

Solutions

Introduction:

In physicochemical terms

- “Solution is a one-phase system consisting of two or more components that form a homogenous molecular dispersion”
(انتشار)

In pharmaceutical terms:

- solutions are “liquid preparations that contain one or more chemical substances dissolved in a suitable solvent or mixture of mutually miscible solvents”

المهم يكونوا miscible

حسب ال (pharmaceutical terms)

Introduction

Advantages of solutions dosage forms:

- Liquids are easier to swallow than solids and therefore are more acceptable for pediatric and geriatric use.
مقبولاً للطفال كبار السن مرحلة الشيخوخة
- Drug administered in the form of solution is immediately available for absorption.
سهولة الامتصاص وأسرع
- The drug is uniformly distributed since the solution is a homogenous system.
التوزيع متساوية في أنحاء الـ solution
- Suitable for administration of some drugs that may irritate the stomach if localized in one area as often occurs after ingestion of a solid dosage form.
تهدئة (الجرعة الدوائية الصلبة) ابتلاع (إذا وقعت في موضع غير الدواء في المعدة)

Introduction:

- Drug absorption from the ^{مسالك الجهاز الهضمي} gastrointestinal tract into the systemic circulation may be expected to occur more rapidly from solution than from suspension or solid dosage forms of the same medicinal agent.

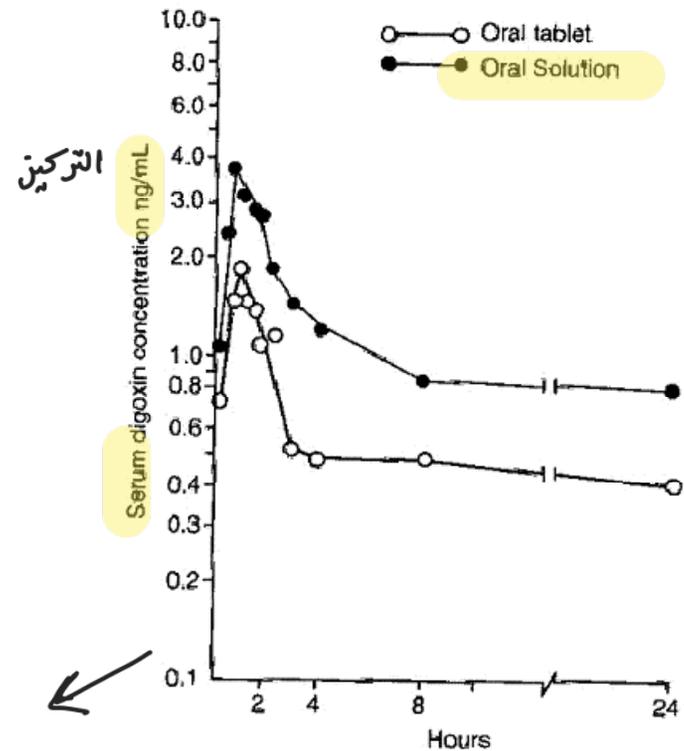


FIGURE 13.2 Serum digoxin concentrations following administration of digoxin 0.5 mg by oral tablet and elixir-like oral solution (Adapted from Huffman DH, Azarnoff DL. Absorption of orally given digoxin preparations. JAMA 1972;222:957).

بوسنج سرعت امتصاص التركيز ل solution مقارنة
 باد (tablets)
 (solid dosage)

Disadvantages of solutions dosage forms

- Liquids are bulky and therefore inconvenient to transport and store.
 (كبير الحجم) (غير مناسبة) (وغير مريحة) (للتقل)
- The stability of drug in solution is often less than in solid dosage form (tablets, capsules, ...).
 (ثباتية الدواء) (انه الدواء يبقى محافظا) (على خصائصه) (التخزين)
- Solutions often provide suitable media for growth of microorganisms.
 (ايكون اكثر عرضة ليتحلل ويغزب بشكل اسرع) (الكائنات الحية الدقيقة)
- Dosage is usually not accurate.
 * تؤثر دقة اخذ الدواء (ملقعة, سرنجة) (مذاق الدواء)
- The taste of drug is usually more pronounced when in solution than when in a solid form.
 (يكون اكثر وضوحا)

Classification

- Classification

A. based on a particular pharmaceutical solution's use: oral, otic, ophthalmic, or topical solution

للأذن

للعين

على الجلد

B. Based on their composition:

(بواسطة الفم)

1. Aqueous solutions:

- Syrups
- Aromatic waters

2. Hydroalcoholic solutions:

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

3. Non-aqueous solutions:

Introduction

- additional agents are frequently included to provide color, flavor, sweetness, or stability

- Sweeteners (المحليات)

- Colorants (الملونات)

- Isotonicity adjustment agents

→ لموازنة الملوحة خارج الخلية وداخلها

- Viscosity enhancing agents ← اللزوجة

- Suspending agents

- Antioxidants →

إذا كانت المواد قابلة للتأكسد
بمنهنيق أو antioxidants

- Chelating agents like EDTA

بمنهنيق أو chelating agents حتى نعمل chelation لبعض الـ metals /
التي يمكن يخرّبوا الـ active ingredients

- Emulsifying agents

لتحويله إلى solution
لمستحلب.

Introduction:

- the pharmacist must use information on the solubility and stability of each solute with regard to the solvent or solvent system.
- Combinations of medicinal or pharmaceutical agents that will result in chemical and/or physical interactions affecting the therapeutic quality or pharmaceutical stability of the product must be avoided.
- Each chemical agent has its own solubility in a given solvent. For many agents, their solubility's in the usual solvents are stated in the *United States Pharmacopeia– National Formulary (USP–NF)* as well as in other reference books.

القدرة العلاجية

الثباتية للنتج

نقدر نطلع معلومات ان solubility لـ solute من pharmacopie

Solutes

- Classified as non-electrolytes and electrolytes
- Non-electrolytes (as dextrose, sucrose, glycerin, ethanol, urea) will not dissociate (ionize) in solvents and the solution will not conduct electricity

← غير موصله للكهرباء

تفكك د
+ , -

- Electrolytes will dissociate or ionize when dissolved in a solvent and these solutions will conduct electricity:

* - Strong electrolytes: almost completely dissociate in a solvent (e.g. sodium hydroxide, sodium chloride, potassium chloride, sulfuric acid) (NaOH) (NaCl) KCl

(تحلل كامل)

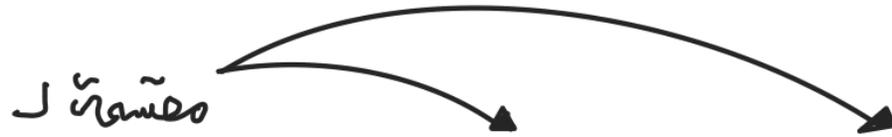
* - Weak electrolytes: dissociate in solvents to a lesser extent (e.g. acetic acid, ammonia, and majority of drugs)

(معظم الادوية)

بتحلل بشكل جزئي

acetic acid form and the ionized form

Solutes



- Weak electrolytes subdivided into weak acids and weak bases

- A way to determine if a compound is weak acid or base is to

انفحص / نتأكد examine the different salts the chemical has

- If the salt form is a sodium, potassium, or calcium ion, the chemical is an acid (e.g. sodium phenytoin, calcium carbonate, sodium phenobarbital)

- If the salt form is a sulfate, hydrochloride, or tartarate, the chemical is a base (e.g. morphine hydrochloride, metoprolol tartarate)

(weak base)



The dissolving of the solute :

Solubility

تركيب الروابط بين جزيئات ال solute و ال Solvent
وارتباط ال solute مع ال solvent

- When a solute dissolves → breaking the solute–solute forces and the solvent–solvent forces to achieve the solute–solvent attraction.

- The **solubility** of an agent in a particular solvent indicates the maximum concentration to which a solution may be prepared with that agent and that solvent.

- When a solvent at a given temperature has dissolved all of the solute possible, it is said to be **saturated**.

وهل المحلول بعد الاشباع

- The solubility is expressed as grams of solute dissolving in milliliters of solvent; for example, “1 g of sodium chloride dissolves in 2.8 mL of water.

نحتاج 2.8ml من الماء لتحيين saturated solution عند تذيب 1g من NaCl

تعتمد على درجة الحرارة ←

When the exact solubility has not been determined, general expressions of relative solubility may be used. These terms are defined in the USP

Descriptive term	PARTS OF SOLVENT REQUIRED FOR 1 PART OF SOLUTE
very soluble	one part needs ↓ of solute less than 1 of solvent (needed)
freely soluble	from 1 to 10 of solvent =
soluble	(from 10 to 30) of solvent =
← sparingly soluble	(from 30 to 100) of solvent =
(قليل) slightly soluble	(from 100 to 1000) of solvent =
very slightly soluble	(from 1000 to 10 000) of solvent
practically insoluble	more than 10 000 of solvent

Solubility

- The maximum possible concentration to which a pharmacist may prepare a solution varies greatly and depends on:
 - Chemical constitution of the solute
 - Chemical constitution of solvent
 - Type of solvent
 - pH
 - Presence of cosolvents or solubilizing agents
 - Temperature

بقدر نتحكم بالـ Solubility
لـ Solute أو الـ solvent عن طريق:

مثال :-
صكّن أحسن الـ Solubility لمادة معينة عن طريق تحويلها لـ (salt form)

في حالات معينة

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible:

Example 1 (Complexation):

- iodine granules are soluble in water only to the extent of 1 g in about 3,000 mL. Using only these two agents, the maximum concentration possible would be approximately 0.03% of iodine.
- However, through the use of an aqueous solution of potassium iodide or sodium iodide as the solvent, much larger amounts of iodine may be dissolved as the result of the formation of a water-soluble complex with the iodide salt.
- This reaction is taken advantage of, for example, in Iodine Topical Solution, USP, prepared to contain about 2% iodine and 2.4% sodium iodide.

very slightly soluble

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible:

- Example 1 (cont'd):
- **Complexation formation**: occurs when an **insoluble solute** reacts with a **soluble substance** to form a **soluble complex** (e.g. the complexation of the soluble potassium iodide (KI) to the insoluble iodine molecules (I_2) to form a soluble triiodide complex (KI_3)).

