Clarification and Filtration

Clarification may be defined as the process that involves the removal or separation of a solid from a liquid, or a fluid from another fluid. The term “fluid” encompasses both liquids and gases. Clarification can be achieved using either filtration or centrifugation techniques. Filtration is mainly required to remove unwanted solid particles from a liquid product or from air and centrifugation is normally used to separate fluid from another fluid or to collect the solid as the product

Filtration is defined as the process in which particles are separated from a liquid by passing the liquid through a permeable material. The permeable medium is a porous material that separates particles from the liquid passing through it and is known as a *filter*.

Thus, filtration is a unit operation in which a mixture of solids and liquid, the *feed, suspension, dispersion, influent* or *slurry*, is forced through a porous medium, in which the solids are deposited or entrapped. The solids retained on a filter are known as the *residue*. The solids form a *cake* on the surface of the medium, and the clarified liquid known as *effluent or filtrate* is discharged from the filter. If recovery of solids is desired, the process is called *cake filtration*

.

There are numerous applications of filtration in pharmaceutical
processing which mainly include:
(i) clarification of products to improve their appearance, i.e. to give them ‘sparkle’ or ‘brightness’,
(ii) removal of potential irritants e.g. from eye drop preparations or solutions applied to mucous membranes

,

(iii) filtration for recovery of desired solid material from a suspension of slurry, e.g. to obtain a drug or excipient after a crystallization process,

(iv) production of water of appropriate quality for pharmaceutical use,

(v) meeting sterility specification (removal of microorganisms) required for some products using *sterile filtration or aseptic filtration*

,
(vi) Sterilization of solutions and suspensions that are chemically or physically unstable under heating conditions

(vii) detect ion of microorganisms present in liquids by analyzing a suitable filter on which the bacteria are retained and
(viii) assessment of the efficacy of preservatives. Recently, techniques such as nanofiltration, ultrafiltration, and microfiltration have been used to recover colloidal delivery systems from mother liquor

MECHANISMS OF FILTRATION

Four different mechanisms of filtration according to the way in which the suspended material is trapped by the filter medium are as follows:

1)Surface Straining

In surface straining, any particle that is larger in size than the pores of the medium deposits on the surface, and stays there until it is removed. Particles that are smaller in size than the pores pass quickly through the medium

2) Depth Straining

Depth straining is also governed by particle size or shape. For filter media that are relatively thick in comparison with their pore diameters, particles will travel along the pore until they reach a point where the pore narrows down to a size too small for the particles to go any further, so that they become trapped

3)Depth Filtration

In depth filtration, the particles becomes entrapped in the depth of the medium, even though they are smaller in diameter, and possibly much smaller, than the pore at that point, They become attached to the pore wall, or to another particle already held by means of van der Waals and other surface forces (*entanglement*)

4)Cake Filtration

Cake filtration (which is a development of surface filtration) begins with the formation of a layer of particles on the surface of the filter medium, with larger pores bridged by a group of smaller particles. On this layer, a cake of particles accumulates to act as the filter medium for subsequent filtration. Cake filtration in which solid recovery is the goal is an important pharmaceutical process

These definitions emphasize that the mechanisms of filtration may result in the trapping of far smaller particles than might be expected from the size of the pores in the medium. The actual mechanism or combination of mechanisms in any specific instance is dependent on the characteristics of both the medium and the suspension being filtered

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THEORY OF FILTRATION

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

$$\text{Rate} = \frac{\text{Driving force}}{\text{Resistance}}$$

The rate may be expressed as volume per unit time and the driving force as a pressure differential. The apparent complexity of the filtration equations arises from the expansion of the resistance term. Resistance is not constant since it increases as solids are deposited on the filter medium. An expression of this changing resistance involves a material balance as well as factors expressing permeability or coefficient of resistance of the continuously expanding cake.

These factors have been taken into account in the formation of the *Darcy's equation:*

$$\frac{dV}{dT} = \frac{KA\,\Delta P}{\eta L}$$

where, *A* = Filter area
P= total pressure drop through cake and filter medium
V = volume of filtrate
T = time
η = filtrate viscosity
L = bed thickness in direction of fluid flow
K = permeability coefficient

It is convenient to summarize the theoretic relationship as:

$$\text{Rate of filtration} = \frac{(\text{Area of filter}) \times (\text{Pressure difference})}{(\text{Viscosity}) \times (\text{Resistance of cake and filter})} \quad \ldots ($$

Interpretation of the basic equations, however, leads to a general set of rules:

1)Pressure increases usually cause a proportionate increase in flow unless the cake is highly compressible. Pressure increases on highly compressible, flocculent, or slimy precipitates may decrease or terminate flow.

