Pharmaceutical technology

Lecture 3 and 4

Types of waters

Assist. Prof. Dr. Wedad K. Ali

Water

- The most important solvent for pharmaceutical solutions is water.
- The standards for which are found in the USP and specify five degrees of purity. These are entitled as follows

1. Water
2. Purified water (Distilled water)
3. Water for injection
4. Sterile water for injection
5. Bacteriostatic water for injection

Water
Tap water or drinking water
Uses

- It is allowed to use in

1. Washing and the extraction of crude drug
2. In the preparation of products for external use
3. In other preparations in which the difference between water and purified water is of no consequence

- Water, USP, is not suitable for general pharmaceutical use because of considerable amount of dissolved solids present

What is the difference between water and purified water

- The only difference between water and purified water lie in the amount of total dissolved solids.
- A 100 ml water evaporation on steam bath and drying in an oven at 105^{o}C results in not more than 100mg residue, dissolved solids (0.1%).
- A 100 ml purified water on evaporation and drying results in not more than 1 mg dissolved solids (0.001%).
- So purified water 100 times more free of dissolved solids than is water

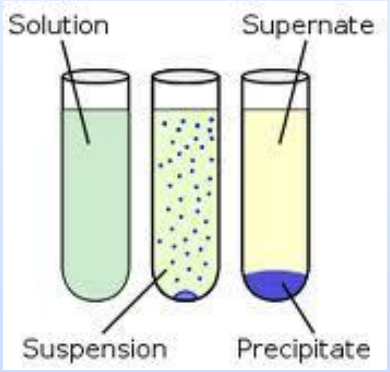
Dissolved solids in water

- Sodium chloride
- Potassium chloride
- Calcium sulfate
- Magnesium bicarbonate

Because of the chemical incompatibilities of dissolved solids present and chemical agent being added; the pharmacist should be aware about specific singes that could be seen during compounding of pharmaceutical solutions.

Signs of incompatibilities

- The development of precipitate



- Effervescence

- Discoloration

Properties of water USP

- Water is clear, colorless and practically tasteless and odorless, even near the boiling point.
- Its pH is neutral or just slightly alkaline.

❖ Note: the deviation from neutrality to slight acidity or alkalinity is due to the composition of the dissolved solids and due to dissolved carbon dioxide or ammonia.

Purified Water, USP

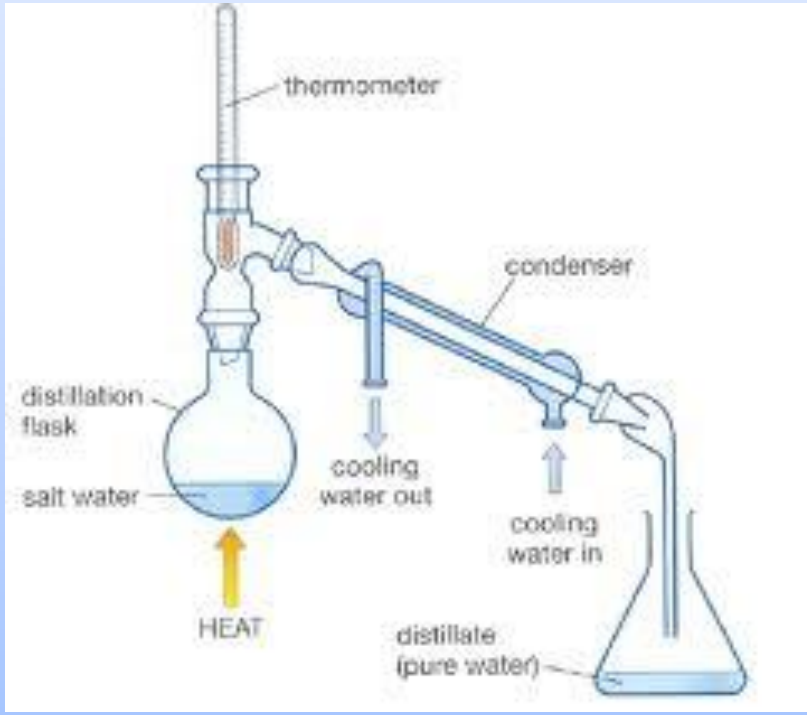
- it is used in the preparation of all medication containing water except ampoules, injections, some official external preparations, such as liniments, and other specialized products.

