Unit-4

Pharmaceutical Engineering

UNIT-IV **10 Hours**

Filtration: Objectives, applications, Theories & Factors influencing filtration, filter aids, filter medias. Principle, Construction, Working, Uses, Merits and demerits of plate & frame filter, filter leaf, rotary drum filter, Meta filter & Cartridge filter, membrane filters and Seidtz filter.

Centrifugation: Objectives, principle & applications of Centrifugation, principles, construction, working, uses, merits and demerits of Perforated basket centrifuge, Non-perforated basket centrifuge, semi continuous centrifuge & super centrifuge.

Filtration: Objectives, applications, Theories & Factors influencing filtration, filter aids, filter medias. Principle, Construction, Working, Uses, Merits and demerits of plate & frame filter, filter leaf, rotary drum filter, Meta filter & Cartridge filter, membrane filters and Seidtz filter.

Filtration:

- It is defined as a process of separation of solid from fluids by passing mixture through a porous medium that retain the solid but allows the fluids to pass through.
- The mixture or suspension to be filtered is known as slurry.
- The porous medium used to retain the solids is known a filter medium.
- The accumulated solid on the filters are referred to as filter cake, while the color liquid passing through the filter is filtrate.
- When solids are present in a very low concentration that is not exceeding 1.0% w/v the process of its separation from liquid is called clarification.

Objectives:

- Separating solids from liquids and gases is the main goal of filtration. It also includes:
- To remove contaminant particles from dispersing fluid so that it can be recovered.
- By removing the dispersing fluid, solid particles can be recovered.
- Solvents and solids must be of high quality.
- Particulates can be removed from the air to enable pharmaceutically useful gases to be purified.
- It is used to sterilize parenteral thermolabile products.

Applications:

1. Production of sterile products:

- Air is filtered through HEPA filters (high efficiency particulate air filters) or laminar air bench to obtain sterile air, which maintain good environment prior to and during manufacturing of sterile products.
- A solution is passed through a bacteria proof filter in order to obtain sterile solution, particularly when heat sterilization is not suitable on account of the thermolabile nature of the contents.
- In case of sterile products particle as small as 0.2µm should be removed, which includes the bio- burden of fungi, bacteria etc.

2. Production of bulk drugs:

- Solids of intermediates and finished products are separated from the reaction mixture by filtration techniques by the method, impurities can be removed.

3. Production of liquid oral formulation:

- Filtration is an essential steps in the production of liquid oral for obtaining clear solution.

4. Affluent and waste water treatment:

- Waste solid must be separated from the waste liquid prior to its disposal.
- Sometimes, the soluble components are precipitated and the separated by filtration.

Theories of filtration:

The flow of a liquid through a filter follows the basic rules that govern the flow of any liquid through the medium offering resistance. The rate of flow may be expressed as—

Rate = driving force/resistance.

- The rate of filtration may be expressed as volume/time.
- The driving force is the pressure differential between the upstream and downstream of the filter.
- The resistance is not constant .it increase with an increase in the deposition of solids on the filter medium.

1. Poiseuille's Equation—

Poiceuille considered that considered that filtration is similar to the streamline flow of a liquid under pressure through Capillaries.

$$V = \pi \Delta P r4 / 8L\eta.$$

Where,

- V = rate of flow, that is volume of liquid flowing in unit time m3 /s.
- ΔP = Pressure difference across the filter. Pascal.
- r = radius of the capillary in the filter bed. Meter
- L = Thickness of the filter cake (capillary length). Meter
- η = Viscosity of the filtrate. Pascal/second.

2. Darcy Equation—

$$V = KA\Delta P/\eta L.$$

- K = permeability coefficient of cake m2 .
- A = Surface area of the porous bed (filter medium) m2 .

The term k depends on the characteristics of the cake, such as porosity, specific surface area and compressibility.

3. Kozeny-Carman Equation—

$$V = A/\eta s2 \times \Delta P/KL \times Ɛ3 /(1-Ɛ)2$$

Where →

- Ɛ = porosity of the cake (bed)
- S = Specific surface area of the particles comprising the cake m2 /m3 .
- K = Kozeny constant (usually taken 5).

Factor influencing filtration.

1. Surface area: According to Darcy's Rate of filtration is directly proportional to surface area of filter media.

2. Particle size of solids:

$$Particle\ Size \uparrow = Rate\ of\ Filtration \uparrow$$

3. Filter Cake:

Filtration is decrease on increasing filter cake.

$$Viscosity \times \frac{1}{Rate\ of\ filterration}$$

4. Viscosity:

$$Viscosity \uparrow = Filtration \downarrow$$

Filter aids:

- The objective of filter aid is to prevent the medium from becoming blocked and to form an open, porous cake, hence, reducing the resistance to flow of the filtrate.
- Filter aid forms a surface deposit which screens out the solids and also prevents the plugging of supporting filter medium.

