# Experiment 1

# Introduction:

## Pharmaceutics principles and pharmaceutical calculations

Dispensing laboratory is one of the most useful labs for pharmacy student, where they learn how to prepare specific medicine in a desired form, to achieve therapeutic effect and patient satisfaction. This lab session will cover aspects you have to know before starting compounding formulation.

*Definitions:*

***Pharmacists*** *are experts on the action and uses of drugs, including their chemistry, the formulation of medicines and the way in which drugs are used to manage diseases.*

***Extemporaneous preparation*** *is defined as a drug that is compounded in a pharmacy according to a prescription and should only be used when manufactured medicines are not available.*

***Dosage forms*** *are the means by which drug molecules are delivered to sites of action within the body.*

There are three main types of dosage forms:

1. **Solid dosage forms**: e.g. tablets, granules, suppositories and lozenges
2. **Liquid dosage forms**: e.g. drops, gargles, mouthwashes and suspension
3. **Semisolid dosage forms**: e.g. emulsions, creams, gels, ointments and pastes

**An Ingredient:** is a chemical or material that is added to a formulation during the formulation process.

A. **Active Ingredients:** are those chemicals or materials that have therapeutic benefits

B. **Inactive ingredients (also called excipients, added substances)** are necessary for preparing dosage forms or for enhancing the stability of finished preparations. They do not give a therapeutic response (or, at least, are not intended to) if given alone in the concentration present in the dosage form.

Packaging

The pharmacist must dispense a compounded formulation in an appropriate package:

- The container should not react with the formulation
- The container should protect the formulation against factors that couldcause deterioration or destruction of dosage form such as humidity, light, airborne contamination, microorganism, ingredient loss and physical damage

Storage Temperature Requirements:

| Descriptors of storage condition | Temperature |
|---|---|
| • Freezer | -25C° to – 10C° |
| • Cold | Not exceeding 8 C° |
| • Refrigerator | 2 C° to 8 C° |
| • Cool | 8 C° to 15 C° |
| • Room | Prevailing temperature |
| • Controlled room temperature | Thermostatically maintained 20 C° to 25 C° |
| • Warm | 30 C° to 40 C° |
| • Excessive heat | Above 40 C° |

**Stability** is defined as" the extent to which a dosage form retains, within specified limits,and throughout its period and use (i.e. its shelf life), the same properties and characteristics that it possessed at the time of its manufacture".

**Expiration dates** are required on commercially manufactured pharmaceutical dosage forms and are determined by extensive study of the product's stability. These studies are conducted with the entire pharmaceutical products-i.e., the active drug in its complete formulation, in its specific container, and under the environmental conditions expected in shipment, storage, and handling. Expiration date is usually in the order of years.

**Beyond-use dates** are used for compounded preparations only and are generally in the order of "days" or "months."

**Assigning a Beyond-Use Date:**

— **Nonaqueous liquids and solid formulations**

— If the source of the active drug is a manufactured drug product, the beyond-use date is not later than 25% of the time remaining until the drug product's expiration date, or 6 months, whichever is earlier.

— If the source of the active drug is a USP or NF substance, the beyond-use date is not later than 6 months.

— **Water containing formulations**

— When prepared from ingredients in solid form, the beyond-use date should be not later than 14 days when stored at cold temperature.

— **For all other formulations**

— The beyond-use date is not later than the intended duration of therapy or 30 days, whichever is earlier.

تاريخ BUD لا يزيد عن: مدة العلاج أو 30 يوم وأيهما أقل.

**Freshly prepared** is defined in the BP as prepared no more than 24 hrs beforeuse but there is no indication when it should be discarded

**Recently prepared** is defined in BP as discarded after 4 weeks

Observing Signs of instability:

| Formulation | Potential sign of instability |
|---|---|
| Solutions | Crystal formation |
| Emulsions | Phase separation |
| Suspensions | Increased Sedimentation |
| Tablets | Cracking |

**Equipment and supplies for measuring, mixing, molding, and packaging:**

- Spatulas
- The Mortar and pestle
- Ointment slabs (pill tiles)
- A stirring hotplate



Labeling of dispensed medicines

It is the pharmacist responsibility to provide the patient with all information necessary so that the medicine is used appropriately.

