Pharmaceutics –II BOP-232
(Unit Operation)
Unit-II

Water system

- **Raw water**
- **Soft water**
- **Purified water**
- **Water for injection**
- **Quality requirement and treatment of water**
- **Washing**
- **Cleaning and standardization of cleaning**

Filtration and centrifugation

- **Theory of filtration**
- **Filter aids**
- **Filter media**
- **Industrial filter**
- **Filter press**
- **Rotary filter**
- **Edge filter**
- **Factor affecting filtration**

Principal of centrifugation

- Industrial centrifugal filter
- Industrial centrifugal sedimenters

Water system

- Definition-; A colorless, transparent, odorless, liquid which forms the seas, lakes, rivers, and rain and is the basis of the fluids of living organisms.
- Water is a polar inorganic compound that is at room temperature a tasteless and odorless liquid, nearly colorless with a hint of blue.
- Water is a universal solvent.
- Water is essential for life without water life cannot exist
- Water is present on earth about 75%.
- Density: -1,000 kg/m³
- Boiling point: -100 °C
- Formula: -H_2O
- Molar mass: -18.01528 g/mol
- Melting point:- 0 °C

Types of water

- Raw water
- Drinking water / potable water (Specification: BIS, WHO, ISO, IPA)
- Purified water (Specification IP, BP, USP & Others pharmacopeia)
- Water for injection (Specification: IP, BP, USP & Others pharmacopeia)

Raw water

- Raw water is a natural water that is obtained from natural origin without passing from potable process
- Raw water sources are rivers lakes ponds etc
- This water is ground water used for many purposes without purification such as washing of dress

Characteristics of raw water

- **Physical characteristics**
  - ✓ Taste and odour
  - ✓ Turbidity
  - ✓ Colour
- **Chemical characteristics**
  - ✓ PH
  - ✓ Hardness

Soft water

- Soft water is a types of water which contain calcium and magnesium ions i.e.(1-60mg/L)
- Soft water comes from peat or igneous rock sources.
- In hard water 120-180 mg/litre

Potable Water:

- Used in early stages of chemical synthesis
- Used Early stages of Equipment Cleaning
- Sources: Public water supply, wells or combination of > 1 of these
- Must meet Requirements of USEPA (40 CFR 141)
- Seasonal variations in quality may occur and must be considered for treatment before usage.

Purified water

- Purified water is water mechanically filtered or processed to be cleaned for consumption.
- Purified water is obtained from distillation method.
- Purified water is originated from tap water and ground water.
- Purified water is used as marine resources such as in aquarium.
- Used as excipients in manufacturing of pharmaceuticals.
- Used for Equipment Cleaning esp. product contact surfaces of nonsterile chemicals
- Preparation of bulk chemicals.
- Types of Purification: Deionization, Distillation, Ion exchange, Reverse Osmosis, Filtration.
- Must meet ionic, organic chemical and microbial requirements.

Water for injection- (*aqua ad iniectabilia* or *aqua ad injectionem*) is water of extra high quality, which is used for production of parenterals (e. g. infusion solution for intravenous therapy or solution for injection) and water-based ophthalmic products according to Pharmacopoeia

- WFI is not sterile.
- WFI is Water for injection is a type of water which is obtained from the distilled water
- Prepared from potable water and purified water source.
- WFI is an intermediate bulk product
- Used as excipient in manufacturing of potentials.
- Used for Equipment Cleaning esp. product contact surfaces of sterile products.
- Preparation of sterile bulk chemicals.
- Method of preparation is multicolumn distillation..
- Must meet ionic, organic chemical, microbial and endotoxins requirements.

Water quality

- Water quality refers to the chemical, physical, biological, and radiological characteristics of water.
- It is a measure of the condition of water relative to the requirements of one or more biotic species and or to any human need or purpose
- The parameters for water quality are determined by the intended use. Work in the area of water quality tends to be focused on water that is treated for human consumption, industrial use, or in the environment.
- Water quality depends on the local geology and ecosystem
- Drinking water quality standards describes the quality parameters set for drinking water

Pharmaceutical water indicators

The following is a list of indicators often measured by situational category:

- ✓ Alkalinity
- ✓ Color of water
- ✓ pH
- ✓ Taste and odor (geosmin, 2-Methylisoborneol (MIB), etc.)
- ✓ Dissolved metals and salts (sodium, chloride, potassium, calcium, manganese, magnesium)
- ✓ Microorganisms such as fecal coliform bacteria (*Escherichia coli*), Cryptosporidium, and Giardia lamblia; *see* Bacteriological water analysis
- ✓ Dissolved metals and metalloids (lead, mercury, arsenic, etc.)
- ✓ Dissolved organics: colored dissolved organic matter (CDOM), dissolved organic carbon (DOC)
- ✓ Heavy metals
- ✓ Hormone analogs

