CHAPTER 8

FILTRATION

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Abstract

Filtration is a critical separation process in pharmaceutical manufacturing used to remove solid particles from liquids or gases. This operation is essential for purifying raw materials, intermediate products, and final drug formulations. Various filtration mechanisms, including surface straining, depth filtration, and cake filtration, are employed depending on the nature of the suspension and desired level of separation. The selection of appropriate filter media, such as membrane filters, depth filters, or cartridge filters, is crucial for achieving optimal filtration efficiency. Factors influencing filtration performance include particle size distribution, filter pore size, pressure differential, and filtration rate. The principles of constant pressure and constant rate filtration are explored, along with their applications in different pharmaceutical processes. Advanced filtration techniques, such as tangential flow filtration and sterile filtration, are discussed in the context of biotechnology products and aseptic processing. Quality control measures, including integrity testing of sterilizing filters and validation of filtration processes, are essential to ensure product sterility and purity. Understanding filtration principles and practices is vital for maintaining product quality and compliance with regulatory standards in pharmaceutical manufacturing

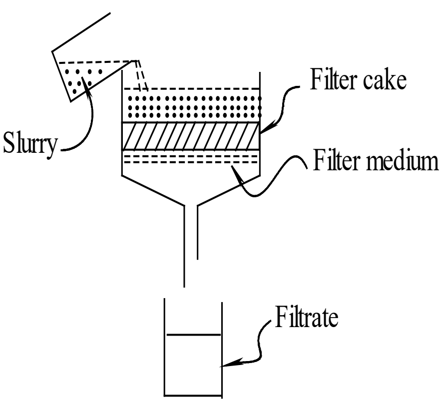
Keywords: *Separation, Filter media, Particle retention, Sterile filtration, Cake formation, Process validation*

Learning Objectives

After completion of the chapter, the student should be able to:

- Define filtration and its role in pharmaceutical processing.
- Explain the principles and mechanisms of filtration.
- Describe different types of filters and filtration equipment used in pharmaceuticals.
- Discuss the factors affecting filtration efficiency and rate.
- Explain the concept of filter aids and their applications.
- Analyze the challenges in filtering different types of pharmaceutical solutions and suspensions.
- Evaluate methods for assessing the quality and effectiveness of filtration processes.

Filtration may be defined as the separation of a solid from a fluid by means of a porous medium that retains the solid but allows the fluid to pass.



THEORIES OF FILTRATION

Slurry: The suspension of solid and liquid to be filtered.

Filter medium: The porous medium used to retain the solids.

Filter cake: The accumulation of solids on the filter medium.

Filtrate: The clear liquid passing through the filter and collected in the receptor.

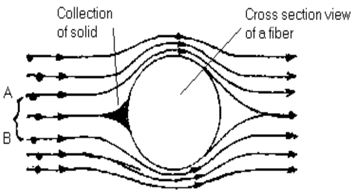
In the early stages of liquid filtration particles are retained on the fibers of filter medium by the following mechanisms:

(i) Straining, (ii) Impingement, (iii) Entanglement and (iv) Attractive forces

After a preliminary layer of particles are deposited on the filter-medium, the filtration occurs through the filter cake. This time filtration obeys Kozeney's equation.

Straining

The particles larger than the pore size of filter medium will be retained on the latter.



Impingement

When a dilute suspension approaches a fiber the fluid passes along the side of the fiber will pass with the fluid but the particles in between A – B region will hit directly on the fiber. Due to their higher moment of inertia they strike (impinge) on the fiber and accumulate to form a ridge, roughly triangular in section.

Entanglement

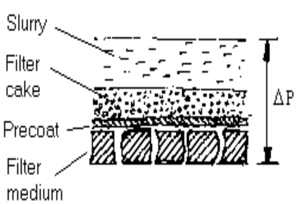
If the filter medium consists of a cloth or is a porous felt, then particles become entangled in the mass of fibers. Usually the particles are smaller than the pores.

Attractive forces

In some cases, particles may collect on a filter medium as a result of attractive forces. Gas flowing through a filter medium causes generation of charges on the filter surface. The particles containing charge gets attracted to the surface.

Kozeny's Equation

In the process of filtration the fluid passes through the filter medium, which offers resistance to its passage. Pressure difference across the filter is the driving force for the operation.



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

$\frac{dV}{d\theta} = \frac{A\,\Delta P}{R}$ where $\frac{dV}{d\theta} =$ volume flow rate

A = Area of filtration

R = Resistance to flow through the filter

Resistance to filtration is offered by the filter medium, precoat and filter cake.

