

## Experiment 2

### Liquid dosage forms: solutions Aqueous solutions and syrups

Solutions are one of the Pharmaceutical dosage forms which are prepared by dissolving the active ingredient(s) in an aqueous or non-aqueous solvent.

Solution:

Is a homogenous mixture of two or more components. They contain one or more solutes dissolved in one or more solvents. They may be used for a variety of purposes both as internal and external dosage forms.

injection, orally  
لما عن طريق الفم او  
عن طريق الابر

#### Isotonic solutions:

Solutions that have same osmotic pressure as body fluids.

#### Hypertonic solutions:

Solutions that have higher osmotic pressure than body fluids.

#### Hypotonic Solutions:

Solutions that have lower osmotic pressure than body fluids.

Solutions can be formulated for different routes of administration

1. **Orally:** Syrups, elixirs, drops
2. **In mouth and throat:** Mouth washes, gargles, throat sprays.
3. **In body cavities:** Douches, enemas, ear drops, nasal sprays.
4. **On body Surfaces:** Collodions.

Advantages of Solutions

- ✓ (1) Easier to swallow therefore easier for: children - old.
- ✓ (2) Faster effect compared to tablets and capsules.
- ✓ (3) Homogenous, therefore, give uniform dose compared to suspension or emulsion which need shaking.
- ✓ (4) Dilute irritant action of some drugs (aspirin, KI, KBr) thus minimize adverse effects in the GIT.

Disadvantages of Solutions

- (1) Bulky therefore difficult to transport and store.
- (2) Unpleasant taste or odors are difficult to mask.
- (3) Needs an accurate spoon to measure the dose.
- (4) Less stable than solid dosage forms.

Additives = Excipients = Inactive ingredient → هم المواد التي يضيفهم مثلاً أحسن من التركيبة لكن ما العلم أي مفعول طبي

- 1- Buffers → PH ← maintain
- 2- Isotonicity modifiers → Isotonicity → ophthalmic
- 3- Viscosity enhancement (NaCl and Dextrose) → بتعدل اللزوجة → orally → satisfied, injection →
- 4- Preservatives ← مواد حافظة
- 5- Antioxidants ← مضادات التأكسد
- 6- Sweetening agents ← محليات
- 7- Flavours and perfumes ← external

### Stability of solutions

- Both physical and chemical stability of solutions in their containers is very important
- A solution must retain its clarity, color, odor, taste and viscosity over its shelf life.

### Classification of Solutions According to Vehicle (solvent)

#### 1. Aqueous solutions:

- Syrups
- Aromatic waters

} Beyond use date = 14 days in cold temperature

#### 2. Hydro-alcoholic solutions: \* Beyond use date

- Elixirs \*
- Spirits \*
- Tinctures
- Fluid Extracts
- Collodions
- Liniments

#### 3. Non-aqueous solutions

oil → hormones Explan

#### Aqueous Solutions

- Drugs are dissolved in water along with any necessary flavorings, preservatives, or buffering salts.
- Distilled or purified water should always be used when preparing pharmaceutical solutions.

Advantages of water as a vehicle: Tasteless, odorless, lack of pharmacological activity, neutral and very cheap. → طعم او رائحة ما يتفاعل مع الدواء, رخيص, متعاد من ناحية ال PH

Purified water is used in preparing pharmaceutical dosage forms. It is prepared by distillation, ion exchange methods or reverse osmosis. It must not be used for the preparations of parenteral formulations. + ophthalmic

sterile ←

Preparation

## ↓ Aqueous Pharmaceutical Solutions:

### I. Nasal Solutions

- Nasal solutions are usually aqueous solutions designed to be administered to the nasal passages, they are used either to exert local effect (in congestion or infection), or for rapid systemic effect by avoiding 1<sup>st</sup> pass effect → drug metabolism يُجَدُّ مِنَ الرِّئَةِ
- E.g. Ephedrine Sulfate or Naphazoline Hydrochloride Nasal Solution USP is administered for their local effect to reduce nasal congestion.
- Generally solutions are administered as drops. Solutions can also be administered as a fine mist from a nasal spray bottle. Nasal sprays are preferred to drops because drops are more likely to drain into the back of the mouth and throat and be swallowed. يَعْرِضُ عَلَى الْفَرْسِجِ

#### Nasal drops:

Solution of medicaments designed to be applied to nasal mucosa in a small volume, usually formulated to be iso-osmotic with nasal secretions or buffered to (6.5) to minimize damage of nasal cilia. السَّجْرَات