Labeling of dispensed medicines has two main functions:

1. To identify the patient with the contents of the container
2. To ensure that the patients have clear and concise information, which will enable them to use their medicine in the most effective way

Any label should contain the following: **(do not use any abbreviations- use full text)**

***A. Main label:***

(1) *Name of Patient* .... (Full name)
(2) *Name of preparation.*
(3) *Form.*
(4) *Strength.*
(5) *Manufacturing date.*
(6) *Use(s): for the whole product " why we use it "*
(7) *Storage conditions*

*B. Auxiliary label:*

**(1) *Direction of use:***
e.g., for external use, for rectal use, …etc

(2) *Warning:*
e.g. keep out of reach of children. Shake well before use" for suspensions and emulsions. "For external use only" for external liquid and semisolid preparations. "May cause drowsiness" for drugs that cause sedation as a side effect

(3) *Interaction with food, drinks or other medicines.*

*Example of Auxiliary labels*

| | |
|---|---|
| *-Swallow whole with a drought of water*<br>*-For external use only*<br>*-Shake the bottle*<br>*-For rectal use only* | *-Not to be swallowed*<br>*-Avoid application to broken skin*<br>*-For external use only*<br>*-For nasal use only* |

| **Hashemite University** | |
|---|---|
| **Pharmaceutics Lab** | **School of Pharmacy** |
| **Patient's Name's:** *_XY* | |
| **$R_x$** *Ketoprofen gel 10%w/w, 10 ml* | |
| **Direction:** *Apply twice daily to affected knee* | |
| **Refill:** *0* | |
| **Storage requirements:** *store at room temperature* | |
| **Dispensed by:**____*ND* | |
| **Manufacturing date:** *1/1/2020* | **Do Not Use Beyond:** *1/2/2020* |
| *For external use only & Avoid application to broken skin* | |

Calculations for compounding

Most of the calculations required for compounding and dispensing involve relatively simple arithmetic. The welfare of patients depends on the accuracy of pharmaceutical calculations and so *careless calculations cost lives*.

Working from a master formula

The master formula is obtained from reference sources such as British Pharmacopeias (BP), British National Formulary (BNF) and United States Pharmacopeias (USP). The master formula lists the ingredients for the total quantities greater than or less than the amount required to be prepared. The formula must therefore be scaled down or scaled up as appropriate.

- Pharmacopeias: Books contain information about drugs, their properties (physical / chemical), assay of drugs, and how to prepare a preparation. They are published by the authority of government, or medical or pharmaceutical society. We will use both USP (United States Pharmacopeia) and BP (BritishPharmacopeia).
- NF (National Formulary): is a manual containing a list of medicines that are approved for prescription throughout the country, includes information of the composition, description, selection, prescribing, dispensing and administration of medicines.

## Dealing with strength expressions:

**1. Percentage Strength:**

- % w/w or percentage weight in weight: this expresses the amount in grams of solute in 100 g of product
- %w/v or percentage weight in volume: this expresses the amount in grams of solute in 100 ml of product
- %v/v or percentage volume in volume: this expresses the number of milliliters of solute in 100 mL of product
- %v/w or percentage volume in weight: this expresses the number of milliliters of solute in 100g of product

2. Other strength expression: strength may be written for the amount of active ingredient(s) in unit dose (e.g. capsules or tablets), so here we write the amount per unit dose; e.g. 10 mg Phenobarbital per capsule.
3. Millimoles: To calculate the number of millimoles of an ingredient in a medicinal product, you will first need to know the molecular weight of an ingredient (listed in pharmacopeias, Martindale…etc). The number of moles of ingredient is the mass of ingredient divided by the molecular mass:

Number of moles= Mass in grams/Molecular mass

Example I

Example: How much sodium Chloride BP is required to prepare 100 ml of sodium Chloride BP solution containing 1.5 mmol sodium chloride per ml? Mwt= 58.4

1.5mmol ⟶ 1ml

?? ⟶ 100ml

150mmol of Sodium chloride

$150 \times 10^{-3}$ = mass / Mwt × mole

$150 \times 10^{-3} \times 58.4$ = mass

mass = 8.76g

100ml of the final solution of 1.5mmol per ml will contain 150 mmol (0.15mol).