Characteristics of filter aids:

- Chemically inert and free from impurities.
- Low specific gravity, so remain suspended in liquids.
- Porous rather than dense, so that pervious cake can be formed.
- Recoverable.

Filter Medium:

- The surface upon which solids are deposited in a filter is called the "Filter medium"

Properties of ideal filter medium are as follows

It should

- Be capable of delivering a clear filtrate at a suitable production rate.
- Have sufficient mechanical strength.
- Be inert.
- Retain the solids without plugging at the start of filtration.
- Not absorb dissolve material.
- Sterile filtration imposes a special requirement since the pore size must not exceed the dimension of bacteria or spores.

Principle, Construction, Working, Uses, Merits and demerits of plate & frame filter, filter leaf, rotary drum filter, Meta filter & Cartridge filter, membrane filters and Seidtz filter.

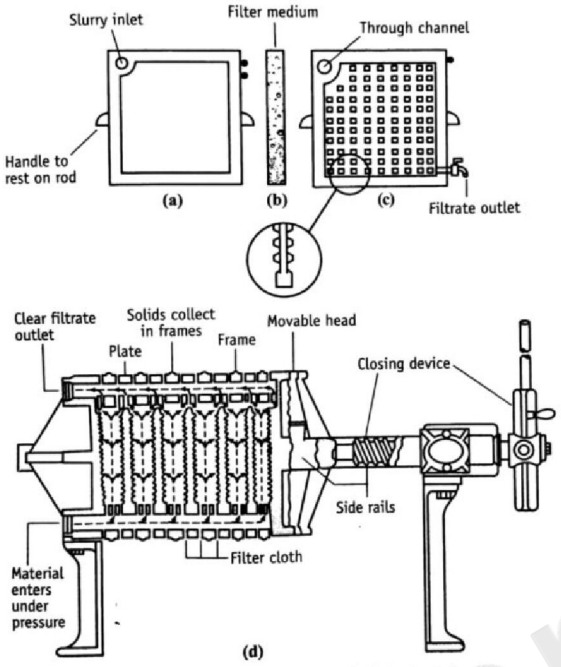
Plate & frame filter:

Principle:

- Plate and frame filters work on the principle of surface filtration.
- The slurry enters the frame by pressure and flows through filter medium.
- The filtrate is collected on the plates and send to outlet.
- A number of frames and plates are used so that surface area increases and consequently large volumes of slurry can be processed simultaneously with or without washing.

Construction:

- It consist of plates and frames.
- The frame is open and is used as an inlet for the material to be filtered. Plate has a groove support to the filter cloth.
- The plates and frame may be made of various metals which provide resistance to corrosion or prevent metallic contamination of the filtrate (usually made up of aluminum alloy)
- Filter cloth is fitted on each side of the plate.
- The plate and frames are placed alternatively and fitted in the outer frame of the press.
- Each plate acts as a single filtration unit. The outlet of each plate is connected to a common outlet pipe.



a) Frame- maintains the slurry reservoir, inlet (eye) for slurry.
b) Filter medium
c) Plate along with section-Supports the filter medium, receiving the filtrate and outlet (eye).
d) Assembly of plate and frame filter press.

Working:

It involves two steps:

1. Filtration:

- The slurry inlet through common inlet pipe of all filter frame which further pass through filter media (cloth) and the filter liquid is collected in the plates from where it is collected through common outlet pipe.
- The cake is deposited in the froms the process of filtration is continued until the frame is filled with filter cake.

2. Washing:

- When the process is stopped the frame is emptied or washed with water.
- It is necessary because filter cake create resistance for filtration.
- After washing the cycle (filtration) is restarted.

Uses:

- Sterile filtrate can by obtain by using asbestos and cellulosev filter sheet (for this, whole filter press and filter medium have been sterilized previously).
- Filtration of viscous liquid can also be done by incorporatingv heating/cooling coils in the press.

Merits:

- Provide large filtration area in relatively small floor space.
- The capacity being variable according to thickness of frames and number used.
- Sturdy construction permits the use of considerable pressurev difference. (2000 Kilopascals normally used)
- Efficient washing of cake is possible.
- Operation and maintenance is easy.
- It produces dry cake in form of slab.
- Construction of filter press is very simple and a variety of materials can be used.

Demerits of plate & frame filter:

- It is a batch filter, so it is a time consuming.
- It is batch filter.
- It is an expensive filter.

