INDUSTRIAL PHARMACY-I

UNIT IV-PARENTERALS

CLASS:27

TOPIC Vehicles, additives, importance of isotonicity

- The vehicle for parenteral can be classified as **aqueous vehicles and non-aqueous vehicles**.

Most commonly used

- water for injection /sterile water for injections as an aqueous vehicle for preparation of parenteral preparations

Non-Aqueous Vehicles

- Generally fixed oils are used as a non-aqueous vehicle.
- The USP provides specifications for such vehicles, indicating that the fixed oils must be of vegetable origin so that they can easily metabolize, will be liquid at room temperature, and will not become rancid readily.
- Corn oil, cottonseed oil, peanut oil, and sesame oil are commonly used non aqueous vehicles Fixed oils are used as vehicles for certain hormone (e.g. progesterone, testosterone, deoxycorticosteron) and vitamin (e.g., Vitamin K, Vitamin E) preparations

Water-Miscible Vehicles

- Water miscible solvents like liquid polyethylene glycol, propylene glycol, glycerin, sorbitol and ethyl alcohol have been used as a portion of the vehicle in the formulation of parenterals.
- Ethyl alcohol is used in the preparation of solutions of cardiac glycosides and the glycols in solutions of barbiturates, certain alkaloids, and certain antibiotics.
- These co-solvents are used carefully keeping in view that it should maintain the integrity of the product in terms of safety and stability of the product.

Water for Injection

- Methods of preparations Water for Injection can be prepared by

- **distillation** or
- by **membrane technologies** (i.e., reverse osmosis or ultrafiltration).
- The EP (European Pharmacopeia) only permits distillation as the process for producing WFI.

The USP and JP (Japanese Pharmacopeia) allow all these technologies to be applied

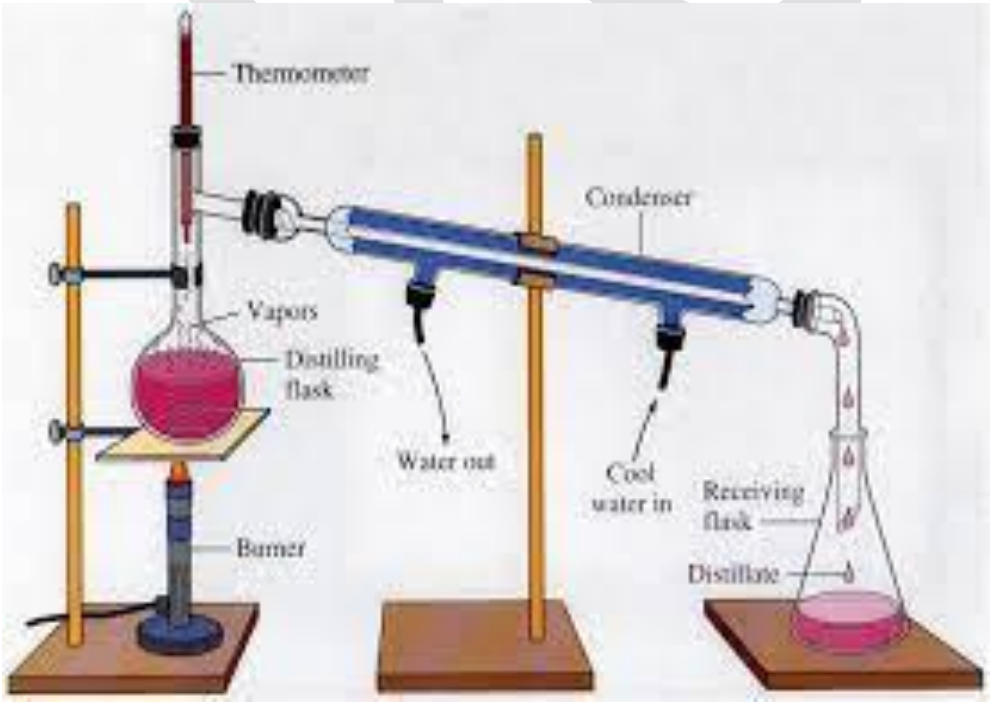
- Distillation is a process of converting water from a liquid to its gaseous form (steam).
- Since steam is pure gaseous water, all other contaminants in the feed water are removed.
- A conventional still consists of Boiler or evaporator, containing feed water.

