Ministry of Higher Education and Scientific Research
Al- Rasheed University College-Department of Pharmacy

Pharmaceutical Technology for 3rd year students, Lec. #2, 2018

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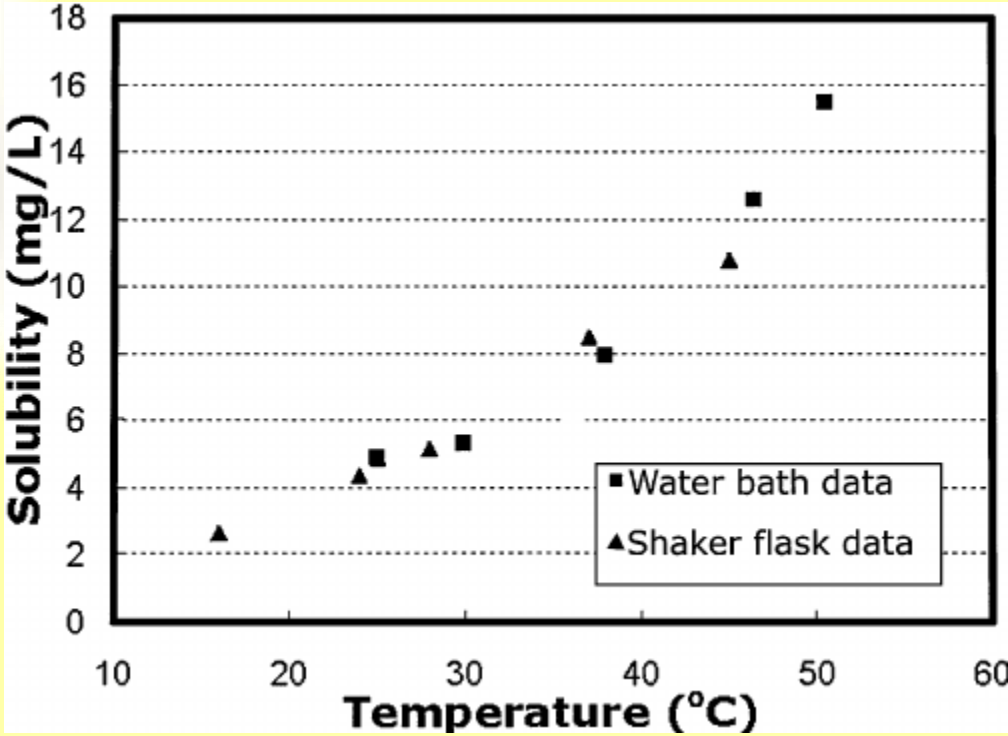
Pharmaceutics PhD.

Solubility Measurement:

- ✓ The amount of solvent required to dissolve the amount of solute can be determined by a simple calculation, & The solubility may then be expressed **as grams of solute** dissolving in **milliliters of solvent**;


Solubility (mg/L)
0
2
4
6
8
10
12
14
16
18
10
20
30
40
50
60
Temperature (°C)
Water bath data
Shaker flask data