8mL REF 6064 NDC 59365-6064-0

EACH mL CONTAINS:
Iodine 0.05gm,
Potassium iodide 0.105gm.

DOSE: SINGLE USE
DO NOT REUSE. DISCARD AFTER USE. KEEP
TIGHTLY CLOSED. PROTECT FROM LIGHT. DO
NOT USE IF SEAL HAS BEEN BROKEN. STORE AT
CONTROLLED ROOM TEMPERATURE 15°-30°C
(59°-86°F).

Manufactured for CooperSurgical
Trumbull, CT 06611 Rev. 02/2002 CAUTION: Federal law prohibits dispensing without prescription.

LUGOL'S
(STRONG IODINE SOLUTION USP)

CooperSurgical

LOT NO.
EXP. DATE



TheHealthyHomeEconomist.com

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Example 2:

- Many of the important organic medicinal agents are either weak acids or weak bases, and their solubility depends to a large measure on the pH of the solvent.
- For instance, the weak bases, including many of the alkaloids (atropine, codeine, and morphine), antihistamine (diphenhydramine and promethazine), local anesthetics (cocaine, procaine, and tetracaine), and other important drugs, are not very water soluble, but they are soluble in

→ (dilute solutions of acids)

* بنحسب ان solubility لـ (weak bases)

عن طريق وضعهم في

dilute solutions of acids.

examples of weak base drugs

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Example 2 (cont'd)

- Organic medicinal that are weak acids include the barbiturate drugs (e.g., phenobarbital) and the sulfonamides (e.g., sulfadiazine and sulfacetamide) form water-soluble salts in basic solution
- The free acid may precipitate from solution by a lowering of the pH

إذا بدنا نرسب الـ weak acid بنخليه الـ acidic ← pH يعني بنقل الـ solubility

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Example 3 (two factors; type of solvent and form of drug):

- Pharmaceutical manufacturers have prepared many acid salts of organic bases to enable the preparation of aqueous solutions.
- Salts of organic compounds are more soluble in water than are the corresponding organic bases.
- Conversely, the organic bases are more soluble in organic solvents, including alcohol, than are the corresponding salt forms.
→ not favored to be used as a solvent

Example 3 (cont'd)

TABLE 13.2 WATER AND ALCOHOL SOLUBILITIES OF SOME WEAK ACIDS, WEAK BASES, AND THEIR SALTS

DRUG	MILLILITERS OF SOLVENT TO DISSOLVE 1 _g OF DRUG	
	WATER	ALCOHOL
Atropine	455.0	2
Atropine sulfate	0.5	5
Codeine	120.0	2
Codeine sulfate	30.0	1280
Codeine phosphate	2.5	325
Morphine	5000.0	210
Morphine sulfate	16.0	565
Phenobarbital	1000.0	8
Phenobarbital sodium	1.0	10
Procaine	200.0	Soluble
Procaine hydrochloride	1.0	15
Sulfadiazine	13000.0	Sparingly soluble
Sodium sulfadiazine	2.0	Slightly soluble

از ابدنا نذوبه ب water
بخواه د salt لتحسن
ذائبه
ذائبه الوقت قلت
ذائبه الملح في
ال organic solvent

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

- Example 4 (co-solvent usage)

- Co-Solvent Systems

س

النزط الانهم

- Solvent blending or co-solvency: by mixing miscible solvents of different polarities to form a solvent system of optimum polarity to dissolve the solute

example:-> Diazepam Injection use a co-solvent mixture that contains 40% propylene glycol, 10% ethanol, and 50% Water for Injection (three solvents)

- Dielectric constant (an index of solvent polarity) is used as a guide to determine a co-solvent system

وبعد معرفة
التراكيب المناسبة التي نختارها من الـ solvents
لحتى نوصل لـ polarity معينة ليناسب المادة التي بدنا نذوبها.

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Example 4

- Temperature: *بحقّ نسرع از Solubility*
هو نحسن از solubility او تزيد كمية الدواء اللي بردنا نذوبها
 - many compounds have greater solubility at elevated temperatures
** بعض المواد بتأثر بار temperature حتى لو كانت قليلة **
** So we have to select the correct temp.*
 - Selecting the correct temperature will cause the solution to hold the required amount of drug in solution
 - Also will help the pharmacist know the correct formulation storage conditions

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Temperature (cont'd):

- However, elevated temperatures cannot be maintained for pharmaceuticals, and the **net effect** of heat is simply an **increase in the rate of solution** rather than an increase in solubility.
- Pharmacists should be careful not to exceed the minimally required temperature, so as to avoid drug deterioration

(تجزیب / تشکیل)

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Temperature (cont'd):

- Some chemical agents, particularly calcium salts, undergo exothermic reactions as they dissolve and give off heat. ^{تشبيط}
- For such materials, the use of heat would actually discourage the formation of a solution.
- The best pharmaceutical example of this type of chemical is calcium hydroxide, which is used in the preparation of Calcium Hydroxide Topical Solution, USP.
- Calcium hydroxide is soluble in water to the extent of 140 mg per 100 mL of solution at 25°C and 170 mg per 100 mL of solution at 15°C .

Notes %

تفاعل $Ca(OH)_2$ ملارد للحرارة (بمعنى حرارة في النواتج) حسب المعادلة ← $Ca(OH)_2 + H_2O \rightarrow heat$
فذائبته يتكون أعلى وأسرع لما يكون عند درجات حرارة منخفضة.

أما لو رفعنا درجة الحرارة فبنتقل الذائبة وبتجه هم للمعادلة باتجاه تكوين التفاعلات فبتسبب $Ca(OH)_2$ فباتالي بتقل ذائبته .

General guideline for solubility:

- the most widely written guideline for the prediction of solubility is “like dissolves like.” Thus, organic compounds are more soluble in organic solvents than in water.
- The greater the number of polar groups present, the greater will likely be the organic compound’s solubility in water. Polar groups include OH, CHO, COH, CHOH, CH₂OH, COOH, NO₂, CO, NH₂, and SO₃H.
- An increase in the molecular weight of an organic compound without a change in polarity reduces solubility in water.

General guideline for solubility:

شرح الذوبان

- To hasten the dissolution rate a pharmacist may employ one or several techniques such as:
 - Applying heat (not suitable for volatile and thermolabile substances)
 - Reducing the particle size (Comminution, grinding)
 - Utilizing a solubilizing agent
 - Vigorous agitation

ex. لحايعون السكر مطحون بشكل ناعم
رج يذوب بشكل أسرع من اذا كان Crystals

(Good and strong stirring)

لما نيجي ببناء نعمل زيادة لدرجة الحرارة نتأكد انه المادة
ما يصير لها تعلق وتخرّب او تكون مادة متطايرة .

TABLE 13.3 SOLUBILITIES OF SELECTED ORGANIC COMPOUNDS IN WATER AS A DEMONSTRATION OF CHEMICAL STRUCTURE–SOLUBILITY RELATIONSHIP

COMPOUND	FORMULA	MILLILITERS OF WATER REQUIRED TO DISSOLVE 1 G OF COMPOUND
Benzene	C_6H_6	1430.0
Benzoic acid	C_6H_5COOH	<u>275.0</u>
Benzyl alcohol	$C_6H_5CH_2OH$	25.0
Phenol	C_6H_5OH	15.0
Pyrocatechol	$C_6H_4(OH)_2$	2.3
Pyrogallol	$C_6H_3(OH)_3$	1.7
Carbon tetrachloride	CCl_4	2000.0
Chloroform	$CHCl_3$	200.0
Methylene chloride	CH_2Cl_2	50.0

زادته زائبيته
لا فنيقنا
polar group

General guidelines for solubility

- Water is the most commonly used solvents for oral solutions
- The physiological actions of many solvents greatly limit their use. With few exceptions, most organic solvents are irritating or toxic.
- Thus, toxicity and irritation limit the solvents employed to a few compounds:
 - For internal use, only a few solvents such as glycerin, alcohol, and propylene glycol are indicated for internal use
 - for topical use, acetone, isopropanol, polyethylene glycols, saturated aliphatic hydrocarbons, ether, and various oils may be used

Some solvents for liquid preparations:

- ALCOHOL, USP: ETHYL ALCOHOL, ETHANOL, C₂H₅OH:
- Next to water, alcohol is the most useful solvent in pharmacy.
- Together with water, it forms a hydroalcoholic mixture that dissolves both alcohol-soluble and water-soluble substances
- **Alcohol, USP:** is 94.9% to 96.0% C₂H₅OH by volume (i.e., v/v) when determined at 15.56°C
- **Dehydrated Alcohol, USP:** contains not less than 99.5% C₂H₅OH by volume and is used when an essentially water-free alcohol is desired.
- It is also used in liquid products as an antimicrobial preservative

المختلطة

بنقدرة

فيه مواد تذوب

ماء الكحول

نصفها الحرارة بدرجة معينة
لأنه الكحول متطاير

(مضاد للميكروبات)

Advantages of hydroalcoholic solutions:

- They generally can dissolve more oil soluble drugs (or the free acid or free base form) compared to aqueous solutions
- They have some preservation capacity because of the presence of alcohol
- They can be used to dissolve either alcohol soluble or water soluble drugs

Disadvantages of hydroalcoholic solutions:

- The used solvents are not always physiologically inert
- Elixirs are less sweet and less viscous than syrups
- Less effective in masking taste compared to syrups

ليست خاصة فسيولوجيا اي انها قد تؤثر سلبا على جسم الانسان
← أقل فعالية في اخفاء الطعم مقارنة بـ syrups

Some solvents for liquid preparations:

- The U.S. Food and Drug Administration (FDA) restrict the use of alcohol in over-the-counter (OTC) oral drug products and include appropriate warnings in the labeling:
 - For OTC oral products intended for children under 6 years of age, the recommended alcohol content limit is 0.5%;
 - for products intended for children 6 to 12 years of age, the recommended limit is 5%;
 - and for products recommended for children over 12 years of age and for adults, the recommended limit is 10%.