2)An increase in area increases flow and life proportional to the square of the area since cake thickness and thus resistance, are also reduced.

3)Cake resistance is a function of cake thickness, therefore, the average flow rate is inversely proportional to the amount of cake deposited.

4) The filtrate flow rate at any instant is inversely proportional to viscosity so, filtration efficiency also may be affected by changes in temperature. The viscosities of most liquids decrease with increase in temperature. Increasing the temperature of heavy pharmaceutical syrups lowers the viscosity and increases filtration rates

5) The permeability coefficient may be examined in terms of its two variables: porosity and surface area

,the cake porosity depends on the way in which particles are deposited and packed. A fast deposition rate, given by concentrated slurries or high flow rates, may give a higher porosity because of the greater possibility of bridging and arching in the cake Surface area

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unlike porosity, is markedly affected by particle size and is inversely proportional to particle diameter. Hence, a coarse precipitate is easier to filter than a fine precipitate even though both may pack with the same porosity.

Most clarification problems can be resolved empirically by varying one or more of these factors

FILTER MEDIA

The surface upon which solids are deposited in a filter is called the filter *medium*. For the pharmacist selecting this important element, the wide range of available materials may be bewildering. The selection is frequently based on past experience, and reliance on technical services of commercial suppliers is often advisable. The ideal filter material should have the following characteristics:

1)A medium for cake filtration must retain the solids without plugging and without excessive bleeding of particles at the start of the filtration. In clarification applications in which no appreciable cake is developed, the medium must remove all particles above a desired size.
2)It should offer minimum resistance and the resistance offered by the medium itself will not vary significantly during the filtration process.
3)It allows easy discharge of cake.
4)It should be chemically and physically inert.
5)It should not swell when it is in contact with filtrate and washing liquid.
6)It should have sufficient mechanical strength to withstand pressure drop and mechanical stress during filtration.

There are a variety of different depth filter and membrane filter materials used in pharmaceutical processes. Depth filters are mainly polymeric fibrous materials. The filter fabrics are commonly woven from natural fibers such as cotton and from synthetic fibers and glass

Filter cloth, a surface type medium, is woven from either natural or synthetic fiber or metal. Cotton fabric is the most common and is widely used as a primary medium, as backing for paper or felts in plate and frame filters, and as fabricated bags for coarse straining. Nylon is often superior for pharmaceutical use, since it is unaffected by molds, fungi, or bacteria, provides an extremely smooth surface for good cake discharge, and has negligible absorption properties. Both cotton and nylon are suitable for coarse straining in aseptic filtrations, since they can be sterilized by autoclaving. Monofilament nylon cloth is extremely strong and is available for openings as small as 10 μm. Teflon is superior for most liquid filtration, as it is almost chemically inert, provides sufficient strength, and can withstand elevated temperatures.

Woven wire cloth, particularly stainless steel, is durable, resistant to plugging, and easily cleaned. Metallic filter media provide good surfaces for cake filtration and are usually used with filter aids. As support elements for disposable media, wire screens are particularly suitable, since they may be cleaned rapidly and returned to service. Wire mesh filters also are installed in filling lines of packaging equipment

Non-woven filter media include felts, bonded fabrics, and kraft papers. A *felt* is a fibrous mass that is free from bonding agents and mechanically interlocked to yield specific pore diameters that have controlled particle retention. High flow rate with low pressure drop is a primary characteristic. Felts of natural or synthetic material function as depth media and are recommended where gelatinous solutions or fine particulate matter are involved.

Porous stainless steel filters are widely used for the removal of small amounts of unwanted solids from liquids (clarification) such as milk, syrup, sulfuric acid, and hot caustic soda. Porous metallic filters can be easily cleaned and repeatedly sterilized

Membrane filter media

are the basic tools for microfiltration, ultrafiltration, nanofiltration and reverse osmosis, Membrane filters, classified as surface or screen filters, are made of various esters of cellulose or from nylon, Teflon, polyvinyl chloride, polyamide, polysulfone, or silver

The filter is a thin membrane, about 150 μm thick, with 400 to 500 million pores per square . centimeter of the filter surface. The pores are extremely uniform in size and occupy about 80% of filter volume

The high porosity permits flow rates at least 40 times higher than those obtained through other media of comparable particle retention capability

Because of surface screening characteristics, prefiltration is often required to avoid rapid clogging of a membrane. The selection of a membrane filter for a particular application is a function of the size of the particle or particles to be removed

Surface-type cartridges of corrugated, resin-treated paper are common in hydraulic lines of processing equipment, but are rarely applied to finished products. Ceramic cartridges have the advantage of being cleanable for reuse by back-flushing. Asbestos and porcelain filter candles are acceptable for some sterile filtrations along with membrane filters

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FILTER AIDS

Usually, the resistance to flow due the filter medium itself is very low, but increases as a layer of solids builds up, blocking the pores of the medium and forming a solid, impervious cake. Poorly flocculated solids offer higher resistance than do flocculated solids or solids providing high porosity to the cake.