- Purified water, USP, formerly official as Distilled water, may be prepared by

1. Distillation
2. Deionization
3. Reverse osmosis

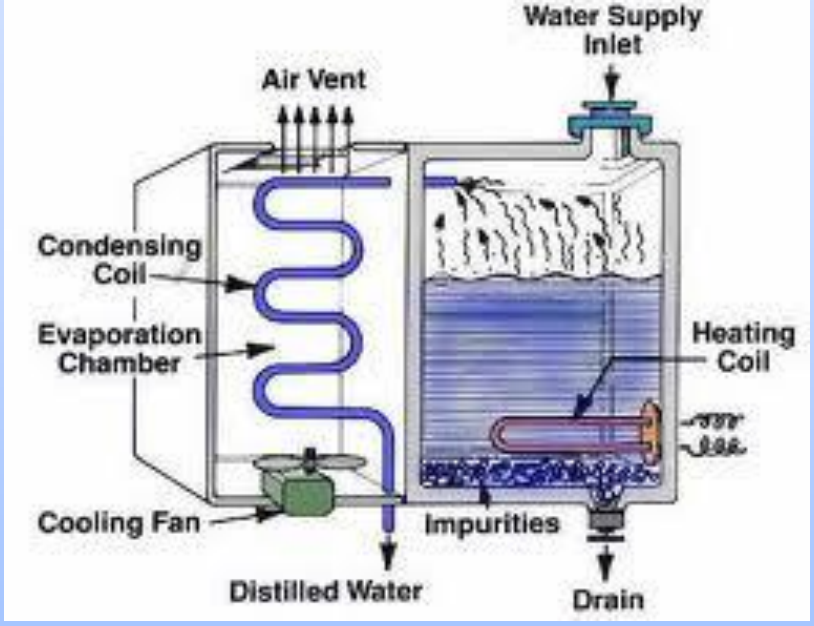
Distillation Method

Distillation involves boiling the water and then condensing the steam into a clean container.



Distillation Method

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

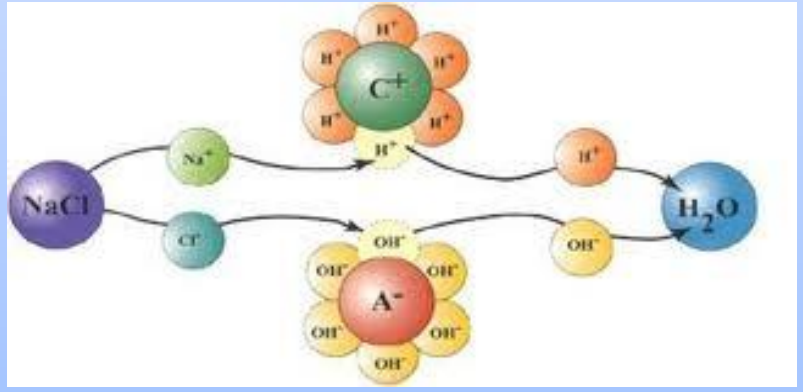


- Generally, the first portion of aqueous distillate (about the first 10% to 20%) must be discarded because it contains many foreign volatile substances usually found in urban drinking water, the usual starting material.
- Also, the last portion of water (about 10% of the original volume of water) remaining in the distillation apparatus must be discarded and not subjected to further distillation because distillation to dryness would undoubtedly result in decomposition of the remaining solid impurities to volatile substances that would distill and contaminate the previously collected portion of distillate.

Deionization methods

- In deionization methods the exchangers are used, they are synthetic, polymeric resins of high molecular weight, which are insoluble in water and characterized by an unusually high content of free amino, sulfonic acid or phenolic functions.
- These resins are mainly of two types;

1. The cation, or acid, exchangers, which permit the replacement of cations in solution with hydrogen ion
2. The anion, or base, exchange resins, which permit the removal of anions.