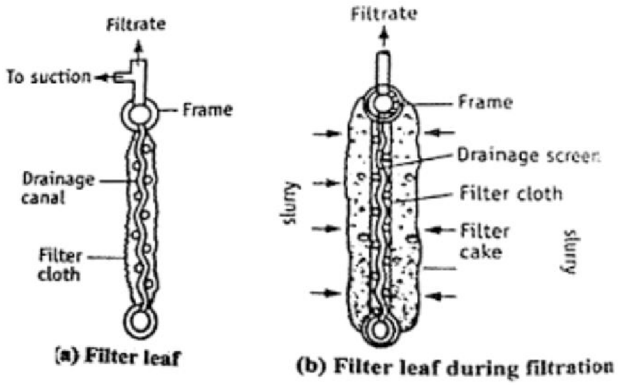
Filter leaf

Principle:

- It is an apparatus consisting of a longitudinal drainage screen covered with a filter cloth.
- The mechanism is surface filtration and acts as sieve or strainer.
- Vacuum or pressure can be applied to increase the rate of filtration

Construction:

- It consists of narrow frame enclosing a drainage screen or grooved plate.
- The frame may be of any shape, circular, square or rectangular.
- The whole unit is covered with filter cloth.
- The outlet for the filtrate connects to the interior of the frame through section.



(a) Filter leaf (b) Filter leaf during filtration

Working:

- The filter leaf is immersed in a slurry.
- Vacuum system is connected to the filtrate outlet.
- The slurry passed through the filter cloth.
- Finally filtrate enters the drainage canal and goes through the outlet into the receive.
- Air is passed to flow in reversed direction which facilitates removal of cake.

Uses:

- The filter leaf is satisfactory if the solid content is not too high, about 5% i.e dilute suspention.
- The vertical leaf filters may be readily jacketed for applications whenever hot or cold temperatures are to be maintained.

Merits:

- A number of leaves can be connected to provide a larger area for filtration.
- Labour costs for operating the filter are comparatively moderate.
- The special feature of the leaf filter is the high efficiency of washing.
- Filter leaf is mechanically simple since there are no complex components in it.

Demerits:

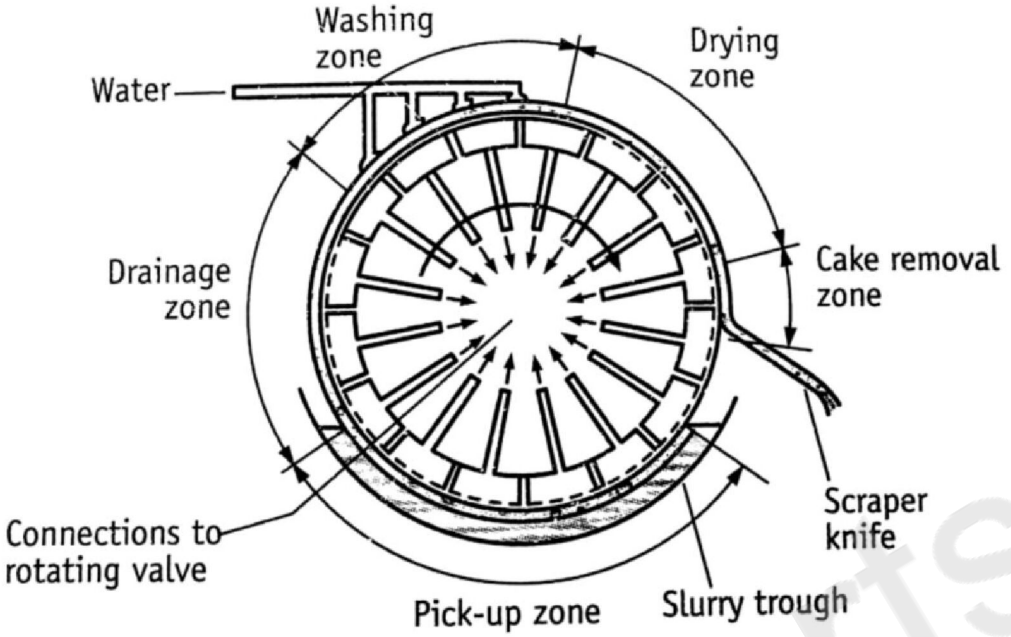
- High headroom is required for dismantling the leaves on vertical vessels.
- Large floor space is required for discharging the cake on horizontal vessels.

Rotary drum filter

Principle: It is based on the principle of filtering the slurry through sieve-like mechanism on a rotating drum surface, under the condition of vacuum.

Construction:

- It consists of a metal cylinder mounted horizontally.
- The drum may be up to 3 metres in diameter and 3.5 metres in length and gives a surface area of 20 metres square. The curved surface is a perforated plate, which supports a filter cloth.
- The drum is radially partitioned dividing the annular space into separate compartments.
- Each of them is connected by an internal pipe to the centre of the drum through a rotating valve.