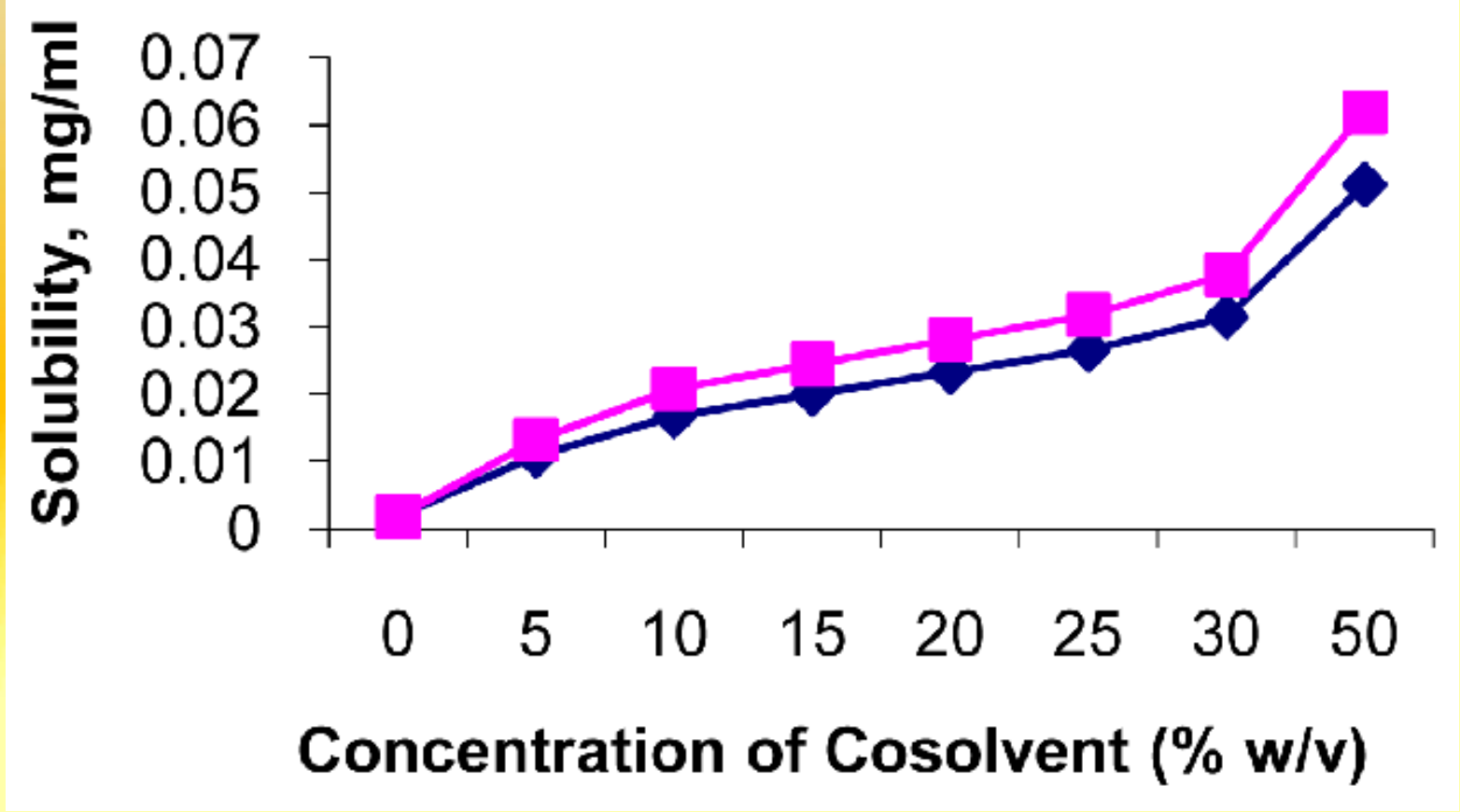
Enhancement of Drug Solubility

1- pH Adjustment

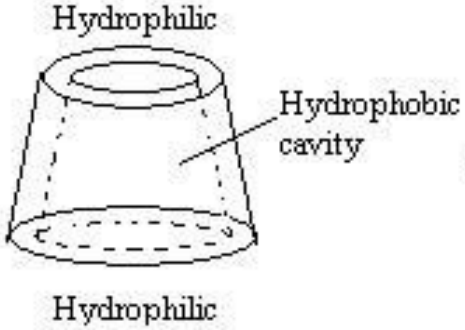
2- Co – Solvents

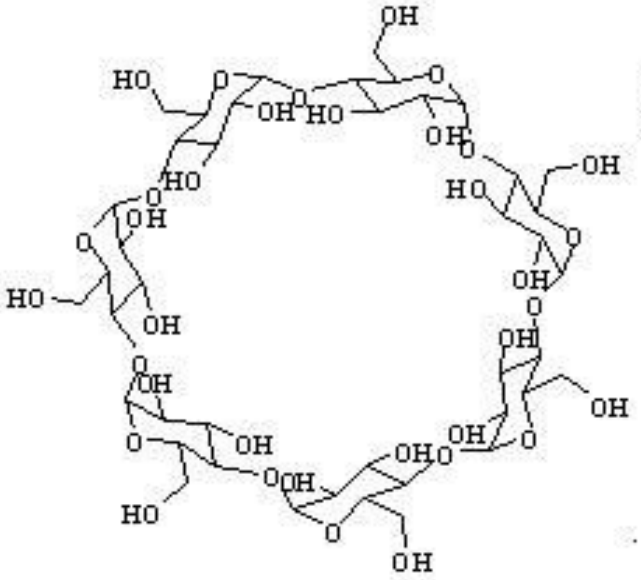
Cosolvency and micellization techniques have been severally used to enhance the solubility of poorly aqueous soluble drugs.

➢Typically, a linear increase in co–solvent fraction results in logarithmic increases in drug solubility.

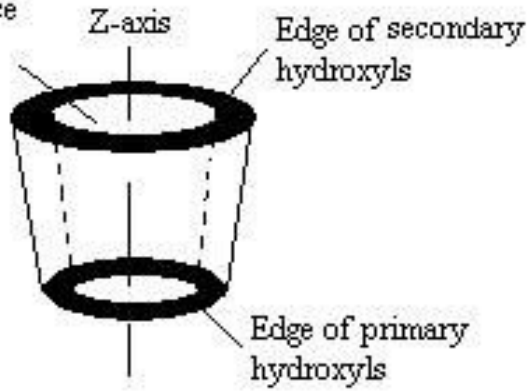

Solubility, mg/ml
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
5
10
15
20
25
30
50
Concentration of Cosolvent (% w/v)

3- Complexation with Cyclodextrins (CDs)