Number of moles (moles)= weight (g)/molecular weight(g/mol)

0.15 =weight/58.44

Weight=0.15*58.44=8.766g of Sodium Chloride BP

Example 2

Calculate the amounts of the ingredients for 200 ml Turpentine liniment BP1988.

| Ingredients | Master formula BP | Scaled quantities |
|---|---|---|
| Soft soap | 75 g | 15 g |
| Camphor | 50 g | 10 g |
| Turpentine oil | 650 ml | 130 ml |
| Water | Up to 1000 ml | Up to 200 ml |

In this example the volume of water can't be calculated because a combination of weights and volumes are present in this formula.

Example 3

Calculate the amounts of the ingredients for 60 g of Zinc oxide and calamine paste BP 1988

| Ingredients | Master formula BP | Scaled quantities |
|---|---|---|
| Zinc oxide | 3.75 g | 7.5 g |
| Calamine | 15%w/w | 9 g |
| Wool fat | 7.5 g | 15 g |
| White soft paraffin | Up to 30 g | Up to 60 g |

Dilutions:

| Meaning | Type |
|---|---|
| Final volume = 10 | 1 in 10 |
| Solvent = 10 | 1:10 |

There are two main methods for expressing dilutions. It is important that the two are not mixed up as there is a key difference between them:

a) 1 in x – 1 part of solute in x parts of final solution. For example 1 in 10 means that there is one part of concentrate in 10 parts of final solution

b) 1: x (or 1 to x)- 1 part of solute to x parts of solvent. For example 1:10 means that there is one part of concentrate to 10 parts of solvent (or 1 in 11) (e.g. 1 ml of concentrate and 10 ml vehicle with a final volume of 11 ml)

Example I:

Prepare 500 ml of a 0.1% w/v solution using a 20% w/v concentrated stock solution?

First, you need to calculate the total amount of active ingredient required in the final solution:

0.1% w/v solution= 0.1g in 100 ml

Therefore, there is 0.5g in 500 ml. Next, you need to calculate the quantity of the concentrated solution that contains the same amount of active ingredient:

20% w/v solution = 20g in 100 ml

So there are 2 g in 10 ml, 1g in 5ml and 0.5g in 2.5 ml. Therefore 2.5 ml of 20% w/v solution would be required to make 500ml of a 0.1% w/v solution.

Example 2

How much solute is required to produce 5 liters of a 0.9% w/v solution?

0.9%= 0.9g in 100 ml

Therefore there are 9 g in 1000 ml and you would need 45g in 5000 ml

Example 3

What quantity of a 40% w/v solution would be required to produce 1 liter of a 1 in 1000 solution?

1 in 1000= 1 g in 1000ml

What volume of a 40% w/v solution contains 1g?

40% w/v = 40g in 100 ml.

There are 4g in 10 ml, therefore 1 g in 2.5ml. Therefore, 2.5 ml of a 40% solution would be required to produce 1 Liter of a 1 in 1000.

# *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.*

- **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, Kl, 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

1- Buffers
2- Isotonicity modifiers
3- Viscosity enhancement (NaCl and Dextrose)
4- Preservatives
5- Antioxidants
6- Sweetening agents
7- Flavours and perfumes

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

1. **Aqueous solutions:**
   - Syrups
   - Aromatic waters
2. Hydro-alcoholic solutions:
   - Elixirs
   - Spirits
   - Tinctures
   - Fluid Extracts
   - Collodions
   - Liniments
3. Non-aqueous solutions

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.

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.

Purified water → oral solutions

Sterile water → injections

# 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 1st pass effect
- E.g. Ephedrine Sulfate or Naphaxoline 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.

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*Nasal drops:* محلول ينحط داخل الأنف بكمية صغيرة

*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.*

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Properties of well formulated Nasal drops:

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

## II. Eye Solutions:

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*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.*

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## 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

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*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.*

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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.

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.