Some solvents for liquid preparations:

- **DILUTED ALCOHOL, NF:**
- Diluted Alcohol, NF, is prepared by mixing equal volumes of Alcohol, USP, and Purified Water, USP.
- **RUBBING ALCOHOL:**
- Rubbing alcohol contains about 70% ethyl alcohol by volume, the remainder consisting of water, denaturants with or without color additives and perfume oils, and stabilizers.
- Each 100 mL must contain not less than 355 mg of sucrose octaacetate or 1.4 mg of denatonium benzoate (bitter substances that discourage accidental or abusive oral ingestion).
- According to the Internal Revenue Service, U.S. Treasury Department, the denaturant employed in rubbing alcohol is formula 23-H, which is composed of 8 parts by volume of acetone, 1.5 parts by volume of methyl isobutyl ketone, and 100 parts by volume of ethyl alcohol.
- The use of this **denaturant mixture** makes the separation of ethyl alcohol from the denaturants **virtually impossible with ordinary distillation apparatus**. This discourages the illegal removal for use as a beverage of the alcoholic content of rubbing alcohol.

Some solvents for liquid preparations:

- Rubbing alcohol is used as:
 - Rubefacient externally → يوضع على الجلد ويحلل مساج وهو يحسن الدورة الدموية
 - Soothing rub for bedridden patients → للمرضى طريحي الفراش
 - Germicide for instruments → معقم للأدوات
 - Skin cleanser before injection → معقم قبل الحقن
 - Vehicle for topical preparations

Rubefacient

From Wikipedia, the free encyclopedia

A **rubefacient** is a substance for topical application that produces redness of the skin e.g. by causing dilation of the capillaries and an increase in blood circulation. They have sometimes been used to relieve acute or chronic pain, but there is limited evidence as to their efficacy,^{[1][2]} and as of 2010 the best evidence does not

Some solvents for liquid preparations:

GLYCERIN, USP (GLYCEROL):

- Glycerin is a clear syrupy liquid with a sweet taste. It is miscible with both water and alcohol (ذائب)
- Glycerin :
 - has preservative qualities
 - and is often used as a stabilizer ← *بشبه التركيبة التي بدنا نعملها*
 - and used as an auxiliary solvent in conjunction with water or alcohol

Some solvents for liquid preparations:

ISOPROPYL RUBBING ALCOHOL:

- Isopropyl rubbing alcohol is about 70% by volume isopropyl alcohol, the remainder consisting of water with or without color additives, stabilizers, and perfume oils.

PROPYLENE GLYCOL, USP:

- Propylene glycol, a viscous liquid, is miscible with water and alcohol. It is a useful solvent with a wide range of applications
- It is sometimes substituted for glycerin in some pharmaceutical formulations.
- Although orally administered propylene glycol has a low toxicity in animals, it may exhibit a weak central nervous system depressant activity

The disadvantage of propylene glycol ←

Some solvents for liquid preparations:

Fixed oils (vegetable oils) (oil solvents) لما يكون الجارة ما بتدوب غير ب
مثل فيتامين (E)

- These are non-volatile oils that consist mainly of fatty acid esters of glycerol.

Liquid paraffin

- It is often used as a solvent for the topical application of drugs
- Liquid paraffin or mineral oil is a transparent, colourless, odourless, or almost odourless, oily liquid composed of saturated hydrocarbons obtained from petroleum
- H.W: history for its use in medicine

قد نبحث عن استخدامها
في الطب

Some solvents for liquid preparations:

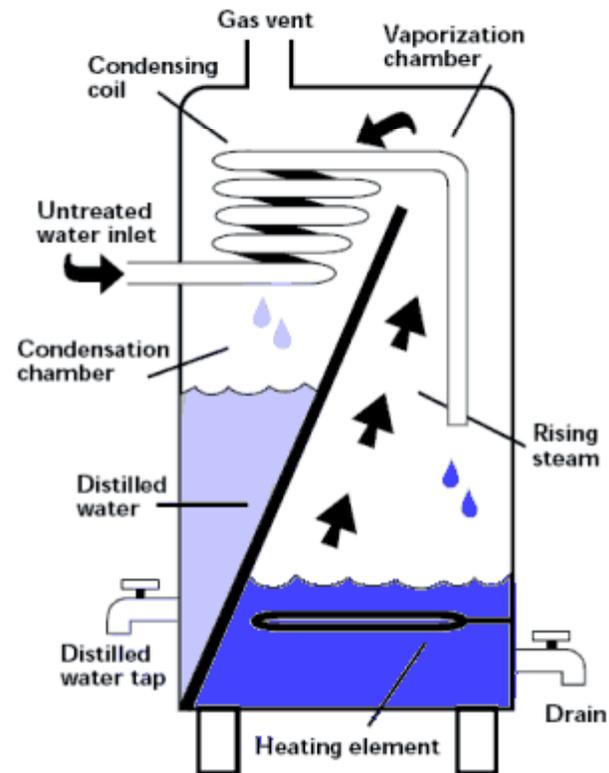
PURIFIED WATER, USP, H₂O

- Naturally occurring water contains various amounts of dissolved inorganic salts, organic matter and microorganisms.
- Ordinary drinking water obtained from the tap is **not** accepted for the manufacture of aqueous pharmaceutical preparations or for the extemporaneous compounding of prescriptions
- Purified water ^{تصفيره} is obtained by distillation, Ion-exchange treatment, reverse osmosis or other suitable process.
- Purified water, USP is intended for use in the preparation of aqueous dosage forms except those intended for parenteral administration (Injections).
- Water for Injection, USP; Bacteriostatic Water for Injection, USP; or Sterile Water for Injection, USP, is used for injections

Methods for preparing Purified water:

1) Distillation method

- **Distillation** is a process of separating the component substances from a liquid mixture by selective evaporation and condensation



Methods for preparing Purified water:

2) Ion-exchange method

- Advantages over distillation method:

- No heat is required

- Ease of operation *يُعتبر طريقةً آهلة*

- Minimal maintenance *لما يغرب بسرعة ← ما يحتاج صيانة بشكل متكرر*

- More mobile facility

- The ion exchange equipment involves the passage of water through a column of cation and anion exchangers, consisting of water insoluble, synthetic, polymerized resins of high molecular weight

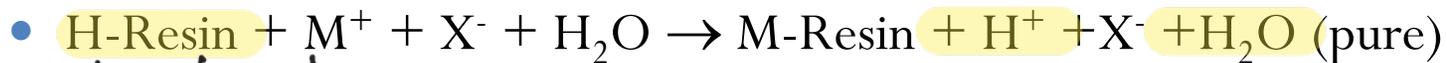
Methods for preparing Purified water:

- Water purified using this method is referred to as ^{پیشی} demineralized or deionized water ²

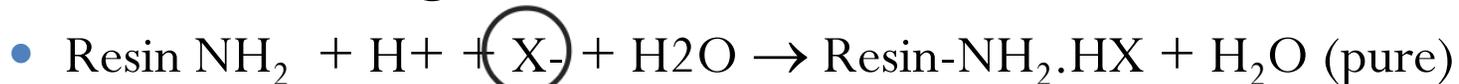
• These resins are mainly of two types:

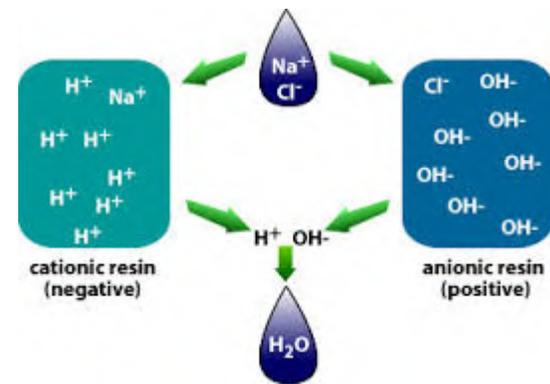
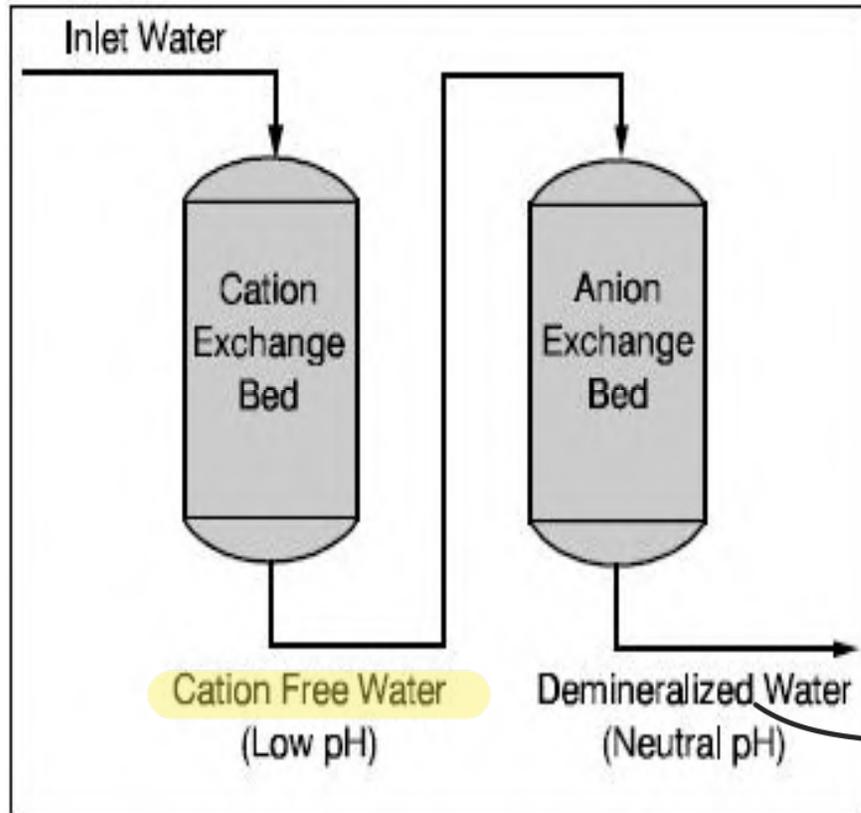
- A) The cation or acid exchanger, which permit the exchange of cations in solutions with hydrogen ion from the resin
- B) The anion or base exchangers which permit the removal of anions