In the case of cake filtration, the rate varies with the square of the volume of liquid. When the volume of the filter cake solids per unit volume of filtrate is low, the solids deposited on the filter medium may penetrate the void space, thus making the filter medium more resistant to flow. At a higher concentration of solids in a suspension, the bridging over of openings over the void space, rather than blinding of the openings, seems to predominate

The filter medium becomes plugged or slimy with the accumulation of solids, and the flow of filtrate stops. A filter aid acts by reducing this resistance.

Filter aids are a special type of filter medium. Ideally, the filter aid forms a fine surface deposit that screens out all solids, preventing them from contacting and plugging the supporting filter medium.

Usually, the filter aid acts by forming a highly porous and noncompressible cake that retains solids, as does any depth filter. The duration of a filtration cycle and the clarity attained can be controlled as density, type, particle size, and quantity of the filter aid are varied.

The quantity of the filter aid greatly influences the filtration rate. If too little filter aid is used, the resistance offered by the filter cake is greater than if no filter aid is used, because of the added thickness to the cake. On the other hand, if high amounts of filter aid are added, the filter aid merely adds to the thickness of the cake without providing additional cake porosity

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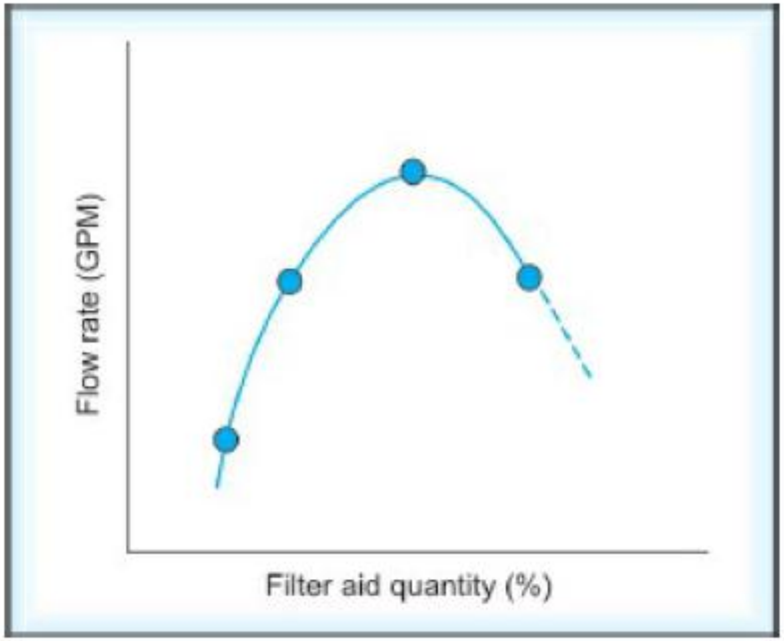


typical plot of filter aid concentration versus permeability. In the figure, flow rate and permeability are directly proportional to each other. At low concentrations of filter aid, the flow rate is low because of low permeability. As the filter aid concentration increases, the flow rate increases and peaks off. Beyond this point, the flow rate decreases as the filter aid concentration is increased

The ideal filter aid performs its functions physically or mechanically and no absorption or chemical action is involved in most cases.

The important characteristics for filter aids are the following:

1)It should have a structure that permits formation of pervious cake.
2)It should have a particle size distribution suitable for the retention of solids, as required.
3)It should be able to remain suspended in the liquid.
4)It should be free of impurities.
5)It should be inert to the liquid being filtered.
6)It should be free from moisture in cases where the addition of moisture would be undesirable

Filter aids are considered to be equivalent in performance when they produce the same flow rate and filtered solution clarity under the same operating conditions when filtering a standard sugar solution

Diatomite (diatomaceous earth) is the most important filter aid. Processed from fossilized diatoms, it has irregularly shaped porous particles that form a rigid incompressible cake. Since diatomite is primarily silica, it is relatively inert and insoluble

Cellulose, asbestos, filter aids are also commercially available. Cellulose is highly compressible and costs two to four times more than diatomite or perlite. It is reserved for applications where the liquids may be incompatible with silica compounds. Cellulose is used as a coarse precoat