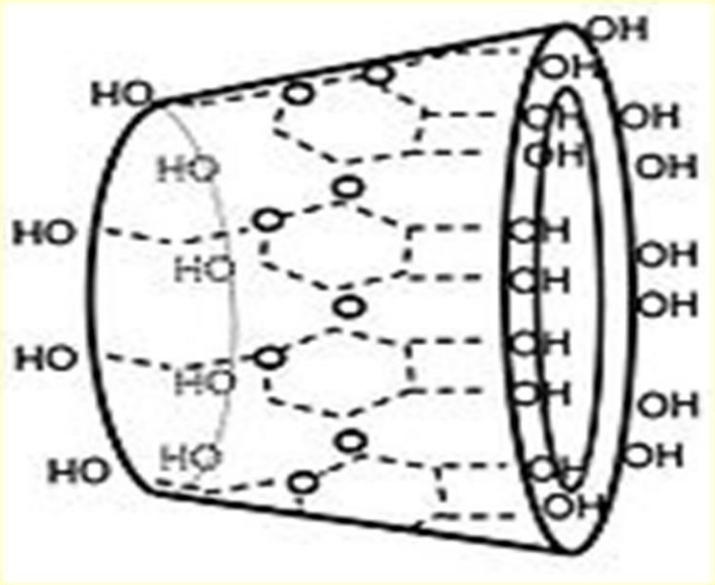




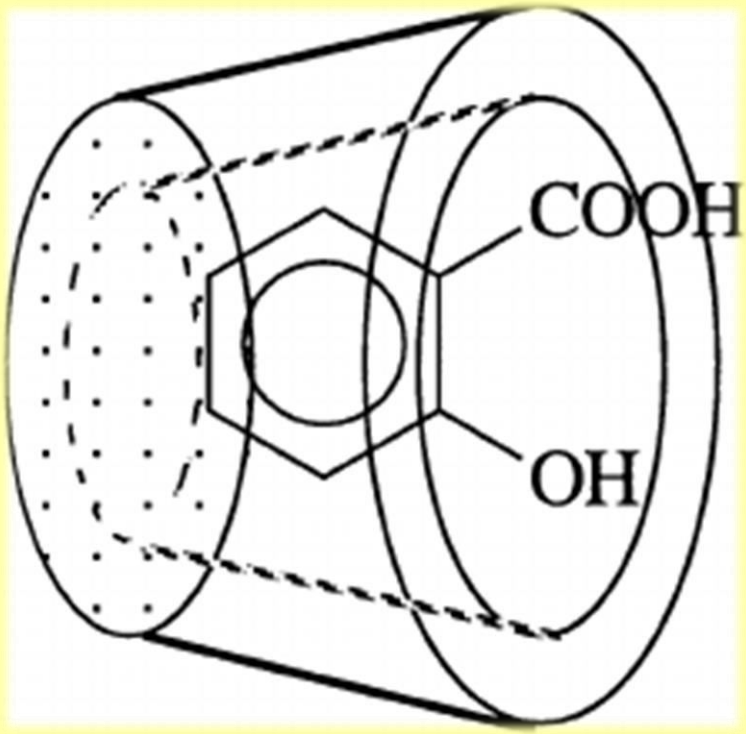
The interior surface of the cavity



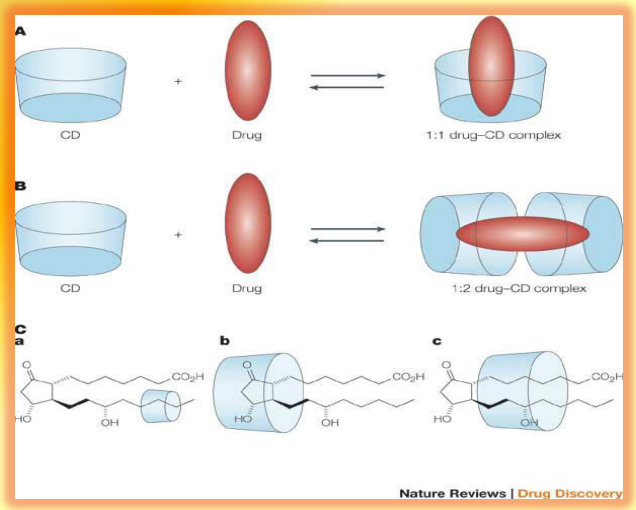
✓ The hydrophilic exterior results in CDs being soluble in water.



- ✓One of the striking feature of CDs is their ability to form **inclusion complexes** with a variety of compounds



- ✓CD-complexing agent are often used, in pharmaceutical formulation of **oral products**, to **increase the bioavailability** of **poorly water soluble or unstable drug.**



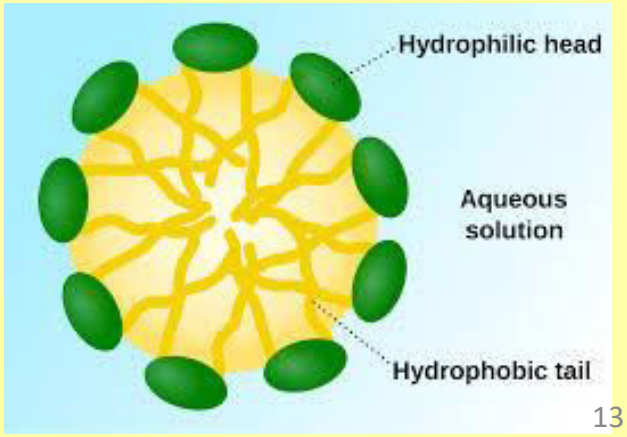
➢ Furthermore, a number of safety evaluations have shown that γ–cyclodextrin,
2-hydroxypropyle-β-cyclodextrin,
sulphobutylether β–cyclodextrin,
sulphated β– cyclodextrin and maltosyl β–cyclodextrin appear to be safe even when administered parenterally.

