Lecture 5 **Pharmaceutical Technology** **3rd Stage**

Solution Using Mixed Solvent System

Spirits, Elixers, and Extracted Products

Lecturer Iman Aldahhan

When substance to be included in liquid dosage form for oral administration are not water soluble or when they exhibit chemical instability in water one must either prepare suspension or utilize non aqueous solvents alone or with a minimum amount of water.

Spirits:

Spirits are alcoholic or hydroalcoholic solution of volatile substances. Generally, the alcohol concentration of spirits is rather high, usually over 60%.Because of the greater solubility of aromatic substances in alcohol than in water, spirits can contain a greater concentration of these materials than corresponding aromatic waters. The amount of volatile materials in spirits varies greatly and no fixed percentage can be given. The alcohol content varies. The lowest percentage is in Aromatic Ammonia Spirit (62 to 68 percent). The highest is in Camphor Spirit (80 to 87 percent).

When mixed with water or with an aqueous preparation, the volatile substances present in spirits generally separate from solution and form a milky preparation. In order to avoid this turbidity,

1. Water except as specified in the formula should be avoided.

2. Graduates and other equipment used should be dry.

3. Filter paper should be moistened with alcohol.

Iman Aldahhan

Methods used to prepare Spirits:

The introduction of spirit into pharmacy and medicine was brought about by the development of distillation procedures. Depending on the materials utilized, spirits may be prepared by:

1. Simple solution

2. Solution by maceration

3. Distillation

4. Chemical reaction

Uses of Spirits:

1. Spirits may be used pharmaceutically as flavoring agent and medicinally for the therapeutic value of aromatic solute.
2. As flavoring agents they are used to impart the flavor of their solute to other pharmaceutical preparations.
3. For medicinal purposes, spirits may be taken orally, applied externally, or used by inhalation, depending upon the particular preparation.
4. When taken orally, they are generally mixed with a portion of water to reduce the pungency of the spirit.

Official Spirits:

The spirits most recently official in the USP/ NF were

1. Aromatic ammonia spirit

2. Camphor spirits

3. Compound orange spirit

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4. Peppermint spirit

There is no classification of spirits because

1. There is small number of spirits

2. Some have therapeutic effect, other are used as flavor.

3. Each spirit has its own method for preparation.

Aromatic Ammonia Spirit, NF:

It acts:

1. as a carminative due to the volatile oils present.

2. as antacid.

3. as a mild reflex circulatory stimulant due to the liberation of ammonia (NH_3) from the ammonium carbonate which the spirit contains so it is used in cases of fainting.

Camphor Spirit, NF:

Camphor spirit, NF like aromatic ammonia spirit, is well known to the lay public. It is referred to as Tincture of camphor and also as camphor. This preparation is a simple solution of 10 percent camphor in alcohol. It is rarely used internally, but its external use is very common. Usually it is applied to “cold sores” and similar ailments.

Compound Orange spirit, USP:

It is a blend of several oils and is readily prepared by simple solution. It is an important ingredient of aromatic elixir.

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Peppermint Spirit, NF:

It is used as a carminative and flavor. Given orally in small doses, usually 1ml, this spirit is an effective carminative, and it is used extensively for that purpose.

Its preparation as follows:

1. The leaves are macerated in water to remove tannins and other water soluble materials.

2. The aqueous extract is discarded, and the leaves are expressed and

3. macerated in alcohol. The alcohol dissolves the chlorophyll giving the product a bright green color.

4. To this alcoholic solution 10% of volatile oil is added.

The leaves used do not impart any medicinal action to the preparation. This action comes from the volatile oil added to the alcohol.

Elixirs:

Elixirs are clear, sweetened, hydroalcoholic solutions for oral use, and are usually flavoured 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

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2. Less effective in masking the taste of medicinal substances.

However, because of their hydroalcoholic character, elixirs are

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

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 adjunct solvents.

Although many elixirs are sweetened with sucrose or with 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 flavouring materials to increase their palatability and most have coloring agent to enhance their appearance.

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

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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 filteration.
- 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.

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- 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 slow the rate of their filtration.