➢ Source of heat to vaporize the water in the evaporator

➢ Headspace above the level of feed water, with condensing surfaces for refluxing the vapor, thereby returning nonvolatile impurities to the feed water.

➢ Provision for eliminating volatile impurities before the hot water vapor is condensed.

➢ Condenser for removing the heat of vaporization, thereby converting the water vapor to a liquid distillate. Distillation unit



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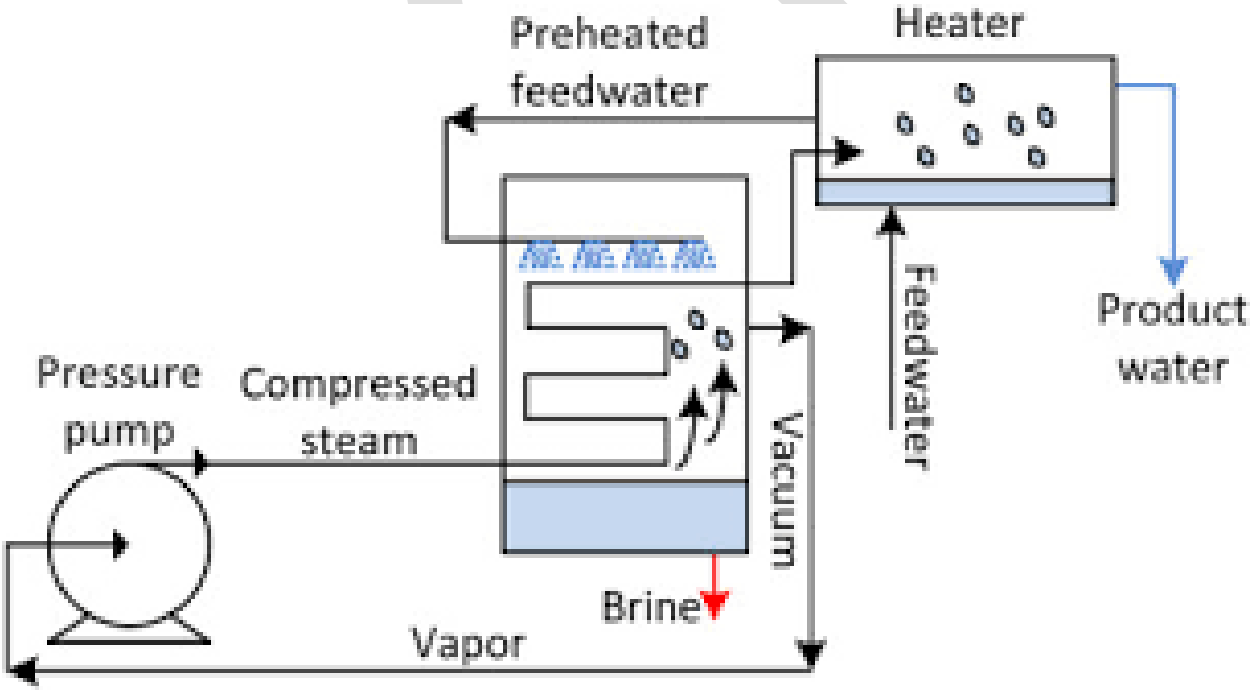
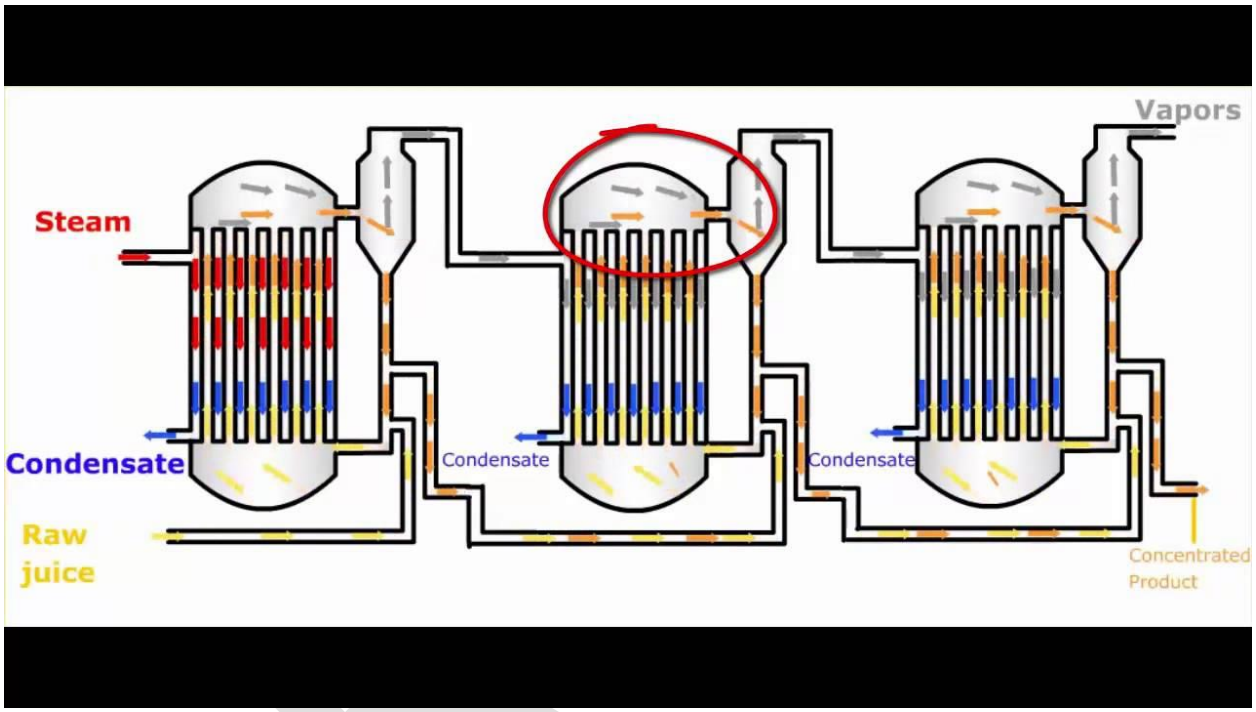
Vapor compression still



