# Drying

lec 1

## DRYING

*Drying is defined as removal of the liquid from a material by application of heat, & is accomplished by transfer of a liquid from the surface into an unsaturated vapor phase.*

**Definition.** For the purpose of this discussion, drying is defined as the removal of a liquid from a material by the application of heat, and is accomplished by the transfer of a liquid from a surface into an unsaturated vapor phase. This definition applies to the removal of a small amount of water from moisture-bearing table salt as well as to the recovery of salt from the sea by evaporation. Drying and evaporation are distinguishable merely by the relative quantities of liquid removed from the solid.

There are, however, many nonthermal methods of drying, for example, the *expression* of a solid to remove liquid (the squeezing of a wetted sponge), the *extraction* of liquid from a solid by use of a solvent, the *adsorption* of water from a solvent by the use of desiccants (such as anhydrous calcium chloride), the *absorption* of moisture from gases by passage through a sulfuric acid column, and the *desiccation* of moisture from a solid by placing it in a sealed container with a moisture-removing material (silica gel in a bottle).

# Drying

# Drying

*- Drying is commonly the **last stage** in a manufacture process.

***- Drying** is the final **removal of water** from material (**usually by heat**)

.**Non –thermal drying**

**1-** As Squeezing wetted sponge

**2-**Adsorption by desiccant (desiccation)

**3-** Extraction.

# Purposes of drying

•- In pharmaceutical technology, drying is carried out for one or more of **the following reasons**:

**1-**To avoid or eliminate moisture which may **lead to corrosion** and decrease the product or **drug stabilit**y.

**2-**To **improve** or keep the **good properties** of a material, e.g. **flowability,** compressibility.

**3-**To r**educe** the cost **of transportation** of large **volume** materials ( liquids)

**4-**To make the **material easy** or more suitable for **handling.**

**5-** Preservative.

**6-** The **final step in**: Evaporation- Filtration- Crystallization.

# Psychrometry

A critical factor in drying operations is the vapor-carrying capacity of the air, nitrogen, or other gas stream passing over the drying material. This carrying capacity determines not only the rate of drying but also the extent of drying, i.e., the lowest moisture content to which a given material can be dried. The determination of the vapor concentration and carrying capacity of the gas is termed *psychrometry*.

**Psychrometric Chart.** The humidity characteristics of air are best shown graphically in a *psychrometric* or *humidity chart.*

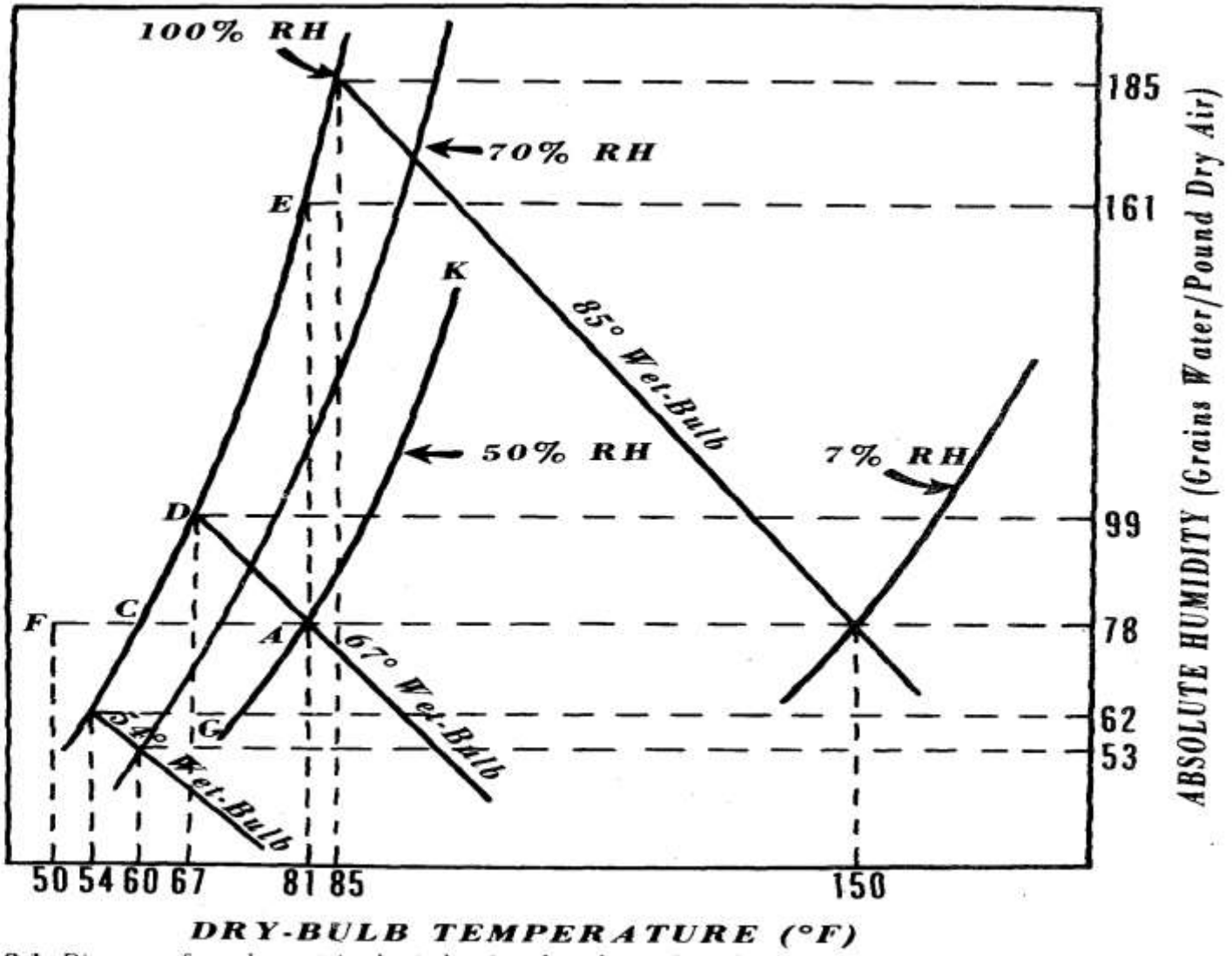



FIG. 3-1. *Diagram of psychrometric chart showing the relationship of air temperature to humidity.*

- Saturation humidity : is absolute humidity at which the partial pressure of water vapor in the air is equal to the vapor pressure of free water at the same temperature.
- i.e. Humidity does not change when it is in contact with liquid water at same temp.
- **Dew point**: temp. at which given mixture of air and water vapor must be cooled to become saturated.(i.e. hold max. amount of moisture without condensation).
- **Relative saturation** ( % Relative humidity RH ): ratio of the partial pressure of water vapor in the air to the vapor pressure of free water at the same temperature.
- Saturation humidity ( 100% R H)
- Relative saturation also express as % humidity or % absolute humidity which is ratio of absolute humidity to saturation humidity at the same temp.

- **Wet- bulb temp**.: is equilibrium temp. reached by evaporating surface when the rate of heat transferred by convection is equal to the rate of heat lost by evaporation.
- It is measured by thermometer whose bulb is covered by wick saturated with water.
- **Dry- bulb temp**.: is the actual temp. of air as measured by ordinary thermometer.

The basic curves of the psychrometric chart are shown in a simplified version in Figure 3-1. These curves are graphic representations of the relationship between the temperature and humidity of the air–water vapor system at constant pressure. The temperature is shown in the horizontal axis; the vertical axis represents *absolute humidity* (weight of water vapor per unit weight of dry air). The most important curve shown is the curve for *saturation humidity,* curve CDE. Saturation humidity is the absolute humidity at which the partial pressure of water vapor in the air is equal to the vapor pressure of free water at the same temperature. Under these conditions, the air is completely saturated with moisture, and the humidity does not change when it is in contact with liquid water at the same temperature.

At point C, the air is saturated with water vapor, and its temperature, 60°F, is referred to as the *dew point.* The dew point is defined as the temperature to which a given mixture of air and water vapor must be cooled to become saturated (i.e., to hold the maximum amount of moisture without condensation taking place). When the mixture is cooled to temperatures below the dew point, such as 50°F (point F), the water vapor condenses to produce a two-phase system of saturated air (condition C) and droplets of free water.

Curves of temperature versus absolute humidity at constant relative humidity are plotted on the same axes at specific interval of the relative humidity . One of these curve is GK with50% RH . The relative saturation also can be expressed as percent humidity or percent absolute humidity , the ratio of absolute humidity to the saturation humidity at the same temperature . For air at condition A , the percent absolute humidity is represented by the ratio of the absolute humidity to the absolute humidity of the saturated air at that temperature(78/161=48%) .

- If air under the condition represented by the point A , is used to dry a wet material , the difference in vapor pressure between the surface water and the air causes some of the liquid to evaporate . The latent heat of vaporization of water cools the evaporating surface below the air temp. . The resultant difference in temp. causes a transfer of heat from air to the liquid at a rate that increases as the temp. difference becomes larger.
- the heat transferred becomes equal to the heat of vaporization and the temperature stabilize. The temp. that is reached is called the wet bulb temp.

The wet-bulb temperature is a function of the temperature and humidity of the air used for the evaporation, and thus can be employed as a means of measuring humidity. For this purpose, a second type of curve is superimposed on the temperature-humidity curves of the psychrometric chart. This is the *constant wet-bulb temperature* line. The constant wet-bulb temperature line is AD for air at condition A, and the temperature corresponding to saturation at point D is the wet-bulb temperature, 67°F.

- For example let us assume a wet- bulb temp. Of 54 $^{o}$F and a dry –bulb of 60F. The 54$^{o}$ F line is followed until it intersect the saturation humidity curve at an absolute humidity of 62 grain water/pound dry air. Then 54 $^{o}$F wet –bulb temp. line is followed until it intersect the 60$^{o}$F dry -bulb temp. line at an absolute humidity of 53 grains /pound dry air .

# Humidity Measurement.

1. Gravimetric method : known amount of air passed over a previously weighed moisture – absorbing chemical (e.g phosphorous pentoxid) and the resultant increase in weight of chemical is measured
2. hygrometer: instrument utilize certain materials whose properties change .

- Mechanical hygrometer
- Electrical hygrometer

3. Based on dew point temp. measurement.: by observing temp. at which moisture begin to form on polished surface contact with air.
4. Sling psychrometer: by measuring both dry and wet bulb temp.

# Theory of Drying

Lec 2

Drying involves both heat and mass transfer operations. Heat must be transferred to the material to be dried in order to supply the latent heat required for vaporization of the moisture. Mass transfer is involved in the diffusion of water through the material to the evaporating surface, in the subsequent evaporation of the water from the surface, and in diffusion of the resultant vapor into the passing air stream.