Physical indicators

- ✓ Water Temperature
- ✓ Specifics Conductance or EC, Electrical Conductance, Conductivity
- ✓ Total suspended solids (TSS)
- ✓ Transparency or Turbidity
- ✓ Total dissolved solids (TDS)
- ✓ Odour of water
- ✓ Color of water
- ✓ Taste of water

Chemical indicators

- ✓ pH
- ✓ Biochemical oxygen demand (BOD)
- ✓ Chemical oxygen demand (COD)
- ✓ Dissolved oxygen (DO)
- ✓ Total hardness (TH)
- ✓ Heavy metals
- ✓ Nitrate
- ✓ Orthophosphates
- ✓ Pesticides
- ✓ Surfactants

Biological indicators

- ✓ Ephemeroptera
- ✓ Plecoptera
- ✓ Mollusca
- ✓ Trichoptera
- ✓ *Escherichia coli* (E. coli)
- ✓ Coliform bacteria

The World Health Organisation (WHO) Guideline for Drinking-water Quality (GDWQ)

Parameter	World Health Organization	European Union	United States	China	Canada
1,2-dichloroethane	“	3.0 µg/l	5 µg/l	“	“
Acrylamide	“	0.10 µg/l	“	“	“
Antimony	ns	5.0 µg/l	6.0 µg/l	“	“
Arsenic	10µg/l	10 µg/l	10µg/l	50µg/l	“
Barium	700µg/l	ns	2 mg/L	“	“
Benzene	10µg/l	1.0 µg/l	5 µg/l	“	“
Benzo(a)pyrene	“	0.010 µg/l	0.2 µg/l	0.0028 µg/l	“
Boron	2.4mg/l	1.0 mg/L	“	“	“
Bromate	“	10 µg/l	10 µg/l	“	“
Cadmium	3 µg/l	5 µg/l	5 µg/l	5 µg/l	“
Chromium	50µg/l	50 µg/l	0.1 mg/L	50 µg/l (Cr6)	“
Copper	“	2.0 mg/l	TT	1 mg/l	“
Cyanide	“	50 µg/l	0.2 mg/L	50 µg/l	“
Epichlorohydrin	“	0.10 µg/l	“	“	“
Fluoride	1.5 mg/l	1.5 mg/l	4 mg/l	1 mg/l	“
Lead	“	10 µg/l	15 µg/l	10 µg/l	“
Mercury	6 µg/l	1 µg/l	2 µg/l	0.05 µg/l	“
Nickel	“	20 µg/l	“	“	“
Nitrate	50 mg/l	50 mg/l	10 mg/L (as N)	10 mg/L (as N)	“
Nitrite	“	0.50 mg/l	1 mg/L (as N)	“	“
Pesticides (individual)	“	0.10 µg/ l	“	“	“
Pesticides — Total	“	0.50 µg/l	“	“	“
Polycyclic aromatic hydrocarbons l	“	0.10 µg/	“	“	“
Selenium	40 µg/l	10 µg/l	50 µg/l	10 µg/l	“
Tetrachloroethene and Trichloroethene	40µg/l	10 µg/l	“	“	
,2-dichloroethane	“	3.0 µg/l	5 µg/l	“	“
Acrylamide	“	0.10 µg/l	“	“	“
Antimony	ns	5.0 µg/l	6.0 µg/l	“	“
Arsenic	10µg/l	10 µg/l	10µg/l	50µg/l	“
Barium	700µg/l	ns	2 mg/L	“	“
Benzene	10µg/l	1.0 µg/l	5 µg/l	“	“
Benzo(a)pyrene	“	0.010 µg/l	0.2 µg/l	0.0028 µg/l	“
Boron	2.4mg/l	1.0 mg/L	“	“	“