Glycerin + Surfactant يخلف الشمع أفضل.

Glycerin:
- Viscous
- Hygroscopic
- Reduce swelling

Oil:
- Lipophilic
- Remove wax

## IV. Aromatic water:

*Aromatic Waters:* الماء فيه كمية من المادة العطرية لحد ما يقدر يذوبها فقط

*Are clear, saturated solutions of aromatic substances (may be volatile oilsor 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.

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, β-pinene and α-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.

المكونات الكيميائية الرئيسية للزيت:
الزيت يحتوي على مواد كيميائية مختلفة تعطيه الطعم والرائحة والخواص العلاجية.

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السلامة:

- غير سام إذا استخدمناه بتركيز منخفض.
- لكن ممكن يسبب تحسس بسبب المينثول.
- ممكن يهيج الجلد أو الأغشية المخاطية.
- يجب تجنب ملامسة العينين.

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التخزين:

- علبة مغلقة
- مكان جاف
- بعيد عن الشمس والمطر

حتى لا يتبخر الزيت أو يتلف.

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التحذيرات:

- لا يُستخدم أثناء الحمل.
- لا يُستخدم للأطفال تحت 7 سنوات.

طريقة التحضير (Practical lab part)

الخطوات:

1 مزج الزيت مع مسحوق Talc

الهدف:

- يعمل كمساعد ترشيح → يجعل المحلول صافٍ Talc
- يعمل كموزع → يزيد سطح الزيت المعرض للماء → يذوب أفضل Talc

2 إضافة Purified water

نحصل على slurry = خليط شبه سائل

3 تحريك الخليط عدة مرات لمدة 30 دقيقة

لضمان التوزيع الكامل

الترشيح = 4 Filtration

للحصول على محلول صافي

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دور Talc:

1 Filter aid: يساعد الترشيح
2 Distributing agent: يوزع الزيت ويزيد فعالية الماء في إذابته

يجب أن يكون inert يعني غير نشط كيميائيًا، حتى لا يتفاعل مع الزيت أو يؤثر على خواصه

***Formula (1):***

**$R_x$ 100 ml Peppermint Water USP**

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

**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

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*Q: What does triturate mean?*

To triturate means to grind and mix a solid substance with a liquid or another substance until it becomes a smooth and uniform mixtur

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*

Storage:

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

Use of preparation:

Carminative and flavoring agent.

1.ضع 0.75 g Talc في الهاون (mortar).
2.إخلط زيت النعنع (0.1 ml = 2 drops) مع التالك جيدًا triturate.
Q: What does triturate mean?
تفسير: طحن وخلط مادة صلبة مع سائل أو مادة أخرى حتى تصبح خليط ناعم متجانس.

3.أضف حوالي 2/3 من الماء المقطر (≈ 33 ml) تدريجيًا مع استمرار الخلط.
4.صفّ المحلول ثم أكمل الحجم النهائي إلى 50 ml باستخدام أسطوانة مدرجة.

### *Formula (2)*

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

| Ingredients | Master formula | Scaled formula |
|---|---|---|
| $NaHCO_3$ | 5gm | |
| Glycerol | 30ml | |
| Water | q.s. 100ml | q.s. 10 ml |

**Procedure**

1. Weigh sodium bicarbonate ($NaHCO_3$)
2. Dissolve $NaHCO_3$ 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) **$NaHCO_3$:** 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.

## 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, what is the concentration in w/w solution?

*(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
- 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.

| النظام | الاسم | التركيز |
|---|---|---|
| أمريكي | USP | 85% w/v |
| بريطاني | BP | 65% w/w |

**الفكرة المهمة**

هم نفس الشراب تقريباً لكن:

- الأمريكان يحسبوه w/v
- البريطانيين يحسبوه w/w

ولهذا طلع معنا:

85% w/v ≈ 65% w/w

**جملة تحفظيها للامتحان:**

USP uses w/v concentration while BP uses w/w concentration.

Disadvantages of simple syrup :

1- Accelerate dental decay.
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.
3- **Ipecac syrup:** emetic agent.