**The general principles for efficient drying can be summarized as:**

- large surface area for heat transfer,
- efficient heat transfer per unit area (to provide sufficient latent heat of vaporization or heat of sublimation in the case of freeze drying).
- efficient mass transfer of evaporated water through any surrounding boundary layers, i.e. sufficient turbulence to minimize boundary layer thickness.
- efficient vapour removal, i.e. low relative humidity air moving at adequate velocity.

# Drying of Solids

**Loss on Drying.** The moisture in a solid can be expressed on a wet-weight or dry-weight basis. On a wet-weight basis, the water content of a material is calculated as a percentage of the weight of the *wet* solid, whereas on the dry-weight basis, the water is expressed as a percentage of the weight of the dry solid.

In pharmacy, the term *loss on drying*, commonly referred to as LOD, is an expression of moisture content on a wet-weight basis, which is calculated as follows:

$$\% \text{ LOD} = \frac{\text{wt. of water in sample}}{\text{total wt. of wet sample}} \times 100 \tag{6}$$

The LOD of a wet solid is often determined by the use of a moisture balance, which has a heat source for rapid heating and a scale calibrated in percent LOD. A weighed sample is placed on the balance and allowed to dry until it is at constant weight. The water lost by evaporation is read directly from the percent LOD scale. It is assumed that there are no other volatile materials present.

**Moisture Content.** Another measurement of the moisture in a wet solid is that calculated on a dry-weight basis. This value is referred to as *moisture content*, or MC:

$$\% \text{ MC} = \frac{\text{wt. of water in sample}}{\text{wt. of dry sample}} \times 100 \tag{7}$$

If exactly 5 g of moist solid is brought to a constant dry weight of 3 g:

$$\text{MC} = \frac{5 - 3}{3} \times 100 = 66.7\%$$

$$\text{whereas} \quad \text{LOD} = \frac{5 - 3}{5} \times 100 = 40\%$$

LOD values can vary in any solid-fluid mixture from slightly above 0% to slightly below 100%, but the MC values can change from

slightly above 0% and approach infinity. Thus, a small change in LOD value, from 80% to 83%, represents an increase in MC of 88%, or a 22% increase in the amount of water that must be evaporated per pound of dry product. Thus, percent MC is a far more realistic value than LOD in the determination of dryer load capacity.

**Classification of Solids Based on Drying Behavior.** Solids may be classified into two major categories on the basis of their drying behavior, namely (1) granular or crystalline type solids and (2) amorphous solids. The water in crystalline solids is held in shallow and open surface pores as well as in interstitial spaces between particles that are easily accessible to the surface. Materials with fibrous, amorphous, or gelatinous structures are in the second category. In these solids, the moisture is an integral part of the molecular structure as well as being physically entrapped in fine capillaries and small interior pores. Typical pharmaceuticals of the first category are calcium sulfate, zinc oxide, and magnesium oxide. Materials that fall into the second category are starch, casein, yeast, insulin, and gelatinous inorganic materials such as aluminum hydroxide. All of the amorphous solid materials are more difficult to dry than granular or crystalline solids.

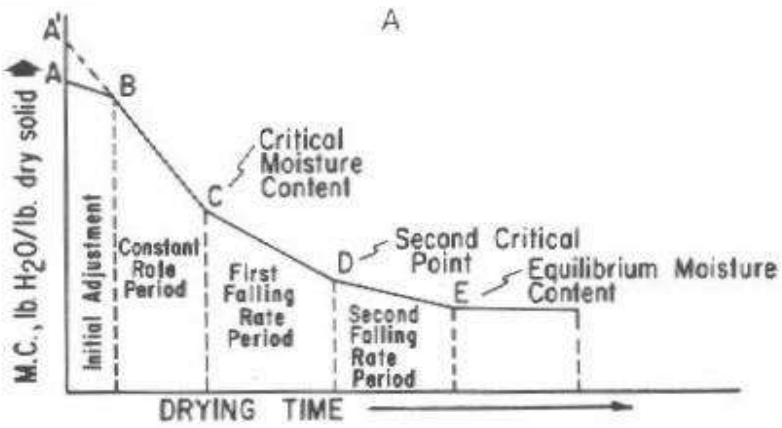
**Behavior of Solids During Drying.** How would one know if 8 or 12 hours are required to dry a batch weight of material in a certain dryer? How can one determine the size of a particular type of dryer required for drying a substance from one moisture level to the desired moisture content?

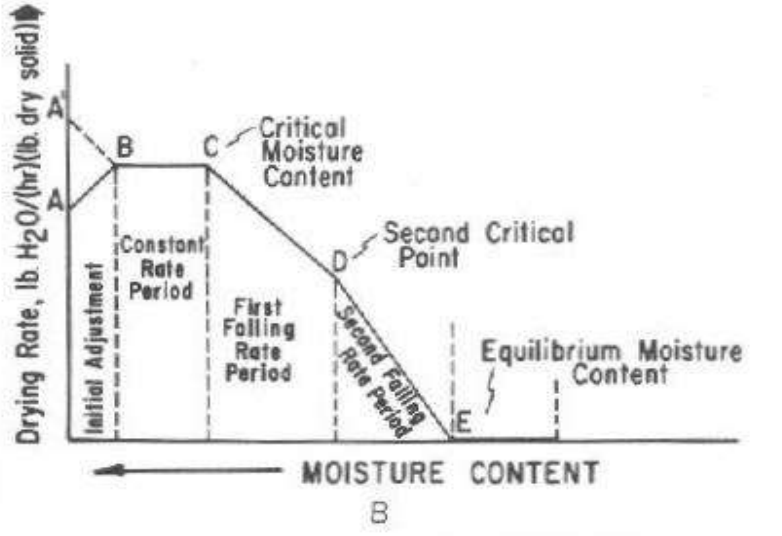
# Rate of drying in a bed of powder:

- **The rate at which drying occurs has been found to show certain phases in which the change in moisture content is plotted against time**. From A to B

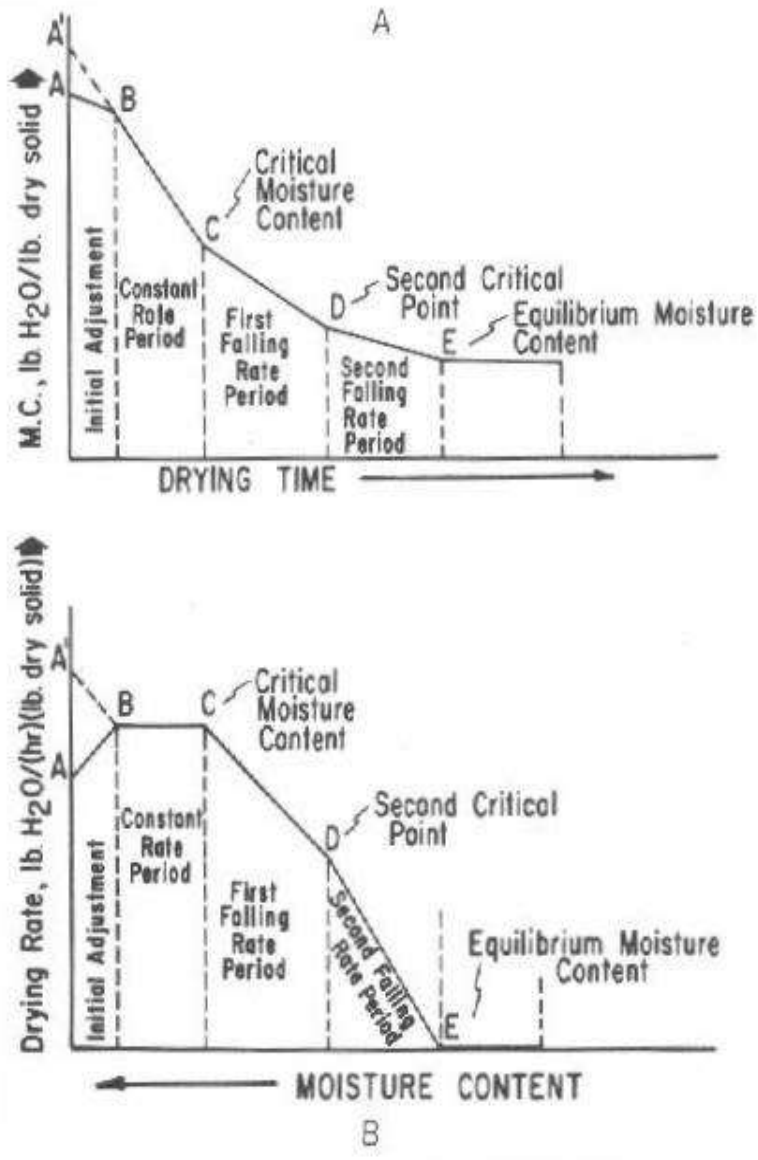
when awet solid is placed in adrying oven It begin to absorbe heat and increase in Temp.at the same time the moisture begins evaporating and thuse tend to cool the Drying solid.this phase is known as **initial Adjustment**.

after aperoid of initial adjustment the rate Of Heating and cooling becomes equal and Temp. of drying materail is stabilizes and Reach to the Wet-bulb temp. of drying air. At point **B** the temp. is stabilized and remain Constant&there is afilm of moisture.



.Between points B&C, the moisture
Evaporating from the surface is replaced by
Water diffusing from the enterior of the solid.
Rate of evaporation is equal to the rate of
Diffusion and the rate of drying is constant.
This phase is termed as **constant rate period.**
At point c the surface water is no longer
Replaced at arate fast enough to maintain
Acontinuous film.
Dry spots begin to appear, this point **C** known
As **Critical moisture cotaint**



Between points C&D .the number and area of the drying spots continous to grow,and the rate of drying falls steadily. The time CD is named as

**First falling rate period. At** point **D** the film of surface water is completely

Evaporated and the rate of drying depend on the diffusion of moisture

To the surface of solid.

Point **D** is referred to as

The second critical point.