Parameter	World Health Organization	European Union	United States	China	Canada
Bromate	“	10 µg/l	10 µg/l	“	“
Cadmium	3 µg/l	5 µg/l	5 µg/l	5 µg/l	“
Chromium	50µg/l	50 µg/l	0.1 mg/L	50 µg/l (Cr6)	“
Copper	“	2.0 mg/l	TT	1 mg/l	“
Cyanide	“	50 µg/l	0.2 mg/L	50 µg/l	“
Epichlorohydrin	“	0.10 µg/l	“	“	“
Fluoride	1.5 mg/l	1.5 mg/l	4 mg/l	1 mg/l	“
Lead	“	10 µg/l	15 µg/l	10 µg/l	“
Mercury	6 µg/l	1 µg/l	2 µg/l	0.05 µg/l	“
Nickel	“	20 µg/l	“	“	“
Nitrate	50 mg/l	50 mg/l	10 mg/L (as N)	10 mg/L (as N)	“
Nitrite	“	0.50 mg/l	1 mg/L (as N)	“	“
Pesticides (individual)	“	0.10 µg/ l	“	“	“
Pesticides — Total	“	0.50 µg/l	“	“	“
Polycyclic aromatic hydrocarbons l	“	0.10 µg/	“	“	“
Selenium	40 µg/l	10 µg/l	50 µg/l	10 µg/l	“

Treatment of water

- Water treatment is any process that makes water more acceptable for a specific end-use. The end use may be drinking, industrial water supply, irrigation, river flow maintenance, water recreation or many other uses including being safely returned to the environment.
- Water treatment removes contaminants or reduces their concentration so that the water becomes fit for its desired end-use, .
- Treatment for drinking water production involves the removal of contaminants from raw water to produce water that is pure enough for human consumption without any short term or long term risk of any adverse health effect.
- Substances that are removed during the process of drinking water treatment include suspended solids, bacteria, algae, viruses, fungi, and minerals such as iron and manganese.
- The processes involved in removing the contaminants include physical processes such as settling and filtration, chemical processes such as disinfection and coagulation and biological processes such as slow sand filtration

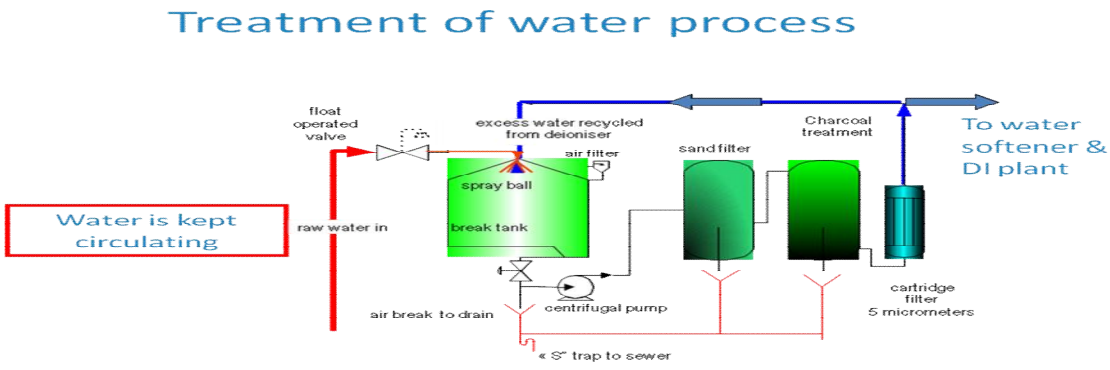
There are the following methods are use for treatment of water

- ✓ a)Boiling
- ✓ b)Filtration
- ✓ c)Addition of ammonia
- ✓ d) Sedimentation
- ✓ e)Chlorination
- ✓ f)Clark lime process

Processes

A combination selected from the following processes is used drinking water treatment worldwide:

- Pre-chlorination for algae control and arresting biological growth
- Aeration along with pre-chlorination for removal of dissolved iron and manganese
- Coagulation for flocculation or slow-sand filtration
- Coagulant aids, also known as polyelectrolytes – to improve coagulation and for thicker floc formation
- Sedimentation for solids separation, that is removal of suspended solids trapped in the floc
- Filtration to remove particles from water
- Disinfection for killing bacteria viruses and other pathogens.