Asbestos has good retention on coarse screens, but has limited application because of its high cost, and leaching of fibers into the filterate that might be toxic. Asbestos filters may be used in pharmaceutical industry if their application is followed by membrane filtration

Water-soluble polymers such as flocculating agents are often used as filter aids. The polymers may be derived from vegetable or animal sources, or they may be produced synthetically. Water-soluble polymers may be classified as nonionic, anionic, or cationic, depending on their property to ionize in water

New, high performance filter aids with self flocking (SF) property provide low tortuosity and fine particle filtration with high flow rates. These filter aids are compounded calcined rice hulls that coagulate extremely fine particles into large, rigid, permeable, flocculated particles

Filter aids may be applied by *precoating* or *body-mix* techniques.
Precoating requires suspending the filter aid in a liquid and recirculating the slurry until the filter aid is uniformly deposited on the filter septum

Body mix (direct addition of filter aid to the filter feed) is more common in batch pharmaceutical operations

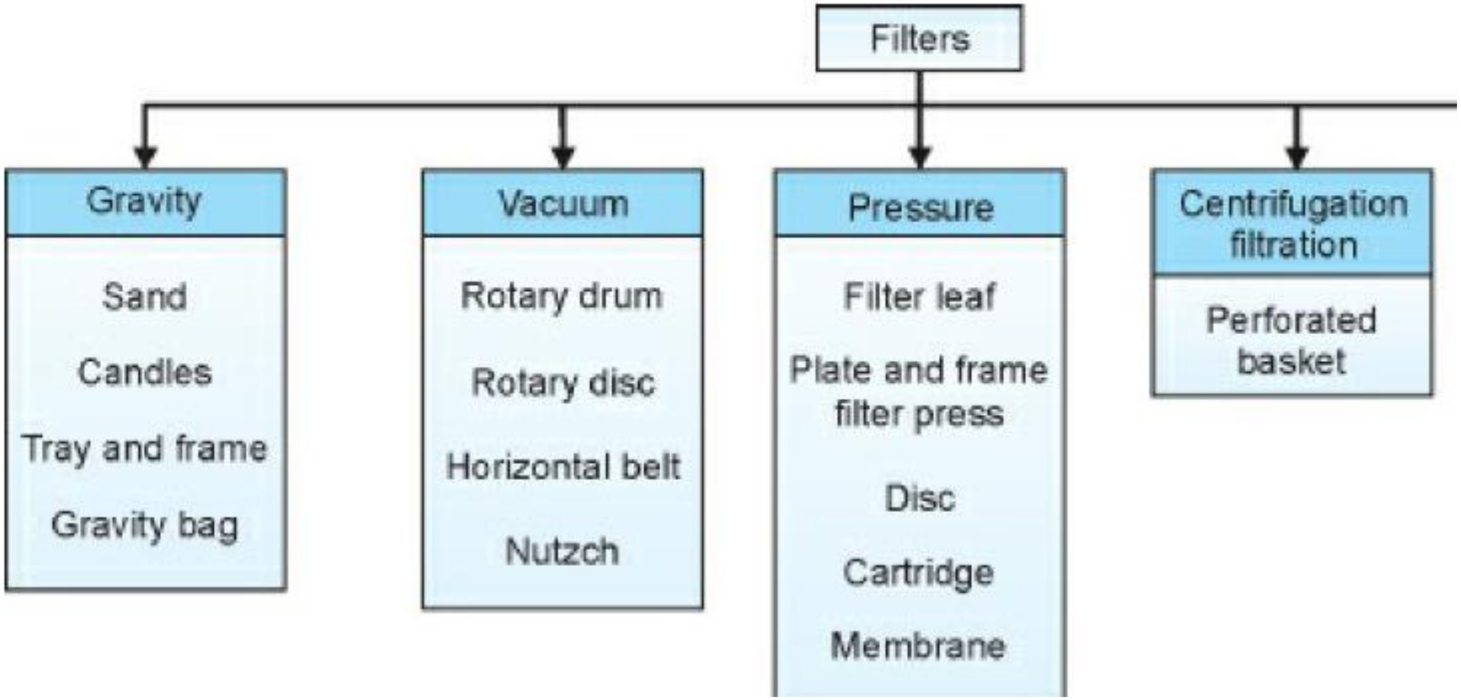
Often, a filter aid performs its function not physically or mechanically, but chemically, by reacting with the solids. These chemicals may cause the solids depositing in a filter bed to adhere more strongly to the filter medium.