Advantages of deionization method

- Deionization possess a number of advantages when compared with distillation

1. Elimination of the use of heat
2. Simpler equipment, with less maintenance
3. Lower long-term costs and
4. Ease of production and storage

Deionization processes

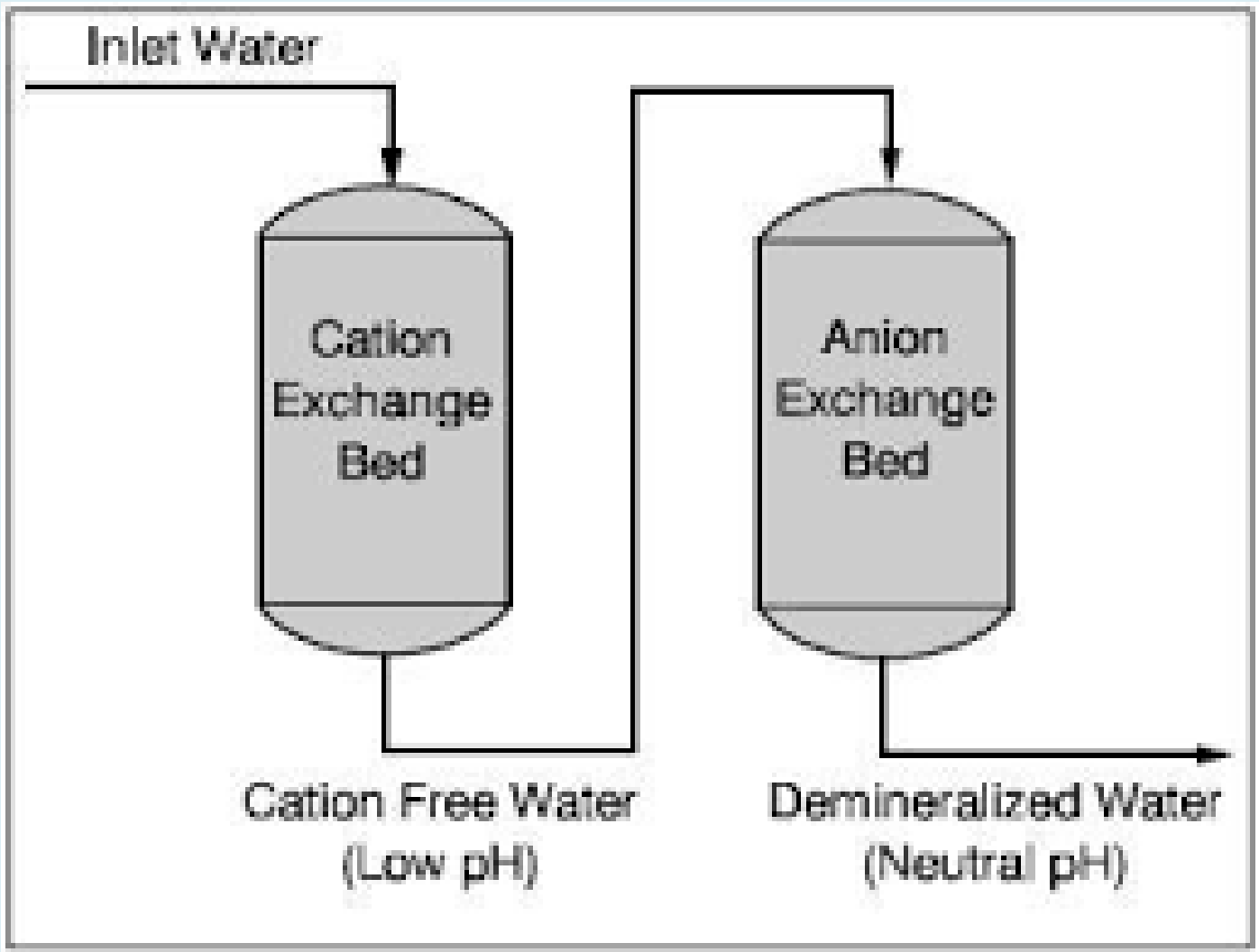
1. Acid or cation, Exchange step: in this step, the cations of the salts are replaced with hydrogen ions. The cations so replaced remain behind, "fixed" to the resin.

- Where M^+ and X^- are the cation and the anion of a salt present in solution.