Working:

- The drum is dipped into the slurry (Speed of drum is less than 1 revolution per minute) and vacuum is applied to the outlet which is connected to the filtrate receiver (Pick-up Zone)
- When the cake has formed the cake drained or partially dried by vacuum (Draining Zone)
- The drum is sprayed with water to wash the cake (Washing Zone)
- Retaining the vacuum connection drains the cake and produces partial dryness (Drying zone)
- Then cake is removed by doctor knife (cake-removal zone)
- A pre-coat of filter aid is deposited on the drum to prevent blocking of filter cloth during filtration process.

Uses:

- In the production of antibiotics, a rotating filter is employed to separate the mycelium from the fermentation liquid.
- Calcium carbonate, magnesium carbonate, and starch are collected using these.
- It is appropriate for slurry having significant levels of particles in the range of 15-30%.

Merits:

- Continuous rotation of the filter is required.
- This filter is ideal for filtering slurries with a high solids content.
- Because of the automated operation, labour expenses are extremely cheap.
- A rotating filter is appropriate for filtering of highly concentrated liquids or thick slurries comprising 15-30% solids.

- The cake thickness may be varied by varying the rotational speed.
- Extremely large capacity.

Demerits:

- A complex design with a lot of moving elements.
- Expensive equipment.
- Cake tends to crack.

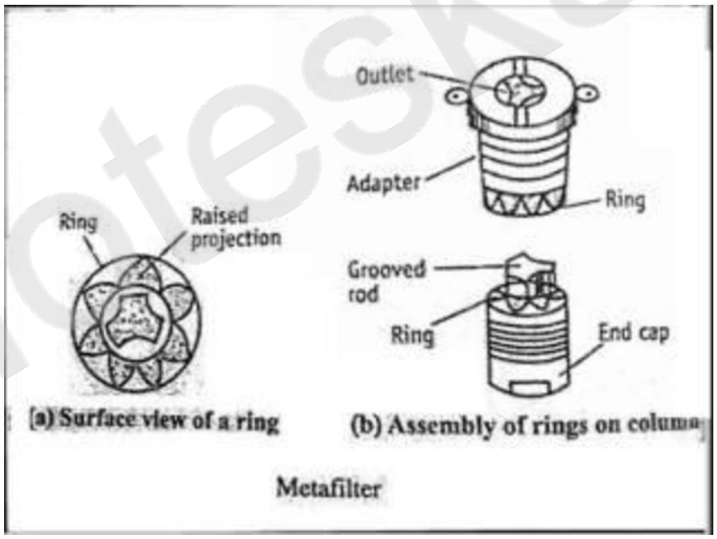
Meta filter

Principle:

- Meta filter function as a surface filtration for the separation of particles.

Construction:

- It consist of a grooved, drainage rod on which are packed a number of metallic rings.
- Rings made up of stainless steel and have thickness 0.8 mm, Inside diameter 15mm, Outside diameter 22mm.
- These rings have a number of semicircular projection on one surface and when they are packed on the rod the opening b/w the rings is about 0.2 mm.



Working:

- Filters are placed in a vessel
- Slurry is pumped under pressure or occasionally by applying reduced pressure to the outlet side
- Slurry passes through the channels formed on the edges between the rings
- The clear liquid rises up and collected from the outlet into receiver
- For separation of fine particles, a bed of suitable materials such as kieselguhr is first built up.
- The pack of rings serves essentially as a base on which the true filter medium is supported.

Uses:

- Clarification of syrups.
- Filtration of injection solutions.
- Clarification of insulin liquors.

Merits:

- Removal of cake can be carried out by simply back- flushing with water.
- Change over from one batch to another or one product to another is easy.
- Sterile products can be handled.
- Can be used under high pressures, without any danger of bursting the filter medium.
- Running cost is low, as separate filter medium is not used.

Demerits:

- It is not a continuous process.
- It is used where the proportion of solid in the liquid to be filtered is about 5% or less.