Filter aids are chosen by trial and error in either laboratory or plant.
Within the ranges previously indicated, the filter aid is usually selected to give acceptable filtrate at the highest flow rate; however, in pharmaceutical operations in which quality is a primary consideration, the selection usually favours the fine grades, which yield low flow rates.

The most important pharmaceutical factor is inertness. A filter aid may have such extensive absorption properties that desired coloured substances and active principles are frequently removed. The total quantity of any ingredient absorbed may be small, but it may be a considerable portion of the original concentration

FILTRATION EQUIPMENT

Commercial filtration equipment is classified by the end product desired (filtrate of cake solids), by the method of operation (batch or continuous), by type of operation (non-sterile filtration, sterile filtration, centrifugation filtration, centrifugation sedimentation), but most importantly by the type of driving force (gravity, vacuum, pressure and centrifugation)



Gravity Filters

Gravity filters rely on gravity generated low operating pressure (usually less than 1.03×10^4 N/m^2) and give low filtration rates unless very large surfaces areas are used, which limits their use on a large scale

However, these are simple and cheap, and are frequently used in laboratory filtration where volumes are small and low filtration rate is relatively insignificant. Gravity filters employing thick, granular beds are common in water treatment, where clarification of water is done prior to deionization or distillation

Small-scale purification of water may use porous ceramics as a filter medium in the form of hollow "*candles*". The fluid passes from the outside through the porous ceramics into the interior of the hollow candles

Various new gravity filter systems are available commercially such as cylindrical gravity filters, rectangular gravity filters, and hydro-clear gravity filters which utilize granular particles in a basin. Fluid streams pass through the basin and particles are physically and/or chemically captured by the media.

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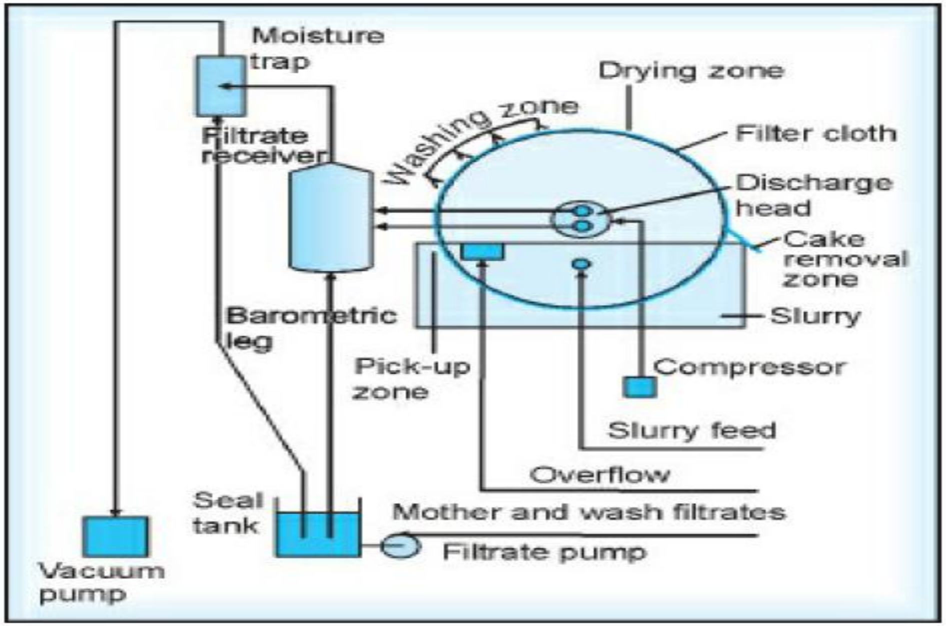
Vacuum Filters

These are employed on a large scale, but are rarely used for the collection of crystalline precipitates or sterile filtration

Vacuum filters are simple and reliable machines, and therefore have gained wide acceptance in the chemical, food and pharmaceutical industries. For large-scale operations, continuous vacuum filters are the most widely used

Rotary Drum Filter

The rotary drum vacuum filter is divided into sections, each connected to a discharge head



Each filter unit is rectangular in shape with a curved profile so that a number can be joined up to form a drum. Each unit has a perforated metal surface and is covered with filter cloth

The slurry is fed to a tank in which solids are held in suspension by an agitator. As the drum rotates, each section passes through the slurry and vacuum draws filtrate through the filter medium at the drum surface (*pick-up zone*).

The suspended solids deposit on the filter drum as a cake, and as rotation continues, vacuum holds the cake at the drum surface. This is followed by washing and further drainage in the drying zone. As the cake moves towards the discharge point, it may be scraped from the drum or it may be supported by strings until it breaks free under gravitational forces (cake removal zone).

