Filtration Sterilization

The major mechanisms of filtration are sieving, adsorption and trapping within the matrix of the filter material.

Sterilizing grade filters are used in the treatment of heat sensitive injections and ophthalmic solutions, biological products and air and other gases for supply to aseptic areas.

Filtration through a membrane with 0.2 micron or smaller pore size removes biological contaminants, including bacteria, mold and yeast.

Aseptic technique means using practices and procedures to prevent contamination from pathogens. It involves applying the strictest rules to minimize the risk of infection.

The elements of aseptic technique are a sterile work area, good personal hygiene, sterile reagents and media, and sterile handling.

FILTRATION

FILTRATION may be define as a process of separation of solids from a fluid by passing the same through a porous medium that retains the solids but allows the fluid to pass through.

Terms Used in Filtration

Slurry: Suspension to be filtered

Filter: Porous medium used to retain solid

Filter cake: Accumulated cake solids on the filter

Filtrate: Clear liquid passing through the filter

Applications of Filtration

- Production of sterile products
- Production of bulk drugs
- Production of liquid dosage forms
- Effluents and waste water treatment

Mechanism 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

Surface/screen filtration

- **It is a screening action by which pores or holes of medium prevent the passage of solids.**
- **Mechanism involved: straining and impingement**
- **For this, plates with holes or woven sieves are used.**
- **Efficacy is defined in terms of mean or maximum pore size.**

Depth filtration

In this method, the removal of suspended particulate material from liquid slurry is done by passing the liquid through a filter bed composed of granular or compressible filter medium.

Mechanism: Entanglement

- **The solids are retained with a gradient density structure by physical restriction or by adsorption properties of medium.**

Theories of Filtration

Poiseullie's Equation

Poiseullie considered that filtration is similar to the streamline flow of liquid under pressure through capillaries.

Poiseullie's Equation is-

$$V = \frac{\Delta P \pi r^4}{8 \eta L}$$

Where, V=rate of flow, m^3/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), m
η = viscosity of filtrate, Pa.s

If the cake is composed of bulky mass of particles and the liquid flows through the interstice, then flow of liquids through these may be expressed by this equation.

Darcy's Equation

Poiseullie's law assumes that the capillaries found in the filter are highly irregular and non-uniform.
Therefore, if the length of capillary is taken as the thickness of bed, a correction factor for radius is applied so that the rate is closely approximated and simplified.
The factors influencing the rate of filtration has been incorporated into an equation by Darcy, which is:

$$V = \frac{K A \Delta P}{\eta L}$$

Where, K = permeability coefficient of cake, m^2
A = surface area of porous bed (filter medium), m^2

Other terms are same as previous equation

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

Permeability may be defined quantitatively as the flow rate of a liquid of unit viscosity across a unit area of cake having unit thickness under a pressure gradient of unity.

This equation is valid for liquids flowing through sand, glass beds and various porous media.

This model is applied to filter beds or cakes and other types of depth filter.

This equation is further modified by including characteristics of K by Kozeny-Carman.

Kozeny-Carman Equation

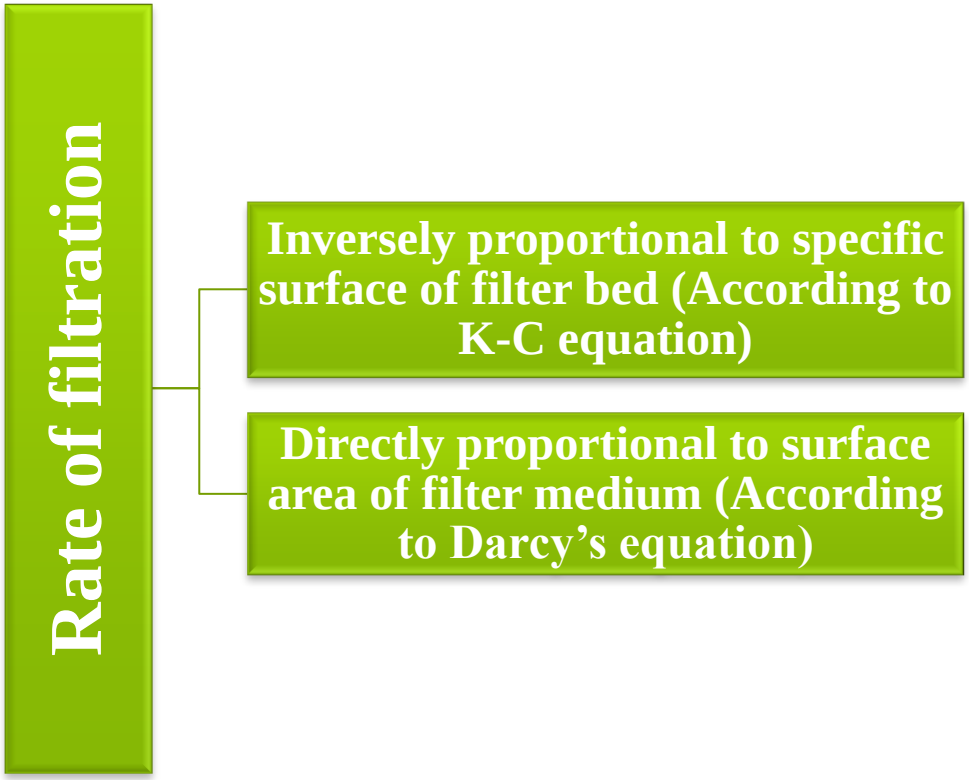
Kozeny-Carman equation is widely used for filtration.

$$V = \frac{\varepsilon^3}{kS^2(1-\varepsilon)^2} \frac{A \Delta P g}{\eta L}$$

Where,
ε = porosity of cake (bed)
S = specific surface area of particles comprising the cake m^2/m^3
K = Kozeny constant (usually taken as 5)

Other terms are same as previous equations

Surface Area of Filter Medium



Rate can be increased either using large filter or connecting a number of small units in parallel.