Properties of well formulated Nasal drops:

- The only vehicle used is aqueous vehicle, because oily vehicle affect ciliary's movement.
- With acceptable viscosity, why? to have longer effect
- Isotonic and buffered → so as not to irritate the nasal mucosa

### II. Eye Solutions: ophthalmic

Eye drops:

Are sterile solutions or suspensions of one or more medicament intended for instillation into the conjunctival sac. They may be packed in single dosage forms or in multiple application containers. الرَّغَائِمُ إِلَى بَيْنِ الْبُحْفَيْنِ حَا

### III. Otic Solutions (Ear solutions):

- Otic formulations are used to treat common ear problems i.e. Exert a local effect, soften the wax, treat local infection and/or to relieve pain, they are not necessary to be sterile.
- Otic formulations include solutions
- Otic Solutions are commonly used to remove ear wax and discharge from infection.
- Otic formulations may contain antibacterial, antifungal, or corticosteroids agents

Ear drops:

They are solutions, suspensions or emulsions of drugs that are installed into the ear to exert a local effect, e.g. by softening earwax, treating infection or inflammation and/or relieving pain.

Ear drops vehicles:

- ✓ - **Aqueous:** e.g. purified water.
- ✓ - **Non-aqueous:** e.g. mineral oil (liquid paraffin) and vegetable oil.

- **Non-aqueous but miscible with water:** e.g. Glycols (propylene glycol or Glycerol).

The viscous glycerin vehicle permits the drug to remain in the ear for a long time. Anhydrous glycerin, being hygroscopic; tends to remove moisture from surrounding tissues, thus reduce swelling. → الانتفاخ

يتمكن الرطوبة

Viscous liquids like glycerin or propylene glycol either are used alone or in combination with a surfactant to aid in the removal of cerumen (ear wax).

In addition, non-aqueous vehicles used in preparation are used to remove wax, as they are lipophilic so solubilize wax.

In order to provide sufficient time for aqueous preparations to act, it is necessary for the patient to remain on his side for a few minutes so the drops do not run out of the ear.

#### IV. Aromatic water:

*Aromatic Waters:*

*Are clear, saturated solutions of aromatic substances (may be volatile oils or volatile solids) in water. Their flavors and taste are similar to the corresponding aromatic substances used.*

Use of aromatic water:

- They are mainly used as the vehicle for oral liquid preparations due to their flavoring properties.  
E.g. Peppermint Water.
- Some aromatic waters have preservative action, hence are used as menstruum to extract crude drugs. E.g. Chloroform Water IP.
- Some aromatic waters have mild therapeutic action. E.g. Camphor Water IP has carminative action and Anise Water has carminative and mild expectorant action.

reduce the thickness of mucus.

تفخة البطن  
يسبب الغازات  
relives  
flatulence

Aromatic water will deteriorate with time **therefore:**

- Should be made in small quantities
- Protected from intense light and excessive heat by storing in air tight, light resistant containers.

If they become cloudy or otherwise deteriorate; they should be discarded. Deterioration may be due to volatilization, decomposition or mould growth.

#### Peppermint Water USP.

- Peppermint oil is extracted from Mentha piperita (Family- Labiatae).
- The main chemical components of peppermint oil are menthol, menthone, 1,8-cineole, methyl acetate, methofuran, isomenthone, limonene,  $\beta$ -pinene and  $\alpha$ -pinene.
- Peppermint oil is non-toxic and non-irritant in low dilutions, but sensitization may be a problem due to the menthol content. It can cause irritation to the skin and mucus membranes and should be kept well away from the eyes. Peppermint oil should be stored in closed containers and kept in a dry place, avoiding sunshine and rain.
- It should be avoided during pregnancy and should not be used on children under seven.

The volatile oil is thoroughly incorporated with powdered talc and to this mixture purified water is added. The resulting slurry is thoroughly agitated several times for the period of 30 minutes and then filtered. Powdered talc work both as filter aid which renders the formulation more clear and as distributing agents for the aromatic substances that ultimately increases the surface area of aromatic substances exposed to the solvent action of water. The distributing agent should be inert in nature.