Multiple-Effect Stills

- Multiple-Effect Stills A multiple-effect still is a simple series of single-effect stills or columns running at different pressures where phase changes of water take place.
- A series of up to seven effects can be used, with the first effect operated at the highest pressure and the last effect at atmospheric pressure.

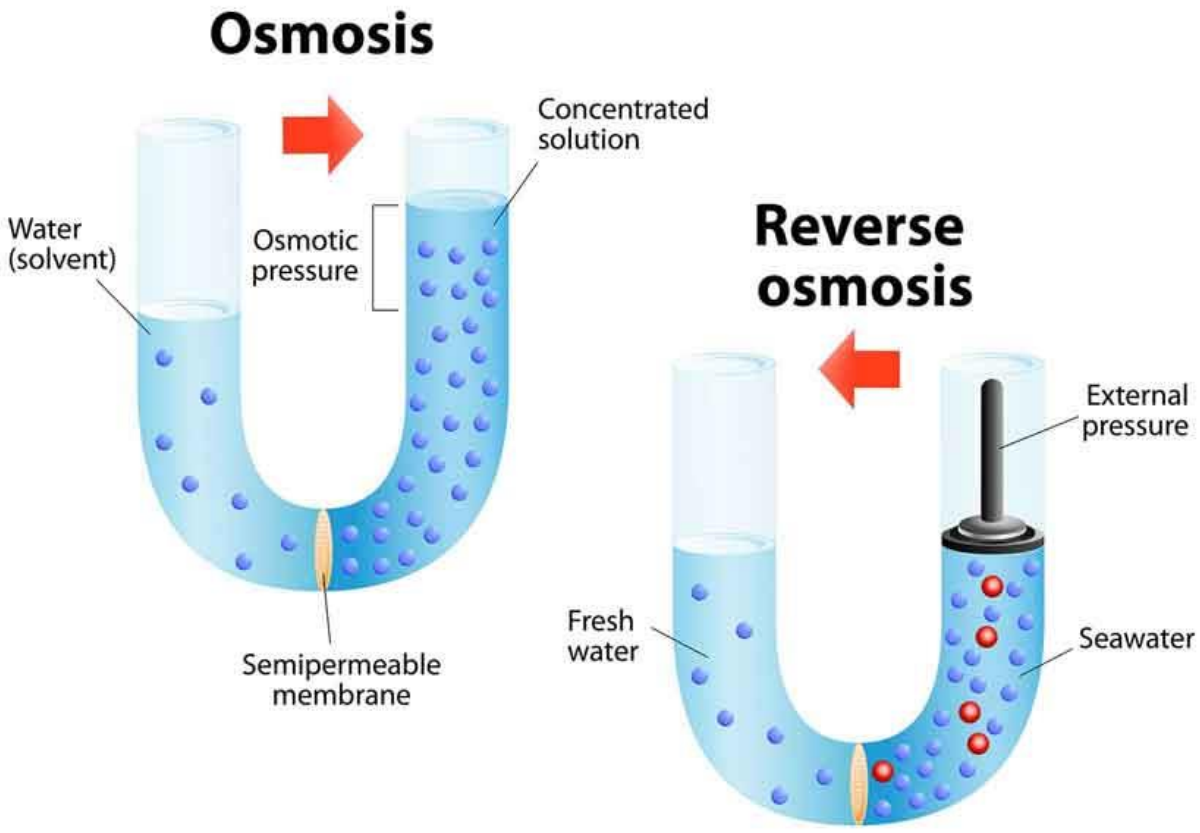
- Steam from an external source is used in the first effect to generate steam under pressure from feed water and it is used as the power source to drive the second effect.
- The steam used to drive the second effect condenses as it gives up its heat of vaporization and forms a distillate.
- This process continues until the last effect, when the steam is at atmospheric pressure. It is condensed in a heat exchanger to get distillate