Resistance, $R = \eta\, r\,(L + L_C)$

where, R = resistance to filtration

η = viscosity of fluid

r = Specific resistance of cake

L_C = Thickness of cake (increases with time)

L = Equivalent length of filter medium and pre-coat (fictitious thickness)

If 'V' volume of liquid is filtered containing 'w' fraction of solid content per unit volume of liquid, then the thickness of the cake formed is :

$$L_C = \frac{w\,V}{A}$$

Therefore,

$$\frac{dV}{d\theta} = \frac{A\,\Delta P}{R} = \frac{A\,\Delta P}{\eta\, r\,(L + L_C)} = \frac{A\,\Delta P}{\eta\, r\left(L + \frac{wV}{A}\right)}$$

$$\boxed{\frac{dV}{d\theta} = \frac{A\,\Delta P}{\eta\, r\left(L + \frac{wV}{A}\right)}}$$

– Kozeny's equation

FACTORS AFFECTING THE RATE OF FILTRATION

1. Properties of the filter medium and filter cake

The resistance of the filter medium and filter cake is denoted by R. The resistance of filter medium is of less significance in industrial scale than the resistance of filter cake. The latter increases with time. The rate of filtration decreases as the thickness of the cake increases. When the rate is uneconomically low the filtration is stopped and the cake is removed mechanically; and the filtration is resumed.

The resistance also depends on the properties of the solids, e.g. particle size, particle size distribution, particle shape, and compressibility of the solid. In case of compressible cake the porosity decreases with increasing pressure drop, so filter aids are incorporated to increase the filtration rate.

2. Area of filter

The rate of filtration can be increased by increasing the area of filtration. This area can be increased by using larger filters or by using a number of small units in combination. In rotary filters the filter cake is continuously removed providing an infinite area of filtration.

3. Pressure drop

Rate of filtration can be increased by increasing the pressure drop across the filter medium. Pressure drop can be achieved by (i) gravity, (ii) negative pressure (reduced pressure or under vacuum), (iii) positive pressure and (iv) centrifugal force.

Gravity: The height of the slurry over the filter medium gives pressure under gravity. By increasing the height of the slurry the pressure drop can be increased.

Negative pressure: The pressure below the filter medium can be reduced below atmospheric pressure by connecting the filtrate receiver to a vacuum pump.

The disadvantage of this method is that the pressure drop can never be increased above one atmospheric pressure.

The second disadvantage is that under reduced pressure the boiling point of liquid is lowered and the liquid may boil in the filtrate receiver that may cause loss of liquid or may damage the vacuum pump.

Positive pressure: The simplest method of raising the pressure difference across the filter membrane is to increase the pressure to the surface of the slurry.

The advantage is that greater pressure difference can be achieved.

Centrifugal force: The gravitational force can be increased by centrifugal force.

4. Viscosity of liquid

An increase in the viscosity of the liquid will decrease the flow rate. The viscosity of the liquid can be decreased by raising the temperature of the slurry or by dilution with a miscible liquid.

5. Thickness of the filter cake

Thickness of the filter cake increases as the filtration progresses. Highly concentrated slurry is first decanted or strained to reduce the solid content and then it is filtered (this reduces the cake thickness). In a rotary drum filter cake is removed continuously so that the cake thickness is minimized.

FILTER MEDIA

The filter medium may be responsible for the collection of solids, while in other cases it is no more than a support for the filter cake.

There are two types of filter media:

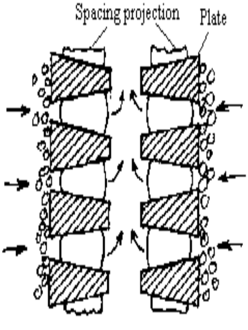
1. Surface filtration media
   A. Screen type B. Edge type C. Stacked disc
2. Depth filtration media
   A. Fibrous media B. Porous media
   C. Cake type media

SURFACE FILTRATION MEDIA

A. Screen type

Examples: Cloths made from wool, cotton, silk, glass, metal or synthetic fibers (rayon, nylon etc.)

Cloths of different weights and weave are used according to the concentration of slurry. The final choice of fiber will depend on the chemical nature of the cloth.



(a) M*uslin cloth* (cotton with duck weave) has high porosity, hard surface, can withstand pressure, allows easy discharge of cake. It is easily damaged by acids and alkalis

(b) *Nitrated cotton cloth* provides much harder surface.

(c) *Glass cloth* offers high thermal and corrosion resistance, high tensile strength but it lacks flexibility.

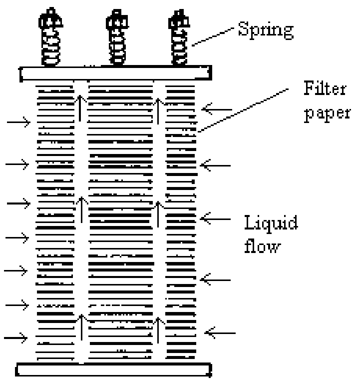
(d) *Synthetic cloths* (nylons) do not swell and have high acid and alkali resistance. They are resistant to fungal or bacterial growth. It resists relatively high temperature and hence smooth surface for esy clening.

(e) *Metallic screens* or *cloth* made up of steel, copper, bronze, nickel are suitable for handling corrosive liquids and high temperature filtration.

(f) *Perforated and screen* are used for coarse solids.

B. Edge type

They involves the use of cartridge type element with flow directed from outside to inside. The element is composed of a stack of discs or washer paper, plastic or metal clamped together by compression. Channels are formed in between the discs by "spacing projection" on the disc surface. Solid particles are retained on the outer surface that may be scraped off regularly.



Stacked Disc Filter

Advantages:

It is not affected by sudden pressure changes.

No clogging takes place.

C. Stacked disc filters

Individual discs are stacked around a perforated inner tube with intermediate spacing washer.