



LEC 3

PHARMACEUTICAL TECHNOLOGY

SOLUTION USING MIXED SOLVENT SYSTEM (ELIXIRS AND SPIRITS)

Stage: 3/ 1st course

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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
- **Medicated** elixirs for the therapeutic effect of the medicinal substances they contain.

When we have to use the mixed solvent systems?

- When substances to be included in liquid dosage forms for oral administration are not water soluble or
- When they exhibit chemical instability in water

One must either prepare **suspensions** or utilize non aqueous solvents alone or with a minimum (**spirit**) or higher (**elixir**) amount of water.

What are the differences between elixirs and syrups?

Compared with syrups, elixirs are usually

- **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. Hence, usually need **flavouring agents**.
- However, because of their **hydroalcoholic** character, elixirs are better able than aqueous syrups to maintain both water-soluble and alcohol-soluble components in solution. Elixirs contain water and alcohol solvents whereas a syrup may or may not use an alcohol for solubility purposes the primary solvent contains only water.
- Also because of their **stable characteristics** (self preserve from alcohol content, more than 10%) and ease with which they are prepared (by **simple solution**), elixirs are preferred over syrups.

Principles

- In the official elixirs, the alcohol content may be reach 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 **glycerine** and **propylene glycol** are frequently employed in elixirs as **adjunct solvents**.
- 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.

- Although many elixirs are sweetened with sucrose or with a sucrose syrup, some utilise sorbitol, **glycerine** 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**.
- All elixirs contain **flavouring** materials to increase their palatability and most have **colouring** agent to enhance their appearance.

- A **disadvantage** of elixirs for children and for adult who choose to avoid alcohol. It contain high percent of alcohol.
- Also it less effective than syrup for masking the test.
- 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.
- **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 may not be clear, but **cloudy**, due principally to the **separation of some of the flavouring oils** by the reduced alcoholic concentration.

- If this occurs (cloudy appearance), 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 glycerine, 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**.

What is the role of each constituent?

Phenobarbital elixir

Phenobarbital	4gm
Orange oil	0.25ml
Propylene glycol	100ml
Alcohol	200 ml
Sorbitol solution	600 ml
Colouring agent	Q.S.
Purified water	q.s.....	1000ml

Theophylline Elixir

Theophylline	5.3 g
Citric acid	10g
Liquid glucose	44g
Syrup	132mL
Glycerin	50mL
Sorbitol solution	324mL
Alcohol	200mL
Saccharin sodium	5g
Lemon oil	0.5g
FD&C Yellow No. 5	0.1g
Purified water, to make	1,000mL

Classification of elixirs

1. Non medicated elixirs

Which is used as vehicles in preparing medicated elixir either by

- The addition of a therapeutic agent to a pleasant tasting vehicle
- The dilution of an existing medicated elixir

The three most commonly used non medicated elixirs were:

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

Aromatic elixir USP

It consists of **compound orange spirit**, **syrup**, **alcohol**, **water**, and **talc**. There is about 10-20% loss in volume due to repeated **filtration**, also the presence of syrup and talc make slow filtration. So, **Dissolve the sugar in the filtrate to increase the rate of filtration, and 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.**



Iso-Alcoholic Elixir, NF

- It is composed of two separate parts, low alcoholic elixir with an alcohol content of 8 to 10 percent, and high alcoholic elixir with an alcohol content of 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.

Compound benzaldehyde elixir, NF

Is prepared by simple solution and is used when a bitter almond-like flavour is desired.

Medicated Elixirs

Medicated elixirs which have therapeutic action, e.g. Phenobarbital elixir.

Medicated elixirs can be described by further classifying them according to their therapeutic activity.

1. Antihistamine elixirs (e.g. diphenhydramine HCL elixir)
2. Sedatives and Hypnotics elixirs (e.g. phenobarbital elixir)
3. Expectorants and cough preparation (e.g. Terpin Hydrate Elixir, NF).
4. Miscellaneous medicated elixirs

PHENOBARBITAL ELIXIR U.S.P

Rx

Phenobarbital	4 g
Tr. of orange peel	30 ml
Solution of amaranth	10 ml
Alcohol	125 ml
Glycerin	450 ml
Syrup	250 ml
D.W	Q.S
	1000 ml

Method:

1. Dissolve the phenobarbital in alcohol
2. Add the tincture of orange peel, glycerin, syrup, amaranth solution and add sufficient water to produce 1000 ml, mix well and filter.

Directions:

- The phenobarbital elixir used as sedative and hypnotic.
- Glycerin used as thickening agent, also increase the solubility of phenobarb.
- Tr. Of orange peel used as flavouring agent.
- Solution of amaranth used as colouring agent.
- Syrup used as sweetening agent.



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 between the dielectric constant of the mixture with the amount of drug solubilised.