Objective of treatment of water

- For the drinking purpose
- For the manufacturing of pharmaceutical product
- For the physical work as bathing
- For the cleaning of utensils
- For the laboratory works
- For removing the microbes and contaminants

FILTRATION

- Filtration is a mechanical or physical operation which is used for the separation of solids from fluids (liquids or gases) by interposing a medium through which only the fluid can pass.
- After filtration the filtrate is transparent liquid free from insoluble solids, collides or insoluble liquid drops

CLARIFICATION

- The term clarification is used when the solids present in the liquid is very small and they do not exceed 1% and filtrate is the required product

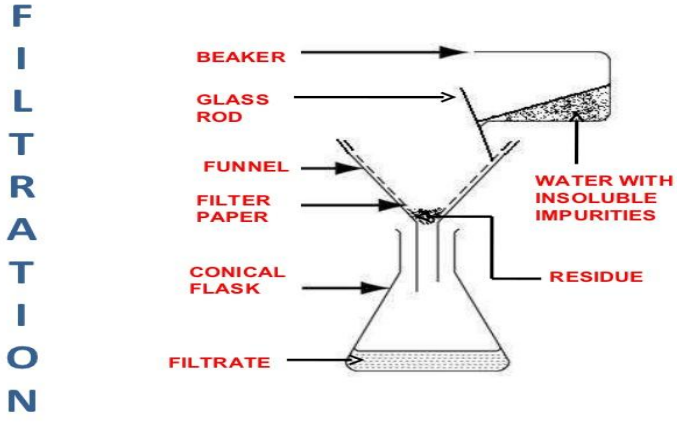
FEED OR SLURRY- The suspension of solids and liquids to be filtered is known as feed or slurry

FILTER MEDIUM The porous medium through which the slurry is forced to pass and provides mechanical supports to filter cake is called filter medium .

FILTER CAKE The solids collected on the filter medium is referred to as filter cake

FILTERATE Clear liquid which passes through the filter is called filtrate

MECHANISM OF FILTRATION The mechanism whereby particles are retained by a filter is significant only in initial stages of filtration.



- **Straining** -Similar to sieving, i.e., particles of larger size can't pass through smaller pore size of filter medium.
- **Impingement-** Solids having the momentum move along the path of streaming flow and strike (impinge) the filter medium. Thus the solids are retained on the filter medium.
- **Entanglement -**Particles become entwined (entangled) in the masses of fibres (of cloths with fine hairy surface or porous felt) due to smaller size of particles than the pore size. Thus solids are retained within filter medium.
- **Attractive forces** -Solids are retained on the filter medium as a result of attractive force between particles and filter medium, as in case of electrostatic filtration.

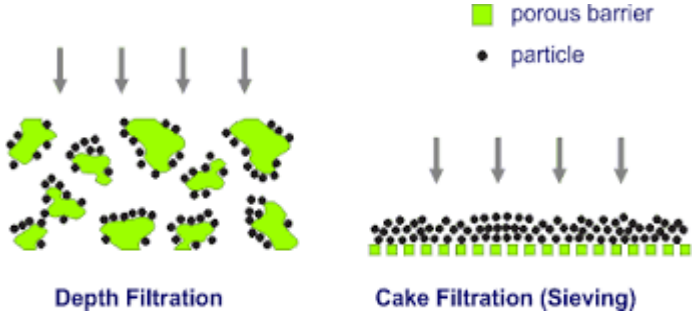
Types of filtration

1) Surface filtration.
2) Depth filtration.

1) Surface filtration: Common process. Porous surface is used for filtration & has pores on it. And to be removed larger size than the pore size of porous medium. So particles can't pass via pores & retain on filter media. Membrane filters are used in it. So, when filter the mixture, the large particles retain on the filter media & clear liquid is obtained.
Mechanism involved: straining and impingement

2) Depth filtration- In this slurry penetrates to a point where the diameter of solid particles is greater than that of the tortuous void or channel.

Mechanism involved- Entanglement



Theories of filtration

- ✓ The flow of 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-volume (litres) per unit time (dv/dt).
- ✓ Driving force = pressure upstream – pressure downstream
- ✓ Resistance is not constant. It increases with an increase in the deposition of solids on the filter medium.
- ✓ **Therefore filtration is not a steady state**.

Rate = driving force / resistance

- ✓ The rate of flow will be greatest at the beginning of filtration process, since the resistance is minimum.
- ✓ After forming of filter cake, its surface acts as filter medium and solids continuously deposit adding to thickness of the cake. Powder or granule bed visualized as a bundle of capillaries

Poiseullie's Equation $V=\pi\Delta Pr^4/8\,\eta L$

Where, V = rate of flow, m3/s (l/s)

ΔP= Pressure difference across the filter, Pa

r = radius of capillary in the filter bed, m

L = thickness of filter cake (capillary length),

η = viscosity of filtrate, Pa.s

Darcy's Equation

$$dv/dt - KA\,\Delta P/\eta\, l$$

Where
V=volume of filtrate
t=time of filtration
K=constant for filter medium & filter cake
A=area of filter medium
Δ **P**=pressure difference above & below the filter medium
η =viscosity of Slurry
l= thickness of the filter bed

- K depends on characteristics of cake, such as porosity, specific surface area and compressibility.