The cake discharge may be done through a scraper, belt, roll or a string. Scraper discharge mechanisms will suit cakes that could be scraped readily and roller discharge mechanism are better for thixotropic cakes

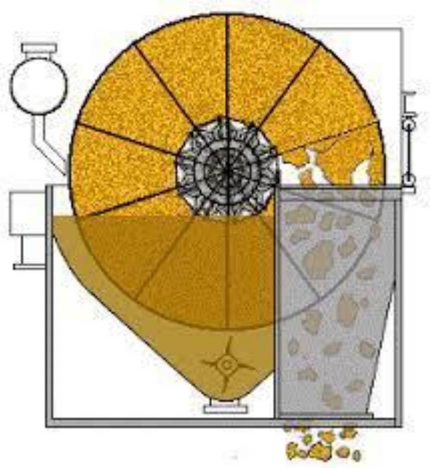
For solids that tend to block the filter cloth, a precoat of filter aids such as diatomaceous earth, perlite and cellulose is deposited on the drum prior to the filtration process

Precoat filters are generally used where a very high degree of clarity is required and solids content is very low (less than 2– 3%) or where solids are sticky and would otherwise clog the filter cloth

Rotary Disc Filter

It consists of several discs, up to 15 in the larger machines, each made up from sectors which are clamped together to form the disc .

Each sector is connected to a vacuum system, compressed air, and appropriate receivers, in the correct sequence, by means of special rotating valve. The operation sequence of a disc filter is similar to a drum filter. The main feature of disc filter is less floor space and the lowest cost of filtration when compared to other vacuum filters.



Pressure Filters

Most of the pressure filters are batch operated but continuous filters are also available. However, owing to the difficulty in removing the cake they are mechanically complex and expensive so mainly used where the added value to the product is high. The filtration rate is influenced, in broad terms, by the properties of the slurry. The trend is that the rate goes up with increased pressure, coarser particles, particle distribution with high uniformity, nonslimy or non-gelatinous solids, noncompressible cakes, lower liquid viscosity and higher temperatures

Plate and Frame Filter Press

The plate and frame filter press is the simplest of all pressure filters and is the most widely used

Filter presses are used for a high degree of clarification of the fluid and for the harvesting of the cake. When clarity is the main objective, a “batch” mode of operation is applied

As the name implies, the plate and frame filter press is an assembly of hollow frames and solid plates that support filter media

One side of the plate is designed for the flow of the feed. After passing the filter media, the filtrate is accommodated on the other side. The solids collect in the frames, and filtrate is removed through place conduits. In cake filtration, the size of the frame space is critical, and wide sludge frames are used

The filter press is the most versatile of filters since the number and type of filter sheets can be varied to suit a particular requirement. It can be used for coarse to fine filtrations, and by special conduit arrangements, for multistage filtration within a single press

The filter press is the most economical filter per unit of filtering surface, and its material of construction can be chosen to suit any process conditions. Labour costs in assembly and cleaning are a primary disadvantage, and leakage between the plates may occur through faulty assembly

Disc Filters

The term disc filter is applied to assemblies of felt or paper discs sealed into a pressure case.

The discs may be preassembled into a self supporting unit, or each disc may rest on an individual screen or plate. Single plate or multiples of single plates may be applied. The flow may be from the inside out wards or outside in wards. The disc filter overcomes some deficiencies of the filter press. Compactness, portability, and cleanliness are obvious advantages for pharmaceutical batch operations

Centrifugation Filtration

In filtering centrifuges, centrifugal force is used to affect the passage of the liquid through the filter medium. This type of filtration is particularly advantageous when very fine particles are involved. Whenever solids recovery is the primary goal, filtering centrifuges must be considered as an alternative to filtration

The advantages of the process are effective washing and drying. Residual moisture after centrifugation is far less than in cakes produced by pressure or vacuum filtration

By this method the moisture content of a cake of coarse crystals can be reduced to as low as 3%., This facilitates the drying operation which normally follows

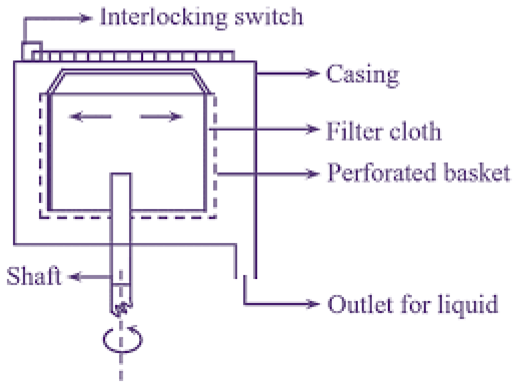
The process is widely used for separating granular products from liquors, but is less effective for concentrated slurries containing smaller particles

