e.g. Phenobarbital elixir.
- Medicated elixirs can be described by further classifying them according to their therapeutic activity.

1. Antihistamine elixirs
2. Sedatives and Hypnotics elixirs
3. Expectorants and cough preparation
4. Miscellaneous medicated elixirs

Antihistamine Elixirs

- This is the largest group of elixirs having a definite therapeutic action.
- Antihistamines are useful primarily in the symptomatic relief of certain allergic disorders.
- In their action, they suppress symptoms caused by histamine, one of the chemical agents released during the antigen-antibody reaction of the allergic response.
- Examples: 1. Diphenhydramine HCl Elixir
  2. Chlorpheniramine HCl Elixir

Sedative and Hypnotics

- This is the second largest group of elixirs
  e.g. Phenobarbital Elixir
- Barbiturate in general used in low dosage as sedatives and in higher dosage as hypnotics.
- They are either long acting sedation, intermediate sedation or short-acting sedation or duration.
- Phenobarbital is used for long-acting sedation.

Phenobarbital elixir

- Phenobarbital elixir is formulated to contain phenobarbital 0.4%, which provides about 20 mg of drug per teaspoonful (5 mL) of elixir.
- The elixir is commonly flavored with orange oil, colored red with an FDA-approved colorant, and sweetened with syrup.
- The official elixir contains about 14% alcohol, which is used to dissolve the phenobarbital. However, this amount is almost the very minimum required to keep the phenobarbital in solution. Therefore, glycerin is often added to enhance the solubility of phenobarbital.

- Frequently, a solute is more soluble in a mixture of solvents than in one solvent alone. This phenomenon is known as cosolvency, and the solvents that, in combination, increase the solubility of the solute are called cosolvents.
- Approximately 1 g of phenobarbital is soluble in 1000 mL of water, in 10 mL of alcohol, in 40 mL of chloroform, and in 15 mL of ether at 25°C. The solubility of phenobarbital in water–alcohol–glycerin mixtures is plotted on a semi logarithm grid in Figure 9–4from the data of Krause and Cross.

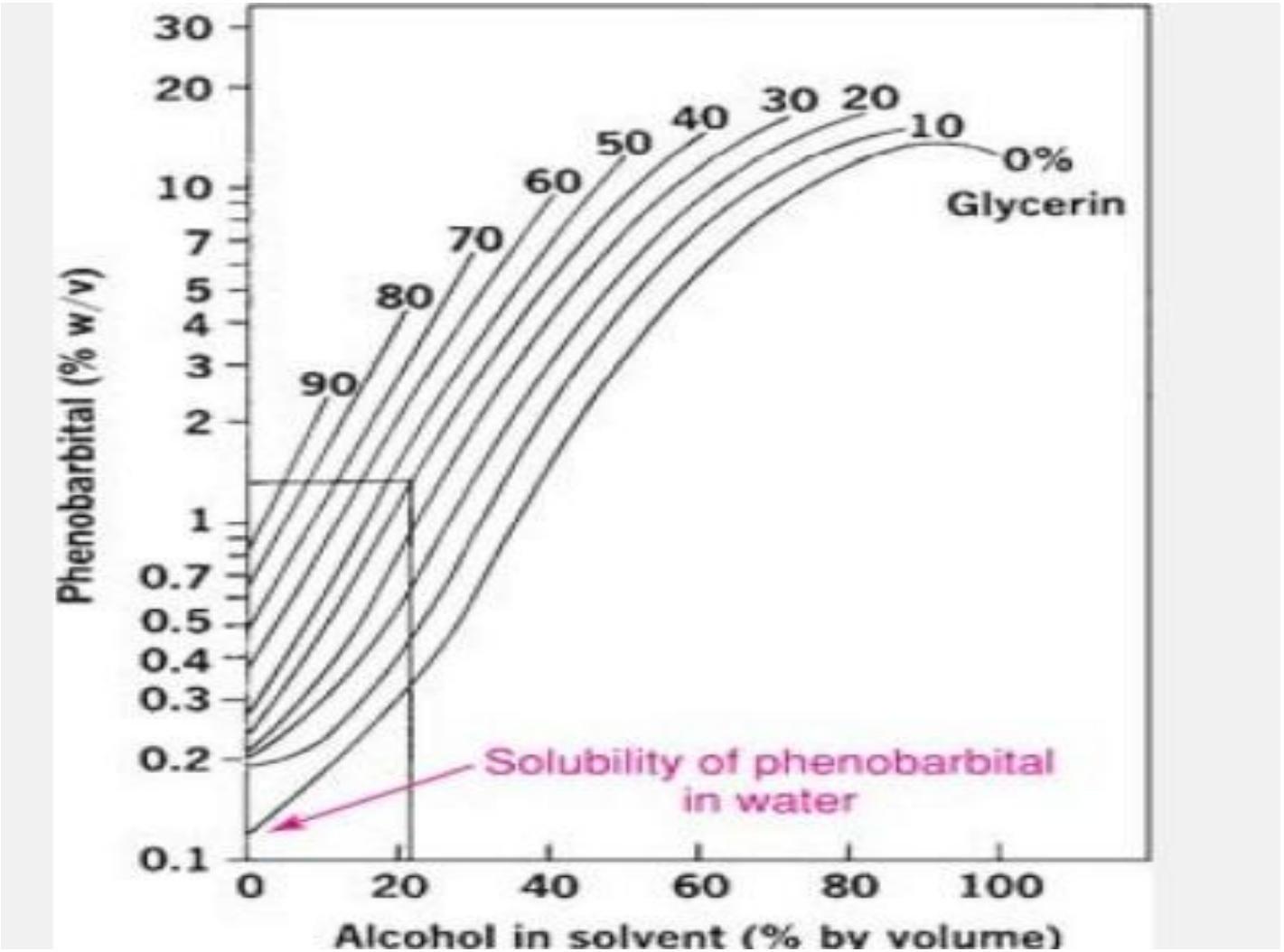

Fig. 9-4. The solubility of phenobarbital in a mixture of water, alcohol, and glycerin at 25°C. The vertical axis is a logarithmic scale representing the solubility of phenobarbital in g/100 mL. (From G. M. Krause and J. M. Cross, J. Am. Pharm. Assoc. Sci. Ed. **40,** 137, 1951. With permission.)

- By drawing lines parallel to the abscissa in Figure 9–4 at a height equivalent to the required phenobarbital concentration, it is a simple matter to obtain the relative amounts of the various combinations of alcohol, glycerin, and water needed to achieve solution.
- For example, at 22% alcohol, 40% glycerin, and the remainder water (38%), 1.5% w/v of phenobarbital is dissolved, as seen by following the vertical and horizontal lines drawn on Figure 9–4.

- In Phenobarbital elixir, the active ingredient first is dissolved in alcohol before adding the other liquids. While phenobarbital dissolves readily in alcohol and will remain in solution when the alcohol content is lowered.
- Mixer of alcohol, water, and glycerin is used in this elixir. The presence of the glycerin prevents the phenobarbital from precipitating.

- Glycerin and glycerin water solutions are poor solvents for phenobarbital. But the solubility of phenobarbital in alcohol is enhanced by the addition of glycerin.

- **Expectorants and cough preparations**

  Terpin Hydrate Elixir, NF.

Miscellaneous Elixirs

1. Digoxin Elixir USP, is used as a cardiotonic.
2. Acetaminophen Elixir, NF, which is used as analgesic.
3. Dexamethasone Elixir, NF, contains a synthetic adrenocorticosteroid and is used in the treatment of rheumatoid arthritis and other conditions for which corticosteroid therapy is indicated.