Reverse Osmosis (RO)

- Reverse osmosis is the natural process of selective permeation of molecules through a semi permeable membrane separating two aqueous solutions of different concentrations is reversed.
- A driving force (usually between 200 and 400 psig) is required to overcome osmotic pressure and to permeate pure water through the membrane.
- RO membranes are typically either cellulose acetate or polysulfone coated with aromatic polyamides.
- The molecules most difficult to remove are small inorganic molecules such as sodium chloride.

- Sometimes Passage through two membranes in series is used to increase the efficiency of removal of these small molecules and decrease the risk of structural failure of a membrane to remove other contaminants such as bacteria and pyrogens



Ultrafiltration

- Ultrafiltration is a type of membrane filtration in which hydrostatic pressure forces a liquid against semipermeable membrane.
- In this solid and solutes of high molecular weight are retained, and low molecular weight solutes passes through the membrane.
- In principle ultrafiltration is not different from reverse osmosis except in terms of size of the molecules it retains

Storage and Distribution

- As per USP

- WFI should be stored at 80°C for prevention of any contamination When the water cannot be used at 80°C, heat exchangers must be installed to reduce the temperature at the point of use
- The USP also permits the WFI to be stored at room temperature but for a maximum of 24 hrs requires frequent sanitization to minimize the risk of viable microorganisms.
- WFI is stored in **stainless-steel** storage tanks.
- These tanks are connected to a welded stainless steel distribution loop supplying the various use sites with a continuously circulating water supply.
- The tank is provided with a hydrophobic membrane vent filter capable of excluding bacteria and non-viable particulate matter.
- Such a vent filter is necessary to permit changes in pressure during filling and emptying.

Bacterial retentive filters should not be installed in such systems because of the risk of bacterial buildup on the filters and the consequent release of pyrogenic substances

- **The Sterile Water for injection (SWFI)** requirements differs in that since it is a final product, it must pass USP sterility test.
- **Bacteriostatic Water for Injection (BWFI)** contains one or more suitable antimicrobial agents in containers 30 ml or less.

This restriction is designed to prevent the administration of large quantity of a bacteriostatic agent that probably would be toxic in the accumulated amount of large volume of solution, even though the concentration was low

Isotonicity

- The most important thing with respect to parenterals is maintaining the isotonisity of product as to avoid any swelling and contraction of blood cells. 0.9% of NaCl is said to be isotonic and used as a standard in pharmaceutical preparations.
- Methods of adjusting tonicity:-