4- Surfactants and Micelles

✓They reduce the surface tension of liquids, and forming micelles once the

critical micellar concentration

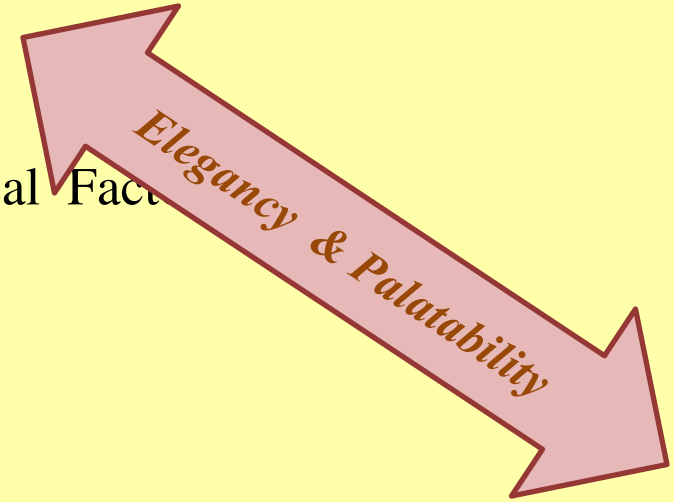
(CMC) is reached.



- ✓ Microbial contamination,
  Light,
  Atmospheric oxygen
  humidity
  Temperature,

  } Enviromental Factors
- ✓ Hydrolytic degradation & autoxidation } Chemical Fact
- ✓ Precipatation,
  alteration in color, odor,
  & viscosity

  } Physical Factors



Solvents for Pharmaceutical Use

1- Water:

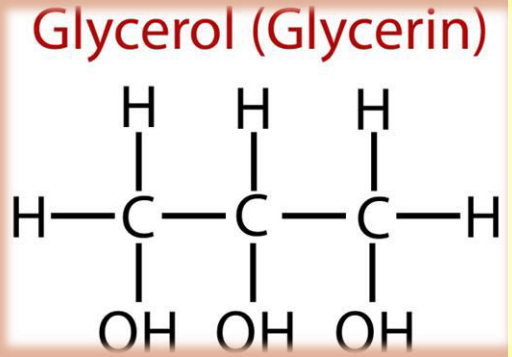
2- Alcohol (ethyl alcohol or ethanol) :

3- Dehydrated alcohol

4- Isopropyl alcohol :

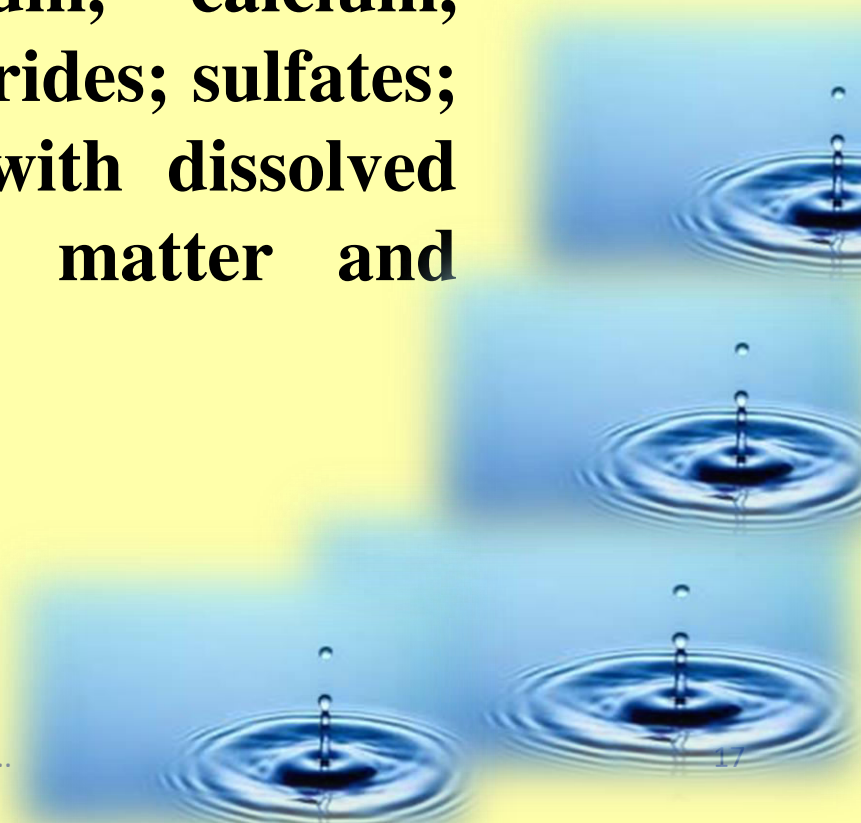
5- Glycerin USP (Glycerol)

6- Propylene Glycol



Purified Water, USP, H2O

- ✓ **Naturally occurring water** exerts its solvent effect on most substances it contacts and, thus, is **impure, containing varying amounts of dissolved inorganic salts**, usually **sodium, potassium, calcium, magnesium, and iron; chlorides; sulfates; and bicarbonates, along with dissolved and undissolved organic matter and microorganisms.**



- ✓Signs of such incompatibilities are precipitation, discoloration, and occasionally effervescence.

- Purified Water, USP, has fewer solid impurities than ordinary drinking water & When evaporated to dryness, it must not yield more than **0.001% of residue**

- Thus, purified water has only 1% as much dissolved solids as tap water.

- Purified Water, USP, is obtained by;

1- distillation method.