Filter press works on principle of connecting units in parallel.

Viscosity of Filtrate

According to K-C equation rate of filtration is inversely proportional to the viscosity of the fluid.

Reason behind this is an increase in the viscosity of the filtrate will increase the resistance of flow.

This problem can be overcome by two methods:

1. **The rate of filtration may be increased by raising the temperature of the liquid, which lowers its viscosity. However, it is not practicable if thermolabile materials are involved or if the filtrate is volatile.**
2. **Dilution is another alternative but the rate must be doubled.**

Filter Media

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

Properties of ideal filter medium:

It should-

1) be capable of delivering a clear filtrate at a suitable production rate.

2) have sufficient mechanical strength.

3) be inert.

4) retain the solids without plugging at the start of filtration.

5) Not absorb dissolve material.

6) Sterile filtration imposes a special requirement since the pore size must not exceed the dimension of bacteria or spores.

Material used as filter media

Woven material

- Made up of wool, silk, metal or synthetic fibres (rayon, nylon etc.).
- These include a) wire screening and b) fabrics of cotton, wool, nylon.
- Wire screening e.g. stainless steel is durable, resistance to plugging and easily cleaned.
- Cotton is a common filter, however, nylon is superior for pharmaceutical use, since it is unaffected by mold, fungus or bacteria and has negligible absorption properties .
- The choice of fibre depends on chemical.

Perforated sheet metal

Stainless steel plates have pores which act as channels as in case of meta filters.

Bed of granular solid built up on supporting medium

- **In some processes, a bed of graded solids may be formed to reduce resistance of flow.**
- **Ex. Of granular solids are gravel, sand, asbestos, paper pulp and keiselgur.**
- **Choice of solids depends on size of solids in process.**

Prefabricated porous solid units

- **Used for its convenience and effectiveness.**
- **Sintered glass, sintered metal, earthenware and porous plastics are used for fabrication.**

Membrane filter media

- These are cartridge units and are economical and available in pore size of 100 µm to even less than 0.2 µm.
- Can be either surface cartridges or depth type cartridges.

Surface cartridges

- These are corrugated and resin treated papers and used in hydraulic lines.
- Ceramic cartridges and porcelain filter candles are examples.
- Can be reuse after cleaning.

Depth type cartridges:

- Made up of cotton, asbestos or cellulose.
- These are disposable items, since cleaning is not feasible.

Properties of Membrane Filter

- **Membrane filters consist of approximately 60-80% air-filled pores.**
- **Filtration is done by applying pressure or vacuum.**
- **The retention feature is low.**
- **The adsorption probability of the active substances is very small.**
- **When used for sterile filtration, the likelihood of bacterial growth in their structures is very small.**
- **They do not give any molecule solution.**
- **They have both in-depth and surface filtering properties.**

Ultrafilter

Membrane filters with pore diameter between 0.001-0.1 µm are called ultrafilters.

They are produced with a support layer which increases the physical resistance of the filter.

Quality Controls of Membrane Filter

Microbiological Methods for Quality Control of Membrane Filters

Pseudomanas diminuta is used for the validation of sterilization.

Filter Integrity Test Methods

Bubble Point Test, Forward Flow Test, Pressure Hold Test

Bubble Point Test

A bubble point test is a test designed to determine the pressure at which a continuous stream of bubbles is initially seen downstream of a wetted filter under gas pressure.

To perform a Bubble Point Test, gas is applied to one side of a wetted filter, with the tubing downstream of the filter submerged in a bucket of water. The filter must be wetted uniformly such that water fills all the voids within the filter media. When gas pressure is applied to one side of the membrane, the test gas will dissolve into the water, to an extent determined by the solubility of the gas in water.

Downstream of the filter, the pressure is lower. Therefore the gas in the water on the downstream side is driven out of solution. As the applied upstream gas pressure is increased, the diffusive flow downstream increases proportionally. At some point, the pressure becomes great enough to expel the water from one or more passageways establishing a path for the bulk flow of air.

As a result, a steady stream of bubbles should be seen exiting the submerged tubing. The pressure at which this steady stream is noticed is referred to as the bubble point.

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.**

Handling of filter aids

Filter aids may be used in either or both two ways:

1) **Pre- coating technique: by forming a pre-coat over the filter medium by filtering a suspension of the filter aid .**

2) **Body- mix technique: A small proportion of the filter aid (0.1-0.5 %) is added to the slurry to be filtered. This slurry is recirculated through the filter until a clear filtrate is obtained, filtration then proceeds to completion.**

Different flow rates can be achieved depending on grade of aid-

1. **Low flow rate: fine grade filter aids- mainly used for clarity**
2. **Fast flow rate: coarse grade filter aids- acceptable filtrate.**

Examples of filter aids

Diatomite (Keiselgur), obtained from natural siliceous deposits.

Perlite, it is an aluminium silicate. Cellulose, Asbestos, charcoal, talc, bentonite , fullers earth etc.