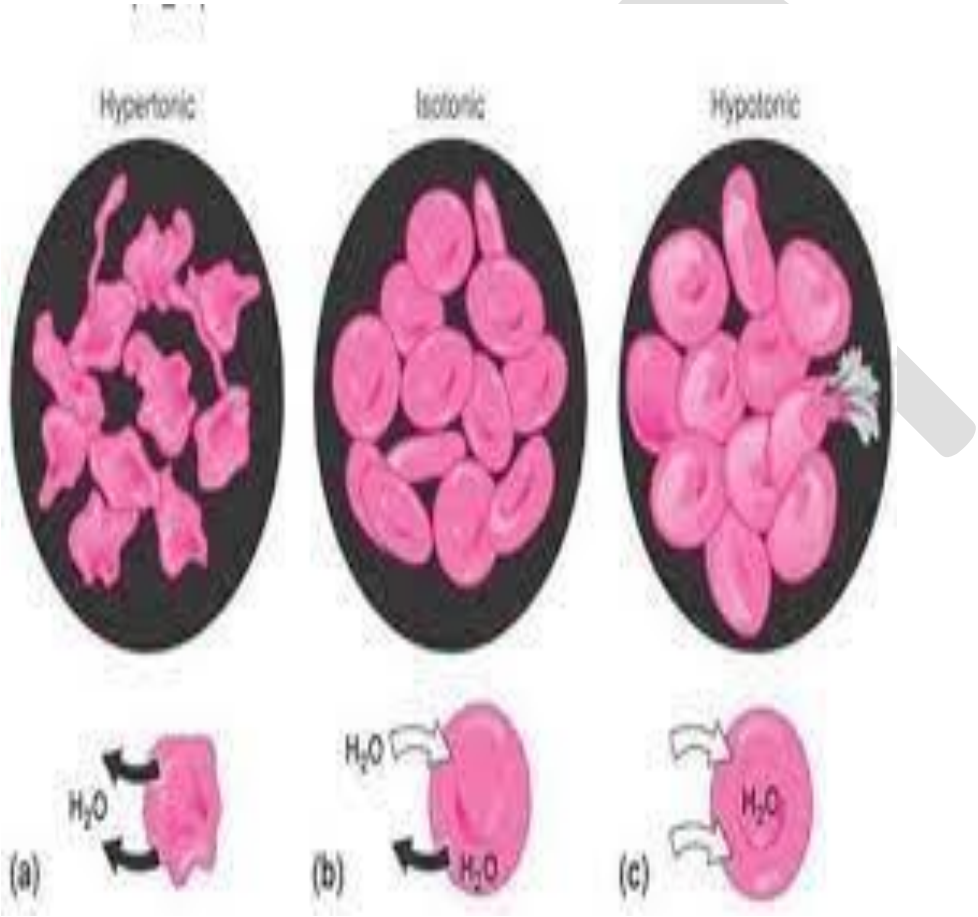
➢ Class I (Freezing point depression and Sodium chloride equivalent method)

➢ Class II (White-Vincent method and Sprowls method)

➢ **Hypotonic**

➢ NaCl0.2% solute inside is greater than solute outside-swelling

- **Isotonic**
- NaCl 0.9%
- Solute inside is equal to outside-equilibrium
- **Hypertonic**
- NaCl 2%
- Solute inside is less than outside-shrinkage



Methods to adjust tonicity

- **Freezing point depression method**
- In this method any substance is added to lower f.p of solution to -0.52º.
- FP of blood and tears is - 0.52º, so any solution having FP 0.52º is isotonic.

- The formula for calculating the amount of adjusting substance to make isotonic solution is w%=(0.52-a)/b
- W%= conc. gm/100 ml of adjusting substance
- a= f.p.d of 1% of unadjusted substance
- b = f.p.d of 1% of adjusting substance

NaCl equivalent method

NaCl equivalent "E" is the amount of NaCl that is equivalent to (i.e., has the same osmotic effect as 1gm of drug).

This method first uses to calculate E NaCl and then calculate the amount of NaCl to reach 0.9%.

E NaCl value is generally given ,And if it is not given it can be calculated by using –

ENaCl = 17Liso (ug M.wt drug % 0.9 (drug% E)

- W%=[0.9-(drug%XENacl)]
- W%=weight of NaCl in gram per100ml
- ENaCl= equivalent weight to1gm of drug
- drug% weight of drug in gm per 100 ml % weight of NaCl in gm per 100 ml (to make solution isotonic

White – Vincent method

- This method involves the addition of H2O to drug to make it isotonic with addition of isotonic vehicle to bring solution to final volume.
- v = wXENaClX111.1
- V=volume of H2O
- W= weight of drug
- 111.1= 100/0.9

Sprawl method

- Sprawl method is a modified white Vincent method in which total volume is kept constant to 30 ml and the drug concentration is kept constant to 1% i.e. 0.3g.

- It was done to make it easy for practicing pharmacist.