PEDIATRIC PARACETAMOL ELIXIR B.P

Rx

Paracetamol		120 mg
Alcohol		0.5 ml
Chloroform spirit		0.1 ml
Propylene glycol		0.5 ml
Conc. rose berry juice		0.125 ml
Amaranth solution		0.01 ml
Invert syrup		1.375
Glycerol	Q.S	5ml

Method:

1. Dissolve paracetamol in alcohol.
2. Add chloroform spirit, propylene glycol, juice, amaranth solution, invert syrup.
3. Complete the volume by addition of glycerol.

Expectorants and cough preparations

- 1. **Terpin Hydrate Elixir, NF.** (Terpin hydrate is an expectorant commonly used to **loosen mucus** in patients presenting with acute or chronic bronchitis, and related conditions. Terpin is derived from oil of turpentine, oregano, thyme and eucalyptus).
- 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.

Expectorants and cough preparations

- 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 Dexamethorphan HBr elixir is non-narcotic elixir.

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.

Spirits

- Spirits are alcoholic or hydroalcoholic solutions 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 %). The highest is in Camphor Spirit (80 to 87 %).

Problem of separation

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.



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

Simple Solution

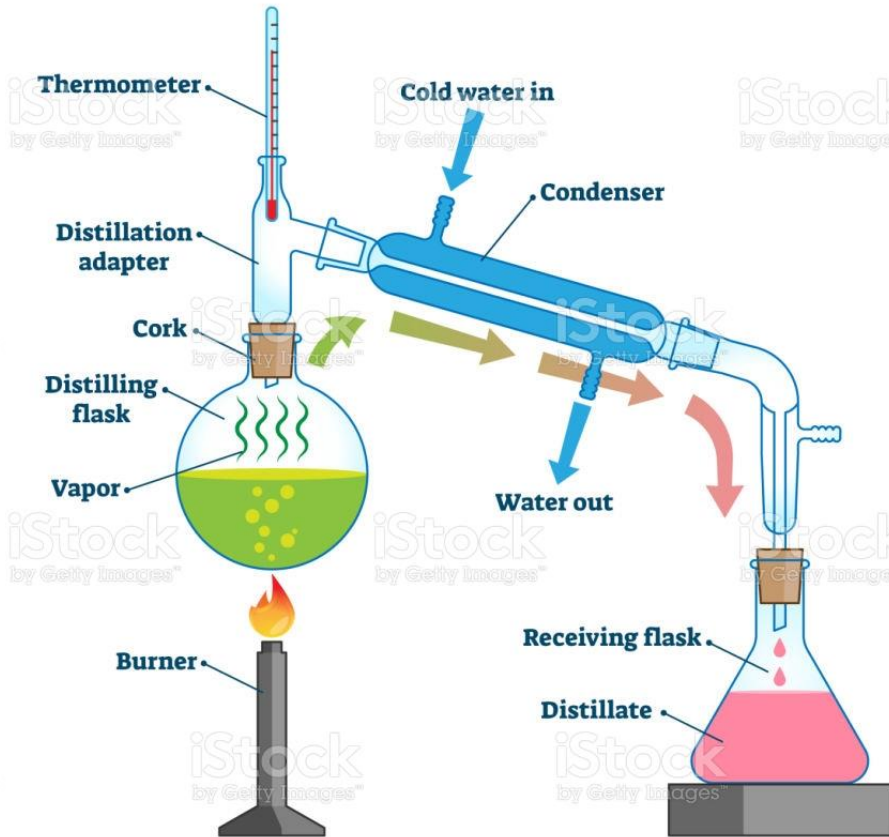
- Majority of spirits are prepared by dissolving the solute in alcohol by agitation. Filtration is generally desirable to obtain a sparkling clear product.
- Example: Aromatic Spirit - 62 to 68% hydroalcoholic solution of ammonia and ammonium carbonate flavored and perfumed with lemon, lavender and myristica oil.