استخدام  
Talc

ما يتفاعل مع مكونات اخرى

يمكن جعلها سائلة وتعتبر للحل أو الأنسجة المخاطية فلازم فصل بعيد عن العين

يمكن جعلها سائلة

تفاعل

**Formula (1):**

**Rx 100 ml Peppermint Water USP**

Ingredients	Master formula	Scaled formula
Peppermint oil	2 ml	4-drops (0.2 ml)
Talc	15 g	1.5g
Water	q.s. 1000 ml	q.s. 100 ml

$$F = \frac{100}{1000} = 0.1$$

$$1 \text{ ml} \rightarrow 20 \text{ drop}$$
$$0.2 \rightarrow ?$$

**Procedure**

1. Put the specified quantity of talc in a mortar
2. **Triturate** the oil of peppermint with the specified quantity of talc
3. Add about 2/3 of the required volume of distilled water gradually, under constant trituration
4. And then filter and bring up to the desired volume in a graduated cylinder.

Note: 1 ml equal 20 drops

Q: What does triturate mean? *mixing the ingredients using mortar & Pestle = Grinding the ingredient to small particles (s.s.)*

Use of ingredients:

- (1) **Peppermint oil:** carminative, flavoring agent.
- (2) **Talc** to clarify solution.
- (3) **Water:** vehicle or solvent

Labeling:

- Main label:-
- Auxiliary label:  
*Keep out of reach of children*

*BBK*

Storage:

*'Store in a cool place', 'Preserve in amber glass well-closed containers'.*

Use of preparation:

Carminative and flavoring agent.

## Formula (2)

Rx 10ml Na-bicarbonate ear drops B.P.C.

$$F = \frac{10}{100} = 0.1$$

Ingredients	Master formula	Scaled formula
NaHCO <sub>3</sub>	5gm	0.5 gm
Glycerol	30ml	3 ml
Water	q.s. 100ml	q.s. 10 ml

### Procedure

1. Weigh sodium bicarbonate (NaHCO<sub>3</sub>)
2. Dissolve NaHCO<sub>3</sub> in 1/3 amount of water in beaker or Erlenmeyer flask
3. Add glycerol and shake
4. Add water to produce 10 ml

### Use of Ingredients

- (1) **NaHCO<sub>3</sub>**: antipruritic
- (2) **Glycerin**: co-solvent, soften earwax, does not support microbial growth. It is hygroscopic so it absorbs water in case of inflammation. It is viscous so it increases contact time, and thus improves the effect.
- (3) **Water**: vehicle or solvent

### Labeling

- Main Label
- Auxiliary Label:  
*Not to be taken orally. Shake well before use.*

### Storage

*'Store in a cool, dry cool place'.*

### Use of Preparation:

Antipruritic (for swimmers).

# Syrup

Is a concentrated or nearly saturated solution of sucrose in water.

- Sweet with pleasant texture

(1) **A simple syrup** contains only sucrose and purified water (e.g. Syrup USP).

(2) **A flavoring syrup** contains a pleasantly flavored substances (e.g. Cherry Syrup, Acacia Syrup, etc.).

(3) **Medicinal syrups** are those to which therapeutic compounds have been added (e.g. Guaifenesin Syrup). Syrups possess remarkable masking properties for bitter and saline drugs. *بعمل تغطية على الطعم المر والمالح*

Cough syrups

## Simple Syrups:

A simple syrup contains only sucrose and purified water (e.g. Syrup USP). *Saturated sugar solution without flavor or medicine.*

### Concentration of Syrup:

According to B.P:

67.7% W/W

According to USP:

85% W/V



- Syrup, USP contains 850 gm sucrose and 450 ml of water in each liter of syrup (85% w/v). Although very concentrated, the solution is not saturated, why?

Since 1 gm sucrose dissolves in 0.5 ml water, only 425 ml of water would be required to dissolve 850 gm sucrose. This slight excess of water enhances the syrup's stability over a range of temperatures, permitting cold storage without crystallization.

- Syrup USP has a specific gravity of 1.313 and a concentration of 85% w/v,  $\rightarrow 1.313 \text{ gm} \rightarrow 1 \text{ ml}$   
what is the concentration in w/w solution?  $85 \text{ gm} \rightarrow ??$

(Answer 65% w/w solution, syrup BP)

- Syrup USP is resistant to microbial growth. If the concentration of sucrose in the syrup is low, preservatives such as glycerin, methyl paraben, benzoic acid and sodium benzoate **may be** added to prevent bacterial and mold growth

Storage Condition

- The USP suggests that syrups be kept at a temperature not above 25°C. In addition, syrups should be preserved in well dried bottles and stored in a cool dark place.