Kozeny-Carman Equation $V=A\Delta P\ \varepsilon^3(1-\varepsilon)/\ S^2\ \eta\ KL$

Where, ε = porosity of cake (bed)

S = specific surface area of particles comprising the cake m2 / m3

K = Kozeny constant (usually taken as 5)

- **Limitations:** It does not consider the fact that depth of granular bed is lesser than the actual path traversed by the fluid. ¬ The actual path is not same through out the bed, but it is sinuous or tortuous.

Factors Effecting Rate of Filtration

- Area of filter surface
- Particle size of the solids to be removed.
- Pore size of the filter media
- The resistance of the filter cake and filter media
- Viscosity of the liquid
- Temperature
- Pressure difference

FILTER MEDIA The surface or medium upon which are retained the solid and allow the filtrate in the process of filtration is known as filtration media

Ideal characteristics of the filter media

- ✓ It should be chemically inert
- ✓ It should have high resistance power for the solids
- ✓ It should have sufficient mechanical strength to withstand filtration pressure
- ✓ should absorb negligible amount of dissolve material
- ✓ should have resistance for the corrosive action of the liquid

Selection of appropriate filter media:

- ✓ Must effectively retain the solid particles.
- ✓ Should not be leakage of solid particles via filter media.
- ✓ Should be chemically inert.
- ✓ Should be physically stable.
- ✓ Should be cost effective.

Types of filter media:

1. Filter cloth
2. Kraft paper
3. Felt
4. Fabric (bounded)
5. Cartridges
6. Glass wool
7. Sintered glass filter

Classification of filtration equipments

- ❖ Based on application of external force:
  - ✓ Filters Pressure filters
  - ✓ Plate and frame filter press
  - ✓ Meta filter
  - ✓ Vacuum filters
  - ✓ Filter leaf
  - ✓ Centrifugal filters centrifuges
- ❖ Based on operation of filtration Filters
  - ✓ **Continuous filtration** -Discharge and filtrate are separated steadily and uninterrupted.
  - ✓ **Discontinuous filtration**- Discharge of filtered solid is intermittent. Filtrate is removed continuously.

Selection of filtration equipment

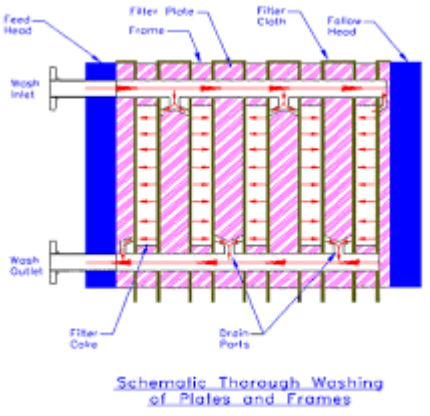
- ✓ Depends upon the properties of fluid- viscosity
- ✓ Nature of solids- size, shape,
- ✓ Distribution and packing characteristics of particles
- ✓ Conc. Of solid in suspension
- ✓ Quantity of material to be handling whether it is necessary to wash the solid whether any form of pre-treatment will be helpful.
- ✓ Equipment and process related Flow rate should be absolute in sense, limit to size of particles passing through the filter should be known.
- ✓ Should be sterilisable by heat, radiation or gas
- ✓ Should be economical.

Plate and frame filter press

Principle: Mechanism is surface filtration. The slurry enters the frame by pressure and flows through filter medium. The filtrate is collected on the plates and sends 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.

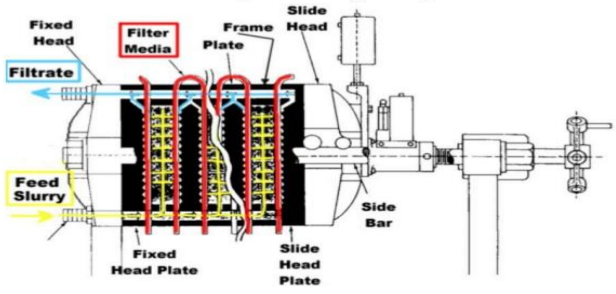
Construction

- ✓ The Filter press is made of two types of units, plate and frames.
- ✓ Usually made of aluminium alloy.
- ✓ Sometimes, these are also lacquered for protection against corrosive chemicals and made suitable for steam sterilization.
- ✓ Frame - It contains a open space inside wherein the slurry reservoir is maintained for filtration and an inlet to receive the slurry. It is indicated by two dots in description.
- ✓ Slurry inlet Handle to rest on rod