Perforated Basket

the device consists of a perforated metal basket mounted on a vertical axis by means of which it can be rotated at a speed of 20 to 25 revolutions per second

The cloth used to retain solids is often supported on a metal screen and the outer casing collects the liquid thrown out from the perforated basket by centrifugal force

Baskets mounted are emptied by shoveling the cake. If, however, top suspension is used, the cake can be more easily withdrawn through traps in the base of the basket



Laboratory Filtration Equipment

Laboratory equipment catalogs offer a wide choice of funnels and flasks adaptable to pharmaceutical filtration studies

For gravity filtration, conventional glass percolators are applicable, in which case the bottom tube is covered with fibrous material. The filtering funnel is the most common of all laboratory filter devices. Filter paper is used with funnels. Sometimes, a plug of fibrous material may be used instead. Filter bags for laboratory use are made of fabric and are mounted for gravity filtration. The uncertainty of adequate clarification with *glass beads* or *sand* has restricted their use as gravity filters for certain operations in the laboratory.

Suction filters are greatly utilized in the laboratory. Usually, a conical funnel and the Buchner funnel are used for suction filtration, as are immersion and suction-leaf filters. Immersion filter tubes, also known as filter sticks, are generally used for small-scale laboratory operations.

Filter paper in circular form is the most common medium for laboratory filtrations. Filter papers are available in a wide variety of textures, purities, and sizes and are available for different uses. They may be circular (1 to 50 cm in diameter), folded, or arranged in sheets or rolls. Some of the special types of laboratory filter papers for pharmaceutical industry are:

1)Filter papers impregnated with activated carbon for the adsorption of colours and odours in pharmaceutical liquids.
2)Filter paper impregnated with diatomaceous earth for the removal of colloidal haze from liquids with low turbidity

Minimum laboratory equipment includes a plate and frame press, a membrane filter holder, and a single-element housing for disposable cartridges.

SPECIALIZED FILTRATION

Sterile/Aseptic Operations

Filtration may be used to clarify and sterilize pharmaceutical solutions that are heat-labile

Membrane filters have become the basic tool in the preparation of sterile solutions

A sterility requirement imposes a severe restraint on filter selection. All sterility tests are presumptive, and one must rely upon total confidence in the basic process, and economics becomes a secondary factor. Membranes with porosity ratings of 0.2 or 0.45 μm are usually specified for sterile filtrations.
In this porosity range, membrane filters may clog rapidly, and a prefilter is used to remove some colloidal matter to extend the filtration cycle

The FDA allows the use of 0.45 μm filters only in cases of colloidal solutions in which 0.2 μm filters have been shown to clog very rapidly

High viscosity or abnormal contaminant levels are the primary restraints to the use of membranes, since an extremely large filtration area is needed for practical flow rates

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Simple formulations such as intravenous solutions, ophthalmics, and other aqueous products may be filtered directly through membranes in an economical manner. Heat-labile oils and liquids containing proteins require pretreatment, e.g. centrifugation or conventional filtration, prior to sterilization filtration, The objective is removal of gross contamination that would rapidly plug the finer membranes

The use of filtration to remove bacteria, particulate matter from air, and other gases such as nitrogen and carbon dioxide is widespread in the pharmaceutical industry. The following are some common applications employing initial gas filtration:

1)Vent filtration

2)Compressed air used in sterilizers

3)Air or nitrogen used for product and in process solution transfers and at filling lines

4)Air or nitrogen used in fermentation

Filtration should be the last step in processing, and the filter should be placed as close as possible to the point of use of final packaging. In serial filtrations, only the final unit needs to be sterile, but minimal contamination in prior steps increases the reliability of the total process. Sterile filtration should always be a pressure operation; a vacuum is undesirable since bacteria may be drawn in at leaky joints and contaminate the product

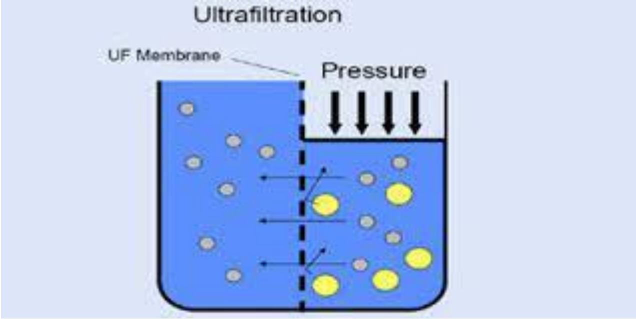
Membrane Ultrafiltration

Unlike conventional filtration, ultrafiltration is a process of selective molecular separation.