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

وظيفتها:
1- تمنع crystallization
→ تمنع تبلور السكر.
2- تزيد solubility
→ تزيد الذوبان.
3- preservative
→ مادة حافظة.

**b- Alcohol** often is included as

- Preservative
- Increase the solubility of added ingredients.

1- preservative
→ يحفظ المحلول.
2- increases solubility
→ يزيد الذوبان

## *Formula (3):*

**Rx 50 ml simple syrup USP**

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

**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

• Master formula: 1000 ml → هذا هو حجم التحضير الأصلي الكامل للمحلول أو الشراب كما هو في الكتاب أو الدستور (USP).
• القيمة بين القوسين (450 ml): هذا غالبًا كمية الماء المطلوبة فعليًا لإذابة السكر في التحضير الأصلي قبل الإضافة للوصول للحجم النهائي 1000 ml.

يعني:
• نحتاج 450 ml ماء أولًا → نضيف إليه 850 g sucrose تدريجيًا مع التسخين.
• بعد إذابة السكر والحصول على محلول واضح → نضيف المزيد من الماء للوصول إلى الحجم النهائي 1000 ml

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 ---- ml Ferrous Sulfate Syrup**

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

**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

الطريقة حسب الفيديو

Aqueous solution (1)

Formula (1)

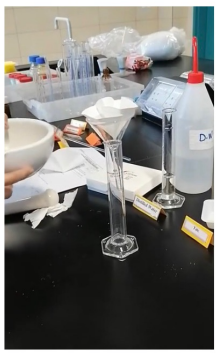
١ اطحن الـ talc

٢ اخلط الزيت واخلط واطحن

٣ اخلط $\frac{2}{3}$ من

$50 \times \frac{2}{3} = 33.3$

اضف اخلط بعدين اصفيها



بعد التصفية اخلط في ٢ وعاء

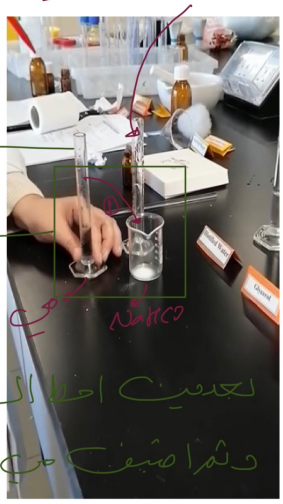
للحجم اي هو ٥٠ واخلط في

حجمها $50 \times \frac{1}{3} = 17$

نفس الشي

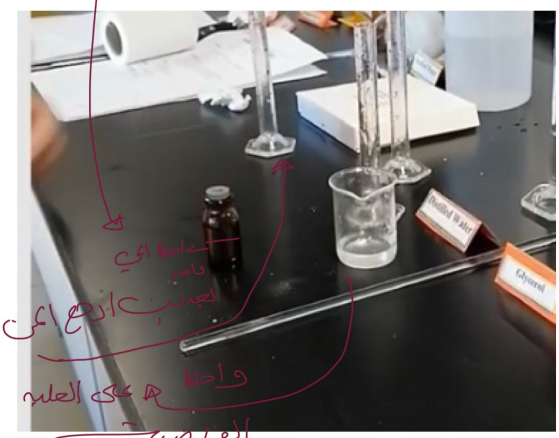
Formula (2) لا

اخلط الـ $NaHCO_3$ بالبيكر والـ glycerol بالثاني




بعدين اخلط الـ glycerol

وثم اضيف حمض و ٧ و صل 10ml




اضيف و

اضيف الماء مكان العلامة

واخلط

هاي خطوات

الحمض خلوها لو بكم

تتذكروا التجربة كيف

تدربوا للصيد (ان شاء الله اخطوات صح)

Formula (3)

هي مسحوق

① اخلط ببيكر واخلطها

على شاي النار

(بالفيديو اخلط شي احسن ما قدرت اميزه)