Example formulations for some medicated elixirs

Phenobarbital elixir

Phenobarbital ..... 4.00 gm

Orange oil ..... 0.25 ml

Propylene glycol ..... 100.00 ml

Alcohol ..... 200.00 ml

Sorbitol solution ..... 600.00 ml

Colouring agent ..... Q.S.

Purified water ad..... 1000.00 ml

Classification of elixirs

1. **Non medicated elixirs**

Which is used as vehicles in preparing medicated elixir either by

1. The addition of a therapeutic agent to a pleasant tasting vehicle
2. The dilution of an existing medicated elixir

The three most commonly used non medicated elixirs were:

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

Aromatic elixir, USP

Is the most widely used. It is a rather simple preparation. Yet it is a difficult to prepare it in small quantities. It consists of compound orange spirit, syrup, alcohol, water, and talc. 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, makes 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 terpeneless 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. The elixir may be

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diluted with water without becoming turbid. Consequently, it can be used with aqueous preparations without producing a milky liquid.

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 an alcoholic content within the ranges has required for elixirs.

If Iso-alcoholic elixir were prescribed, the drug could be dispensed in solution by using the right proportion of the low and high alcoholic elixirs. It is easy to prepare, and both forms are stable. The product is similar in flavor and odor to aromatic elixir.

Low alcoholic elixir:

Compound orange spirit	10 ml
Alcohol	100 ml
Glycerin	200 ml
Sucrose	320 g
Purified water q.s.	1000 ml

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High alcoholic elixir

Compound orange spirit	4 ml
Saccharin	3 g
Glycerin	200 ml
Alcohol q.s .	1000 ml

Medicated Elixirs

Medicated elixirs which have therapeutic action, sometimes 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. .e.g.

1. Diphenhydramine HCl Elixir

2. Chlorpheniramine HCl Elixir

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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.

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.

Role of glycerin in phenobarbital elixir

Glycerin and glycerin water solutions are poor solvents for phenobarbital. But the solubility of phenobarbital in alcohol is enhanced by the addition of glycerin. The solubility of phenobarbital in 10% alcohol solution is 0.19% while the solubility is increased to 0.5% by using 10% alcohol + 40% glycerin. Glycerin cause a correlation the dielectric constant of the mixture with the amount of drug solubilised.

Medicated elixirs

- Amobarbital Elixir: It is used for intermediate duration. In this elixir, methanamine is used to increase the solubility of amobarbital.
- Pentobarbital Elixir; it is used commonly as short-acting barbiturates.
- Sodium salt of pentobarbital is used in preparation of elixir, which is readily water-soluble. This compound, after being dissolved later is converted to

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pentobarbital by adding diluted hydrochloric acid. The conversion is necessary because sodium pentobarbital is not stable in solution but decomposes on standing.

Expectorants and cough preparations

1. Terpin Hydrate Elixir, NF.

2. Terpin hydrate and dextromethorphan Hydrobromide Elixir, NF.

3. Terpin Hydrate and codeine Elixir, NF

The latter two are made by dissolving the respective drugs in Terpin Hydrate Elixir. These elixirs cannot be diluted with much water because the slightly water soluble terpin hydrate will precipitate.

These elixirs contain the highest percentage of alcohol (39 to 44%) of all elixirs in order to keep the terpin hydrate in solution. Terpin Hydrate and codeine elixir is an example of narcotic elixir. Terpin Hydrate and Dextramethorphan HBr elixir is non-narcotic elixir.

Terpin hydrate and codeine elixir

A preparation of the expectorant terpin hydrate, with sweet orange peel tincture, benzaldehyde, glycerin, alcohol, syrup, water, and the antitussive opiate codeine. Terpin hydrate diminishes secretions and promotes healing of the mucous membrane, and codeine depresses the cough center in the medulla oblongata. Prolonged use may lead to addiction.

Terpin hydrate

Terpin hydrate is prepared by the action of nitric acid on oil of turpentine in the presence of alcohol, the resulting crystals being filtered off and crystallized

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from alcohol. The yield of crystallizable material is largely dependent upon the temperature at which the reaction is allowed to proceed. If the temperature be too high, polymerization of the turpentine takes place; if too low, the yield is insufficient.

Though it was quite popular in the USA since the late nineteenth century, it was banned by the U.S. Food and Drug Administration (FDA) in the 1990s due to lack of proof of efficacy

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.

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