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**. 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.

» **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**.

» 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**.

» The term **clarification** is applied when the solids do not exceed 1% and filtrate is the primary product.

Recently, techniques such as **nanofiltration, ultrafiltration, and microfiltration** have been used to recover colloidal delivery systems from mother liquor.

There are numerous **applications of filtration in pharmaceutical processing** which mainly include:

1. Clarification of products **to improve their appearance.**

2. **Removal of potential irritants** e.g. from eye drop preparations or solutions applied to mucous membranes.

3. **Filtration for recovery of desired solid material from a suspension of slurry**, e.g. to obtain a drug or excipient after a crystallization process.

4. Production of water of appropriate quality for pharmaceutical use.

5. Meeting sterility specification (removal of microorganisms) required for some products using **sterile filtration or aseptic filtration**.

6. **Sterilization of solutions and suspensions** that are **chemically or physically unstable under heating** conditions.

7. **Detection of microorganisms** present in liquids by analyzing a suitable filter on which the bacteria are retained.

8. **Assessment of the efficacy of preservatives**.

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**
2. **Depth straining**
3. **Depth filtration**
4. **Cake filtration**

Clarification methods

1. Settling

Settling is the simplest method of clarification is to allow the liquid to stand in a suitable container until the suspended matter either has settled or has risen to the top of the liquid. The latter occurs when the density of the suspended matter is less than that of the fluid medium.

The insoluble matter may be separated from the clear liquid phase by:

1. Skimming
2. Decantation
3. Siphoning

Characteristics of settling method

1. Settling may be advantageous when the suspended particles are large and settle rapidly, it is also may be used to remove fine particles, especially those which tend to flocculate, (if along waiting-period is feasible).
2. If the viscosity of the liquid is high, as is true of syrup, the waiting period may be excessive.
3. The method fails when the suspended matter is colloidal or when its density is approximately equal to that of the liquid phase.
4. Acceleration of settling process can be accomplished by centrifugation. In this operation, the liquid is rotated in a special container at high speeds. The centrifugal forces developed in the rotating container drive the suspended particles to the bottom and the sides of the container.

2. Filtration and collation

» Filtration is the process of removing solid particles from a fluid by passing the suspension through a porous, fibrous or granular substance.

» Collation or straining is crude filtration.

» The distinction between the two processes is based only on the degree of fineness of the straining or filtration medium involved.

» A filter (or strainer) functions primarily by impeding the passage of suspended particles with diameters greater than that of the pores, while allowing the liquid to pass. The retentiveness of filters varies over a wide range, depending on the average pore size.

Factors affecting filtration rate

The factors which influence the rate at which fluids can be passed through a porous medium are summarized in their simplest form in the following expression:

$$\text{Rate of filtration} \propto \frac{(\text{filter area})(\text{pressure drop})}{(\text{liquid viscosity})(\text{filter resistance})}$$

» The rate of filtration, measured as the volume of liquid passed through the filter per unit time.

» It will be increased in proportion to the pressure drop across the filter and filter area; and will be reduced in proportion to the filter resistance and viscosity of the filtrate.

» Pressure drop is determined by the weight of the liquid above the filter. Usually, this is not great enough to effect filtration in reasonably short periods if highly retentive filters are employed or highly viscous liquids such as syrups are being filtered.

The pressure drop can be altered by using:

1. **Suction filter**, which may be employed with properly designed equipment to increase the pressure drop by lowering the pressure beneath the filter,

or

2. **Pressure filtration** (in which the pressure above the liquid is increased).

Filter media

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

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:

1. 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. **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**.

Figure 1 : Cotton fabric filter cloth Nylon filter cloth

2. 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**.

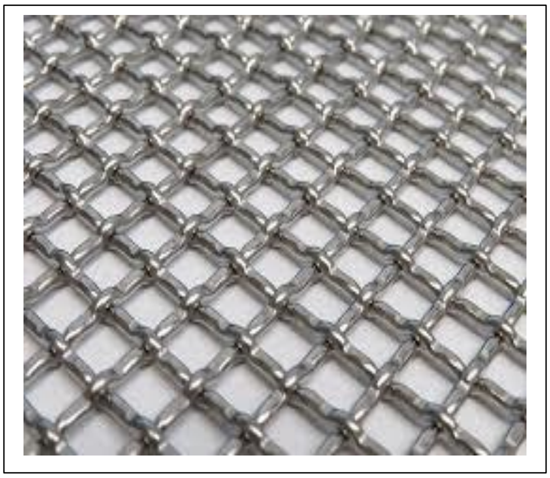

Figure 2 : Woven wire cloth

3. Nonwoven filter media: include **felts, bonded fabrics, and kraft papers**.

A **felt** is a **fibrous mass** are recommended where gelatinous solutions or fine particulate matter are involved.

Figure 3: Nonwoven filter media; felt

Bonded fabrics are made by **binding textile fibers with resins, solvents, and plasticizers**. These materials have not found wide acceptance in dosage form production because of interactions with the additives.

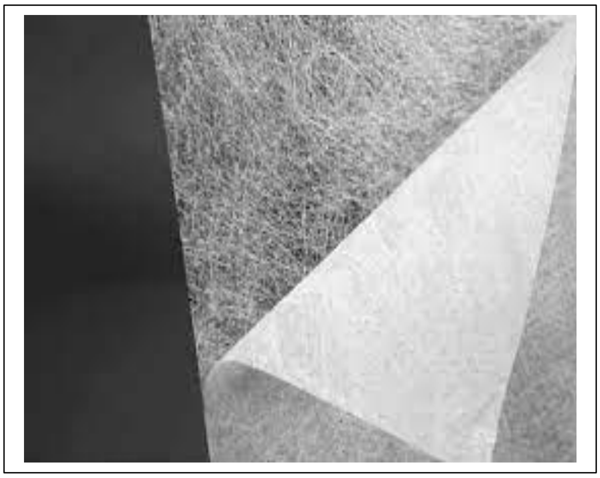

Figure 4 :Nonwoven filter media, bonded fabrics

Kraft paper is a pharmaceutical standard. Although limited to use in plate and frame filters and horizontal-plate filters, it offers controlled porosity, limited absorption characteristic, and low cost.