② اخلط على امي

Sucrose على دفعات واضل اقلب لاذابة

③ نفلتر لو نحتاج وبس

اضيف

Formula

اذوب الـ ferrous sulfate

واضيف الـ Citric acid

احط الـ peppermint

احط $\frac{1}{4}$ من الـ sucrose

$\frac{1}{2}$ من الـ purified water 30 ml

واخلط واضيف ثم فلترة

اعيد اكليط على النار

مرة ثانية واضل اضيف

Sucrose على فترات

احط جامي امي بجنبه

الماء واخلط

افلتر بعدين اعمل

نفس التجربة الـ 2

# Simple Syrup USP

- Calculation of Sucrose Required to Prepare 85 mL of Simple Syrup USP
- **Step 1: Understanding Simple Syrup USP Composition**
- Simple Syrup USP is a concentrated aqueous solution of **sucrose (85% w/v)**.
- This means **85 g of sucrose is dissolved in sufficient purified water to make 100 mL of syrup**.
- We use the formula:

850gm.....1000 ml
??.....75ml

**Formula(3):**
**$R_x$ 75 ml simple syrup USP**

| Ingredients | Master formula | Scaled formula |
|---|---|---|
| sucrose | 850 g | |
| Purified Water | q.s. 1000 ml (450 ml) | q.s.75 ml (---ml) |

$$= \left(\frac{75}{1000}\right) \times 850$$

$$= 0.075 \times 850$$

$$= 63.75 \text{ g}$$

1

**Amount of Water Needed**
•The total volume should be **75 mL** after dissolving sucrose.
•The required water is not simply **75 mL – 63.75 g**
• sucrose dissolves and increases the final volume.
•From USP formulation data, the approximate volume of water required is **45-50% of the final syrup volume** =33.75-37.5.

•Taking an average, **water required ≈ 35.5 mL**.
**Final Answer:**
To prepare **85 mL of Simple Syrup USP**:
•**Sucrose required = 63.75 g**
•**Water required = ~35.5 mL** (to dissolve the sucrose and makeup to 75 mL).

2

# Calculation of Sucrose Required to Prepare 85 mL of Simple Syrup BP

- According to the **British Pharmacopoeia (BP)**, simple syrup contains **66.7% w/w of sucrose**.
- This means that **66.7 g of sucrose is dissolved in enough purified water to make 100 g of syrup** (not mL).
- The density of the final syrup is **approximately 1.313 g/mL**.
- **Step 2: Finding the Mass of 85 mL of Syrup**
- We first calculate the total mass of 75 mL of syrup using its density:

$$\text{Mass of 85 mL Syrup} = \text{Density} \times \text{Volume}$$
$$= 1.32 \times 85$$
$$= 112.2 \text{ g}$$

3

- **Calculating the Required Sucrose Amount**
- Since **66.7% w/w** of the syrup is sucrose, we calculate:

66.7gm.....100 gm
??.....112.2gm

$$\text{Sucrose required} = \left(\frac{66.7}{100}\right) \times 112.2$$
$$= 74.87 \text{ g}$$

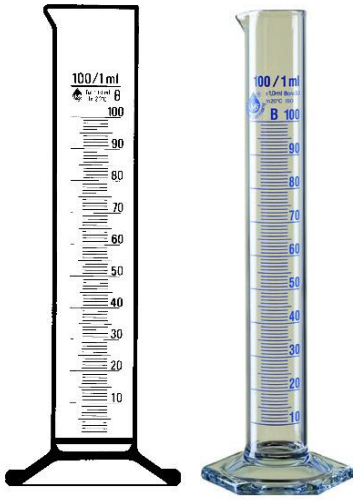
- **Calculating the Required Water Volume**
- The remaining mass is from water:

$$\text{Water required} = 112.2 - 74.87$$
$$= 37.33 \text{ g} \approx 37.33 \text{ mL (since density of water is } 1 \text{ g/mL})$$

- To prepare **85 mL of Simple Syrup BP**:
- **Sucrose required = 74.87 g**
- **Water required = ~37.33 mL** (to dissolve the sucrose and reach the final weight).

4

# Taring of the bottle


5

5

# *Experiment 3*

## *Liquid dosage forms: solutions*

## *Hydro- alcohol solutions*

### I. Spirits:

Are alcoholic and hydro-alcoholic solutions of volatile substances.