It is defined as a process of removing dissolved molecules on the basis of membrane size and configuration by passing a solution under pressure through a very fine filter. Ultrafiltration membrane retains most macromolecules while allowing smaller molecules and solvent to pass through the membrane

The difference between microfiltration and ultrafiltration is significant. The former removes particulates and bacteria; the latter separates molecules

Separation of a solvent and a solute of different molecular size may be achieved by selecting a membrane that allows the solvent, but not the solute, to pass through. Alternatively, two solutes of different molecular sizes may be separated by choosing a membrane that allows the smaller molecule, to pass through but holds back the larger one



The selectivity and retentivity of a membrane are characterized by its molecular weight cut off. It is difficult to characterize the porosity of an ultrafiltration membrane by means of precise molecular weight cut off. The configuration of the molecule and its electrical charge may also affect the separation properties of the membrane

Applications in the pharmaceutical industry are predominantly in the concentration of heatlabile products, such as vaccines, virus preparations, and immunoglobulins. Ultrafiltration also has been used to recover antibiotics, hormones, or vitamins from fermentation broths, to separate cells from fermentation broth, to clarify solutions, and to remove low-molecular-weight contaminants prior to using conventional recovery techniques. The most important application of ultrafiltration is the removal of pyrogens.

Integrity Testing

- An important feature of a filtration system is its ability to be tested for integrity before and after each filtration, which is of high importance especially in sterilization filtration.
- An integrity test is a nondestructive test used to predict functional performance of a filter.
- Each filter has characteristic bubble point and diffusion rate of air through water in a wetted filter as a function of porosity ,
- The common integrity test used to predict the performance of the filter are the bubble point test and the diffusion test.
- The integrity test detect a damage membrane ,system leak, ineffective sealing

Bubble Point Test

- The bubble point is a direct measure of the largest pore in the filter.
- The filter is first wetted and has a liquid above(liquid is held inside the channel by surface tension) and a gas below.
- Since the pores are full of liquids , there will be no passage of gas at zero pressure.(The minimum pressure required to force the liquid outside the capillary should be sufficient to over come the surface tension).
- There is still no passage of gas if pressure is increased slightly.
- When the bubble point pressure is reached, a small bubble forms at the largest opening .
- As the pressure is further increased ,rapid bubbling begins to occur.
- Bubble point pressure for a given membrane is different for different liquids

Bubble Point Test

Failure to hold rated pressure is indicator of inefficient membrane or improper assembly

Diffusion Test

- This test is usually recommended for high volume system like multi-cartridge or other systems with high filtration areas.

- When pressure is applied to a wetted membrane filter, air dissolves in the liquid, diffuses through the film, and is released on the low pressure side

- The diffusion test measure the volume of air that flow through a wet filter membrane from the pressurized site to the atmospheric site

- The air will flow by diffusion process. Pressure is applied using air at 80% of the bubble point pressure for particular membrane.

- Applying pressure at 80% of the bubble point validate filter integrity since there would be a significant increase in air flow at lower pressure indicating damaged membrane ,ineffective seal or system leak.

FILTER SELECTION

In designing or selecting a system for filtration, the specific requirements of the filtration problem must be defined. The following consideration should be addressed before any assistance is requested from the manufacturers of filtration equipment

Once the purpose of the process has been determined, the selection of the filter medium can be made. For example, for a sterilizing filtration, a 0.2 μm pore size is used; for clarification, a plate and frame filter or woven-fiber filter may be used. In general, a pore size smaller than the smallest particle to be removed is selected. The filter medium should be compatible with the liquid or gas to be filtered. It is advisable to check the chemical compatibility charts provided by the vendors for selection of filter type. Filter type, cellulose, poly tetrafluoroethylene (PTFE), fiber, metal, nylon, may be selected based on the chemical resistance to the most aggressive ingredient in the liquid

Filtration surface area is calculated after the filter media, pore size, required flow rate, and pressure differentials are established

For a liquid having a viscosity significantly different from that of water (1 cp), the clean water flow rate is divided by the viscosity of the liquid in centipoises to obtain the approximate initial flow rate for the liquid in question

The broad span of pharmaceutical requirements cannot be met by a single type of filter. The industrial pharmacist must achieve a balance between filter media and equipment capabilities, slurry characteristics, and quality specifications for the final product. The choice is usually a batch pressure filter, which uses either surface or depth filtration principles.

Thank You