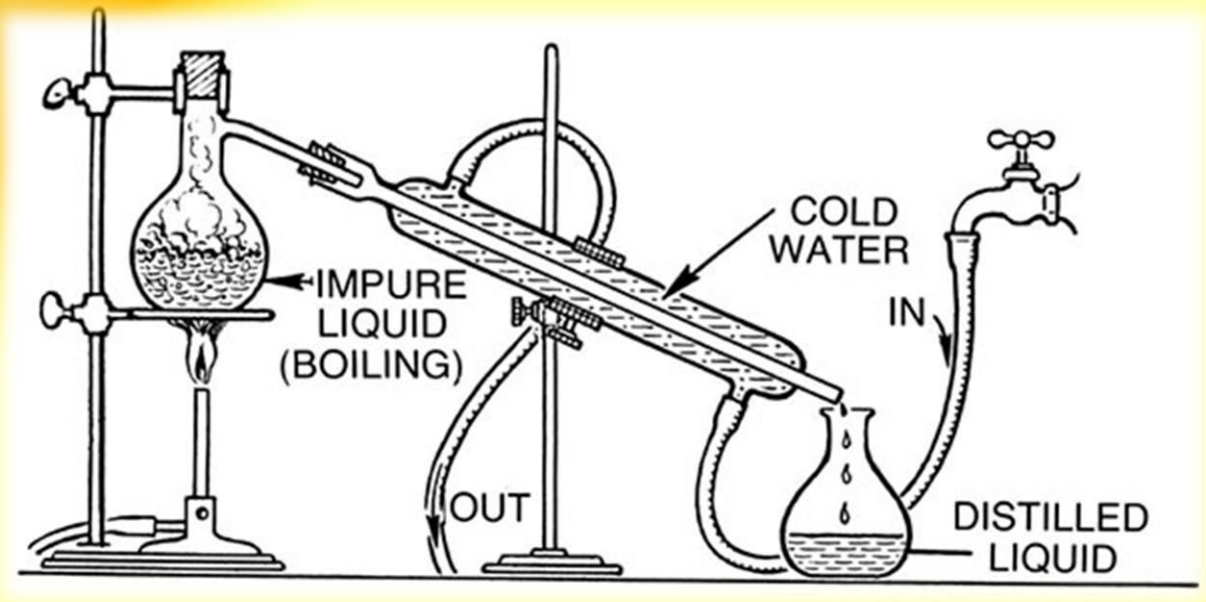
2- ion exchange treatment,

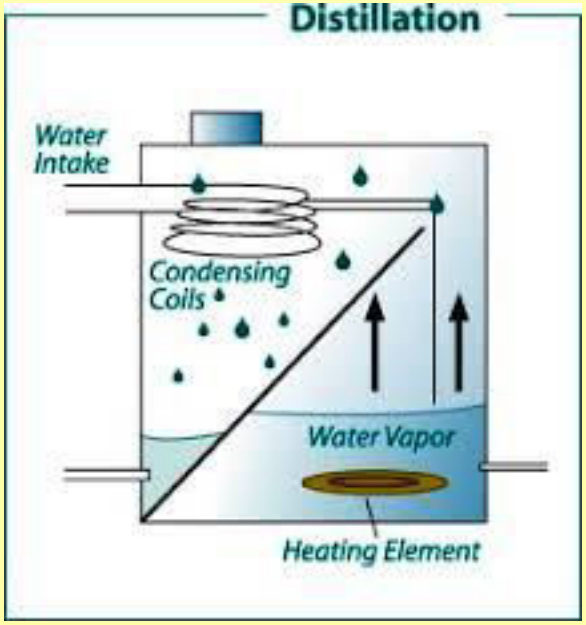
3- reverse osmosis method.

1- Distillation Method

Many stills in various sizes and styles with capacities ranging from about 0.5 to 100 gallons of distillate per hour are available to prepare purified water.

the last portion of water (about 10% of the original volume of water) remaining in the distillation apparatus must be discarded and not subjected to further





Distillation Method

2- Ion Exchange Method

- ✓ On a large or small scale, ion exchange for the preparation of purified water offers a number of advantages over distillation; .

1. The requirement of heat is eliminated,
2. The costly & troublesome maintenance frequently encountered in the operation of the more complex distillation apparatus.
3. Because of the simpler equipment & the nature of the method, ion exchange permits ease of operation, minimal maintenance, and a more mobile facility.

✓These resins are mainly of two types:

(a) the **cations,** or **acid exchangers**, which permit the exchange of the **cations** in solution (in the tap water) with **hydrogen ion** from the **resin**, and

(b) the anions, or **base exchange** resins, which permit the removal of anions.

These two processes are successively employed to remove cations and anions from water.