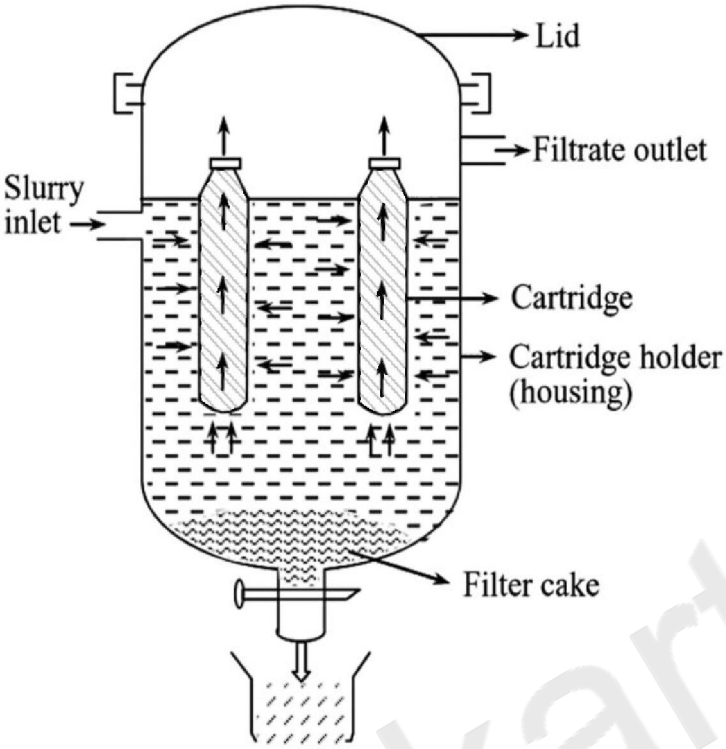
Cartridge filter

Principle:

- Cartridge filter is a thin porous membrane in which pre-filter and membrane filter are combined into a single unit.
- The filtration action is mainly sieve-like and the particles are retained on the surface.

Construction:

- In a cartridge filter, the filter media is disposable and not interchangeable.
- Metal or plastic can be used.
- It has two membrane filters, which are similar to sieves. There is a pre-filter as well as an actual filter for filtration, made from polypropylene.
- The actual filter or membrane filter, depending on the pore size, comes in various sizes in the market and is used according to the type of water we are filtering.
- Cartridges are placed in holders.
- The housing can hold multiple cartridges at the same time.
- A lid closes the housing.
- An inlet and outlet for slurry are provided in the housing.



Working:

- As the slurry is introduced into the housing, it is filtered through the cartridge filter by surface filtration and by the mechanism of straining.
- The filtrate drains to the centre and is collected through the filtrate outlet.

Uses:

- Used for preparation of particulate free solution for parenteral and ophthalmic uses

Merits:

- Along with filtration, simultaneous sterilization with auto- claving can be carried out with stainless steel construction.
- Nowadays, cartridges are available with self-cleaning devices.
- The construction allows dismantling.
- Applicable for continuous filtration thereby reducing the chances of contamination.

Demerits:

- High labour cost is required for dismantling the machine and also for its cleaning.
- The components of the machine cannot be bought from dif- ferent manufacturers because they differ from manufacturer to manufacturer

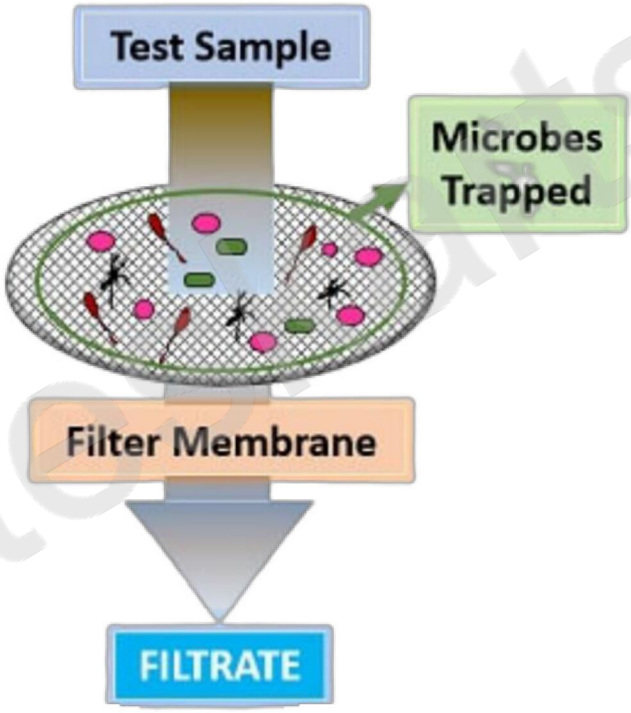
Membrane filters

Principle:

- It act like a sieve and the particulate matter is retained on the surface of membrane.

Construction:

- Membrane filters are made of thin and flat membranes of cellulose derivates, (eg: cellulose acetate, and cellulose nitrate). These filters are brittle when it is stored in dry conditions.
- The filters are 50-150m thickness, and available in sizes up to 60cm². It has 400-500 million pores per square centimeter of filter surface.