- Generally, the alcoholic content of spirits is rather high, usually over 60 %.
- Because of greater solubility of aromatic substances in alcohol, spirits can contain a greater concentration of these materials than in corresponding aromatic water.
- They are most frequently used as flavoring agents, e.g. Peppermint Spirit USP.
- Some spirits are used for their medicinal effect, but most spirits are used as stock solutions for obtaining a proper amount of flavoring oil.

لذلك الجملة تقصد:
لأن الزيوت العطرية تذوب في الكحول أكثر من الماء فإن Spirits تستطيع أن تحتوي كمية أكبر من هذه الزيوت مقارنةً بـ Aromatic water

- ✓ *Spirits should be stored in **tight, light-resistant containers** and **in a cool place.***
- ✓ *Spirits are preparation of high alcoholic strength and when diluted with aqueous solutions or liquids of low alcoholic content turbidity may occur.*
- ✓ *The addition of water **invariably** causes turbidity and separation (alcohol soluble drugs or oils precipitate out of the diluted alcohol).*

لو أضفنا ماء → الكحول أصبح أقل تركيزًا → الزيوت أو الأدوية لم تعد ذائبة
المحلول يصبح عكر (turbid) وبعض المواد تترسب (separation)

***Formula (1):***

**Rx --- ml peppermint spirit B.P.1980**

| Ingredients | Master formula | Scaled formula |
|---|---|---|
| Peppermint oil | 100ml | |
| Ethanol 90% | q.s. 1000ml | |

**Procedure**

1. Dissolve peppermint oil in alcohol and mix
2. Complete to the required volume with ethanol
3. If not clear add talc, shake well
4. Then filter solution with paper wetted with alcohol.
5. Keep in a dispensing bottle to use it in the preparation of the next formula (medicated syrup)

Use of ingredients:

(1) **Peppermint oil:** carminative, flavoring agent.

(2) **Talc** to clarify solution.

(3) **Ethanol (Alcohol):** vehicle (or solvent) and preservative

labeling:

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

Storage:

*'Store in a cool place',*

*'Preserve in amber glass well-closed containers'.*

Use of preparation

Carminative.

**II.** Tincture:

Alcoholic or hydroalcoholic solutions prepared from animal or vegetable drugs or from chemical substances.

Ex: $R_x$ 15 mL Iodine Tincture USP. 1980. used as antiseptic.

Tincture = محاليل كحولية أو كحول-مائية تُحضّر من أدوية حيوانية أو نباتية أو من مواد كيميائية.

## III. Elixirs: *Defined by the USP as:*

"Clear, sweetened, hydroalcoholic liquids intended for oral use".

- Nonmedicated elixirs are employed as vehicles and medicated elixirs for the therapeutic effect of the medicinal substances
- In comparison with syrup elixirs are:
  - *(1) Less sweet*
  - *(2) Less viscous*
  - *(3) Less effective in masking bitter taste*
  - *(4) Better able to maintain both water soluble and alcohol soluble components in solution*
  - *(5) Easier to prepare, thus, from a manufacturing standpoint, elixirs are preferred to syrups.*
- Elixirs containing over 10-12% of alcohol are usually self-preserving and do not require the addition of antimicrobial preservative.
- Because of their usual content of volatile oils and alcohol, elixirs should be stored in tight, light-resistant containers and protected from excessive heat.

---

Preparation of Elixir:

- Alcohol-soluble and water-soluble components 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, to maintain the highest possible alcoholic strength at all times so that minimal separation of the alcohol-soluble components occurs.
- Frequently, the final mixture will be cloudy, principally because of separation of some of the flavoring oils by the reduced alcoholic concentration when an aqueous solution is added to the elixir.
- If this occurs, the elixir is usually permitted to stand for a prescribed number of hours to ensure 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, absorbs the excessive amounts of oils and therefore assists in their removal from the solution.

إذا أضفنا الماء إلى الكحول تدريجيًا → الكحول يظل قويًا

إذا أضفنا الكحول إلى الماء → التركيز الكحولي يصبح أقل فجأة → مشكلة

Alcohol-soluble components = المواد التي تذوب في الكحول (مثل الزيوت العطرية أو الأدوية) إذا الكحول ضعُف فجأة → هذه المواد قد تترسب أو يخرج بعضها من المحلول لذلك نضيف الماء تدريجيًا للكحول لتجنب التعكر والفصل.