2. Base, or anion, Exchange step: water is passed through a basic resin (usually a poly amine) and the anion remaining after step 1 is removed according to

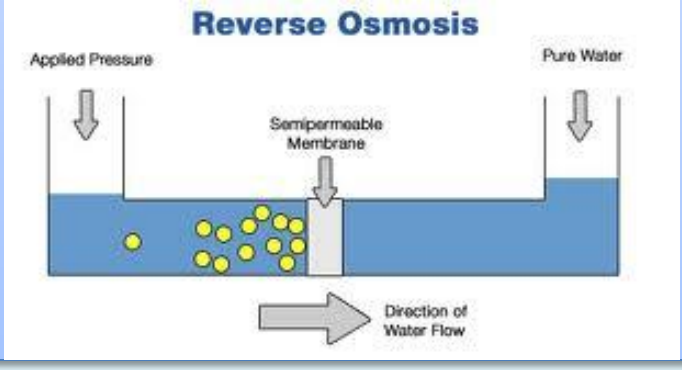
- These two processes are successively or simultaneously employed to remove both cations and anions from water

Ion-exchange equipment
involves the passage of water through a column of cation and anion exchangers



Reverse osmosis

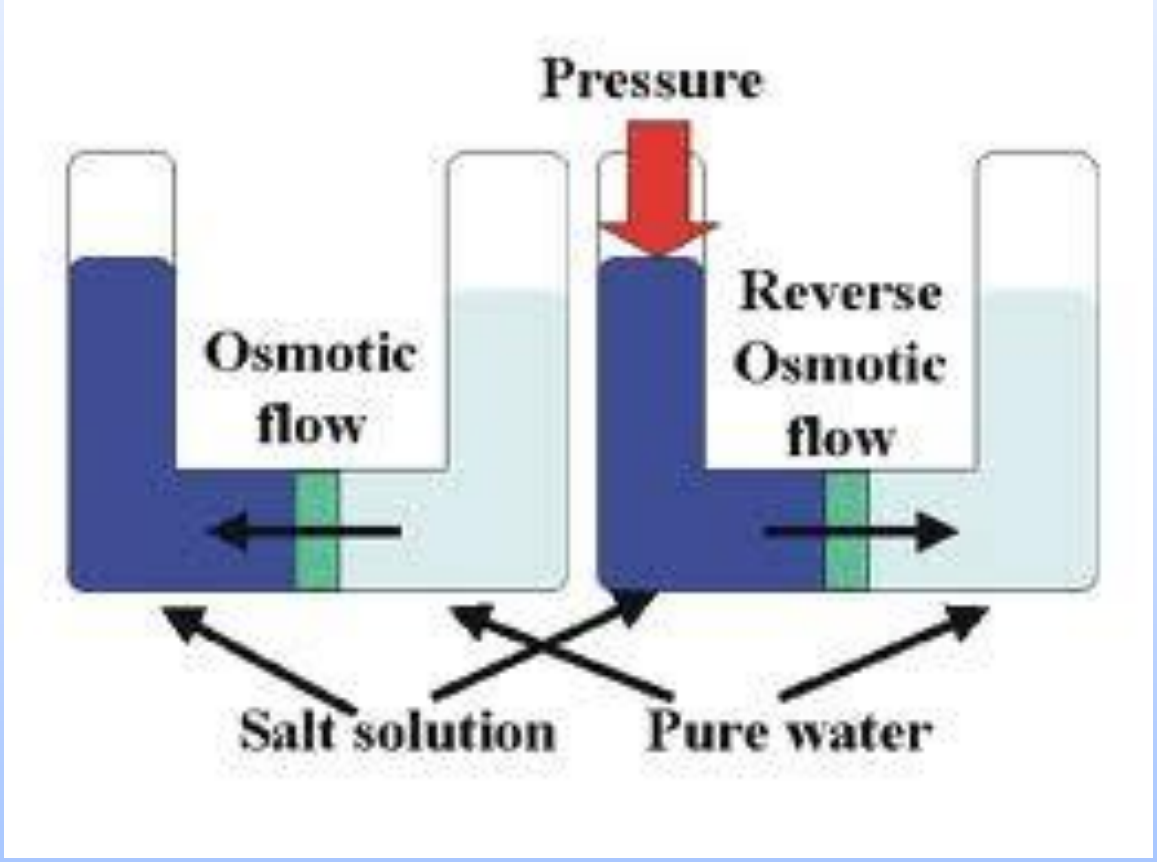
is a membrane-technology filtration method that removes many types of large molecules and ions from solutions by applying pressure to the solution when it is on one side of a selective membrane. The result is that the solute is retained on the pressurized side of the membrane and the pure solvent is allowed to pass to the other side. To be "selective," this membrane should not allow large molecules or ions through the pores (holes), but should allow smaller components of the solution (such as the solvent) to pass freely.