Working:

- The membrane filter pores are uniform in size and occupy about 80% of the filter volume to avoid clogging the membrane, pre-filtration is often required.
- The selection of membrane filter depends upon the particles to be removed.
- Eg: 0.2m for filtering of all bacteria. 1.2µ for filtering non-living particles.

Uses:

- These filter are mainly used for sterilization of both aqueous and oily liquids.

Merits:

- It is rapid.
- These are available as disposable items and hence cross contamination is prevented.

Demerits:

- It cannot be used for filtration of organic solvents, such as alcohols, ketones, ester and chloroform.

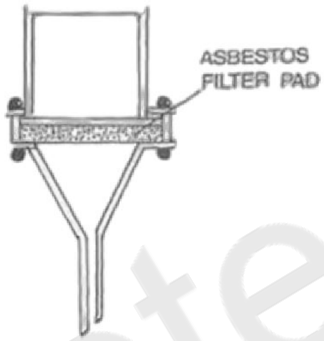
Seitz filter.

Principle:

- Based on sieve-like mechanism through asbestos pad filter disc.

Construction:

- It consist of a pad of compressed asbestos as a filtering medium.
- One upper part to fill the slurry.
- Lower part (Funnel like structure) to receive filtrate.
- Typical seitz pads are about 2mm thick.



Working:

- Add slurry from upper part
- Slurry deposite on asbestos pad and filtrate is passed through it.
- The finest pore size gives almost perfect filtration and retain viruses.

Uses:

- Useful for sterile filtration.
- Also used for air filtration.

Merits:

- It is simple to use
- Useful for viscous solution.

Demerits:

- It is delicate on fragile.
- A new pad must be used for each filtration in order to avoid residue of previous filtration.

Centrifugation: Objectives, principle & applications of Centrifugation, principles, construction, working, uses, merits and demerits of Perforated basket centrifuge, Non-perforated basket centrifuge, semi continuous centrifuge & super centrifuge.

Centrifugation:

- Centrifugation is a mechanical process that uses centrifugal force to separate particles from a solution according to their size, shape, density, and viscosity of the medium.
- Centrifuges are used in a wide variety of applications, including biology, chemistry, medicine, and industry.

Objectives

- Separating immiscible liquids
- Eliminate impurities in the supernatant fluid by purifying the substance.
- This process separates crystallized drugs from their mother liquor.
- To check if the suspensions and emulsions are creaming or sedimenting at an increased speed.

Principle

- The technique of centrifugation operates using the concept of sedimentation, where the centrifugal force causes denser liquids and particles to travel in the radial direction outwards.
- Around the same time, objects with relatively low densities are displaced and pushed towards the centre.

Applications of Centrifugation

- Bulk drug production.
- Manufacturing of biological products.
- Suspension and emulsion evaluation.
- Determination of collide molecular weight.
- Separation of chalk powder and water.
- Skimming milk is made by removing the fat from milk.
- The wine's clarification and stabilisation.
- Drug biopharmaceutical analysis.
- Application in water treatment.
- Draining lettuce after washing it in a salad spinner.

Perforated basket centrifuge

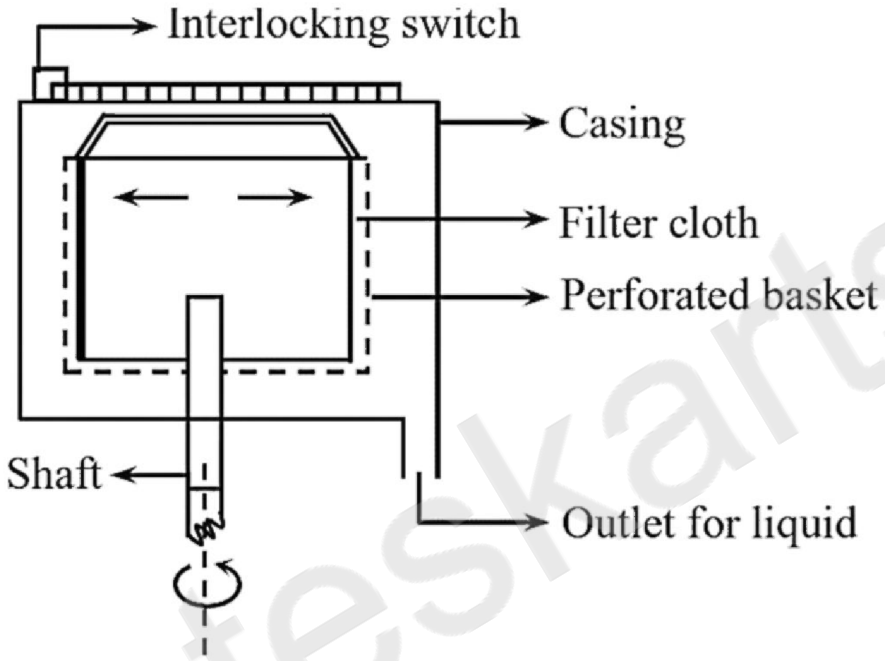
Principles:

- Separation occurs through perforated wall depends on the difference in the densities of solids and solids and liquid phases.