Cation exchange



Anion exchange





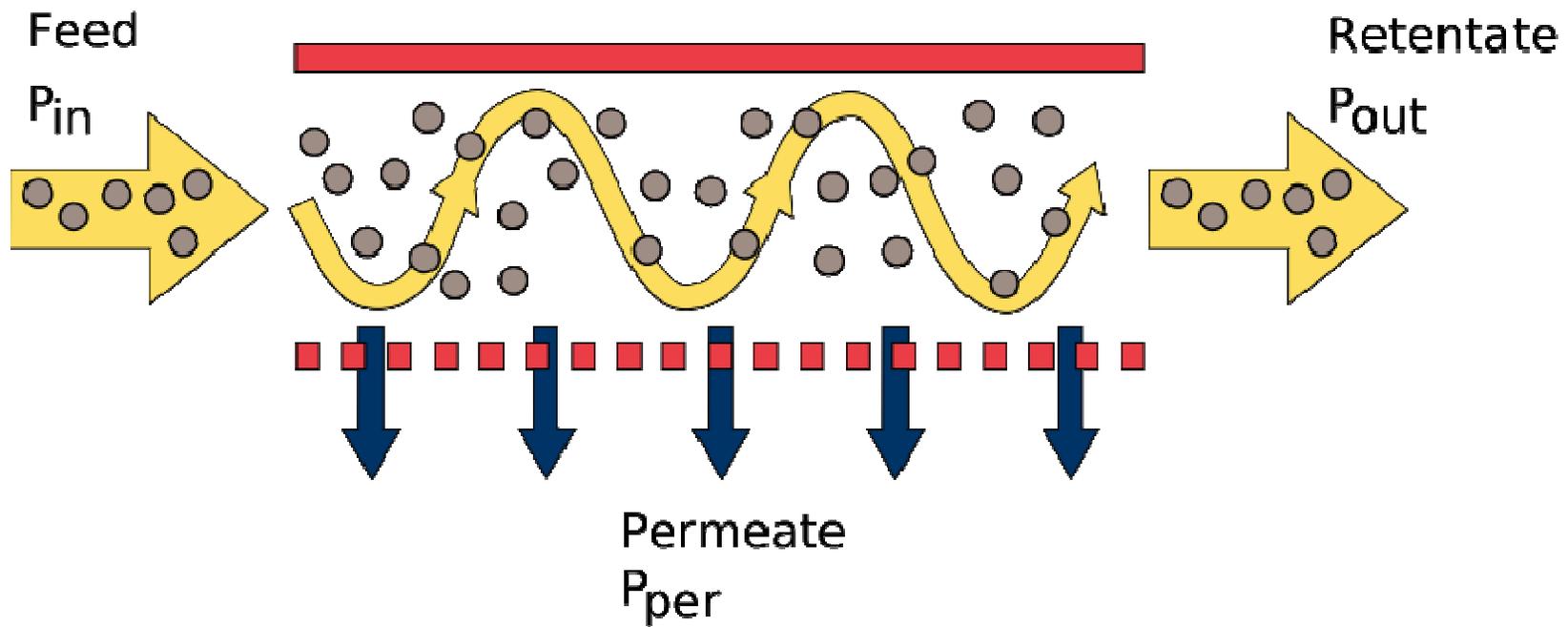
خالي من المعادن

Methods for preparing Purified water:

3) Reverse osmosis

- Formally, reverse osmosis is the process of forcing a solvent from a region of high solute concentration through a semipermeable membrane to a region of low solute concentration by applying a pressure in excess of the osmotic pressure.
- This is one of the processes referred to in industry as cross-flow (or tangential flow) membrane filtration
- In this process a pressurized stream of water is passed parallel to the inner side of a filter membrane core.
- A portion of the feed water permeates the membrane as filtrate
- In the normal [osmosis](#) process, the solvent naturally moves from an area of low solute concentration (high water potential), through a membrane, to an area of high solute concentration (low water potential).
- Whereas the flow in this crossflow system is from a more concentrated to less concentrated and therefore it is termed *reverse osmosis*.

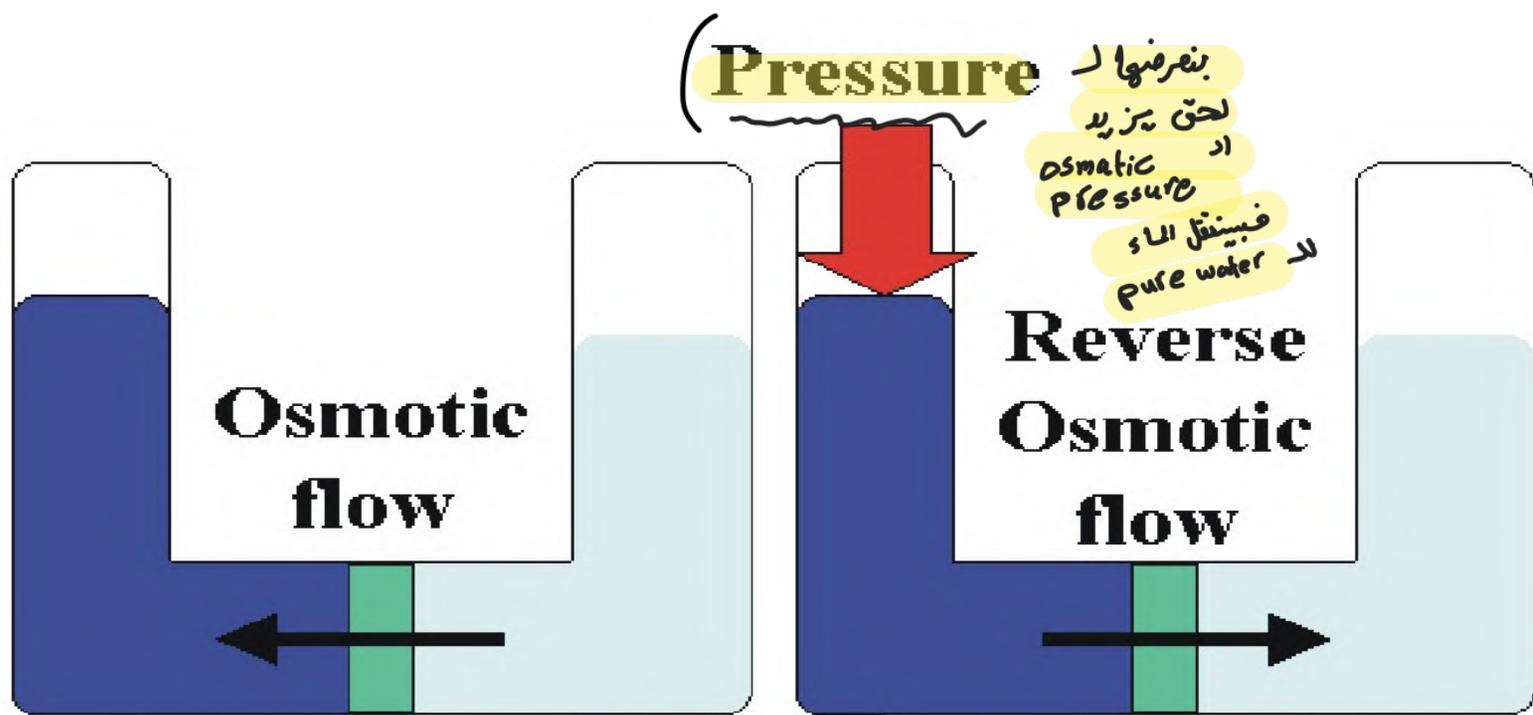
Cross-Flow Filtration



Methods for preparing Purified water:

- Reverse osmosis can remove many types of molecules and ions from solutions, including bacteria
- The result is that the solute is retained on the pressurized side of the membrane and the pure solvent is allowed to pass to the other side
- Depending on their pore size, cross flow membranes can remove particles defined in the range of:
 - Micro filtration (0.1 – 2 microns)
 - Ultrafiltration (0.01 to 0.1 microns)
 - Nanofiltration (0.001 to 0.01 microns)
 - Reverse osmosis (Less than 0.001 microns) : Reverse osmosis removes virtually all viruses, bacteria, pyrogens, and organic molecules and 90% to 99% of ions