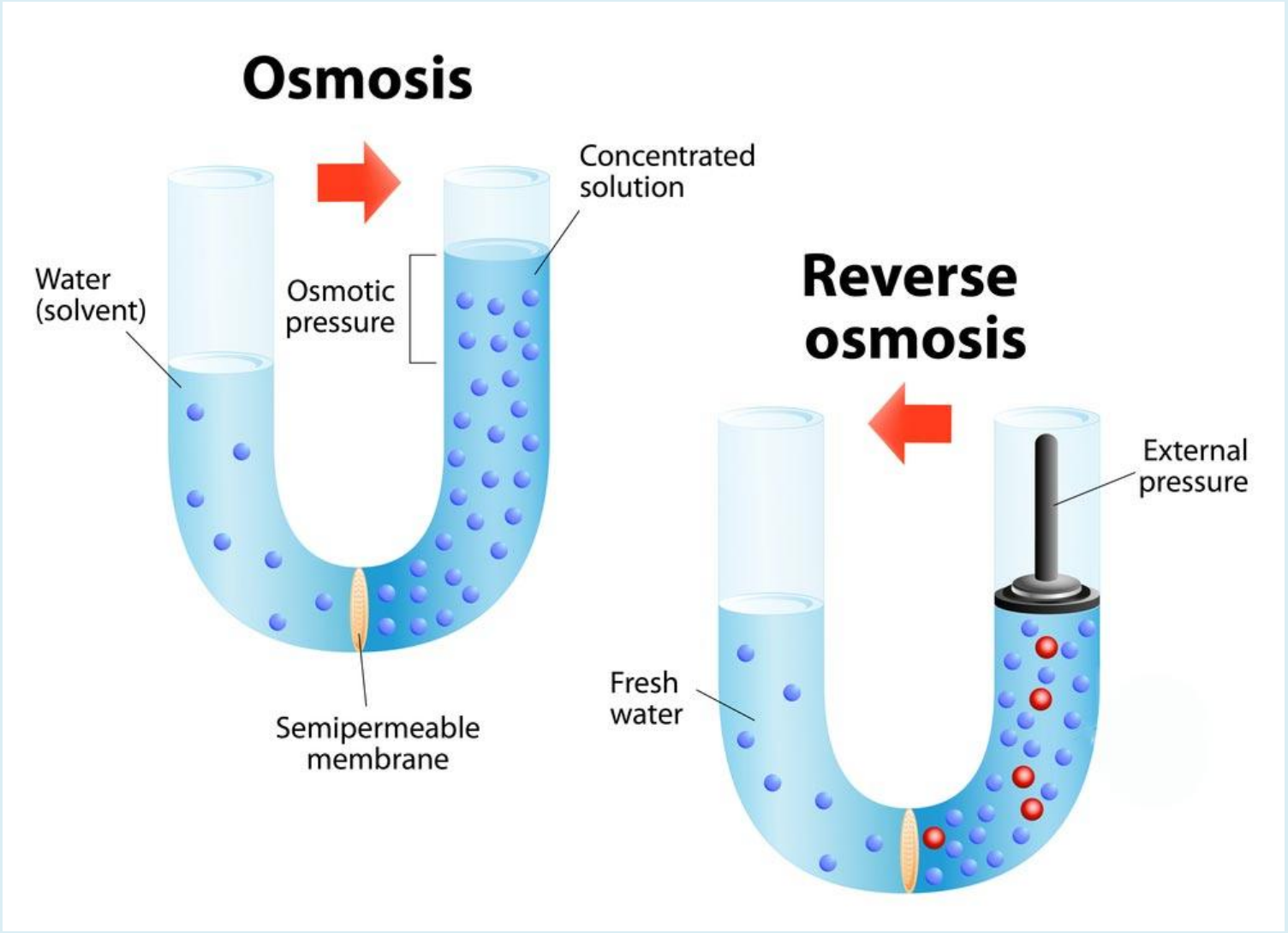


Osmosis and Reverse osmosis

- 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). The movement of a pure solvent to equalize solute concentrations on each side of a membrane generates osmotic pressure.
- Applying an external pressure to reverse the natural flow of pure solvent, thus, is reverse osmosis. The process is similar to other membrane technology applications.
- Reverse osmosis, however, involves a diffusive mechanism so that separation efficiency is dependent on solute concentration, pressure, and water flux rate.
- Reverse osmosis is most commonly known for its use in drinking water purification from sea water, removing the salt and other substances from the water molecules.