Construction:

- It consists of a basket made up of steal or any other suitable metal.

- It is perforated with filter cloth.
- The basket is suspended on vertical shaft and driven by a motor.
- The basket is surrounded by casing which collect the filtrate and discharge through outlet.
- The diameter of basket is 0.9 meter.
- The diameter of perforation depends on crystal size.
- The basket operated at speed of 1000 rpm.



Working:

- The material is loaded in to the basket when it is in stationary.
- Power is applied to rotate (5kw) then power reduced to 2 kw (speed 1000RPM).
- The Liquid passes through perforated wall while solid retains in the basket.
- Liquid is collected through casing, centrifuge is stopped by applying brake. Now unload the solid.

Uses:

- A perforated basket centrifuge is extensively used for separating crystalline drugs (such as aspirin) from the mother liquor. The free-flowing product can be obtained because the mother liquor is removed completely.
- It is also used for removing unwanted solids from a liquid. For example, precipitated proteins are removed from insulin.
- Sugar crystals are separated using a perforated basket centrifuge.

Merits:

- The centrifuge is very compact and it occupies very little floor space.
- It can handle slurries with a high proportion of solids and even those having paste-like consistency.
- The final product has a very low moisture content.
- In this method, the dissolved solids are separated from the cake.
- The process is rapid.

Demerits:

- The entire cycle is complicated resulting in considerable labour costs.

- It is a batch process.

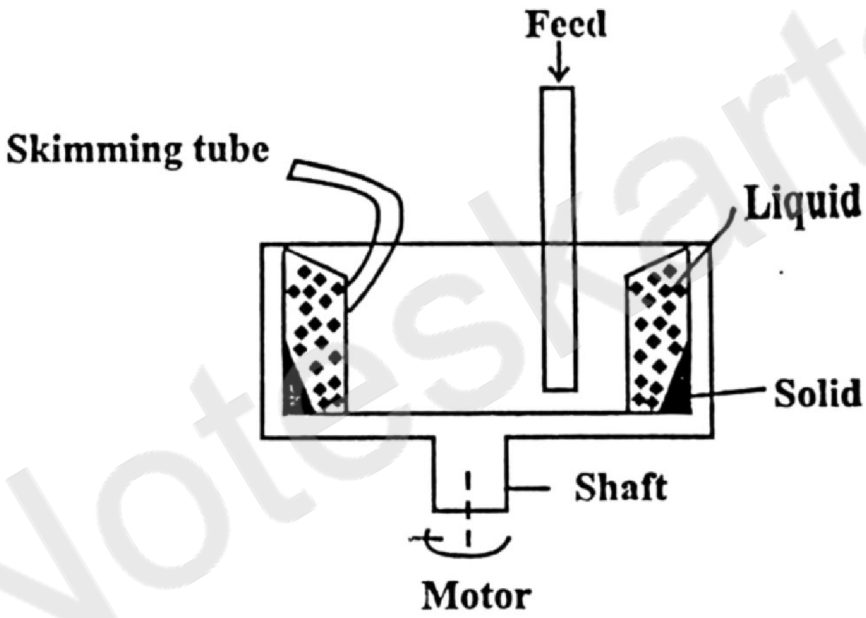
Non-perforated basket centrifuge

Principles:

- The separation of solids and liquids phase depends on difference in densities of both phases without porous barriers (Sedimentation)

Construction:

- It consists of a non-perforated basket made of steel.
- The material is loaded into a basket through a feed tube.
- The basket is mounted on a vertical shaft which is rotated by the motor.
- The liquid is removed with the help of a skimming tube.



Working:

- The suspension is fed into the basket continuously through a feed tube.
- During centrifugation solid is deposited at the side of the basket while liquid remained at the top which is removed by a skimming tube.
- When a sufficient amount of solid gets deposited at the side of the basket then it is removed intermittently by hand and continuously by a scraper blade.

Uses:

- This centrifuge is employed when deposited solids provide high resistance to the flow of liquid.
- Wastewater treatment: Reducing sludge volume and material recovery.
- Mining industry: Dewatering and clarifying mineral mixtures.
- Biotechnology industry: Biomolecule separation and concentration.

Merits:

- Increased solids recovery.
- Improved product quality.

- Reduced operating costs.
- Lower maintenance requirements.