Figure 5 : Kraft paper

4. 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.

Figure 6:Porous stainless-steel filters

5. Membrane filter media: are the basic tools for microfiltration, ultrafiltration, nanofiltration and reverse osmosis. They are used commonly in the preparation of sterile solutions.

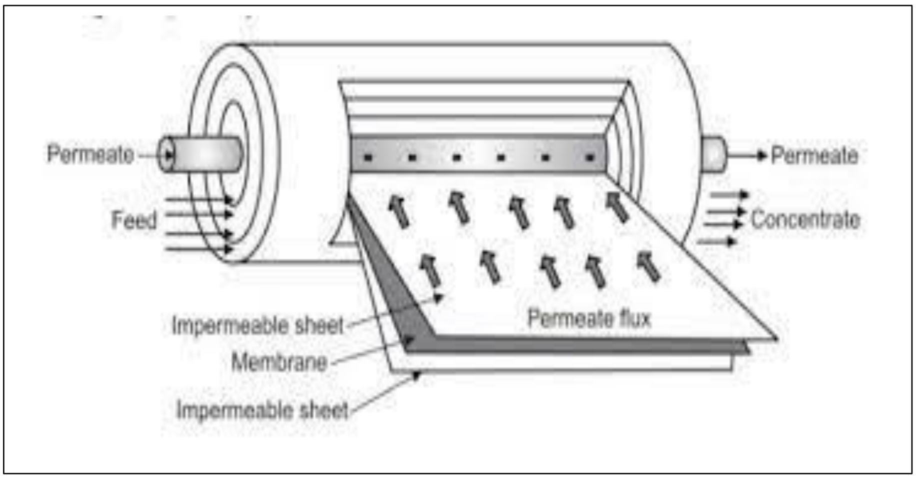

Figure 7: Membrane filter media

The selection of a membrane filter for a particular application is a function of the size of the particle or particles to be removed. An approximate pore size reference guide is given in Table 1.

Table 1: Tabular representation of pore size reference guide

Pore size (μm)	Particle removed
0.2 (0.22)	All bacteria
0.45	All coliform group of bacteria
0.8	All airborne particles
1.2	All nonliving particles considered dangerous in IV fluids
5	All significant cells from body fluids

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**. A filter aid acts by reducing this resistance. 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**.

Figure 2: is a 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 due to the high amounts of filter aid are added, the filter aid merely adds to the thickness of the cake without providing additional cake porosity.**

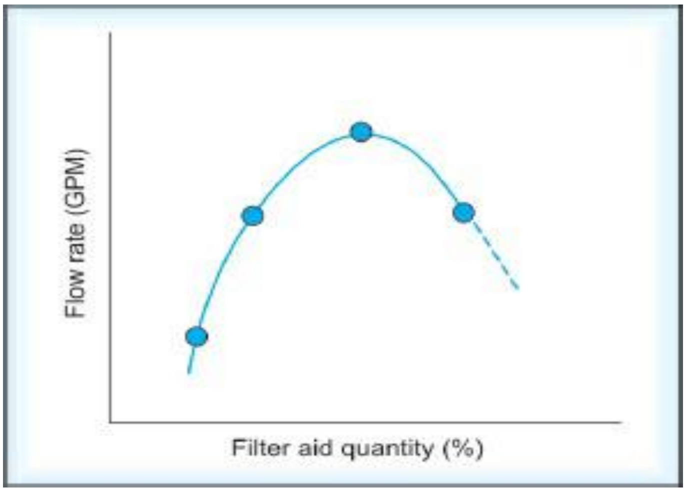

Figure 8: Experimental determination of flow rate as a function of filter aid quantity discloses correct operating level.

The important characteristics for filter aids are the following:

1. It **should have a structure that permits formation of pervious cake**.
2. It should be **able to remain suspended in the liquid**.
3. It should be **free of impurities**.
4. It should be **inert to the liquid** being filtered.
5. It should be **free from moisture** in cases where the addition of moisture would be undesirable.

» Filter aids are classified from low flow rate (fine: Mean size in the range of 3 to 6 µm) to fast flow rate (coarse: Mean size in the range of 20 to 40 µm). Table 2 lists the advantages and disadvantages of filter aid materials.

Table 2: Advantages and disadvantages of filter aid materials.

Material	Chemical composition	Advantages	Disadvantages
Diatomaceous earth	Silica	Wide size range available; fines reduced by calcination; can be used for very fine filtration.	Slightly soluble in dilute acids and alkalies.
Expanded perlite	Silica and aluminosilicates	Wide size range available; not capable of finest retention	More soluble than diatomites in acids and of diatomites. alkalies; may give highly compressible cakes.
Asbestos	Aluminosilicate	Usually used in conjunction with diatomites; very good retention on coarse screens.	Chemical properties similar to perlite.
Cellulose	Cellulose	Used mainly as a coarse precoat; high purity; excellent chemical resistance, slightly soluble in dilute and strong alkalies, none in dilute acids.	Expensive
Carbon	Carbon	May be used for filtering strong alkaline solutions.	Available in coarser grades only; expensive.