Schematic Through Washing of Plates and Frames

Gambar plate and frame filter



Working -Working can be divided into two steps-

1. Filtration operation
2. Washing of cake (if desirable)

1**. Filtration operation**

- ✓ Slurry enters the frame from the feed channel and passes through the filter medium on the surface of the plate .
- ✓ The solid forms a filter cake and remain in the frame .
- ✓ The thickness of the cake is half of the frame thickness, because on each side of frame filtration occurs Thus two filter cakes are formed , which meet eventually in the centre of the frame.
- ✓ The filtrate drains between the projections of the surface of the plate and escape from the outlet .
- ✓ As filtration proceeds, the resistance of the cake increases and filtration rate decrease A

Washing operation

- ➢ When washing of cake is also required modified plate and frame filter is used.
- ➢ For this purpose an additional channel is included called as washing plate .
- ➢ In the half of the washing plate, there is a connection from wash water cannel to the surface of plate.

Procedure for washing the press

- ✓ Step 1 • Filtration proceeds in the ordinary way until the frames are filled with cake.
- ✓ Step 2 • To wash the filter cake, the outlets of washing plates are closed.
- ✓ Step 3 • Wash water is pumped in the washing channel. • The water enters through the inlets on the surface of washing plate.
- ✓ Step 4 • Water passes through the filter cloth and enters frame which contains the cake. • Then water washes the cake, passes through the filter cloth and enters the plate down the surface.
- ✓ Step 5 • finally washed water escapes through the outlet of that plate.

Advantages

- ✓ Construction of filter press is very simple and a variety of materials can be used.
- ✓ 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 pressure difference
- ✓ Efficient washing of cake is possible. • Operation and maintenance is easy.
- ✓ It produces dry cake in form of slab.

Disadvantages

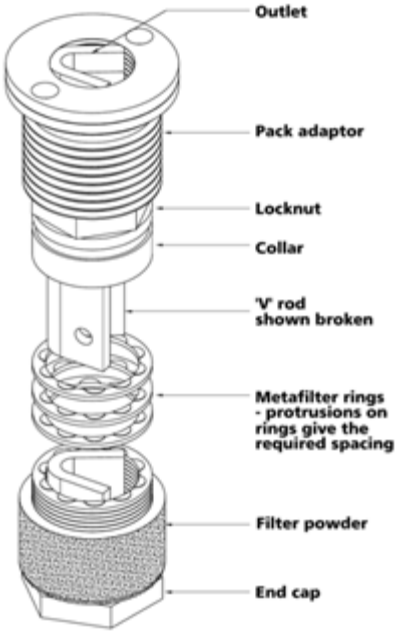
- ✓ It is a batch filter, so it is a time consuming.
- ✓ The filter press is an expensive filter, the emptying time, the labour involved, and the wear and tear on the cloths resulting in high costs.
- ✓ Operation is critical, as the frames should be full, otherwise washing is inefficient and the cake is difficult to remove.
- ✓ The filter press is used for slurries containing less about 5 % solids
- ✓ In view of the high labour costs, it is most suitable for expensive materials e.g. the removal of precipitated proteins from insulin liquors.

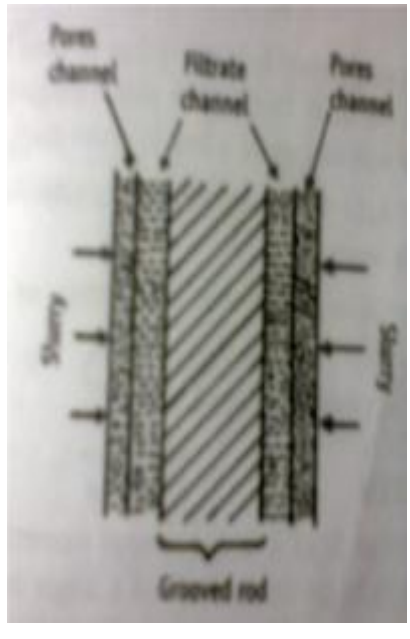
Meta filter

Principle: Mechanism is surface filtration. In this, metal rings contain semicircular projections, which are arranged as a nest to form channels on the edges. This channel offers resistance (strainer) to the flow of solids (coarse particles). The clear liquid is collected into receiver from the top.