من المعترضين ←



Pressure بنظرینوا ل
 لحن یزید
 اد
 Osmotic
 Pressure
 فیننقل الاء
 ل pure water

**Osmotic
 flow**

**Reverse
 Osmotic
 flow**

Salt solution

Pure water

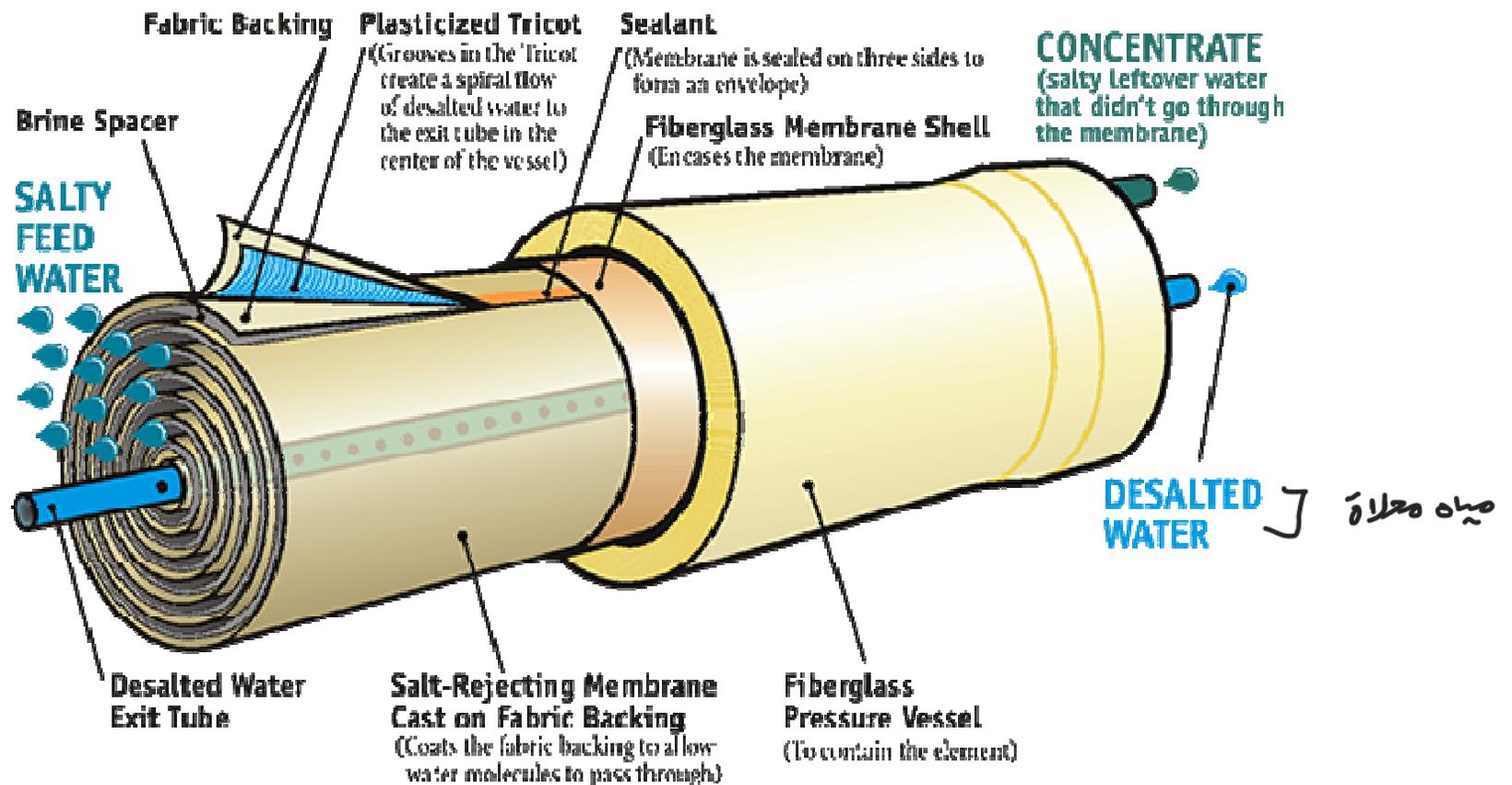
quality of pure water
 ان
 semi permeable
 membrane
 ان

- % reverse osmosis

ماي العلية بدما ملاقة يعني it's not cheap



Reverse Osmosis Membrane Element inside a Pressure Vessel



RO Membrane

- https://www.youtube.com/watch?v=rK7UVY_7K8w

بوضوح السلايد السابق

Common Additives in the solutions.

- **Buffers**
- **Preservatives**
- **Antioxidants**
- **Viscosity enhancers**
- **Sweetening agents**
- **Flavours**

Buffers

- **Buffers** are compounds that resist changes in pH upon the addition of limited amounts of acids or bases.
- Buffer systems are usually composed of a weak acid or base and its conjugate salt.
- The components act in such a way that addition of an acid or base results in the formulation of a salt causing only a small change in pH.

Buffers

- **Buffer capacity** is a measure of the efficiency of a buffer in resisting changes in pH. Conventionally, the buffer capacity (β) is expressed as the amount of strong acid or base, in gram-equivalents, that must be added to 1 liter of the solution to change its pH by one unit.
- Buffer capacities ranging from 0.01 - 0.1 are usually adequate for most pharmaceutical solutions.

* Buffer capacity لازم ما تكون كثير تا resistant او قليل

Buffers

- Once the optimal solution pH for the drug has been determined, buffers are needed to maintain that pH for the expected shelf life of the product
- The buffer capacity must be large enough to maintain the product pH for a reasonably long shelf life
- Change in product pH may result from the interaction of components with one another or with the package (glass, plastic, rubber, closure)
- On the other hand, the buffer capacity must be low enough to allow rapid adjustment of the formulation's pH to the physiological pH upon administration

Buffers

يعني صاير بين ال Buffer و ال Components of the solution
تفاعلات بتخرب المستحضر

- Buffer should have low toxicity and compatible with other ingredients.
- As the pH of most body fluids is 7.4, products such as injections, eye drops and nasal drops should, ideally, be buffered at this value.
- Formulating a product at (7.4) this pH is not always possible because of the drug's solubility, chemical stability, or therapeutic activity. Therefore, some compromise in the formulation pH may be necessary

Buffers

- However, many body fluids have a buffering capacity and when formulating low volume intravenous injections or eye drops a wider range of pH can be tolerated
- Ophthalmic solutions generally are buffered in a pH range from 4.5 to 11.5
- When a formulation is administered to the eye, it stimulates the flow of tears that is capable of quickly diluting and buffering small volumes of formulations
- Usually a compromise between a pH which is physiologically acceptable and a pH of optimum stability and solubility

فلما نستخدم قطارة العين
بكون Buffer capacity
قليلة - لكن يغير لها
adaptation
مع pH الجسم

Preservation of oral solutions:

- Oral aqueous solutions can support growth especially if sucrose is present
- Preservatives are added to prevent microbial growth.
- Methods to preserve solutions:
 1. Add a known **preservative** in the **correct concentration** that is **soluble** in the formulation
 2. If absolute alcoholic content is high → alcohol can act as preservative: a minimum of 15% absolute alcohol is adequate to preserve products with pH 5, and 18% for neutral or slightly alkaline preparations (tinctures, spirits, and some elixirs require no preservatives)

Preservatives

- Ex. Benzoic acid, sodium benzoate, methylparabens, propylparabens and butylparabens.
- When choosing a suitable preservative the following points should be considered:
 - No adsorption of the preservative into the container occurs
 - The preservative is not impaired by the pH of the solution or by interaction with other ingredients

water واغنا همدنا يضلوا بال water
partition into (flavoring oils) كل ما صار لهم
C-chain تبعتهم
Molar weight بتزيد
الحق نعمل preservation
اذا كانوا موجودين في المستحضر
The problem

Preservatives

- (methyl-, ethyl-, propyl-, and butylparabens) frequently used preservatives in oral preparations, have a tendency to partition into certain flavoring oils. بصيلا لحتى ينقسموا
- This partitioning effect could reduce the effective concentration of the preservatives in the aqueous medium of a pharmaceutical product below the level needed for preservative action.

Table 6 Preservatives used in pharmaceutical systems

Preservative	Usual concentration (%)
Acidic	
Phenol	0.2–0.5
Chlorocresol	0.05–0.1
α -Phenylphenol	0.005–0.01
Alkyl esters of <i>p</i> -hydroxybenzoic acid	0.001–0.2
Benzoic acid and its salt	0.1–0.3
Boric acid and its salts	0.5–1.0
Sorbic acid and its salts	0.05–0.2
Neutral	
Chlorobutanol	0.5
Benzyl alcohol	1.0
β -Phenylethyl alcohol	0.2–1.0
Mercurial	
Thiomersal	0.001–0.1
Phenylmercuric acetate and nitrate	0.002–0.005
Nitromersol	0.001–0.1
Quaternary ammonium compounds	
Benzalkonium chloride	0.004–0.02
Cetylpyridinium chloride	0.01–0.02

(From Ref.^[16].)

Antioxidants

تحلل

- Some drugs can be chemically degraded by oxidation.
- If such a drug is present in the formulation, an antioxidant should be added.
- These are materials added to reduce the decomposition (oxidation) of pharmaceutical product.
- These include:
 - ascorbic acid,
 - citric acid,
 - sodium metabisulfite
 - sodium sulfite.
- * Sulfites can cause allergic-type reactions in certain people and so patients should be questioned about this potential reaction before the antioxidant is included in the formulation.

Flavoring agents:

مذاق غير مرغوب

- Most drugs have disagreeable tastes
- A formulation that is disagreeable in **appearance and texture or taste** will not encourage patient **compliance**

مستساغ

- more attractive and palatable formulation → more acceptable to the patient → compliance will be improved

(الفترة الزمنية المقررة لأخذ الدواء للصغير)
(أو الحمل الدواء)

Flavoring agents:

- Children prefer sweet, fruity, and candy-like tastes
- Adults tend to tolerate a reasonable level of bitterness or less sweet, tart, fruity flavors → *tasting buds aren't mature enough.*
- For infants under 3-6 months of age flavoring agents are unnecessary and are not recommended
- In addition to the active drug, formulation components may produce characteristics tastes or odors:
 - alcohol: biting taste (روائح از مذاق) مذاق لاذع
 - Glycerin: sweet taste
 - Methylparaben: floral like aroma
 - Propylparaben: produces a numbing feel in the mouth خدران
 - Menthol and mannitol: impart a cooling sensation

(يعطي احساس بالبرودة)

Flavoring techniques:

- blending: the use of a flavor that blend with drug tastes:

- Drugs with acidic taste can be blended with citrus fruit flavors

- Overshadowing (masking, overpowering): involves using a flavor with a stronger intensity and longer residence time in the mouth (e.g. wintergreen oil)

- Physical methods:

- Use insoluble form of drug \rightarrow like (suspension)

- Make an o/w emulsion of an oily drug and flavor the external aqueous phase

(oil in water)

بعمل مثل masking لطعم الدواء (overshadowing way)

Flavoring techniques:

- Chemical methods: by adsorbing, complexing or making a pro-drug of the drug that eliminate the undesirable taste

مثلاً انه ناخذ الدواء بشكل آخر ولما يدخل الجسم، الانزيمات بتعاله وبتأخذ اد drug.