Osmosis and Reverse Osmosis





https://www.water-rightgroup.com/resources/how-do-reverse-osmosis-drinking-water-systems-work/

Water for injection

- This is pyrogen-free water
- Purified by distillation
- For preparation of products for parenteral use
- It is intended for use as a solvent only in solutions that are to be sterilized after preparation.
- If it is to be used as a solvent in parenteral solutions prepared under aseptic conditions, water for injection must be sterilized before use.
- It contains no added substance and meets the requirements of the tests for purified water.
- It must meet the requirements of pyrogen test
- It must be made isotonic (by the addition of 900mg pyrogen-free sodium chloride for each 100ml)

Sterile water for injection, USP

- Used as a solvent vehicle or diluent for already sterilized and packaged injectable medication.
- The preparation must meet the requirements of the sterility test and pyrogen test and other tests under purified water.

Bacteriostatic water for injection, USP

- It is sterile water for injection containing bacteriostatic agents
- It may be packaged in single containers of not larger than 5 ml size and in multi-dose containers of not larger than 30 ml, the label of which indicates the name and the proportion of added agent
- Not for use in newborns

Lecture 4
Aromatic Waters

- Aromatic waters are examples of the simplest of formulated dosage forms, consisting only of the solvent water and the volatile solute.
- The British Pharmacopoeia (BP) defines aromatic waters as clear, saturated aqueous solutions of volatile oils or other aromatic or volatile substances.
- Aromatic waters are aqueous solutions, usually saturated, of volatile substances characterized by very low water-solubilities.
- Aromatic waters provide a pleasantly flavored medium for the administration of water-soluble drugs and for the liquid phase of emulsion and suspensions.
- Aromatic waters are not therapeutically potent because of the very small proportion of active ingredient present in them.

The official aromatic waters

- The official aromatic waters are

1. Cinnamon water, NF: flavored vehicle
2. Orange flower water, NF: flavored vehicle
3. Stronger rose water, NF: perfume
4. Peppermint water, USP: flavored vehicle, carminative (15 ml dose)
5. Camphor water, NF: flavored vehicle
6. Chloroform water, NF: flavored vehicle

Peppermint oil and waters

Camphor water and ointment

Examples of Aromatic waters

1. Aromatic waters prepared from essential oils e.g. peppermint water, have been used as carminative and as vehicle.
2. Chloroform water: was used in expectorant preparations (dose 5-15ml).
3. Several aromatic waters are not used as vehicles for oral medication. These include: Rose water, Hamamelis water and camphor water.