Construction

- ✓ Metafilter consists of a series of metal rings.
- ✓ These are threaded so that a channel is formed on the edges.
- ✓ It contains a grooved drainage column on which a series of metal rings are packed.
- ✓ These rings are usually made up of stainless steel and have dimensions of about 15.0 mm internal diameter and 22.0 mm external diameter.
- ✓ Each metal ring has a number of semicircular projections (0.8 mm in thickness) on one side of surface.
- ✓ The projections are arranged as a nest to form channels on the edges.
- ✓ These rings are tightened on the drainage column with a nut.
- ✓ Metafilters are also known as edge filters.





Working

- In the working of the Meta filters involves filters are placed in a vessel and may be operated by pumping the slurry under pressure or occasionally by the applications of reduced pressure to the outlet side.
- The slurry passes through the channels formed on the edge between the rings.
- The clear liquid rises up and collected from the outlet into the receiver.
- Meta filter functions as a strainer. For the separation of the fine particles, a bed of suitable materials such as kieseluhr is first built up.
- The pack of the rings serves essentially as a base on which the true filter medium is supported.

Advantages

- ✓ 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.
- ✓ Can be constructed from a material that can provide excellent resistance to corrosion and avoid contamination of sensitive products.
- ✓ It is extremely versatile filter because fine as well as large both types of particles can be separated.
- ✓ 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.

Uses -Meta filters can be used for-

- ✓ Clarification of syrups
- ✓ Filtration of injection solutions
- ✓ Clarification of insulin liquors
- ✓ Filtration of viscous liquids can be achieved by applying pressure.

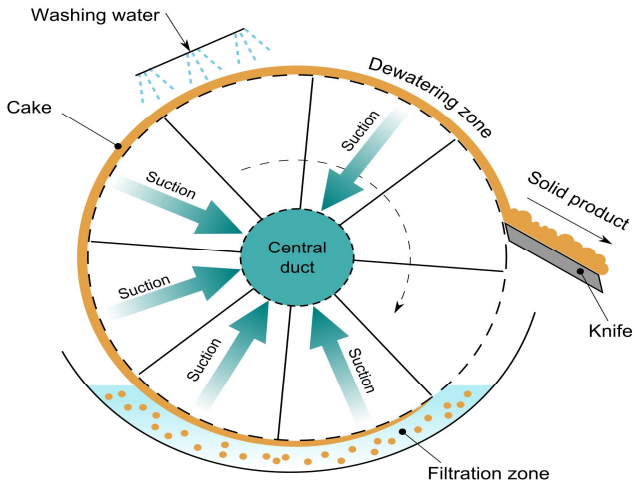
Rotary drum filter

Principle:

Slurry filtered through sieve like mechanism on the rotation drum surface, under the condition of vacuum. In addition compression, drying (using hot air), and removing the filter cake (using knife) are possible.

Construction –

- ✓ It consists of a metal cylinder mounted horizontally.
- ✓ The drum may be up to 3 meters in diameter and 3.5 meters in length and gives surface area of 20 meter square.
- ✓ The curved surface being a perforated plate, supporting a filter cloth.
- ✓ Internally, it is divided into several sectors and a separate connection is made between each sector and a special rotary valve



Working

- ✓ The drum is dipped into the slurry and vacuum applied to the outlet, which is connected to the filtrate receiver.
- ✓ When the cake has formed, the cake drained or partially dried by vacuum.
- ✓ The drum is sprayed with water to wash the cake.
- ✓ Retaining the vacuum connection drains the cake and produces partial dryness then, removed by a doctor knife.

- ✓ When the solids of the slurry are too much that the filter cloth becomes blocked with the particles, a pre-coat filter may be used.
- ✓ A pre-coat of filter aid is deposited on the drum prior to the filtration process.

Advantages

- ✓ The rotary filter is automatic and is continuous in operation, so that the labour costs are very low.
- ✓ The filter has a large capacity, so it is suitable for the filtration of highly concentrated solutions.
- ✓ Variation of the speed of rotation enables the cake thickness to be controlled.
- ✓ Pre-coat of filter aid could used to accelerate the filtration rate.
- ✓ Filter has large surface area.

Disadvantages

- ✓ The rotary filter is a complex piece of equipment, with many moving parts and is very expensive.
- ✓ In addition to the filter itself, some accessories are connected, e.g., a vacuum pump, vacuum receivers, slurry pumps and agitators are required .
- ✓ The cake tends to crack due to the air drawn through by the vacuum system, so that washing and drying are not efficient.
- ✓ Being a vacuum filter, the pressure difference is limited to 1 bar and hot filtrates may boil.
- ✓ It is suitable only for straight- forward slurries

Uses

- ✓ The rotary filter for continuous operation on large quantities of slurry.
- ✓ Suitable for slurry contains considerable amounts of solids in the range 15-30%.
- ✓ Examples of pharmaceutical application include ¬the collection of calcium carbonate, magnesium carbonate, and starch.
- ✓ The separation of the mycelium from the fermentation liquor in the manufacture of antibiotics.