Demerits:

- Lower processing capacity.
- Longer processing times.
- Higher energy consumption.
- Limited solids discharge options.
- Higher initial cost.

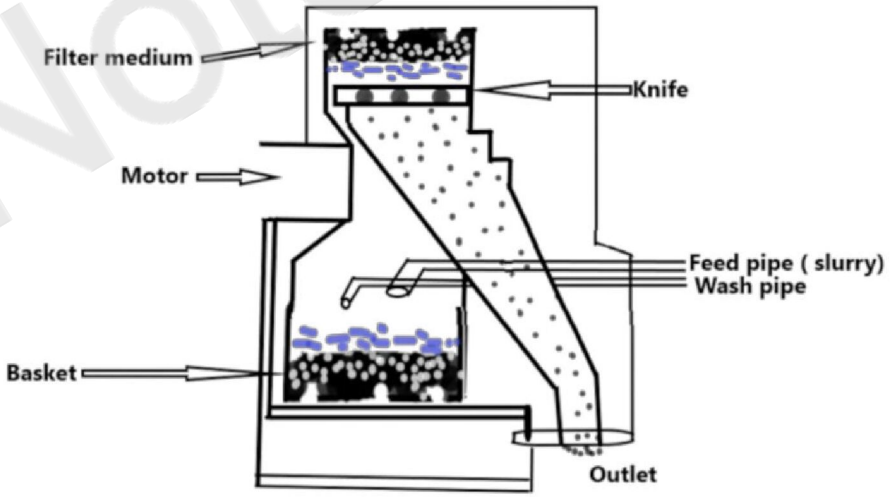
Semi continuous centrifuge

Principles:

- In Semi Continuous centrifuge, separation occurs through a perforated wall depending on the difference in the densities of solid and liquid phases.

Construction:

- It consists of a vertical shaped basket.
- A motor, which will drive the basket.
- A feed pipe and wash pipe introduced to the side of the basket.
- A feeler is adjusted to feed which help to control thickness of slurry by controlling proper air supply.
- A hydraulic cylinder attached to basket for filtrate discharge.



Working:

- The basket is rotated horizontally with a motor.
- The suspension is introduced through the pipe. The slurry passes through the perforated side.
- The crystals remain inside the basket. The filtrate is eliminated from the outlet.

- When the height of the cake is approximately 2-3 inches, the suspension inlet is stopped by a "feeler diaphragm valve assembly".
- The basket rotates at a predetermined time and then the cake is washed with water. The basket is rotated for another predetermined time.
- After that, the hydraulic apparatus raises the knife-chute assembly to cut the cake.
- The cake is collected.

Uses:

- Used to separate crystal from mother liquor.
- Used to clarify liquid removing unwanted solids dirt from oils

Merits:

- This centrifuge is used to separate crystals from the mother liquor.
- This is used to clarify Liquids by removing unwanted solids and dirt from oils.

Demerits:

- Complicated process
- Sometimes chances of breakage of the crystal during discharge.
- High power consumption

Super Centrifuge

Principles:

- Super centrifuge is a continuous centrifuge used to separate two immiscible liquid phases.
- It is a sedimentation type centrifuge.
- During centrifugation, the heavier liquid is thrown against the container wall while the lighter liquid remains as an inner layer. The two layers are simultaneously separated.

Construction:

- It consists of a long hollow cylindrical bowl of small diameter.
- It is suspended from a flexible spindle at the top and guided at the bottom by loose-fit bushing.
- Two liquid outlets are provided at different heights at the top of the bowl, for simultaneous recovery of the separated liquids using modified weirs.

Working:

- Rotate the centrifuge at high frequency about 2000 revolutions per minute rotate on its longitudinal axis with the help of motor drive assembly.
- The feed is introduced to centrifuge bowl from the bottom of the centrifuge using suitable pressure system.
- During centrifugation, two liquid phases separate based on the difference in their densities.
- The heavier liquid is thrown against the wall, while the lighter liquid found at inner layer. Both liquids rise to the top of the vertical bowl.
- Both liquid phase interfaces are maintained by a hydraulic balance.
- Two layers of liquids are consistently separated from different heights by using modified weirs.

Thus, supercentrifuge can work for continuous separation of two immiscible liquid phases.

Uses:

- It is used for separating liquid phases of emulsions in food and pharmaceuticals.
- Super centrifuge is widely used for separating liquid phases of emulsions in food, biochemical, and pharmaceutical industries.

Merits:

- This type of centrifuge is employed in the case where the amount of solid removes only at long intervals.
- Operational continuity.
- Capable of handling much higher concentrations.
- Produces solids when dried.

Demerits:

- The structure of sediments is not uniform.