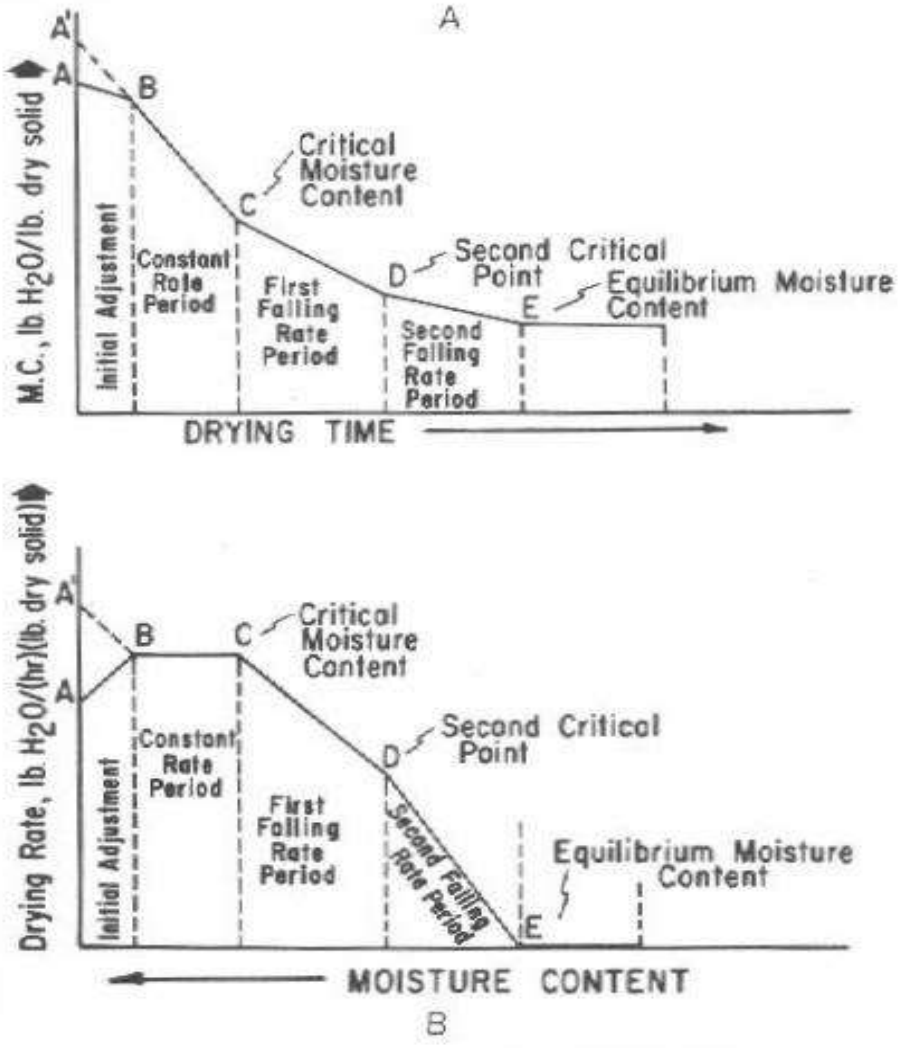
Between points D&E the rate of

Drying falls even more rapidly

Than the fist falling rate and the

Time DE is named as

**Second falling rate peroid**



At point **E** the drying rate is equal

To zero.

The equilibrium moisture peroid

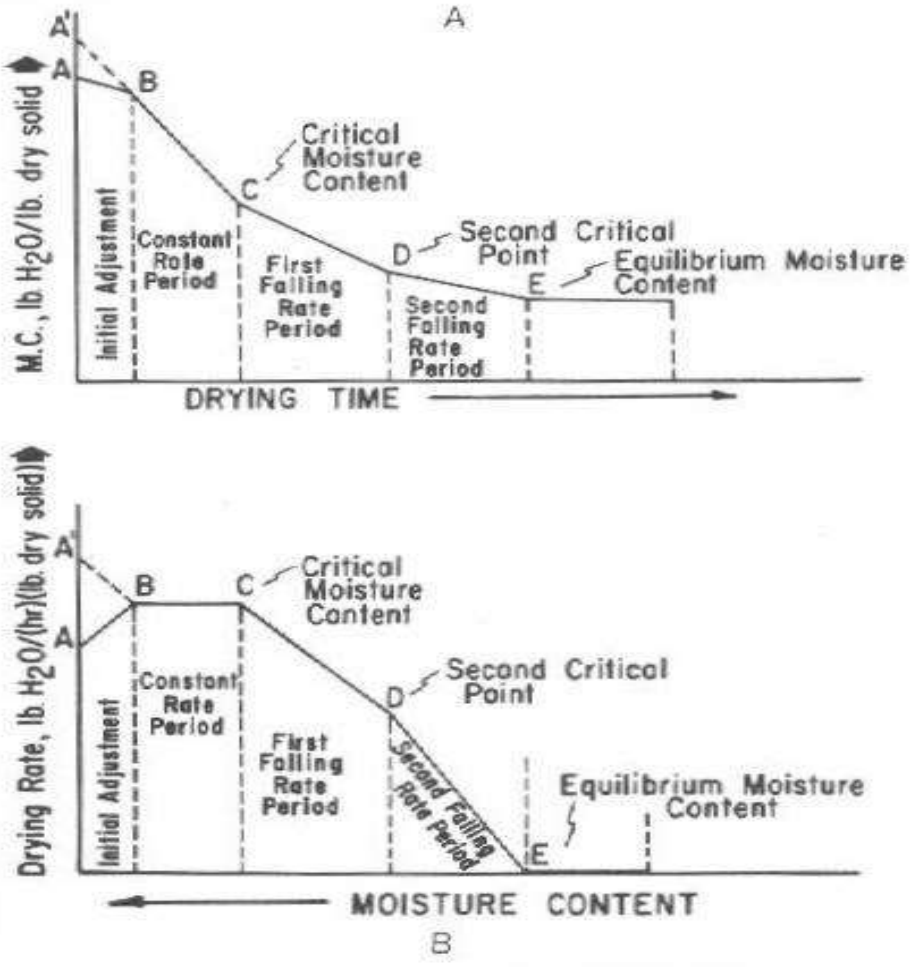
Begins,and **the solid is in**

**Equilibrium with its surroundings**.

Its temp. and moisture content

Remain constant.continued drying

After this point is awaste of time.



# Relative humidity (RH) of air

- Air at a given temperature is capable of taking up water vapour until it is saturated (at 100% RH ). If the temperature is raised then the air will be able to take up more moisture and the relative humidity falls.
- The RH of air is dependent not only on the amount of moisture in the air , but also on its temperature, as the amount of water required to saturate air is itself dependent on temperature.

- It should be noted that in convective drying, where warm air is passed over the surface of a wet solid, the relative humidity may rise during the drying process as a result of two separate factors:-

- 1- Uptake of evaporated water vapour from the wet solid,
- 2- The cooling of the supply air as it transfers heat to the wet solid (evaporative cooling).

The condition in which the material is in equilibrium with its surrounding neither gaining ,nor losing water ,may be expressed in term of its equilibrium moisture content ,equilibrium relative humidity or water activity.

Equilibrium moisture content(EMC):

It’s the moisture content at which the material exert a water vapor pressure equal to the pressure of the atmospheric surrounding ;thus it has no driving force for mass transfer.

EMC values of certain material may differ greatly under same condition . This difference is due to the manner in which water is held by the material. Water may be hold in fine capillary pores that have no easy access to the surface , or the water may be molecularly bounded.

Equilibrium relative humidity (ERH):

The relative humidity surrounding the material at which the material neither gains nor loses moisture is called ERH. At given temperature ERH for a material is determined by its MC, just as the ERH is determined by surrounding RH.

**Water Activity.** The *water activity* ($a_w$) of a material is the ratio of the water vapor pressure exerted by the material to the vapor pressure of pure water at the same temperature. Pure water is assigned an $a_w$ of unity, equivalent to an ERH of 100%. Thus, the water activity value for a material is the decimal fraction corresponding to the ERH divided by 100. For example, an ERH of 50% corresponds to an $a_w$ of 0.5.

# Classification of dryers lec 3

Dryers can be classified according to:

- ***Heat transferring* methods:** this is important in demonstrating gross differences in dryer design ,operation and energy requirement

  **Direct:** Fluidised, Tray, Spray, Rotary Dryers.

  **Indirect:** Cone, Tumble, Pan Dryers.

- ***Continuous/ Batch processing***

  **Continuous:** large quantities/small residence time

  **Batch:** small quantities/ long residence time.

- ***Method of handling the solids***. this method is important when special attention must be given to the nature of the material to be dried.the major criterion is the presence or absence of agitation of the material to be dried friable material should not be subjected to excessive agitation :

  static bed dryer

  moving bed dryer

  fluidize bed dryer

  pneumatic system

**When considering how to dry a material, the following points should be considered:**

- heat sensitivity of the material being dried
- physical characteristics of the material
- nature of the liquid to be removed
- the scale of the operation
- the necessity for asepsis
- available sources of heat (steam, electrical)

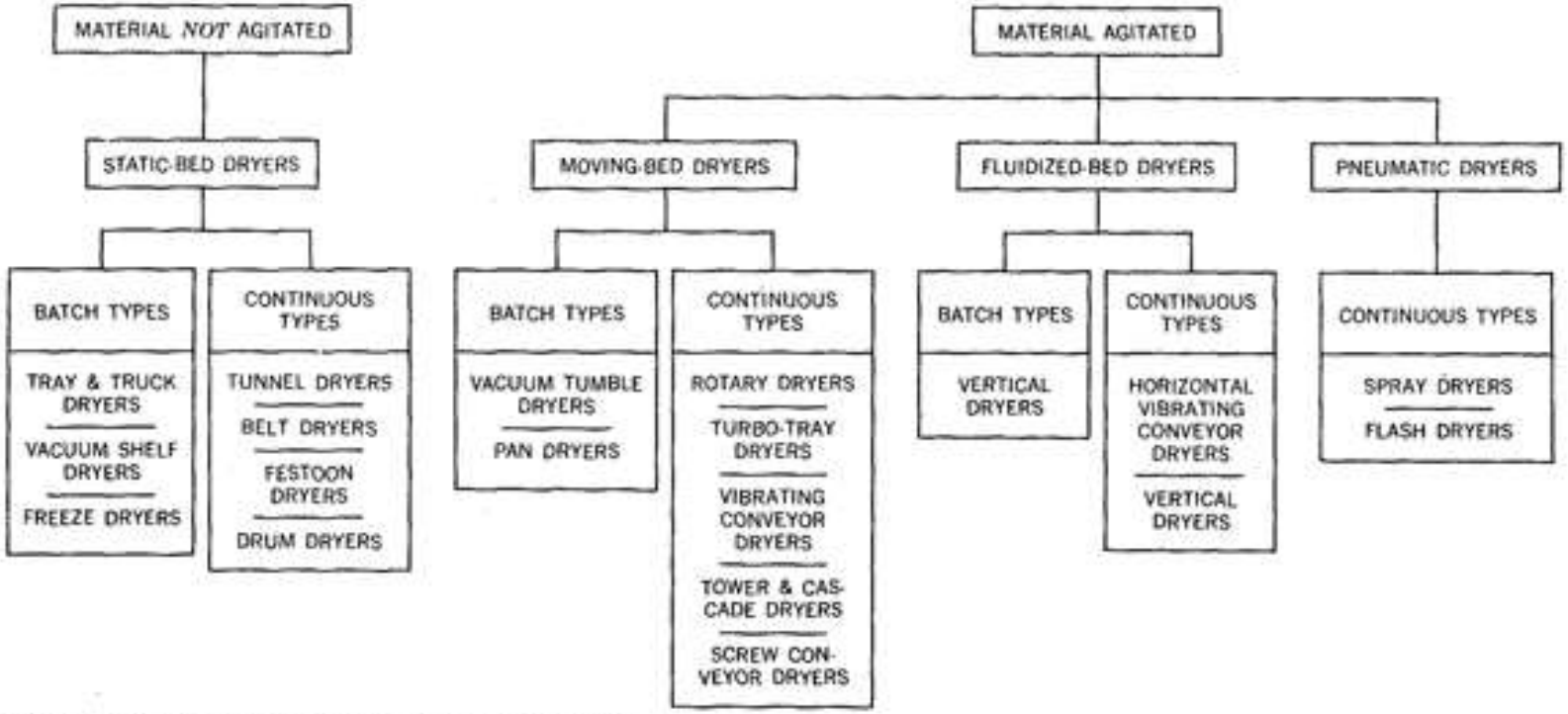



**FIG. 3-5.** *Classification of dryers, based on methods of solids handling.*

# Classification of Dryers

Classification based on the method of solids handling is shown schematically in Figure 3-5. Dryers in this classification scheme are divided into the following types:

1. *Static-bed dryers*—systems in which there is no relative movement among the solid particles being dried, although there may be bulk motion of the entire drying mass. Only a fraction of the total number of particles is directly exposed to heat sources. The exposed surface can be increased by decreasing the thickness of the bed and allowing drying air to flow through it.