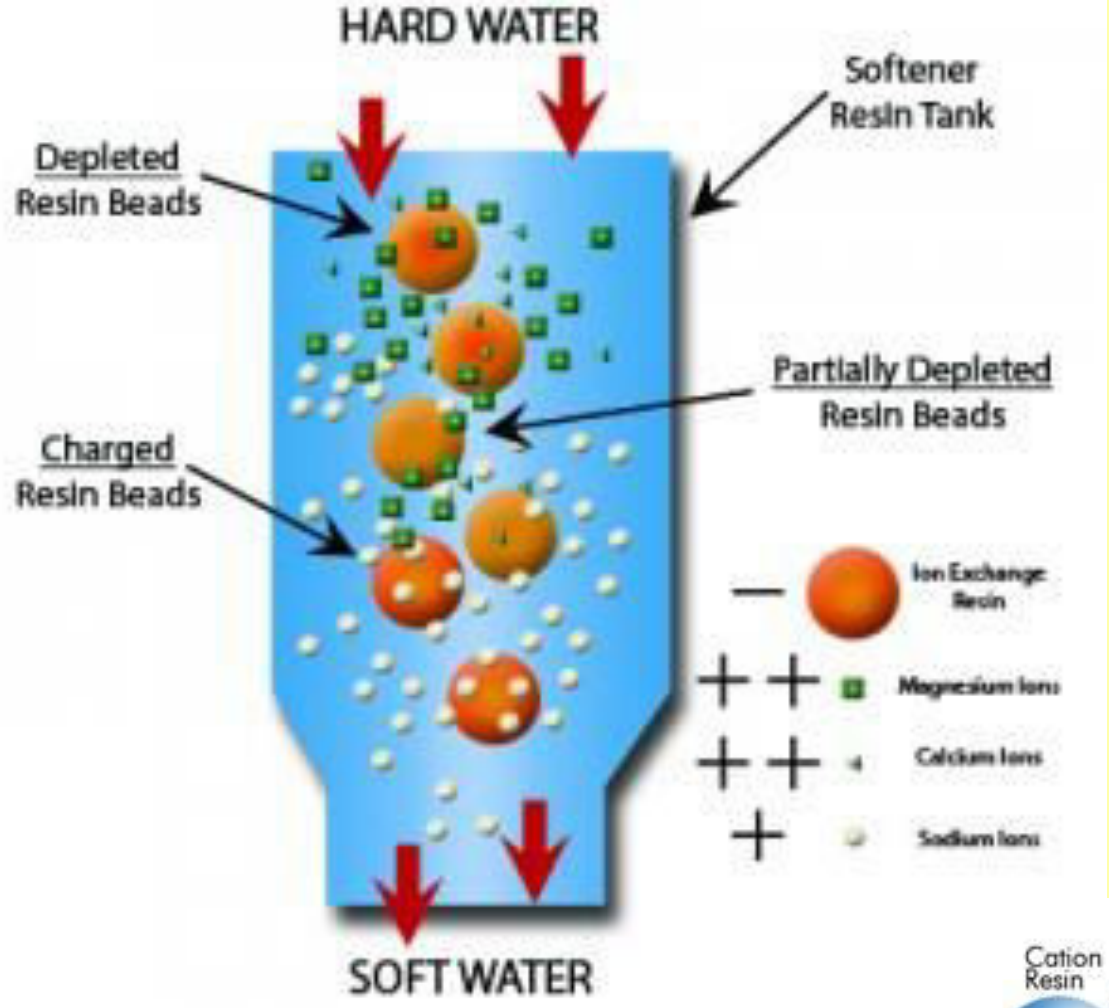
- ✓ **with M+ indicating the metal or cation (as Na+) and the X− indicating the anion (as Cl−).**

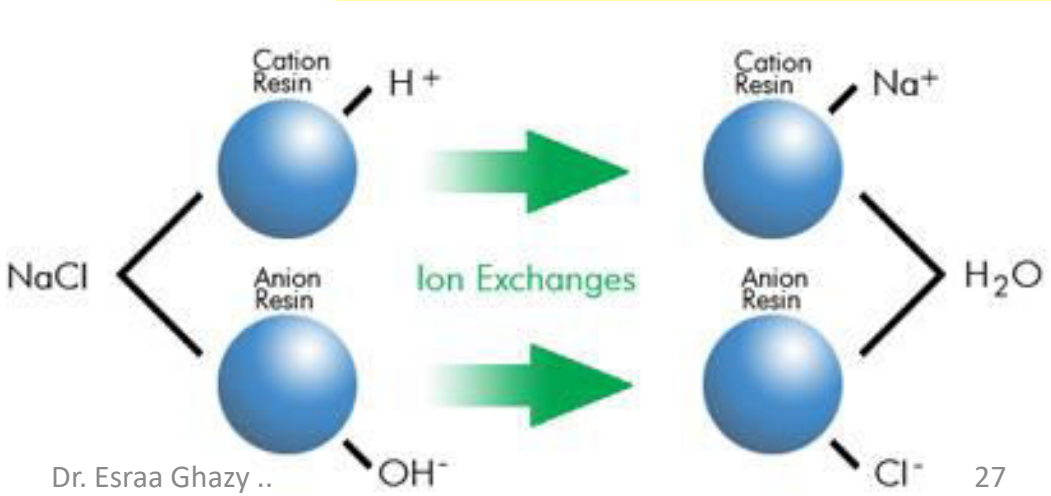
1-Acid or cationic exchanger

$$H\text{- resin} + M^+ + X^- + H_2O \rightarrow M\text{-resin} + H^+ + X^- + H_2O \text{ (pure)}$$

2- Base or anionic exchanger

$$Resin\text{-}NH_2 + H^+ + X^- + H_2O \rightarrow Resin\text{-}NH_2 + HX + H_2O \text{ (pure)}$$


HARD WATER
Softener
Resin Tank
Depleted
Resin Beads
Partially Depleted
Resin Beads
Charged
Resin Beads
Ion Exchange
Resin
Magnesium Ions
Calcium Ions
Sodium Ions
SOFT WATER


Cation
Resin
H +
Cation
Resin
Na+
NaCl
Anion
Resin
Ion Exchanges
Anion
Resin
H2O
OH-
Cl-

3- Reverse Osmosis

In the industry “Reverse osmosis” is one of the processes referred to 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.