- Physiological techniques:

- Use additives that cause a cooling sensation (e.g. mannitol, menthol)
- Menthol, peppermint oil and chloroform mask the taste also by acting as desensitizing agents.

تعمل زي ازالة الاحساس (بجلم الدواء)

Sweeteners

- Low molecular weight carbohydrates and particularly sucrose are traditionally the most widely used sweetening agents in oral solutions.
- Polyhydric alcohols such as glycerol, sorbitol, mannitol and xylitol possess sweetening properties, and can be used for diabetic patients.
- Artificial sweeteners (saccharin, aspartame and cyclamates) can be used. Saccharin and cyclamates are suspected to be carcinogenic and so aspartame is the most accepted one.

(قصومًا)

مرضى السكري

يشبه به ان يكون مادة مسرطنة.

Sweeteners

- Advantages of sucrose:

- colorless

- very soluble in water

- stable over a pH range of about 4 - 8

- It increases the viscosity of solutions which will give them a pleasant texture in the mouth

قوامه لطيف في الفم .

- It masks the taste of both salty and bitter drugs

- It has a soothing effect on the throat which makes it suitable for

ضاد للسعال antitussive preparations

- The main disadvantages of sucrose is that it initiates dental caries and is not suitable for diabetic patients.

تسوس الأسنان

بغطي على الطعم المر للأدوية
والمالح .

Coloring agents

- Colors are substances added to a formulation for the sole purpose of imparting color to promote patients' acceptance of a formulation via visual appeal

- Coloring agents are not required in every formulations and they are contraindicated in all sterile solutions

لا تستخدم في ال sterile solutions

- Pleasant fruity colors are generally preferred and should be coordinated with flavors and scents (yellow with lemon, red with cherry)

يكون اللون متناسق مع الطعم

Coloring agents

المواد اللّية في ار solution

- Physicochemical reactions with other formulation ingredients must be considered when choosing a colorant
- Many colors are salts of sulfonic acids and may be incompatible with large cationic compounds such as alkaloids
- The pharmacists should also consider how pH changes or light exposure alters the color or stability of the product

تغير

Coloring agents

- Colors used in pharmaceutical preparations are either natural colors or synthetic dyes
- Natural colors include red ferric oxide, titanium oxide
- The synthetic dyes are certified by FDA and are:
 - FD&C dyes: used in food, drug, and cosmetics
 - D&C dyes: used in drugs and cosmetics
 - External D&C dyes: used in externally applied drugs and cosmetics

الاستساعة

Viscosity Enhancers:

- It is sometimes desired to increase viscosity to enhance palatability and pourability.
- This can be achieved by increasing sugar concentration or by incorporating viscosity controlling agents such as polyvinylpyrrolidone (PVP) or various cellulose derivatives
- Palatability (palatable)???

Isotonicity modifiers:

- Solution for injection, for application to mucous membranes and large volume solutions for ophthalmic use must be made iso-osmotic with tissue fluid to avoid pain and irritation.
- Other additives should be considered when adjusting tonicity because of their effect on the osmotic pressure of solution.

Preparations of solutions:

- Most solutions are prepared by simple mixing of the solutes with the solvent.
- On an industrial scale, solutions are prepared in large mixing vessels with ports for mechanical stirrers.
- When heat is desired, thermostatically controlled mixing tanks may be used.



Oral solutions:

- The solutions are formulated so that the volume administered for each dose may be:
 - Small: one or more drops
 - 5ml (teaspoonful)
 - 10 ml
 - 15 ml (tablespoonful)
 - Large volume (ex. Usual adult dose for Magnesium citrate oral solution, USP is 200 ml)
- *Even though these are liquids, it is recommended that the patient follow the administration of the liquid dosage form with a glassful of water.

Dry mixtures for solutions:

- A number of medicinal agents, particularly certain antibiotics, have insufficient stability in aqueous solutions to meet extended shelf half-life
- The products are provided to the patient in dry powder or granule form for reconstitution before dispensing to the patient.
- The dry powder contain all the formulation components except the solvent.
- Once reconstituted by the pharmacist, the solution remains stable when stored in the refrigerator for the labeled period, usually 7 to 14 days
- In case the medication remains after the patient completes the course of therapy, the patient should be instructed to discard the remaining portion, which would be unfit for use at a later time.
- Steps of reconstitution

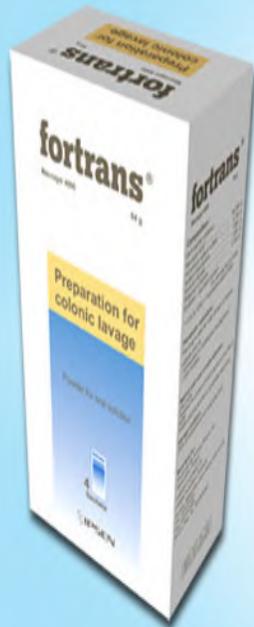
ع ان يتخلص من الجزء المتبقي من الدواء
بعد انتهاء الفترة المحددة لأخذ الدواء.

Dry mixtures for solutions:

ORAL REHYDRATION SOLUTIONS

معالجة الجفاف

- A typical oral rehydration solution contains 45 mEq Na⁺, 20 mEq K⁺, 35 mEq Cl⁻ 30 mEq citrate, and 25 g of glucose per liter.
- These formulations are available in liquid or powder for reconstitution.
- It is important to:
 - Add the specific amount of water to prepare the powder
 - Not to mix these products with other electrolyte containing liquids such as milk or fruit juices



دواء لخسيل القولون
Colon Lavage



NDC 10572-400-01
FILL TO THE TOP OF THE LINE ON BOTTLE

To Pharmacist:

Patient instructions are on base label. Discard unused flavor packs.
Package insert may be removed before dispensing.
Dispense the enclosed Medication Guide to each patient.

**PEG-3350, Sodium Chloride,
Sodium Bicarbonate
and Potassium Chloride
for Oral Solution**

With Flavor Packs

When reconstituted with water to a volume of 4 liters, this solution contains PEG-3350 31.3 mmol/L, sodium 65 mmol/L, chloride 53 mmol/L, bicarbonate 17 mmol/L and potassium 5 mmol/L

Each disposable jug contains, in powdered form: polyethylene glycol 3350 420 g, sodium bicarbonate 5.72 g, sodium chloride 11.2 g, potassium chloride 1.48 g.

PULL DOWN TO OPEN



Rx only **Affordable**
Pharmaceuticals LLC

Braintree, MA 02185

K 09/13

Dry mixtures for solutions: ORAL COLONIC LAVAGE SOLUTION

- Before dispensing it to the patient, the pharmacist reconstitutes this powder with water, creating an isotonic solution having a mildly salty taste. *علم مائع بشكل متساوي*
- The recommended adult dosage of this product is 4 L of solution before the gastrointestinal procedure.

first type of solutions:

Syrup

Like glycerin ←

- Syrups are concentrated aqueous preparations of a sugar or sugar substitute with or without flavoring agents and medicinal substances
- Sweet with pleasant texture
- A **simple syrup** contains only sucrose and purified water (e.g. Syrup USP). (زجاجة القطر)
- Syrups containing pleasantly flavored substances are known as **flavoring syrups** (e.g. Cherry Syrup, Acacia Syrup, etc.). ↗ flavor في syrup
- **Medicinal syrups** are those to which **therapeutic** compounds have been added (e.g. Guaifenesin Syrup).

Syrup

TABLE 13.6 EXAMPLES OF NONMEDICATED SYRUPS (VEHICLES)

SYRUP	COMMENTS
Cherry syrup	Sucrose-based syrup with cherry juice about 47% by volume. Tart fruit flavor is attractive to most patients and acidic pH makes it useful as a vehicle for drugs requiring an acid medium.
Cocoa syrup	Suspension of cocoa powder in aqueous vehicle sweetened and thickened with sucrose, liquid glucose, glycerin; flavored with vanilla, sodium chloride. Particularly effective in administering bitter-tasting drugs to children.
Orange syrup	Sucrose-based syrup uses sweet orange peel tincture, citric acid as sources of flavor and tartness. Resembles orange juice in taste; good vehicle for drugs stable in acidic medium.
Ora-Sweet, Ora-Sweet SF	Commercial vehicles for extemporaneous compounding of (Paddock Laboratories) syrups. Both have pH of 4–4.5 and are alcohol free. Ora-Sweet SF is sugar free.
Raspberry syrup	Sucrose-based syrup with raspberry juice about 48% by volume. Pleasant-flavored vehicle to disguise salty or sour taste of saline medicaments.
Syrup	85% sucrose in purified water. Simple syrup may be used as basis for flavored or medicated syrups.

Syrup

- Syrup, USP (simple syrup) contains 850 gm sucrose and 450 ml of water in each liter of syrup (85% sucrose in purified water)
- Although very concentrated, the solution is not saturated in order to prevent crystallization by decrease in temperature.
- 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

- Sucrose is the most frequently used sugar in syrups.
- Most syrups contain a high proportion of sucrose, usually 60 to 80% to give the desired:
 - Viscosity ✓
 - Sweetness ✓
 - Resistance to microbial growth ✓] صافي ناعمي للمواد الحافظة ←

- Syrup USP is resistant to microbial growth. ↘
high osmotic pressure because of the high conc. sugar.

- If one wants to formulate a syrup containing less sucrose, the quantity of alcohol, or other preservatives, may be estimated by considering the USP Syrup equivalent and the free water equivalent. One may assume that free water is preserved by 18% alcohol.