2. *Moving-bed dryers*—systems in which the drying particles are partially separated so that they flow over each other. Motion may be induced by either gravity or mechanical agitation. The resultant separation of the particles and continuous exposure of new surfaces allow more rapid heat and mass transfer than can occur in static beds.

3. *Fluidized-bed dryers*—systems in which the solid particles are partially suspended in an upward-moving gas stream. The particles are lifted and then fall back in a random manner so that the resultant mixture of solid and gas acts like a boiling liquid. The gas-solid contact is excellent and results in better heat and mass transfer than in static and moving beds.

4. *Pneumatic dryers*—systems in which the drying particles are entrained and conveyed in a high-velocity gas stream. Pneumatic systems further improve on fluidized beds, because there is no channeling or short-circuiting of the gas flow path through a bed of particles. Each particle is completely surrounded by an envelope of drying gas. The resultant heat and mass transfer are extremely rapid; thus, drying times are short.

# Static –Bed System

Tray and truck dryer

Tray dryer consist of cabinet shelf or compartment .This dryer consist of cabinet in which the material to be dried is spread on tiers of tray.

# Static-Bed Systems

A truck dryer is one in which the trays are loaded on trucks (racks equipped with wheels), which can be rolled into and out of the drying cabinet. In plant operations, the truck dryer is preferred over the tray dryer because it offers greater convenience in loading and unloading.

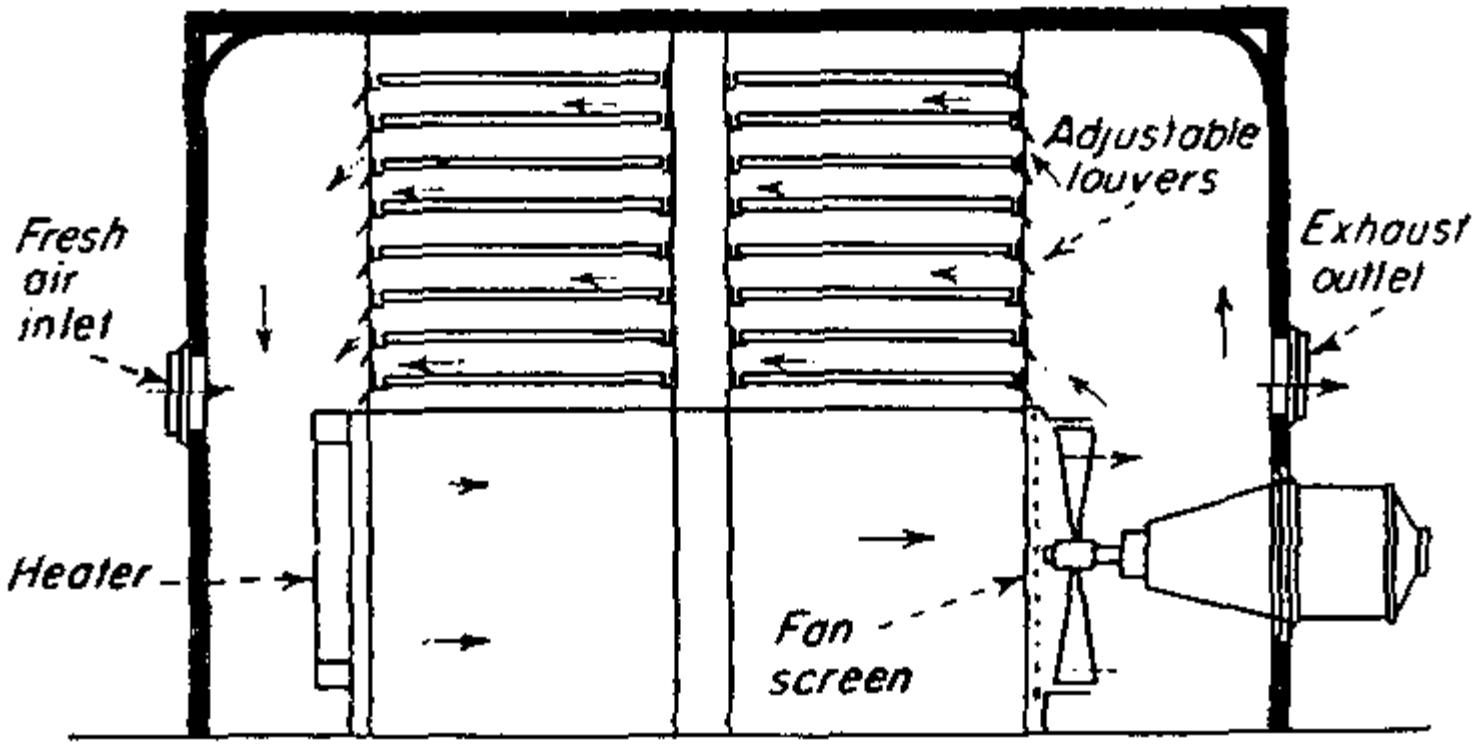


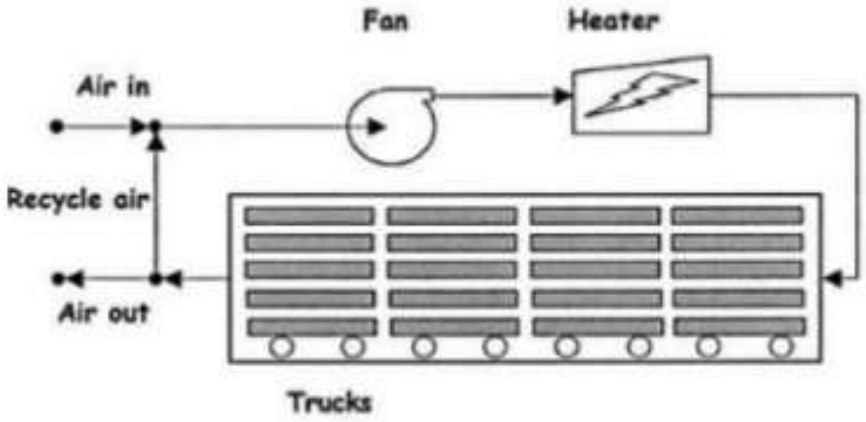

**FIG. 3-6.** *Tray dryer. (Courtesy of the Proctor and Schwartz Company.)*

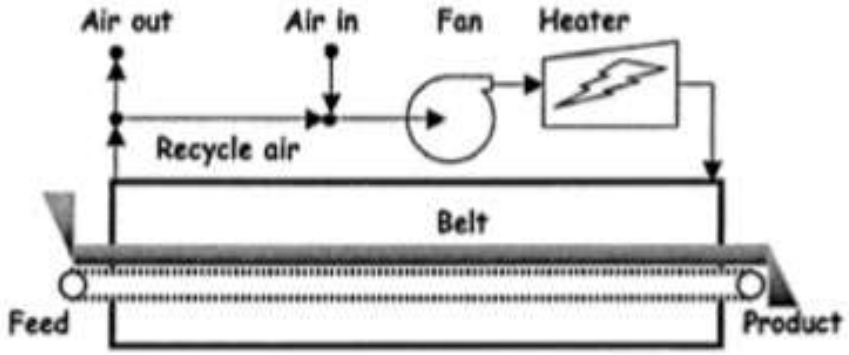
Tray dryers may be classified as direct or indirect. Most tray dryers used in the pharmaceutical industry are of the direct type, in which heating is accomplished by the forced circulation of large volumes of heated air. Indirect tray dryers utilize heated shelves or radiant heat sources inside the drying chamber to evaporate the moisture, which is then removed by either a vacuum pump or a small amount of circulated gas.

To achieve uniform drying, there must be a constant temperature and a uniform airflow over the material being dried.

**Tunnel and Conveyor Dryers.** Tunnel dryers are adaptations of the truck dryer for continuous drying. The trucks are moved progressively through the drying tunnel by a moving chain. These trucks are loaded on one side of the dryer, allowed to reside in the heating chamber for a time sufficiently long to effect the desired drying, and then discharged at the exit. The operation may be more accurately described as *semicontinuous*, because each truck requires individual loading and unloading before and after the drying cycle. Heat is usually supplied by direct convection, but radiant energy also may be used.

# Tunnel (truck) Dryer and Conveyor Dryer



# Lec 4

## Moving-Bed Systems

**Turbo-Tray Dryers.** The turbo-tray dryer, illustrated in Figure 3-7, is a continuous shelf, moving-bed dryer. It consists of a series of rotating annular trays arranged in a vertical stack, all of which rotate slowly at 0.1 to 1.0 rpm. Heated air is circulated over the trays by turbo-type fans mounted in the center of the stack. Wet mass fed through the roof of the dryer is leveled by a stationary wiper. After about seven-eighths of a revolution, the material being dried is pushed

## Moving-Bed Systems

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through radial slots onto the tray below, where it is again spread and leveled. The transfer of mass from one shelf to the next is complete after one revolution. The same procedure continues throughout the height of the dryer until the dried material is discharged at the bottom. Because the turbo-tray dryer continuously exposes new surfaces to the air, drying rates are considerably faster than for tunnel dryers.