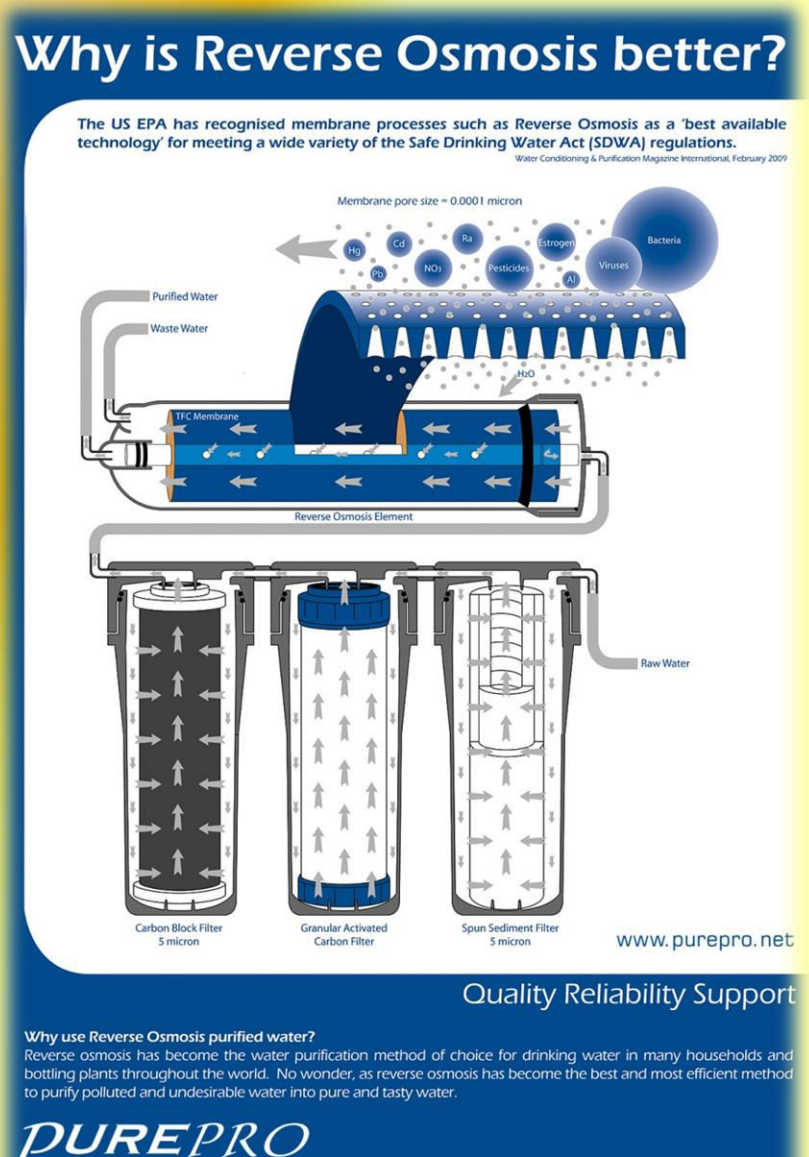
- ✓ Depending on their pore size, cross-flow filter membranes can remove particles defined in the range of

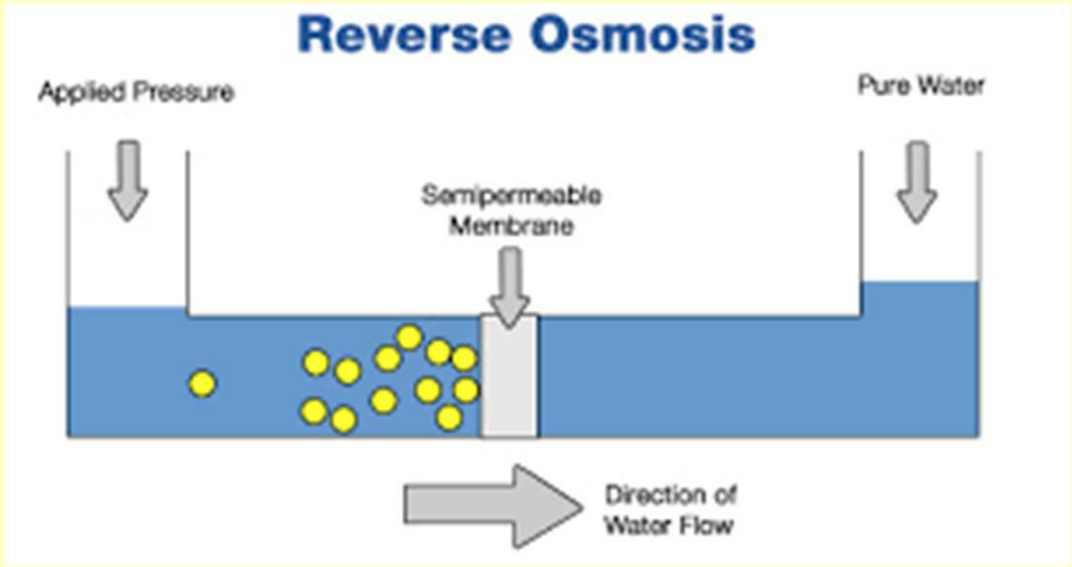
1- microfiltration (0.1 to 2 μm, e.g., bacteria),

2-ultrafiltration (0.01 to 0.1 μm, e.g., virus),

3-nanofiltration (0.001 to 0.01 μm, e.g., organic compounds in the molecular weight range of 300 to 1,000), and reverse osmosis (particles <0.001 μm).