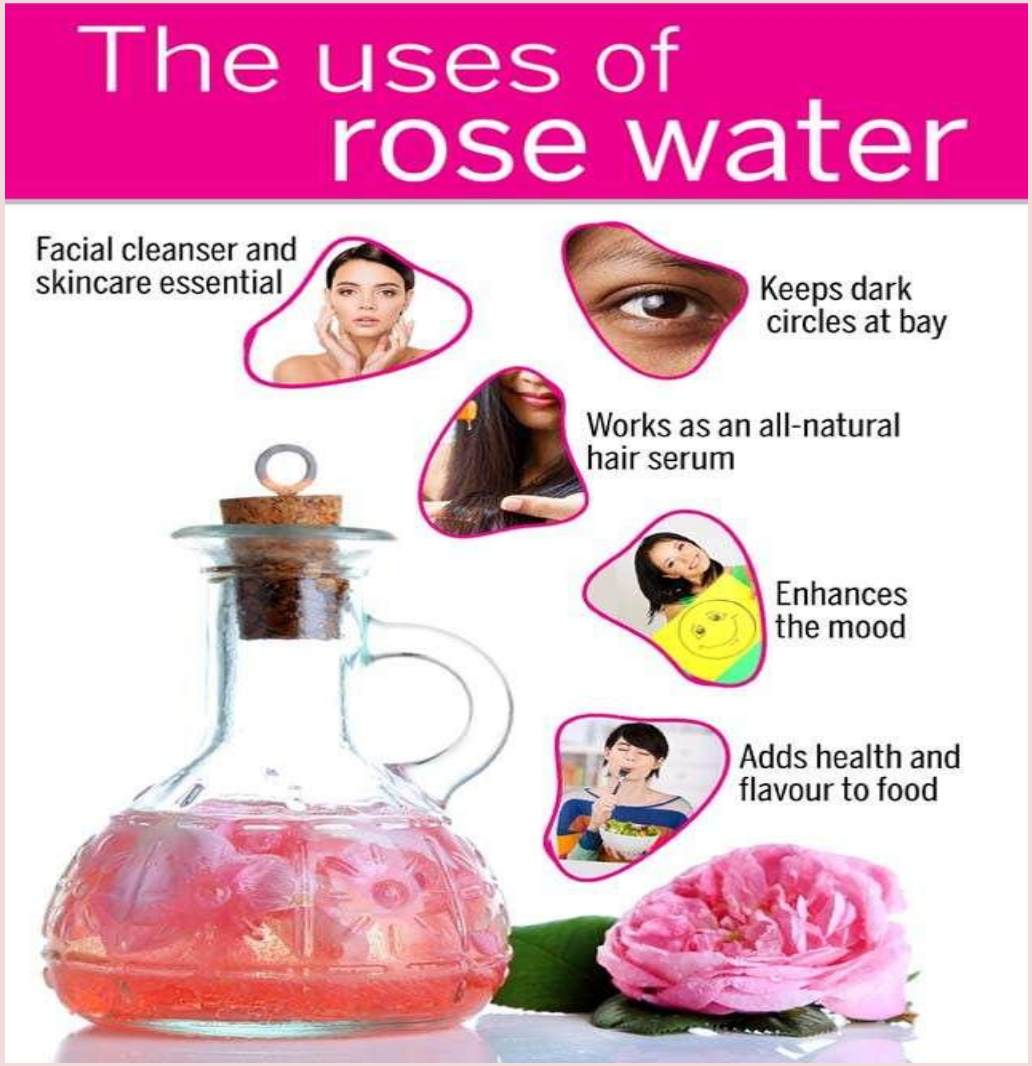
A. Rose water used as perfume

B. Hamamelis water or witch Hazel, is employed commonly as a rub and also is used as an astringent and perfume in aftershave lotion and other cosmetic products. Hamamelis water 12.5% v/v and naphazoline 0.01% w/v is used for temporary relief of eye redness due to minor eye irritations.

C. Camphor water: is frequently used in eye drops for its refreshing properties

- Other uses of Camphor: it is frequently used as rubefacient, Soothing eye, soothing cough

Rose water



https://www.femina.in/beauty/skin/what-are-the-uses-of-rose-water-140781.html

Hamamelis waters

Hamamelis waters preparations

Hamamelis water 12.5% v/v and naphazoline 0.01% w/v

Temporary relief of eye redness due to minor eye irritations

Preparation of aromatic waters

1. Distillation: most of aromatic waters can be prepared by distillation. However, it is not practical or economically feasible to use this method in most cases, since other method is of low cost and with simple apparatus required.

- Note: aromatic waters which are prepared directly from fresh plant material, e.g. stronger rose water, orange flower water, and Hamamelis water can not be prepared by any method other than distillation.
- The distillation method consists of placing the odoriferous portion of the plant in a suitable still with sufficient purified water and then distilling most of the water, carefully. The excess oil is separated from the distillate. The aqueous phase, which may require further clarification is the product.

- The product is labeled as X's, for example XX, XXX . Each X representing one distillation.
- So XXXX means that four times repeated process.
- This process is called re-distillation. This is done or carried on to get a saturated solution if it is not obtained from the 1st distillation.

Preparation of aromatic waters

2. Solution: for most waters excess volatile substances 2 ml or 2 g per liter be agitated with purified water for a period of 15 minutes. The mixture is then set a side for at least 12 hours, to ensure saturation, then it is filtered through wetted filter paper. The filter paper must be wet to prevent the passage of excess oil into the filtrate and to eliminate absorption of dissolved aromatic by the filter.

- The disadvantage of this method is that in-spite of repeated filtration, it is difficult to obtain a brilliant clear preparation owing to the formation of extremely fine particles.
- Chloroform water is prepared by solution without clarification problem exists in this case, since a slight excess of chloroform must remain in the bottle.