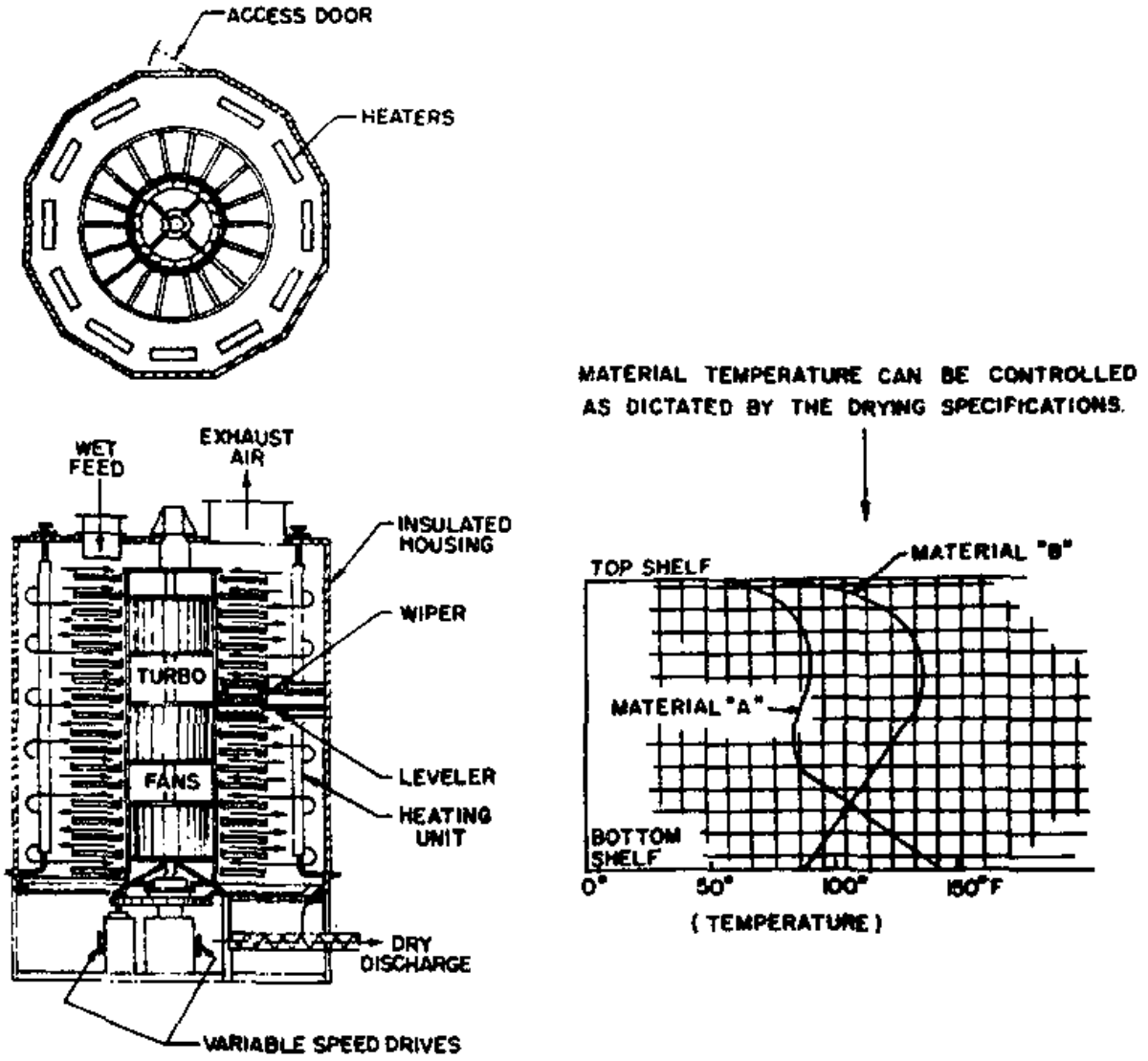
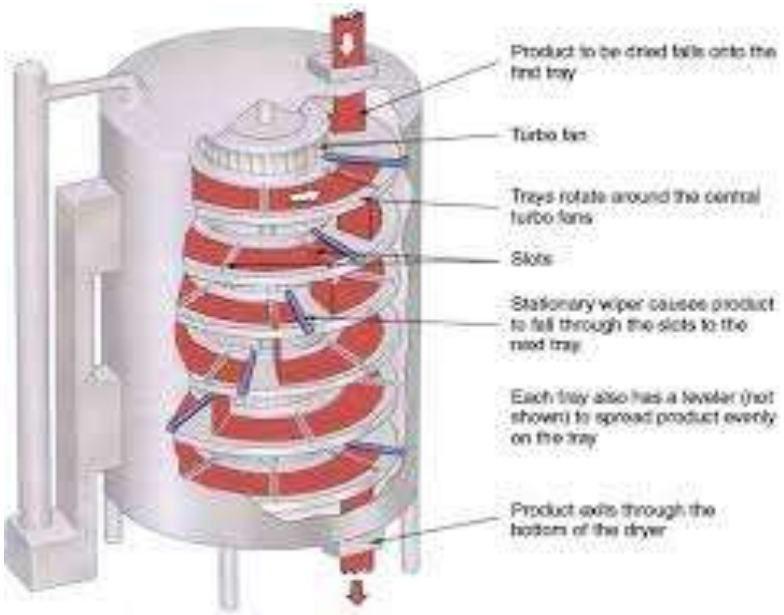
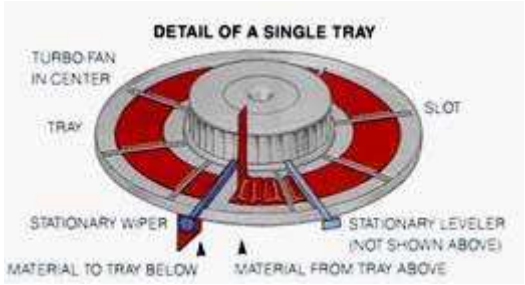
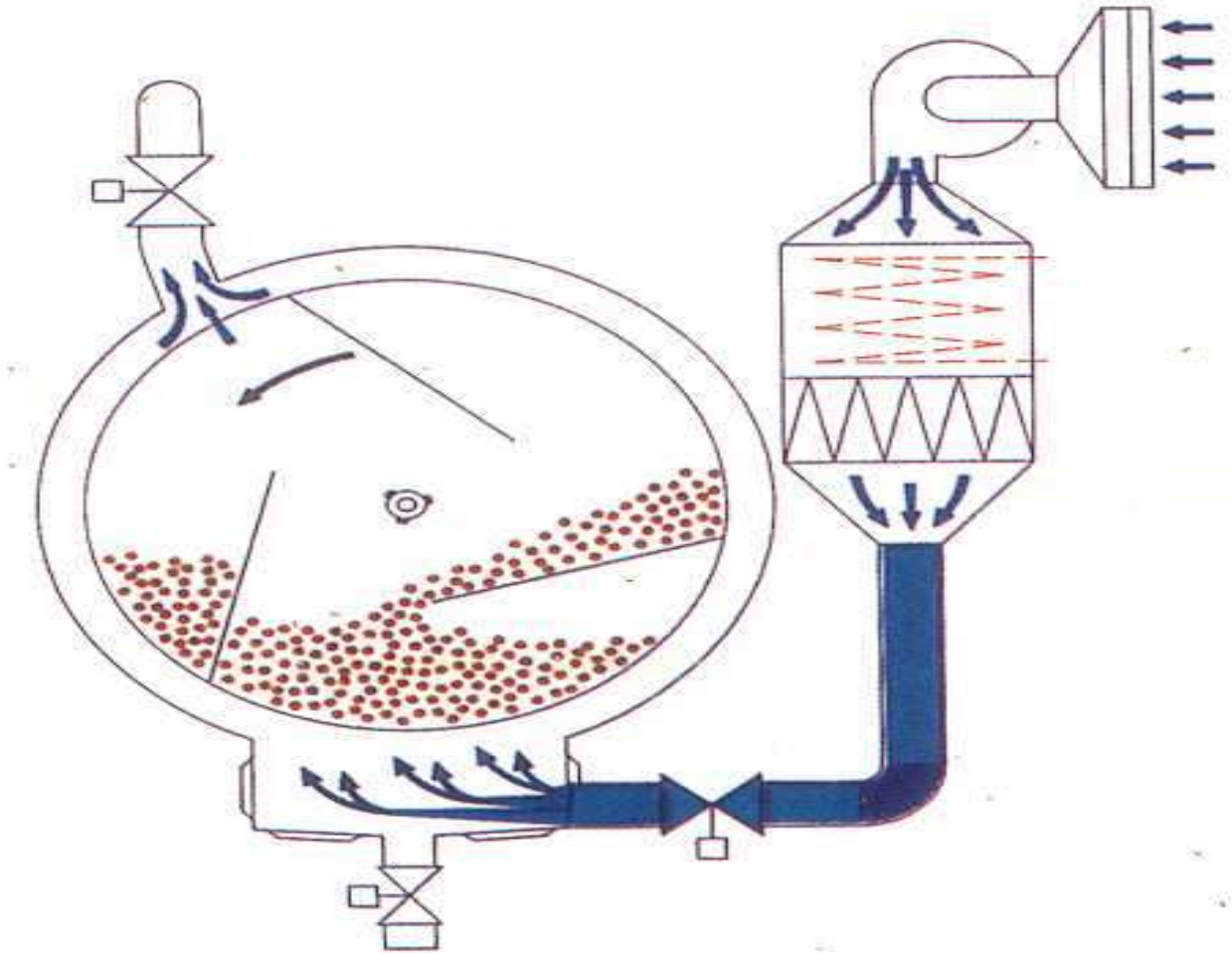



**FIG. 3-7.** *Turbo-tray dryer. (Courtesy of the Wyssmont Company.)*


Product to be dried falls onto the first tray
Turbo fan
Trays rotate around the central turbo fans
Slots
Stationary wiper causes product to fall through the slots to the next tray
Each tray also has a leveler (not shown) to spread product evenly on the tray
Product exits through the bottom of the dryer


DETAIL OF A SINGLE TRAY
TURBO FAN IN CENTER
TRAY
SLOT
STATIONARY WIPER
STATIONARY LEVELER (NOT SHOWN ABOVE)
MATERIAL TO TRAY BELOW
MATERIAL FROM TRAY ABOVE

**Pan Dryers.** Pan dryers are moving-bed dryers of the indirect type that may operate under atmospheric pressure or vacuum, and are generally used to dry small batches of pastes or slurries. The dryer consists of a shallow, circular jacketed pan having a diameter of 3 to 6 feet and depth of 1 to 2 feet, with a flat bottom and vertical sides. Heat is supplied by steam or hot water.