- ✓ Reverse osmosis removes virtually all viruses, bacteria, pyrogens, and organic molecules and 90 - 99% of ions.





Reverse Osmosis Method


AROMATIC WATERS

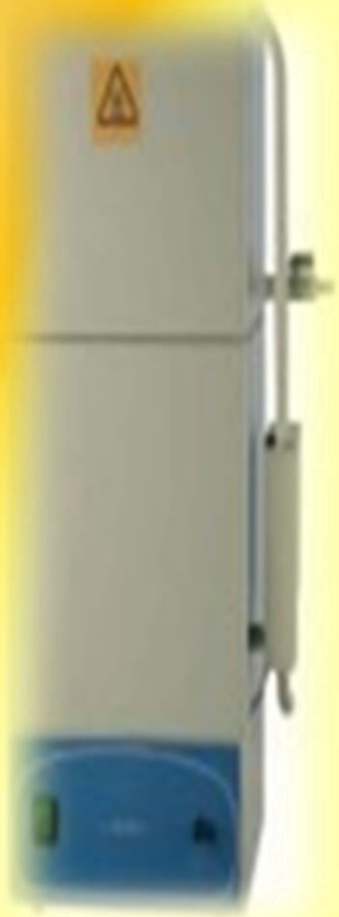
Aromatic waters (flavored & medicated preparations)

- ✓ The British Pharmacopoeia (BP) defines ***Aromatic waters*** are clear, aqueous solutions saturated with volatile oils (characterised by very low water solubilities) or other aromatic or volatile substances.
- ✓ Naturally, they possess an odor and taste similar to that plant or volatile substance from which they are prepared.
- ✓ Aromatic waters are clear and free from solid impurities and are free from empyreumatic (smoke like) or foreign odors.
- ✓ They are examples of simplest formulated dosage forms consisting only of the solvent water & the volatile solute. Ex., Cinnnamon water N.F., Orange flower water N.F. (Aqua Neroli).
- ✓ They include solutions of many chemicals as well as essential oils used in flavoring & perfumery. Ex., peppermint water, chloroform water.
- ✓ Several aromatic waters are not used as vehicle for oral medication. Ex., Rose water N.F., Hamamelis water N.F.

Methods of Preparation Aromatic waters

1- ***Distillation Method***

- involves the placing of the ***coarsely ground odoriferous*** portion of the plant or drug from which the aromatic water is to be prepared with sufficient purified water. Then most of the volume of water is distilled. The excess oil collected with the distillate rises to the top of the aqueous product and is removed. The remaining aqueous solution, saturated with volatile material requires clarification by filtration.
- ***Advantages Vs Disadvantages:***



2. ***Solution Method***

- ✓ In this method, aromatic water is prepared by intermittently shaking 2 ml (if liquid) or 2 g (if solid) of the volatile substance with 1000 ml of purified water in suitable container for a period of 15 minutes. After the period of agitation the mixture is set aside for 12 hours or longer ***to permit the excess oil and the solid substance to settle***. Without further agitation the mixture is passed through a wetted filter paper why?? and purified water added as needed to bring the volume of the filtrate up to the prescribed quantity.
- ✓ ***Advantages Vs Disadvantages:***

3. ***Alternative Solution***

this method, the volatile oil or suitably comminuted aromatic solid is thoroughly incorporated with 15g of powdered talc (or siliceous earth (silica) or pulp filter paper) and to this mixture is added 1000 ml of purified water.

- ✓ The resulting slurry is thoroughly agitated several times for the period of 30 minutes and then filtered.
- ✓ Powdered talc, works as
- ✓ 1- filter aid which renders the formulation more clear

  2- distributing agents for the aromatic substances that ultimately increases the surface area of aromatic substances exposed to the solvent action of water. The distributing agents should be inert in nature.

Advantages Vs Disadvantages:

Time saving factor is an important advantage.

The alternate method has not proven to be entirely satisfactory ???

4- Dilution method

In this method the oil is dissolve in alcohol, prepared the ***concentrate*** which designed to be ***diluted*** with appropriate volume of water when need.

In this method some times S.A.A such as tween is mixed with water to increase the solubility

Advantages Vs Disadvantages:

Easy , time-saving method

Due to presence of alcohol these preparations are prone to alteration in flavor and aroma due to oxidative degradation of the alcohol
Excessive Foam on agitation may formed???

Therapeutic Uses of Aromatic waters

1- Aromatic waters are pharmaceutical aid & used principally for perfuming and flavoring the formulation.

2- They can be used as an excipients or bases or vehicles for formulation of other pharmaceutical preparations.

3- Aromatic waters may be used for some special purposes like,

(a) Camphor water has been used as the vehicle in ophthalmic solutions owning to its ability to contribute refreshing and stimulating effect to the preparation.

(b) Rose water has an antioxidant activity. It cleanses, tones & protects skin from harmful environmental impacts.

(c) Hamamelis water known as witch hazel is employed as a rub, perfume & as an astringent in various cosmetic preparations, particularly in after-shave lotions.

(d) Chloroform water has been used as preservative apart from its flavoring nature.

Storage Conditions of Aromatic waters

- ✓ They should be stored in air tight, light resistance container in cool place & preferably stored in containers which are stoppered with purified cotton to allow access of some air but to exclude dust.

Best Wishes …

Dr. Esraa Ghazy