Preparation of chloroform water

- A saturated solution is prepared and maintained by adding an excess of chloroform to a given quantity of purified water, shaking vigorously, and a taking care that an excess of chloroform is always present . Since chloroform is heavier than water, the excess will remain at the bottom of the container.
- The high volatility of chloroform creates an equilibrium of loss and restoration of strength by evaporation .
- When it is dispensed, the bottle should not be shaken, and only the supernatant liquid should be used.

Preparation of aromatic waters

3. Alternate solution: this method has been developed to overcome difficulties in the simple solution method; *clarification* and *amount of time consumed*.

- In this method the volatile material is mixed thoroughly with 15 g of purified talc, this mixture is agitated with a liter of purified water for 10 minutes, prior to filtration. The talc or other inert material functions as both a filter aid and a distribution agent.
- It serves to accelerate the rate of solution by adsorbing and facilitating the breaking up of the aromatic substance into fine particles, thus increasing the surface area exposed to solvent action, and it facilitates the clarification of the solution.

Disadvantage of alternate solution method

The purified talc pass through the filter paper because purified talc is subdivided too finely.

In order to remove finely divided material other material also used purified siliceous earth and pulped filter paper.

Preparation of aromatic waters

4. Dilution: An alcoholic solution of the essential oil is mixed with water and talc. The mixture is agitated; after several hours it is filtered.

The concentrate contains between 50 and 55 percent alcohol by volume. The concentrate, containing the dilute alcohol. Soluble fraction of 2 ml of oil in each 100 ml.

One volume of concentrate is diluted with 39 volume of water, producing an aromatic water contains less than 1.5 percent of alcohol.

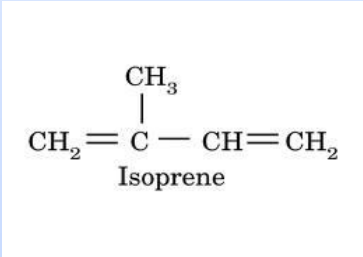
Disadvantage: aqueous preparation that contain small amounts of alcohol are prone to alterations in flavor and aroma, as a consequence of oxidative degradation of the alcohol.

Preparation of aromatic waters

- The other method to prepare concentrates is by using surface-active agent e.g., polysorbate 80 USP (Tween 80) due to solubilization by micelles formation.

Essential oils

- Essential oils are complex mixtures of hydrocarbons, alcohols, ethers, aldehydes and ketone.
- The hydrocarbon fraction of many essential oils is made up of terpenes.



Isoprene

- These components are the least water-soluble and, Consequently, constitute most of the insoluble matter removed in the clarification process. The other substances, are the "aroma carriers"

Stability of aromatic waters

- many waters support the growth of mold. No preservatives are added to aromatic waters
- Excessive exposure to light and to changes in temperature cause aromatic waters to loss some of their desirable characteristics, since

1. The solutes are volatile materials, loss of aroma occurs on prolonged exposure to atmosphere, particularly at elevated temperatures.
2. Aromatic waters are saturated solutions, lowering the temperature causes separation of the aromatic component, thus producing cloudiness.

Stability of aromatic waters

3. The aromatics may be salted out when the aromatic water is used as a vehicle for drugs which are electrolytes. The insoluble material may collect on the top of the liquid, imparting a burning taste to the first dose.
4. Many of the aroma-bearing solutes, as well as the terpenes, are oxidizable compounds. Oxidative degradation, involving dissolved atmospheric oxygen, is likely. This autoxidation can be catalyzed by light and trace quantities of metal ions such as iron (III) and copper (II). For example chloroform water is stored in light-resistant bottles since light catalyze the oxidation of chloroform to the poisonous gas, phosgene. Other example, bitter almond water, deposits crystals of benzoic acid which result from the autoxidation of benzaldehyde.

Terpeneless oils

- Terpeneless oils are commercially available. They are prepared by fractional distillation and/ or extraction.
- They are concentrated products which, therefore, are stronger in aroma and more soluble; also, they may be more stable than the natural essential oil.
- Their use in the preparation of aromatic waters should result in less difficulties in clarification, but the greater cost.

References

- Lewis W. Dittert, “American pharmacy”, Lippincott. company, 1974.
- British Pharmacopeia (BP)