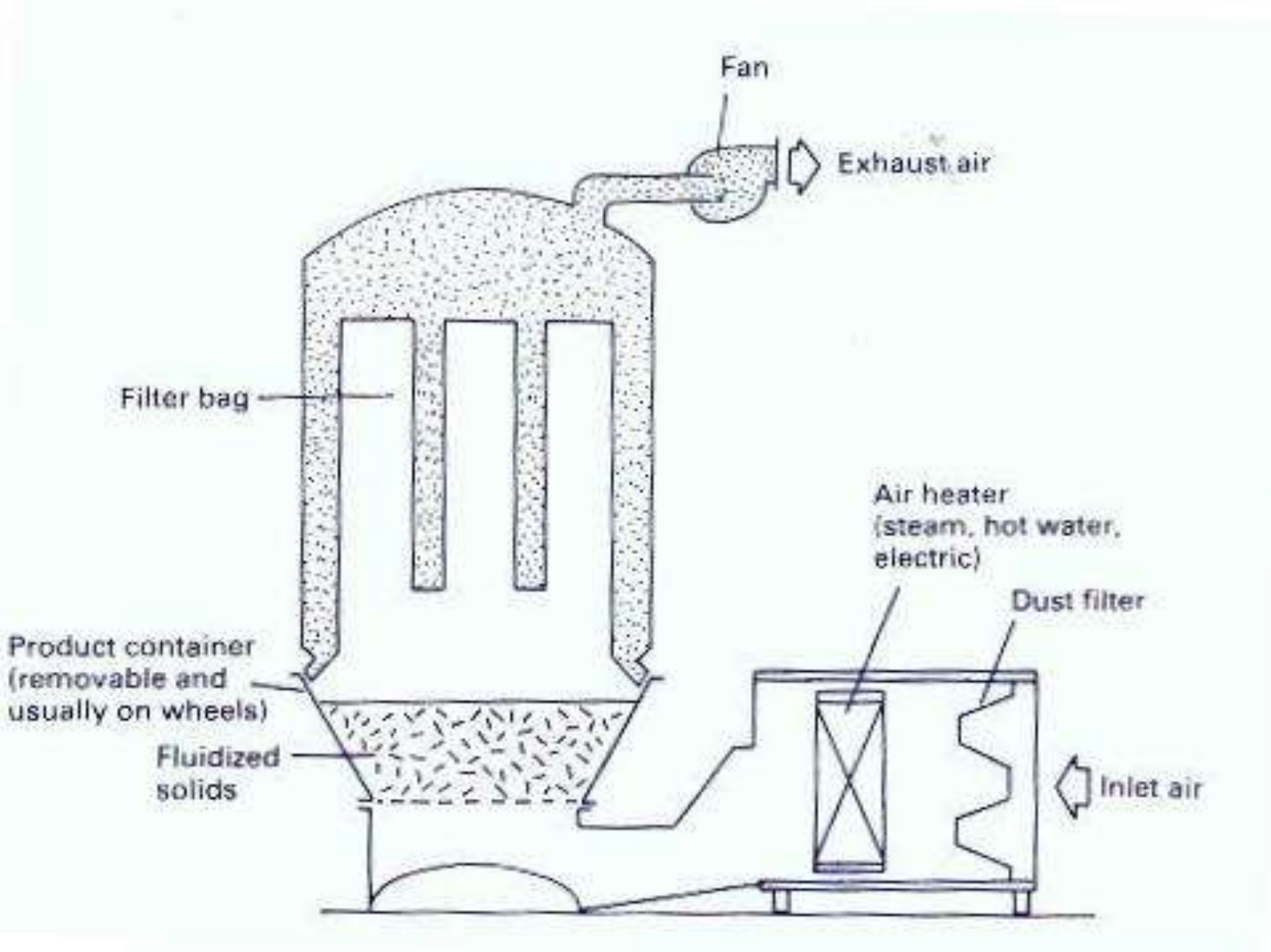
Pan dryer

# Fluidized-bed.dryer

An excellent method of obtaining good contact between the warm drying air and wet particles. The general principles of the technique of *fluidization*. the **term boiling bed** being commonly used to describe it .

particulate matter is contained in a vessel, the base of which is perforated, enabling a fluid to pass through the bed of solids from below. The fluid can be liquid or gas, but air will be assumed for the purposes of the drying process.

The important factor is that fluidization produces conditions of great turbulence, the particles mixing with good contact between air and particles. Hence, if hot air is used, the turbulent conditions lead to high heat and mass transfer rates, the fluidized-bed technique therefore offers a means of rapid drying compared with the older static tray dryers




**Fluidized-bed.dryer**

The fluidization technique is efficient for the drying of granular solids, because each particle is completely surrounded by the drying gas. In addition, the intense mixing between the solids and gas results in uniform conditions of temperature, composition, and particle size distribution throughout the bed.

## Advantages of fluidized-bed drying

- 1- high drying rates.
- 2- most of the drying will be at constant rate.
- 3-The temperature of a fluidized bed is uniform.
- 4- It produces more spherical free-flowing product.
- 5- The free movement of individual particles eliminates the risk of soluble materials migrating, as may occur in static beds.

# Pneumatic Systems

**Spray Dryers.** Spray dryers differ from most other dryers in that they can handle only fluid materials such as solutions, slurries, and thin pastes. The fluid is dispersed as fine droplets into a moving stream of hot gas, where they evaporate rapidly before reaching the wall of the drying chamber. The product dries into a fine powder, which is carried by the gas current and gravity flow into a collection system.

Spary dryer atomizer are:

- Pneumatic atomizer
- Pressure nozzle
- Spinning disc atomizer

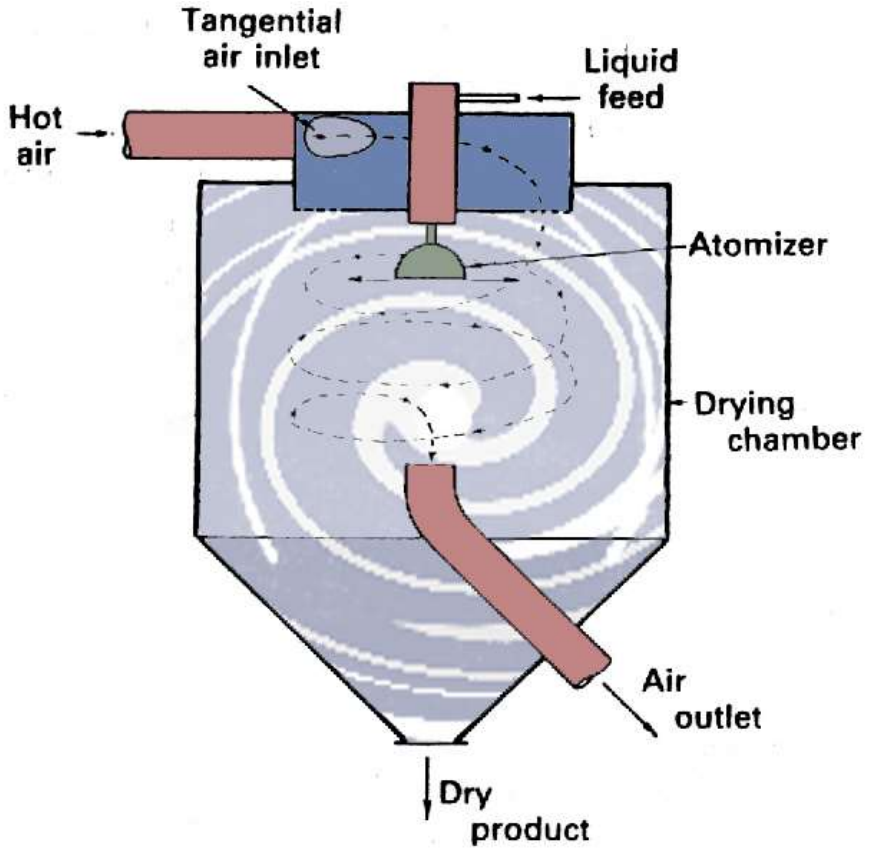
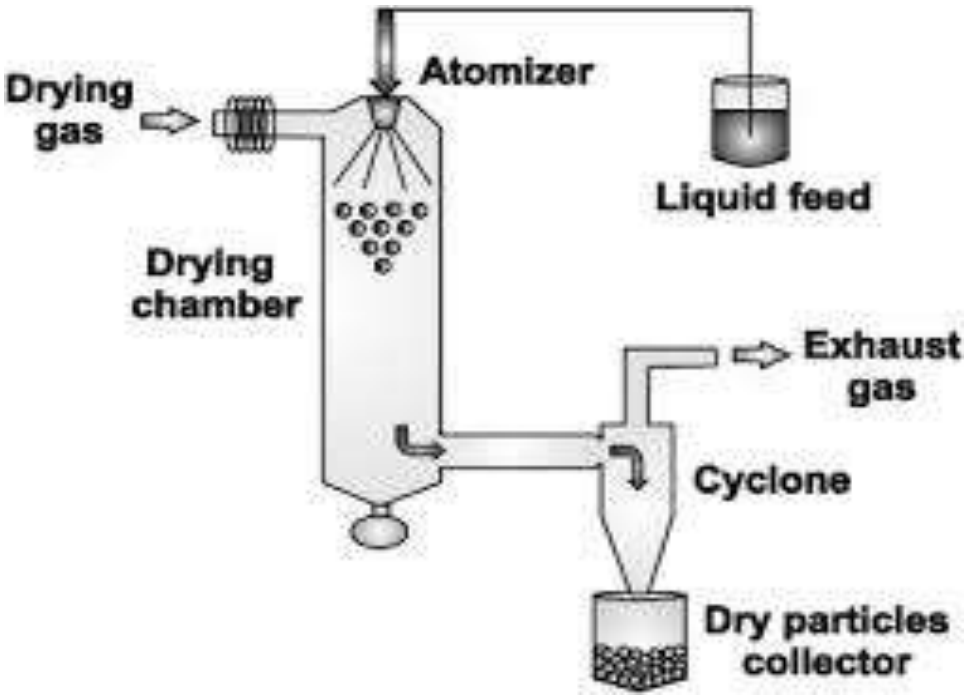



Fig. 38.13 Spray drier


Drying
gas
Atomizer
Liquid feed
Drying
chamber
Exhaust
gas
Cyclone
Dry particles
collector

**Spray Drying and Spray Congealing of Pharmaceuticals.** Spray drying finds great utility in the pharmaceutical industry because of the rapidity of drying and the unique form of the final product. There are three major uses for the spray drying processes: (1) drying heat-sensitive materials, (2) changing the physical form of materials for use in tablet and capsule manufacture, and (3) encapsulating solid and liquid particles.

An alternative to spray for the encapsulation of solid particles is *spray chilling* or *spray congealing*. This process consists of suspending the particles in a molten coating material and pumping the resultant slurry into a spray dryer in which cold air is circulated. The slurry droplets congeal on coming into contact with the air and are collected in the same manner as the spray dried product. The coating agents normally employed are low melting materials such as waxes. The congealing process requires a much higher ratio of coating agent to active material than does spray drying, because only the molten coating agent constitutes the liquid phase. Spray congealed coatings are used mainly for taste masking and for sustained-release formulations.

# Characterization of spray dried products ;

- The products are uniform in appearance and have characteristic shape, in the form of hollow spheres with a small hole.
- This method of drying allows a dry product to retain some properties of feed , e.g., a drop from an emulsion dries with continuous phase on the outside.When reconstituted, the emulsion is easily re- formed.
- Spray drying is useful in the coating and encapsulation of both solid and liquid solid particle are coated by spray drying a suspension of material in solution of the coating agent . As the solvent is evaporated , the coating material envelope the suspended particle.This method is useful as taste and odor masking ,enteric coating ,sustained release and improving stability.