Unsaturated  $\rightarrow$  يحاول التراكيبه فيك  
عشان لو تخفضت بدرجة حرارة منخفضة ما ييسر عندي  
crystalization

saturated  $\leftarrow$  لو كان ال syrup  
supersaturated او  
على اقل تغير بدرجة الحرارة ييسر  
crystalization

Disadvantages of simple syrup :

- 1- Accelerate dental decay. تسوس الأسنان
- 2- Not suitable for diabetic patients, we can use sorbitol instead of sucrose

Example of pharmaceutical syrups :1-

Liquorice syrup: **expectorant**.

2- **Ginger syrup**: carminative and laxative. مادة مسهلة

3- **Ipecac syrup**: emetic agent. يساعد على الاستفراغ

Three methods may be used to prepare syrups:

- (1) Solution with heat
- (2) Agitation without heat
- (3) Percolation

Syrup may contain:

**a- Polyols** (e.g. glycerin) may be added to

- retard crystallization of sucrose or

- Increase the solubility of added ingredients.

- Aid in preservation

**b- Alcohol** often is included as

- Preservative

- Increase the solubility of added ingredients.

2(OH)  
alcohol

في حالات  
التسمم

**Formula (3):**

**Rx 50 ml simple syrup USP**

Ingredients	Master formula	Scaled formula
Sucrose	850 g	42.5
Purified Water	q.s. 1000 ml (450 ml)	q.s. 50 ml 22.5 (---ml)

$$F = \frac{50}{1000} = 0.05$$

**Procedure**

1. Heat water on hot plate then add sucrose gradually with stirring until you get a clear solution
2. Filter if needed when it is hot using cotton.

\*Note: During syrup preparation do not heat above 60 C°

**♣ Notes :**

- Filtration of hot syrup and not cold syrup is done to avoid crystallization of sucrose on cotton.
- Do not heat above 60° C to avoid hydrolysis of sucrose (to fructose and glucose) that will change both the color and the taste of the syrup.

NOTE : Simple syrup will not have a strength unless it contain an active ingredient

**Use of ingredients:**

- (1) **Sucrose:** sweetening agent
- (2) **Water:** vehicle or solvent

**Labeling**

- Main label:
- Auxiliary label:  
*Not to be used for Diabetic patients.*  
*May cause dental decay.*

**Storage:**

*'Store in a cool, dry place'.*  
*Avoid temperature fluctuation (why).*  
*In a well closed amber glass container.*

**Use of preparation:**

Sweetening vehicle, preservative.

**Packaging:**

Preserve in air tight, light resistant containers, and prevent exposure to excessive heat.

Formula (4):

**Medicated syrup or Medicinal syrups:** are those syrups to which therapeutic compounds have been added (e.g. Guaifenesin Syrup, Ferrous Sulfate Syrup).

Rx 50 ml Ferrous Sulfate Syrup

Ingredients	Master formula	Scaled formula
Ferrous sulfate	40.0 g	2 g
Citric Acid	2.1 g	0.105 g
Peppermint spirit	2 ml	0.1 - drops (-2 ml)
Sucrose	825 g	41.25 g
Purified water	q.s. 1000 ml	50 ml

$$F = \frac{50}{1000} = 0.05$$

### Procedure

1. Dissolve the ferrous sulfate, citric acid, peppermint spirit, and 1/4 of the sucrose in 1/2 of the purified water
2. filter the solution
3. Dissolve the remainder of the sucrose in the clear filtrate and complete the volume with purified water to make -- ml
4. Mix and filter if necessary through cotton

### Use of ingredients:

- (1) **Ferrous sulfate:** active ingredient (iron source)
- (2) **Citric Acid:** added to enhance iron absorption in GI (Explain Why?)
- (3) **Peppermint spirit:** preservative and flavoring agent that have a carminative effect too.
- (4) **Sucrose:** sweetening agent and work as preservative.
- (5) **Water:** vehicle or solvent

### Labeling

- Main label:
- Auxiliary label:  
*Not to be used for Diabetic patients.*  
*May cause dental decay.*

### Storage:

*'Store in a cool, dry place'.*  
*Avoid temperature fluctuation (why).*  
*In a well closed amber glass container.*

### Use of preparation:

Iron supplement

**Packaging:** preserve in air tight, light resistant containers, and prevent exposure to excessive heat