الكمية المتوفرة للميكروبيوم تكون عند $free\ water$ فكون $available\ for\ microorganism$ يكون التركيز قليل من الكحول أو المواد الحافظة مع أد السكرز

Syrups

- Syrups may be prepared from sugars other than sucrose (glucose, fructose), non-sugar polyols (sorbitol, glycerin, propylene glycol, mannitol), or other non-nutritive artificial sweeteners (aspartame, saccharin) when a reduction in calories or glucogenic properties is desired, as with the diabetic patient.
- The non-nutritive sweeteners do not impart the characteristic viscosity of syrups and require the addition of viscosity adjusters, such as methylcellulose. ←
- The polyols, though less sweet than sucrose, have the advantage of providing favorable viscosity, reducing (cap-locking) crystallization (which occurs when sucrose crystallizes), and in some cases acting as cosolvents and preservatives. A 70% sorbitol solution is commercially available for use as a vehicle.

Syrup

Most syrups contain the following agents in addition to the purified water and any medicinal agent:

1. Sugar

2. Antimicrobial preservative

according to the amount of free water

- The amount of preservative required varies with
 - the proportion of water available for microbial growth
 - The inherent preservative activity of some formulative materials
 - The capability of preservative itself

3. Flavorants

- Sometimes a small amount of alcohol is added to solve poorly water-soluble flavors

4. Colorants:

- To enhance the appeal of the syrup, a coloring agent that correlates with the flavorant employed (i.e., green with mint, brown with chocolate, etc.) is used

الجاذبية لتحسين

يرتبط

Antihistamine Syrup [↖] medicinal syrup.

Chlorpheniramine maleate	→ المادة الفعالة (الدواء)	0.4 g
Glycerin	sweeteners / preservative	25.0 mL
Syrup (vehicle)		83.0 mL
Sorbitol solution	same like Glycerin	282.0 mL
Sodium benzoate	preservative	1.0 g
Alcohol	co solvent / preservative	60.0 mL
Color and flavor		q.s.
Purified water, to make		1000.0 mL

Preparation of syrups:

- Syrups should be carefully prepared in clean equipment to prevent contamination. Three methods may be used to prepare syrups (See *Remington's* for a full explanation):
 - Solution with heat
 - Agitation without heat
 - Percolation
- Although the hot method is quickest, it is not applicable to syrups of (thermolabile) or volatile ingredients. المكونات المتطايرة تتجزئ بالحرارة
- When using heat, temperature must be carefully controlled to avoid decomposing and darkening the syrup (caramelization).
undesired ↓

Solution with the aid of heat:

- The use of heat facilitates rapid solution of the sugar and certain other components of syrups; however, caution must be exercised against becoming impatient and using excessive heat.
- Sucrose, a disaccharide, may be hydrolyzed into monosaccharides, dextrose (glucose), and fructose (levulose).
- This hydrolytic ^(ریمی) reaction is **inversion**, and the combination of the two monosaccharide products is invert sugar
- If inversion occur:
 1. the sweetness of the syrup is altered because invert sugar is sweeter than sucrose,
 2. and the normally colorless syrup darkens because of the effect of heat on the levulose portion of the invert sugar.

another name: ^{تبدیل} fructose

Solution by agitation without the aid of heat:

- To avoid heat-induced inversion of sucrose
- On a small scale, sucrose and other formulative agents may be dissolved in purified water by placing the ingredients in a vessel larger than the volume of syrup to be prepared, permitting thorough (agitation of the mixture.)
- This process is more time consuming than the use of heat, but the product has maximum stability.

Solution by agitation without the aid of heat:

- When solid agents are to be added to a syrup, it is best to dissolve them in minimal amount of purified water and incorporate the resulting solution into the syrup.
- When solid substances are added directly to a syrup, they dissolve slowly because:
 1. the viscous nature of the syrup does not permit the solid substance to distribute readily throughout the syrup to the available solvent
 2. and also because a limited amount of available water is present in concentrated syrups.

not commonly used these days.

Percolation [←] (filtration)

- In the percolation method, either sucrose may be percolated to prepare the syrup or the source of the medicinal component may be percolated to form an extractive to which sucrose or syrup may be added. (gelatin) ^{mem}
- **percolation** (from Lat. *percōlāre*, to filter or trickle through) refers to the movement and filtering of fluids through porous materials



Elixirs

- Elixirs are clear, sweetened hydro alcoholic solutions intended for oral use and are usually flavored to enhance palatability.
- Nonmedicated elixirs are employed as vehicles and medicated elixirs are employed for the therapeutic effect of the medicinal substances
- In comparison with syrup elixirs are:
 - Less sweet
 - Less viscous
 - Less effective in masking bitter taste
 - Better able to maintain both water soluble and alcohol soluble components in solution
 - Easier to prepare thus, from a manufacturing standpoint, elixirs are preferred to syrups.

Elixirs

- Each elixir requires a specific blend of alcohol and water to maintain all of the components in solution.
- 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 addition to alcohol and water, other solvents, such as glycerin and propylene glycol, are frequently employed in elixirs as adjunctive solvents.
- Elixirs containing over 10-12% of alcohol are usually self-preserving and do not require the addition of antimicrobial preservative.

→ زيادة تركيز
الكحول

as co-solvents →
affects

Elixirs

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

Table 1.1 Phenobarbital Elixir

Phenobarbital (therapeutic agent)	0.4% w/v
Orange oil (flavour)	0.025% v/v
Propylene glycol (co-solvent)	10% v/v
Alcohol	20% v/v
Sorbitol solution (sweetener)	60% v/v
Colour	As required
Purified water	ad 100%

Preparation of elixirs

بندرج للمواد الذائبة في الكحول
في الكحول

المواد الذائبة في الماء في الماء فبندرج كل مادة في المذيب تبعها

- Alcohol-soluble and water-soluble components are generally dissolved separately in alcohol and in purified water,

respectively. ← على التوالي

بالترتيب الاضافة روح تكون :

①

on

- 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.

اذا كانت الاضافة بالعكس الكحول روح يتجز فبتقل نسبة الكحول في ال mixture
فالتالي خردج للمواد الذائبة في الكحول من ال Elixir

Preparation of elixirs

في ار Final mixture بتقل نسبة
الكحول في Elixir فبعض المواد التي كانت
ذائبة في الكحول بتقل ذائبتها فيصير cloudy

- Frequently, the final mixture will be cloudy, principally because of separation of some of the flavoring oils by the reduced alcoholic concentration. soluble in alcohol

- 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

(يتجمعوا) (coalesce) so that they may be more easily removed by filtration.

- Talc بودرة 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.

Elixirs

- For elixirs the pharmacist should be aware about:
 - If the patient receives concurrent medicines that possess an antabuse-like activity
 - If the patient is receiving another drug that causes drowsiness

Tinctures

- Tinctures are alcoholic or hydroalcoholic solutions prepared from vegetable materials or from chemical substances.
- Wikipedias: A **tincture** is typically an alcoholic extract of plant or animal material or solution of such or of a low volatility substance (such as iodine). ⇒ *iodine tincture*: *يعني مذوبينه في alcoholic or hydroalcoholic*
- Tinctures contain alcohol in amounts ranging from approximately 15% to 80%.
- The alcohol content protects against microbial growth and keeps the alcohol-soluble extractives in solution
- When they are prepared from chemical substances (e.g., iodine), tinctures are prepared by simple solution of the chemical agent in the solvent



Tinctures

- Tinctures have a rather high alcoholic content
- Because of the alcoholic content, tinctures must be tightly stoppered and not exposed to excessive temperatures and should be stored in light-resistant containers and protected from sunlight.



Tinctures

IODINE TINCTURE *(Hydroalcoholic solution)*

- Iodine tincture is prepared by dissolving 2% iodine crystals and 2.4% sodium iodide in an amount of alcohol equal to half the volume of tincture to be prepared and diluting the solution to volume with sufficient purified water.
- The tincture is a popular local anti-infective agent applied to the skin in general household first aid.
- The reddish-brown color, which produces a stain on the skin, is useful in delineating the application over the affected skin area.
- The tincture should be stored in a tight container to prevent loss of alcohol.

Topical solutions vs. tinctures

- Generally, the topical solutions employ an aqueous vehicle whereas the topical tinctures employ an alcoholic vehicle.

Examples	Use
Aluminum acetate topical solution	astringent
Coal tar topical solution	Local antieczematic
Hydrogen peroxide topical solution Povidone Iodine topical solution (<i>water used</i>) Thimerosal topical solution Iodine tincture (<i>alcoholic used</i>) Thimerosal tincture //	Anti-infective, anti-bacterial, antiseptic

Sprays

(زيتي)

ممکن ہے کہ
powder ←

- Sprays are aqueous or oleaginous solutions in the form of coarse droplets or as finely divided solids to be applied topically, most usually to the nasopharyngeal tract or to the skin
- To achieve the break up of solution into small particles so that it may be effectively sprayed or to facilitate the spraying of powders, several mechanical devices have been developed.
- Many commercial sprays are used intranasally to relieve nasal congestion and inflammation. Intranasal administration administer drugs to the upper respiratory tract.
- Other sprays that are employed against sunburn and heat burn contain local anesthetics, antiseptics, skin protectants, and antipruritics.
- All medications intended for external use should be clearly labeled for external use only and kept out of the reach of children

(منفلة الفم)

→
تخديرات صوف منعيه
المطهرات

→
مضادات
الحكة

Sprays

- The absorption of some drugs intranasally give blood concentrations that are very similar to concentrations seen when the drug is intravenously administered.
- Because of this favorable absorption, intranasal administration has been investigated as a possible route of systemic administration for drugs such as insulin, glucagon, progesterone, propranolol, and narcotic analgesics (to mention a few).

Sprays

Commercially available sprays include:

Intranasal sprays

- Contain antihistamines, decongestants, sympathomimetics.
- Because of the noninvasive nature and the quickness with which nasal sprays can deliver medications systemically, the future will demonstrate the administration of several drugs by this route.