- Oily liquid may be encapsulated by emulsification in water with aid of emulsifying agent (acacia or starch )as the water is dry the oil drop is encapsulated in shell of gum this process is used .This process is used for preparation of (dry)flavor oil.

# Advantages of the spray drying process

- 1-The droplets are small, giving a **large surface area** for heat transfer, so that **evaporation** is very **rapid**. The actual **drying time** of a droplet is only a **fraction of a second**, and the **overall time** in the dryer is only a few **seconds**.

- 2- Because **evaporation** is very **rapid,** the droplets **do not** attain a **high** temperature, most of the **heat** being used as **latent heat** of vaporization.

- 3- The characteristic **particle** form gives the product a **high bulk density** and, in turn, **ready solubility.**

# Flash Dryers.

**Flash Dryers.** In flash drying, the moistened solid mass is suspended in a finely divided state in a high-velocity (3000 to 6000 feet per minute), high-temperature (300°F to 1300°F) air stream.

The drying process is referred to as *flash drying*, because the drying time is extremely short.

# Specialized Drying Methods

**Lec 5**

- Freeze drying (lyophilization)is a process **used to dry extremely heat – sensitive** materials**.** It allows the drying , without excessive damage, of **proteins, blood products** and even microorganisms, which retain a small but significant viability. It is used for batch drying.

In this process the initial liquid solution or suspension is frozen, the pressure above the frozen state is reduced and the water removed by sublimation.

Freeze drying depend on the phenomenon of sublimation , where by water passes directly from the solid state to the vapor state without passing through the liquid phase .

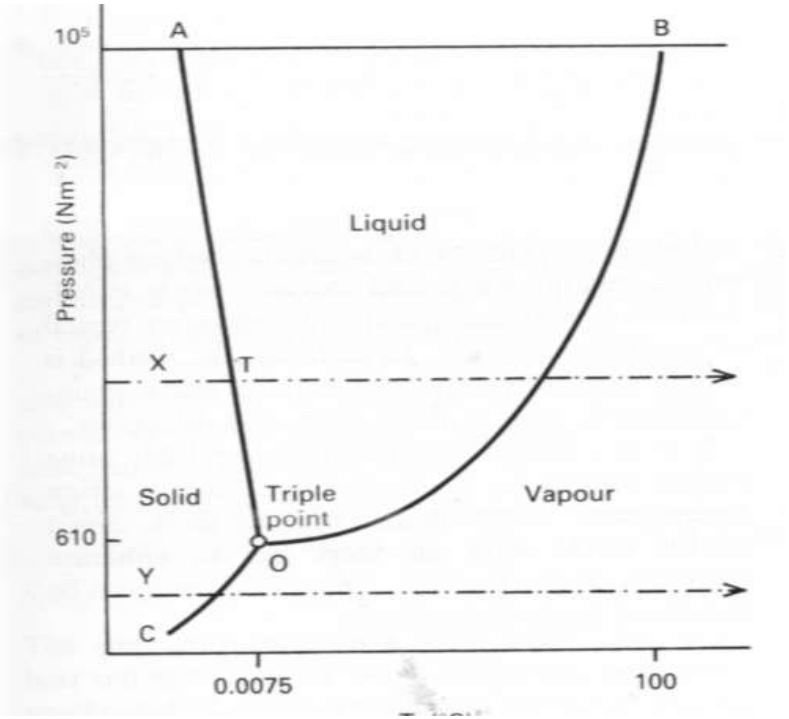
Freeze drying must meet the three basic requirement of all types of drying despite this unusual type of drying:

1-There must be a positive vapor pressure driving force (the vapor pressure of water on the surface of material to be dried must be higher than the partial pressure of the enveloping atmosphere).

2-Adequate latent heat of vaporization must be introduced to the drying solid to maintain the desirable tempareture level at both the surface and the interior .

3-Removal of evaporated moisture.

# The phase diagram for water

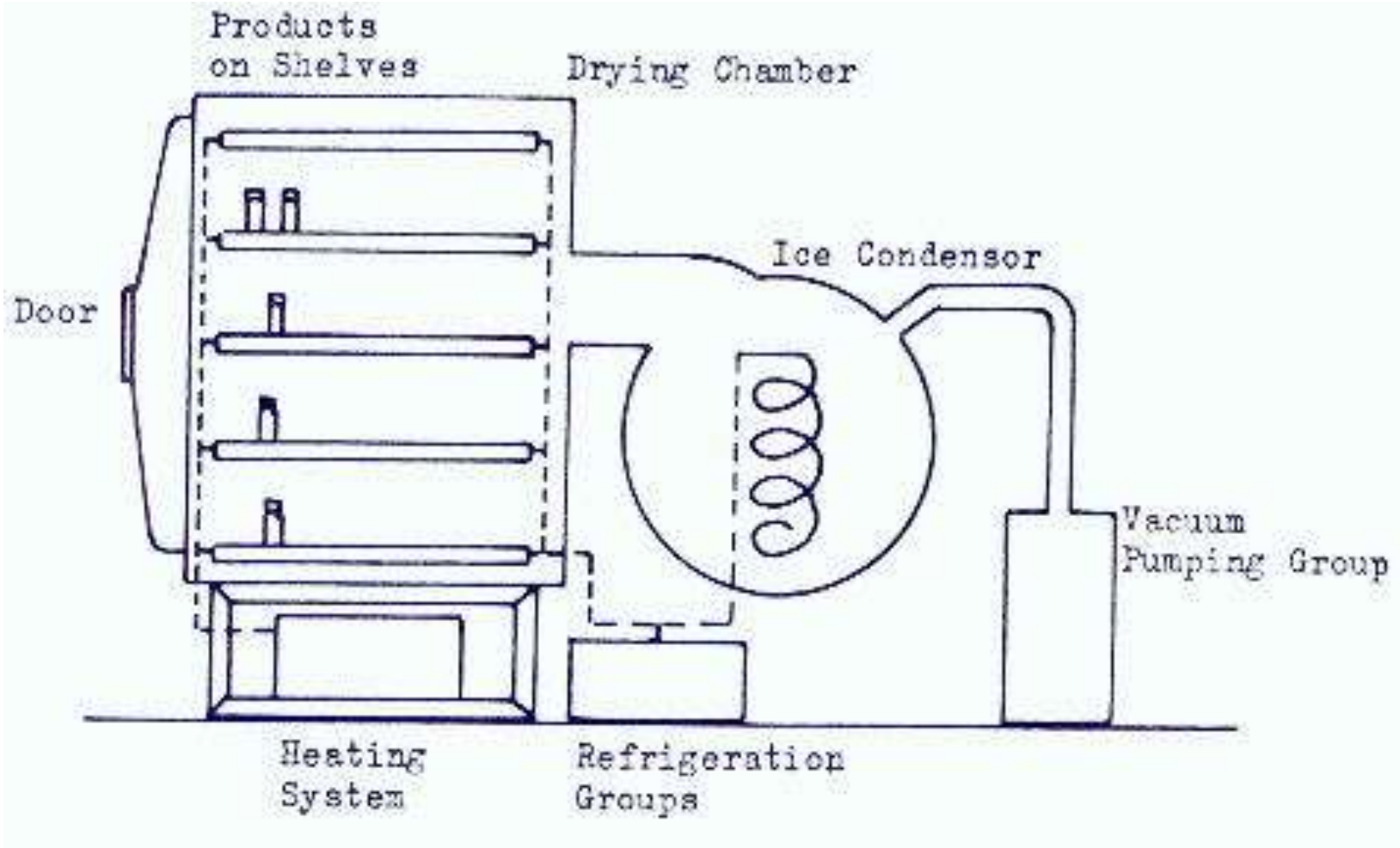



- The diagram consists of three separate areas representing the phases of water, solid, liquid, and vapour . The point O is the only point where all the three phases can coexist, and is known as **the triple point .**

On heating at constant **atmospheric pressure** ice will melt when the temperature rises to 0 C . At this constant temperature and pressure it will then change to water. Continued heating will raise the temperature of the water to 100 C where, if heat addition is continued, the liquid water will be converted into water vapour at 100 C.

- If , however, solid ice is maintained at a pressure below the triple point then on heating the ice will sublime and pass directly to water vapour without passing through the liquid phase.
- This sublimation, and therefore drying, can occur at a temperature below triple point(to prevent ice converted to liquid).
- This will only happen if the pressure is prevented from rising above the triple point pressure .
- It may be thought that as the process takes place at a low temperature the heat required to sublime the ice will be **small**.
- **Pharmaceutical product intended for freeze drying contain dissolved solid resulted in different pressure /temperature relationship**

# Freeze Dryer



# Limitations of the freeze drying process.

- **T**he freeze drying of products such **as blood plasma,** although simple in theory, presents a number of practical problems:-

- 1-The depression of the **freezing point** caused by the presence of **dissolved solutes** means that the solution must be **cooled below** the normal freezing temperature for pure water (-10-30° C).

- 2-Sublimation can only occur at the **frozen surface** and is **slow** process (1mm thickness of ice per hour). So, the **surface area** must therefore be **increased** and

- 3-the **liquid thickness** prior to freezing be **reduced** in order to reduce the thickness of ice to be **sublimated.**

- 4-At low pressure **large** volumes of **water vapour** are produced which must be removed to **prevent** the **pressure rising** above the **triple point** pressure.

- 5-The dry material often needs to be **sterile,** and it must also be **prevented** from **regaining** moisture prior to the final packaging.

# Stages of the freeze drying process

- ***1- Freezing stage*:**
- The liquid material is frozen before the application of vacuum to avoid frothing, and several methods are used to produce a large frozen surface.
- a- Shell freezing : This is employed for large **volumes** such as blood products. The **bottles** are **rotated** slowly and **almost horizontally** in a **refrigerated bath**. The liquid freezes in a **thin shell** around the inner surface of the bottle.
- Freezing is **slow** and **large ice** crystals form, which is a **drawback** of this method.
- In **vertical** spin **freezing the bottles** are spun individually in a **vertical position ,** centrifuged and **cooled** by a blast of cold air. The solution super cools and freezes rapidly, with the formation of **small ice** crystals.
- b- Centrifugal evaporative freezing: The solution is spun in small containers within a centrifuge. This prevents the foaming when a vacuum is applied. The vacuum causes boiling at room temperature. About 20% of the water is removed prior to freeze drying and there is no need for refrigeration. Ampoules are usually frozen in this way

- ***2 - Vacuum application stage:*** The containers and the frozen material must be connected to a vacuum source sufficient to drop the **pressure below the triple point** and remove the larger volumes of low – pressure vapour formed during drying.