Solution with Maceration

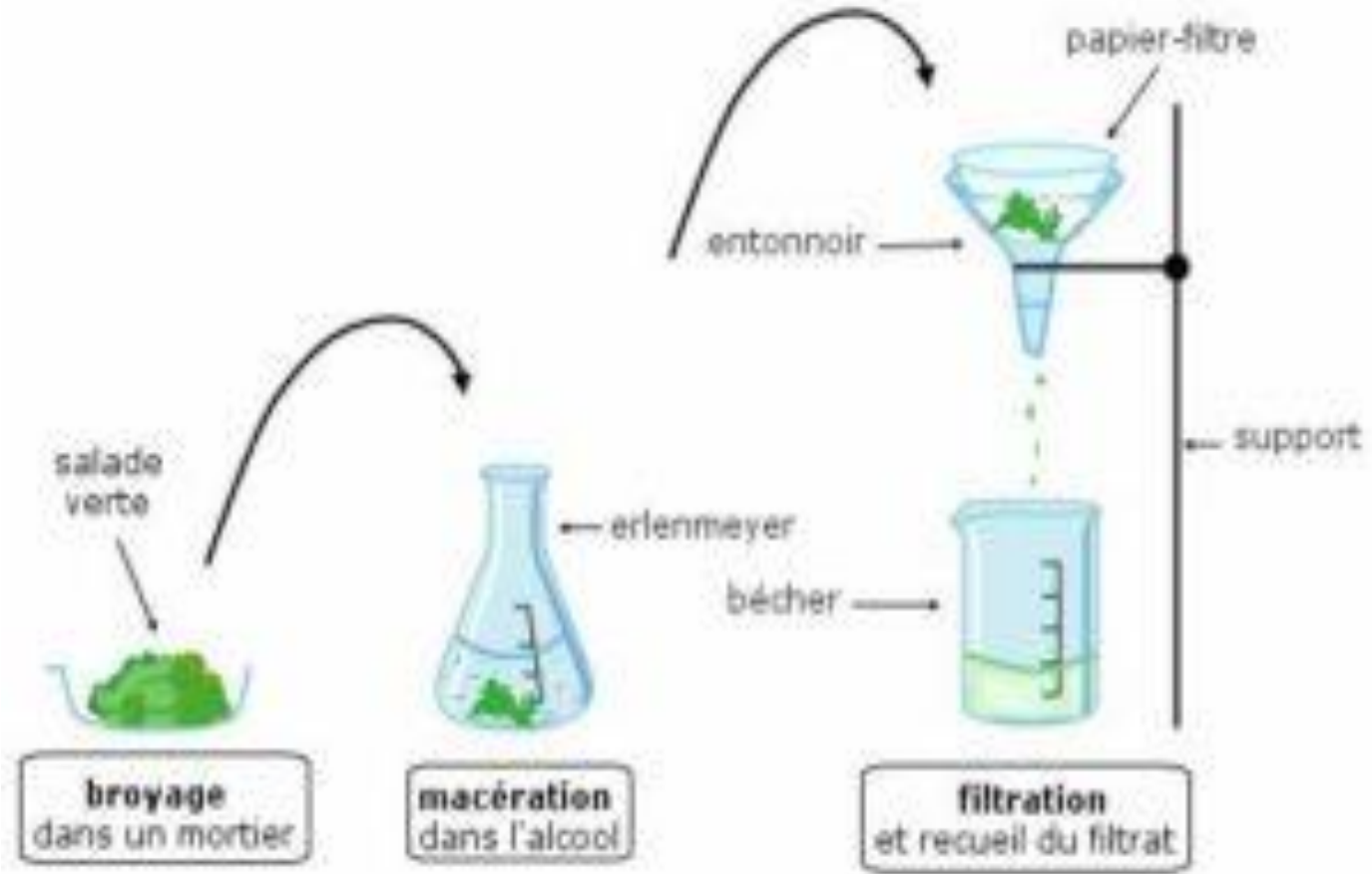
- Macerate the vegetable materials in a suitable solvent to remove the undesired constituents or to extract one which is desired.
- Example: Peppermint Spirit (Spiritus Menthae Piperitae) – 79 to 85% hydroalcoholic solution containing 10% peppermint oil
 - ❑ Oil of peppermint 100 ml
peppermint, bruised, 10 Gm
alcohol, a sufficient quantity to make 1000 ml
 - ❑ First **macerate the peppermint leaves in water** to get rid of tannins and xanthophylls then strongly expressed then macerated them for 6 hours to dissolve the oil of peppermint in nine hundred ml of alcohol, add the peppermint. Then filter through paper, and add, through the filter, enough alcohol to make the spirit measure 1000 ml -(U. S. P.). The purpose of adding peppermint is to give the preparation a green color.

Use: digestive aid or carminative

DISTILLATION



Maceration



Uses of Spirits

Spirits may be used pharmaceutically as **flavoring agent** and medicinally for the **therapeutic value of aromatic solute**.

- As flavoring agents they are used to impart the flavor of their solute to other pharmaceutical preparations.
- For medicinal purposes, spirits may be taken **orally** (peppermint spirit), applied **externally** (camphor spirit), or used by **inhalation** (aromatic spirit of ammonia), depending upon the particular preparation.
- 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
4. Peppermint spirit

There is no classification of spirits because:

1. There are 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 an **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**.

Store in a closed container at room temperature, away from heat, moisture, and direct light.



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.

It contains

Camphor 10% **Active Ingredient**

Alcohol 84% (Range 80-87%) and Purified Water. (Inactive Ingredients)

Uses: For temporary relief of minor aches and pains of muscles and joints associated with simple backache, arthritis, strains, bruises and sprains.



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.

It contains oil of orange peel, (200 Cc.) oil of lemon, (50 Cc.) oil of coriander, (20 Cc.) oil of anise, (5 Cc.) deodorized alcohol, a sufficient quantity to make one thousand (1000 Cc.). Mix them. Keep the product in completely filled, well-stoppered bottles, in a cool and dark place.

Uses: This is a pleasant **carminative** and **flavoring agent**, used chiefly, for the latter purpose,

Peppermint Spirit, NF

It is used as a **carminative** and **flavor**.

The Tincture of oil of peppermint, more commonly known as *essence of peppermint*

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.





THANK YOU