(Throat) sprays

- May be effectively employed to (relief states) like sore throat, laryngitis, halitosis.
- Contain antiseptics, deodorants and flavorants. (المنكهات)

Skin sprays

- These are applied for:
 - Fungal infections (in foot)
 - Against sun burn (contain local anesthetics, antiseptics, skin protectants and antipruritics).
 - For cosmetic uses.

لا تخترق الجلد
يعمل له
امتصاص

رائحة الفم الكريهة، التهاب الحنجرة، (ألم الحلق) → (تحفف حالات)

المطهرات

Vaginal and rectal solution:

- Vaginal douches:
 - solutions for irrigation cleansing of the vagina. prepared from either powder or liquid concentrate
 - The powders may be prepared and packaged in bulk or as unit packages.
 - The user simply adds the prescribed amount of powder or prescribed volume of liquid concentrate to the appropriate volume of warm water and stirs until dissolved.
 - Douches are used for their hygienic effects. A few douche containing specific therapeutic anti-infective agents

Vaginal and rectal solution:

Evacuation Enema:

- These are rectal enema used to cleanse the bowel
- Commercially, many enemas are available in disposable plastic squeeze bottles
- The agents present are solutions of sodium phosphate and sodium biphosphate, glycerin and docustae potassium, and light mineral oil. عباره عن املاح :-
- The patient should be told that the product will most probably work within 5 to 10 minutes.

Topical oral (dental) solution:

- A variety of medicinal agents are employed topically in the oral cavity for a number of purposes.
- These include:
 - Local anesthetics
 - Anti-infective agents
 - Cleansing agents
 - Analgesics → المسكنات
 - Saliva substitutes → للناسي التي عندها نقص في افراز اللعاب
 - Dental caries prophylactics → الوقاية من خوس الأسنان
 - Antifungals
 - Anti-inflammatory agents
صناد التهاب

الماء المعطر

Aromatic Water

- Aromatic waters are clear aqueous solutions saturated with volatile oils or other volatile or aromatic substances.
- Aromatic waters are no longer in wide-spread use.
- They were prepared from a number of volatile substances including: orange oil, rose oil, anise oil, peppermint oil, camphor and chloroform.
زيت الياسون زيت النعناع
- Aromatic waters may be used in perfuming and/or flavoring
- Most of the aromatic substances in the preparation of aromatic waters have very low solubility in water, and even though the water may be saturated, its concentration of aromatic material is still rather small

Aromatic water

- A dispersant (1-3 gm of talc per 100 ml of solution) is used
- The volatile substance is first mixed with talc, then the water is added and the mixture is agitated periodically over a period of time
- Finally the aromatic water is collected by filtration
- Talc:
 1. increases the surface area of the volatile substance that is exposed to water to facilitate saturation of the solution with volatile substances (dispersing agent)
 2. Also used as a clarification agent (remove haziness) to remove excess volatile oil from a solution by making aromatic water first and then added to the talc. The mixture is agitated briefly then filtered

Spirits

- Spirits are alcoholic and hydroalcoholic 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.

• Spirits can be prepared by:

• Simple solution

• Solution by (maceration) ^{التقعير}

• Distillation

(Volatile oil + hydroalcoholic)

نذوبهم مع بعض

الجزء المراد استخلاصه من النبات على سبيل المثال

Spirits

Maceration

- It is a process in which the properly ^{hydroalcoholic} comminuted ^{منقسم} drug is permitted to soak in the menstruum until the cellular structure is softened and penetrated by the menstruum and the soluble constituents are dissolved.
- Maceration is usually conducted at a temperature of 15°C to 20°C for 3 days or until the soluble matter is dissolved.

Spirits

- Spirits may be used
 - pharmaceutically as flavoring agents
 - medicinally for the therapeutic value of the aromatic solute
 - Taken orally (generally mixed with a portion of water)
 - Applied externally
 - Used by (inhalation) → الاستنشاق
- Peppermint spirit is an example of official spirit

قدِيمًا تُسَمَّى (لبخات)

Liniments:

- Liniments are alcoholic or oleaginous solutions or emulsions of various medicinal substances intended to be rubbed on the skin. (وضعها على البشرة)
- Liniments are not applied to skin areas that are broken or bruised because excessive irritation might result. كدمات
- All liniments should bear a label “for external use only”
- The vehicle for liniments should be selected on the basis of:
 - 1) type of action desired (rubefacient, counterirritant or just massage)
 - 2) The solubility of ingredients in various solvents

Liniments

for
muscle
pain
and rubbing it
on the skin



- **Liniment** (or embrocation), from the Latin *linere*, to anoint, is a medicated topical preparation for application to the skin. Sometimes called balms, liniments are of a similar or lesser viscosity than lotions and are rubbed in to create friction, unlike lotions, ointments or creams.^{[1][2]}
- Liniments are typically sold to relieve pain and stiffness, such as from sore muscles or arthritis. These are typically formulated from alcohol, acetone, or similar quickly evaporating solvents and contain counterirritant aromatic chemical compounds such as methyl salicylate, benzoin resin, or capsaicin. (Wikipedia)

زصلب

it's taken of the pepper to make irritation.

Liniments:

Liniments with alcoholic or hydroalcoholic vehicles

- are useful in instances in which rubefacient, counterirritant, or penetrating action is desired.

Oleaginous liniments

- are employed primarily when massage is desired.
- Less irritating than alcoholic liniments
- The solvent may be:
 - a fixed oil (ex, almond oil, peanut oil, sesame oil, or cottonseed oil)
 - a volatile substance (cx. Wintergreen oil, turpentine)
 - combination of volatile and fixed oils

بجيت يحون
معنا للتهديج

Collodions:

- Liquid preparations containing nitrocellulose proxylin in a mixture of alcohol and ethyl ether.
- They are used as topical protective or as a topical drug vehicle and are made “flexible” by the addition of castor oil.

- e.g. Flexible Collodion USP, Salicylic Acid Collodion USP

contains castor oil

Collodions

يجف و يصير طبقة شفافة

- **collodion** dries to a transparent, tenacious film;
- used as:
 - a topical protectant,
 - to close small wounds, abrasions, and cuts,
 - to hold surgical dressings in place,
 - and to keep medications in contact with the skin
- There are two basic types: flexible; non-flexible.
- While it is initially colorless, it discolors over time.



Collodions

- **Flexible Colloidon**

USP:

- A preparation of camphor, castor oil, and collodion
- Used as a topical protectant

- **Salicylic Acid**

Colloidon USP:

- Flexible collodion containing salicylic acid
- Used topically as a keratolytic

Fluid extracts:

- are liquid preparations of vegetable drugs prepared by percolation. They contain alcohol as a solvent, preservative, or both and are made so that each milliliter contains the therapeutic constituents of 1 g of the standard drug that it represents.
- Because of their concentrated nature, many fluid extracts are:
 1. considered too potent to be self administered
 2. too bitter and unpalatable
 3. and their use per se is almost not existent in medical practice.
- most fluid extracts today are either modified by the addition of flavoring or sweetening agents before use or used as the drug source of other liquid dosage forms, such as syrups.

Non-Aqueous Solutions

- **Glycerins or Glycerites** are solutions composed of no less than 50% glycerin by weight. They are extremely viscous and are rarely used in practice and are generally limited to use in topical products, e.g. Glycerin Otic Solution. قطرات الأذن →
- **Oleaginous Solutions** are solutions of fat soluble vitamins (Vitamin A, O, and E), or other fat soluble substances in vegetable oils (corn, cottonseed, olive, peanut, and sesame seed oils) or mineral oil. Oleaginous solutions may be formulated for oral, topical or parenteral administration.

↳ intra muscular

Liquid Aliquot Method

- Can be used when a formulation calls for an amount of drug that is less than what can be weight by balance
- Example:
 - Prepare 100 ml of a solution contain 0.2 mg/ml clonidine
 - Answer:
 1. $100 \text{ ml} * 0.2 \text{ mg/ml} = 20 \text{ mg}$ clonidine
 2. 20 mg is less than the least weighable quantity (120 mg is the least weighable quantity for class A balance)
 3. Select a volume of solution that is large enough to solubilize the drug but small enough so it does not exceed the total volume of prescription

Liquid Aliquot Method;

- Clonidine solubility in water is 1 gm/13 ml
- If 5 ml is selected as the aliquot volume the concentration in that solution will be 20 mg / 5 ml
- 120mg → ? ml water
20 mg → 5 ml (aliquot)

30ml water

So prepare 120 mg of clonidine in 30 ml water and take 5 ml from this solution to another container and bring it to its final volume (100 ml)

Packaging

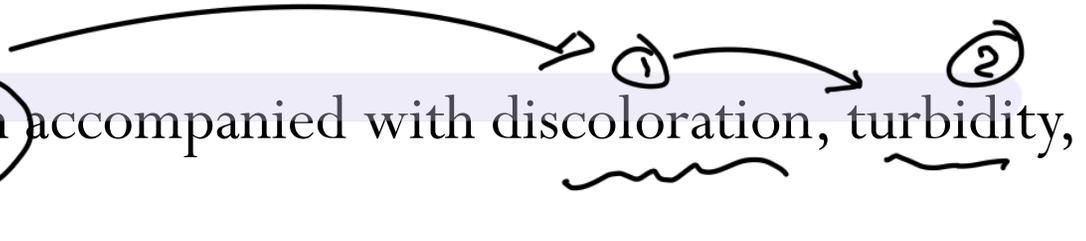
حسب التركيبة
والهدف والعجم

- Solutions are used for many different purposes and route of administration
- Packaging are diverse and vary from simple prescription bottles to sprays and nebulizers to roll on applicators to parenteral containers such as vials and bags

Observing formulations for evidence of instability

صغير مواد حافظه

- Beyond use date for aqueous solutions without preservative is 14 days if stored at cold temperature

- (Microbial growth) accompanied with discoloration, turbidity, gas formation (3)
- 

- Precipitation in a solution (4)