CENTRIFUGATION

PRINCIPLES OF CENTRIFUGATION- Particles having a size above 5μm sediment at the bottom due to gravitation force. Such a suspension can be separated by simple filtration techniques. If the size of particles are less than 5μm they undergo Brownian motion. In such suspension a stronger centrifugal force is applied to separate the particles.

- Centrifugation is a process which involves the application of the centripetal force for the sedimentation of heterogeneous mixtures with a centrifuge,
- This process is used to separate two miscible substances, but also to analyze the hydrodynamic properties of macromolecules.
- More-dense components of the mixture migrate away from the axis of the centrifuge, while less-dense components of the mixture migrate towards the axis.
- There is a correlation between the size and density of a particle and the rate that the particle separates from a heterogeneous mixture, when the only force applied is that of gravity.
- The larger the size and the larger the density of the particles, the faster they separate from the mixture.
- The rate of centrifugation is specified by the angular velocity usually expressed as revolutions per minute (RPM), or acceleration expressed as *g*.
- The general formula for calculating the revolutions per minute (RPM) of a centrifuge is

$$,RPM= \sqrt{g/r}$$

where g represents the respective force of the centrifuge and r the radius from the center of the rotor to a point in the sample

Application

1. Production of bulk drugs

After crystallization the drugs are separated from the mother liquor by centrifugation. For example traces of mother liquor is separated from aspirin crystals by centrifugation method.

2. Production of biological products

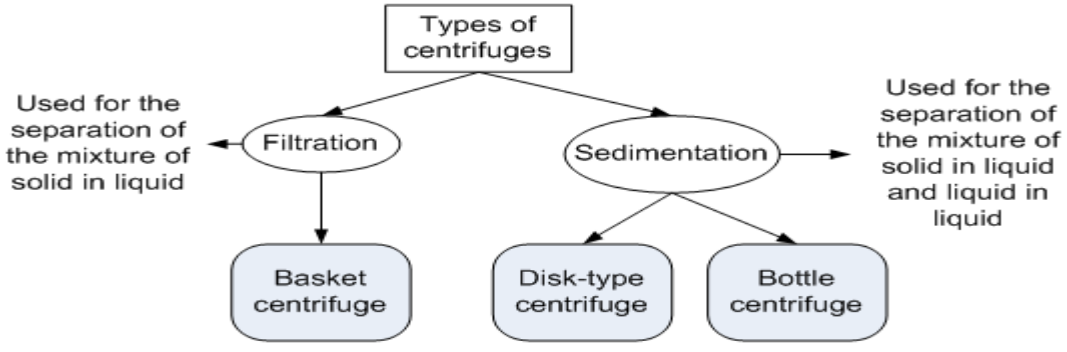
Most of the biological products are either proteinaceous or macromolecules. During manufacturing they remain in colloidal dispersion in water. By normal methods of filtration it is difficult to separate the colloid particles. In those cases centrifugal methods are used. Insulin is purified from other precipitates of protein materials by centrifugation. Blood cells are separated from plasma by centrifugal method. Bacterial enzymes are separate from bacterial culture medium by sedimenting the bacterial cells by centrifugation. Dirt and water are separated from olive oil and fish-liver oils.

3. Evaluation of suspensions and emulsions

One of the problems of suspensions is sedimentation and one of the problems of emulsions is creaming. Immediately after the preparation of a suspension or emulsion this problems may not appear quickly. To enhance the rate of sedimentation and creaming the suspension or emulsion is introduced in a centrifuge and rotate at an rpm of 200 to 3000. If still the problems do not appear then the suspension or emulsion can be taken as stable formulation.

4. Determination of molecular weight of colloids

Polymers, proteins and such macromolecules often forms colloidal dispersions. The molecular weights of those molecule can be determined by ultracentrifugation. The larger molecules will be arranged at periphery and the lighter molecules near the centre



Conical Disc Centrifuge

- ✓ Large particles have higher settling velocities than small particles
- ✓ Cellular debris ends up at the outer edge of the bowl
- ✓ Soluble intracellular material passes through with the clarified liquid
- ✓ Discs give a higher sigma factor