Saturated solution (محلول مشبع) = محلول لا يستطيع أن يذوب فيه المزيد من المادة في الظروف الحالية. أي: كل الزيت العطري أو الدواء اللي ممكن يذوب في الكحول أو المحلول ذاب بالكامل.

***Formula (2):***

**Rx -- ml Aromatic elixir N.F. 1980**

| Ingredients | Master formula | Scaled formula |
|---|---|---|
| Compound Orange Spirit* (Prepared by the lab instructor) | 12ml | ---ml (---drops) |
| Syrup | 375ml | |
| Talc | 30gm | |
| Ethanol (Alcohol) | 240ml | |
| Water | q.s. 1000ml | |

****Compound orange spirit***

| | |
|---|---|
| *Orange oil* | *200 ml* |
| *Lemon oil* | *50 ml* |
| *Coriander oil* | *20 ml* |
| *Anise oil* | *5 ml* |
| *Alcohol q.s* | *1000 ml* |

Procedure:-

1. Mix orange spirit withalcohol in E. Flask.
2. Add syrup portion wise with vigorous shaking
3. Add water portion wise until reaching the required volume
4. Use talc as a clarifying agent (If needed).
5. Filter the elixir using filter paper wetted with alcohol (to get rid of talc).

*Note: Filtration require wetting of the filter paper with the solvent to avoid cellulose fibers from breaking out during filtration.*

***Notes on procedure:*** *Elixir should be clear after filtration, if not (i.e. separationof volatile oil) this could happen due to either hurrying up in adding water or syrup, or not mixing well with talc.*

Use of the ingredients:-

(1) **Compound orange spirit:** flavoring agent.
(2) **Syrup:** sweet vehicle, sweetening agent, preservative.
(3) **Talc:** clarifying agent
(4) **Alcohol:** co solvent, preservative
(5) **Water:** vehicle (or solvent)

labeling:

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

1.Nonmedicated elixir = vehicle → مجرد ناقل
2.Medicated elixir = يحتوي active ingredient → يعطي تأثير علاجي

*Note: Elixir will not have a strength unless it contains an active ingredient, but alone it is considered a vehicle for other drugs .*

Use of preparation:

Flavoring vehicle

Storage:-

*In dry cool place, in tight amber glass (to protect volatile oils from light)*

## IV. Linctus:

A viscous liquid preparation for oral use only usually used to relief cough. It usually contains sucrose and is administered in small dose volume. It should be sipped and swallowed slowly without addition of water.

- The viscous nature of the preparation coats the throat and helps to alleviate the irritation which is causing the problem.

***Formula (3):***

**Rx …… mL Pediatric Codeine Linctus BP.1980**

| Ingredients | Master formula | Scaled formula |
|---|---|---|
| Codeine | 3 gm | |
| Water | 20 ml | |
| Compound tartrazine solution | 10 ml | |
| Benzoic acid | 20 ml | |
| Chloroform | 20 ml | |
| Lemon syrup | 200 ml | |
| Syrup | q.s. 1000 ml | q.s. 50 ml |

**Procedure:**

1. Dissolve codeine in water, mix well.
2. Add compound tartrazine.
3. Add Benzoic acid, mix.
4. Add Chloroform (CHCl3) and mix.
5. Add lemon syrup, mix.
6. Complete volume with syrup up to 50 ml.

Use of Ingredients:

(1) **Codeine phosphate:** antitussive
(2) **Lemon syrup:** flavoring agent
(3) **Benzoic acid:** preservative
(4) **CHCl3:** expectorant
(5) **Compound tartrazine:** coloring agent
(6) **Syrup:** sweetening vehicle.

Labeling:

- Main label
- Auxiliary label:

*Shake well before use.*
*The linctus should be sipped and swallowed slowly undiluted.*

Storage:

*'Store in a cool, dry place.' And Store in amber glass container* ***(why)***

Use of preparation:

Antitussive