- ***3 - Sublimation stage:***
- Heat of sublimation must be supplied. Under these conditions the ice slowly sublimes, leaving a porous solid which still contains about 0.5% moisture after primary drying .
- **Primary drying**: It can reduce the moisture content of a freeze-dried solid to around 0.5%. Further reduction can be affected by secondary drying .
- **Heat transfer:** Insufficient heat input prolongs the process, which is already slow, and excess heat will cause melting.
- **Vapour removal:** The vapour formed must be continually removed to avoid a pressure rise that would stop sublimation.
- **Rate of drying**: The rate of drying in freeze drying is very slow, the ice being removed at a rate of about only 1mm depth per hour.

***4- Secondary drying:***

The removal of residual moisture at the end of primary drying is performed by raising the temperature of the solid to as high as 50 or 60 C .

***5- Packaging:***

Attention must be paid to packaging freeze-dried products to ensure protection from moisture. Containers should be closed without contacting the atmosphere.

## Advantages of freeze drying

1- Drying takes place at very low temperatures, so the chemical decomposition, particularly hydrolysis is minimized.

2- The solution is frozen occupying the same volume as the original solution, thus , the product is light and porous.

3- The porous form of the product gives ready solubility.

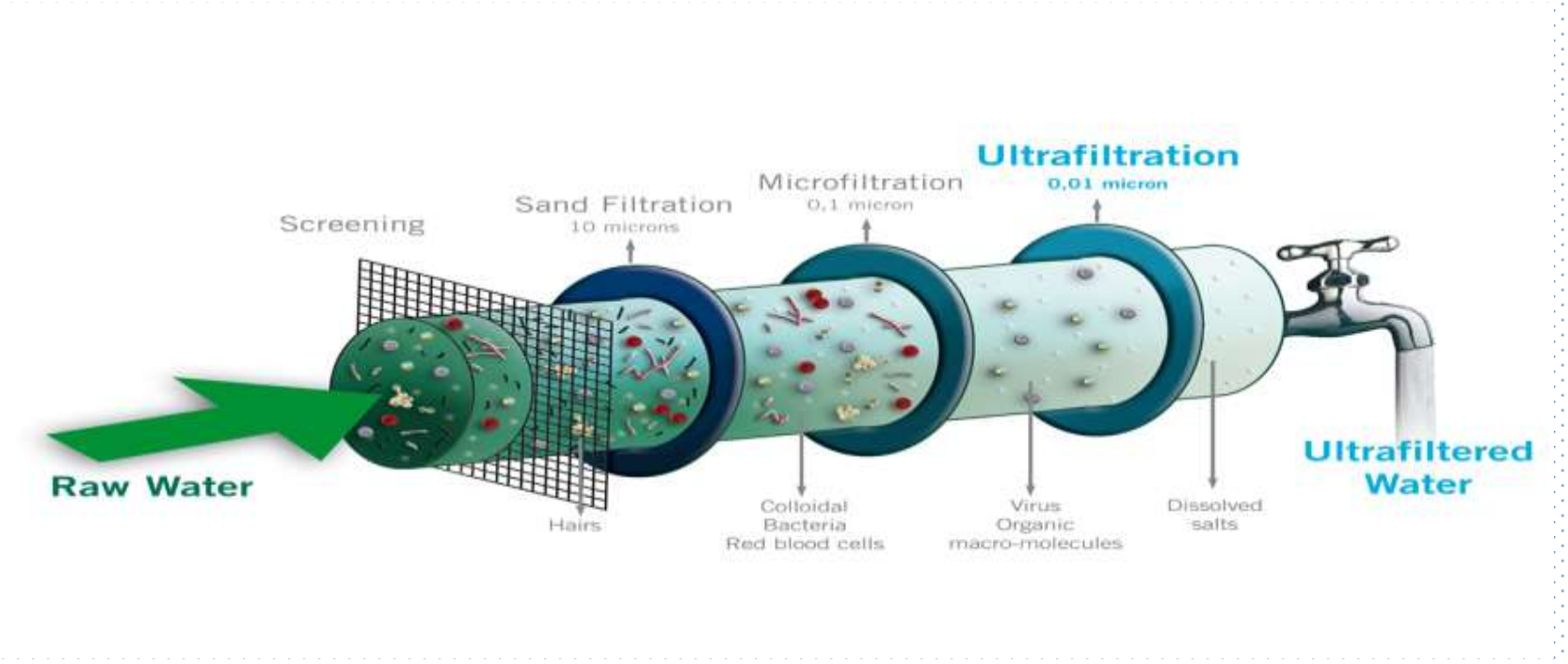
4- There is no concentration of solution prior to drying. Hence, salts do not concentrate and denature proteins, as occurs with other drying methods.

5- As the process takes place under high vacuum there is little contact with air, and oxidation is minimized.

**Microwave Drying.** The application of microwave energy to the drying of solids represents a radical departure from conventional means of drying. Instead of applying heat externally to a material, energy in the form of microwaves is converted into internal heat by interaction with the material itself. This permits extremely rapid heat transfer throughout the material, which in turn can lead to rapid drying.


thank you

# Clarification and Filtration



- **Introduction**
- Filtration is a separation process in which a solid-liquid mixture called the feed (or the suspension) is forced through a porous medium on which the solids are deposited or in which they are entrapped.
- The porous medium which allows the liquid to go through while retaining the solids is called **the filter**.
- The retained solid is called "**the residue**" or "the **cake**".
- The clarified liquid is called "**the effluent**" or the "**filtrate**".
- Filtration can be broadly classified into three categories according to the purpose of it: (see Fig. 1).

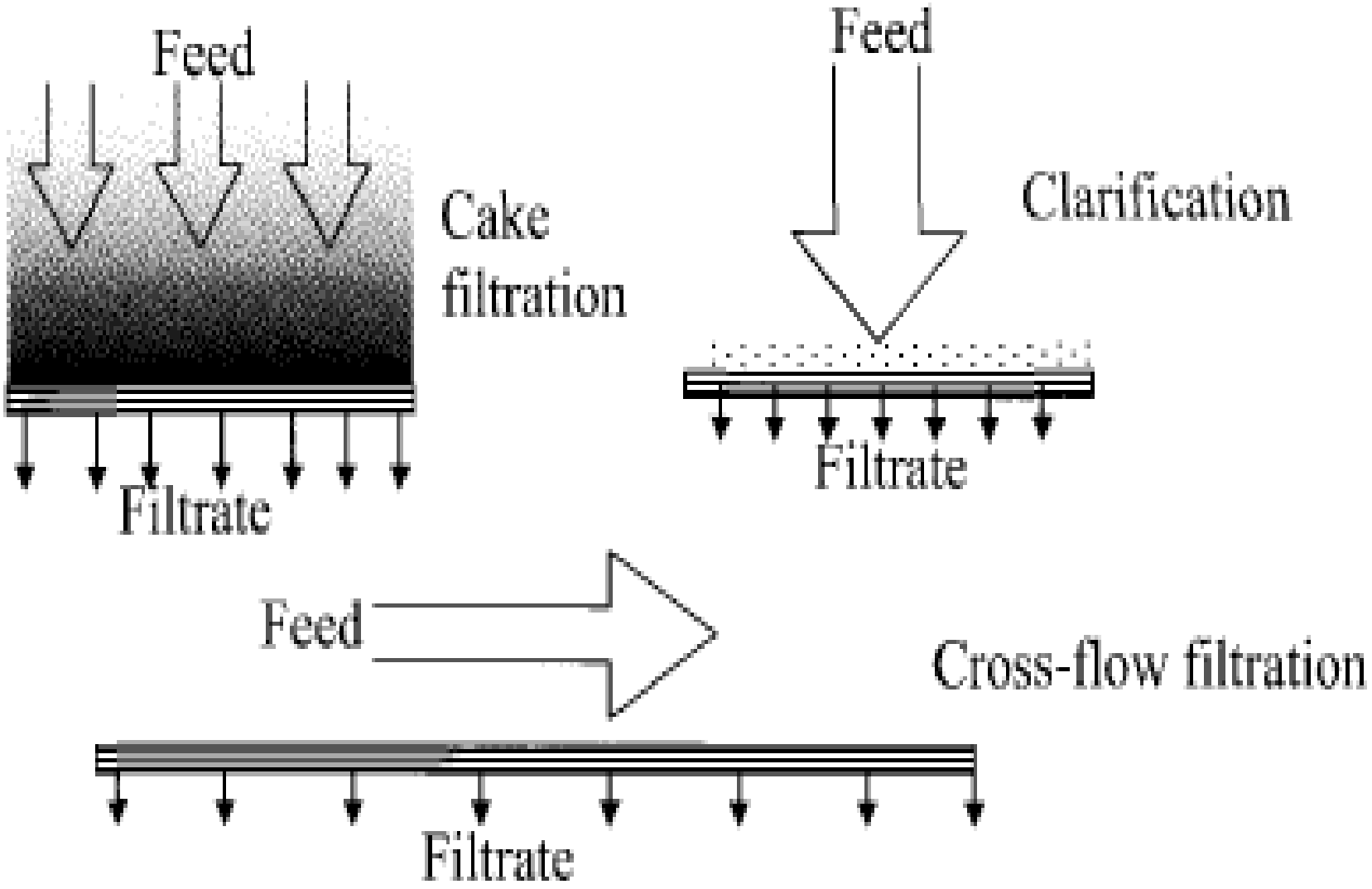



Fig1- type of filtrations

- If recovery of solids from high solid content slurry is desired, the process is called **cake filtration**.
- The term **clarification** is applied when the solid content in the feed does not exceed 1 %.
- In a clarification process the filtrate is the primary product.
- The third type of filtration is called cross-flow filtration in which the liquid flows parallel to the filtration medium
- **Cross-flow filtration ( ultrafiltration)** is separation of intermicellar liquid from solids by use of pressure on semipermeable membrane.
- **sterilization** is the method of choice for seperation of micoorganisms from solution which is physically and chemically unstable under heating condition.

# Application of solid/liquid filtration

- 1- Improvement of the appearance of solutions, mouth washes, etc.....
- 2- Removal of potential irritants, e.g. from eye drop preparations or solutions applied to mucous membranes.
- 3- Recovery of desired solid material from suspension or slurry ,e.g. to obtain drug after crystallization process.
- 4- Certain operations, such as the extraction of vegetable drugs with a solvent, may yield a turbid product with a small quantity fine suspended colloidal matter; this can be removed by filtration.
- 5- Detection of microorganisms present in liquids, This can be achieved by analyzing a suitable filter on which the bacteria are retained .This method can also be used to assess the efficiency of preservatives.

- **Mechanism of filtration:**
- Based on the mechanisms by which solids are retained by a filter .we have these type of filteration :
  - ***Surface filtration:*** The particles are retained by a screening action and held on the external surface of the filter. The mechanisms are straining and impingement

  The particles are not allowed to enter the filtration medium.

- ***Depth filtration:*** Particles are allowed to penetrate pores and pore networks present in the filtration medium to point where diameter of solid particle is greater than the diameter of tortuous void or channel. The solids are retained by physical restriction or by adsorption properties of the medium.

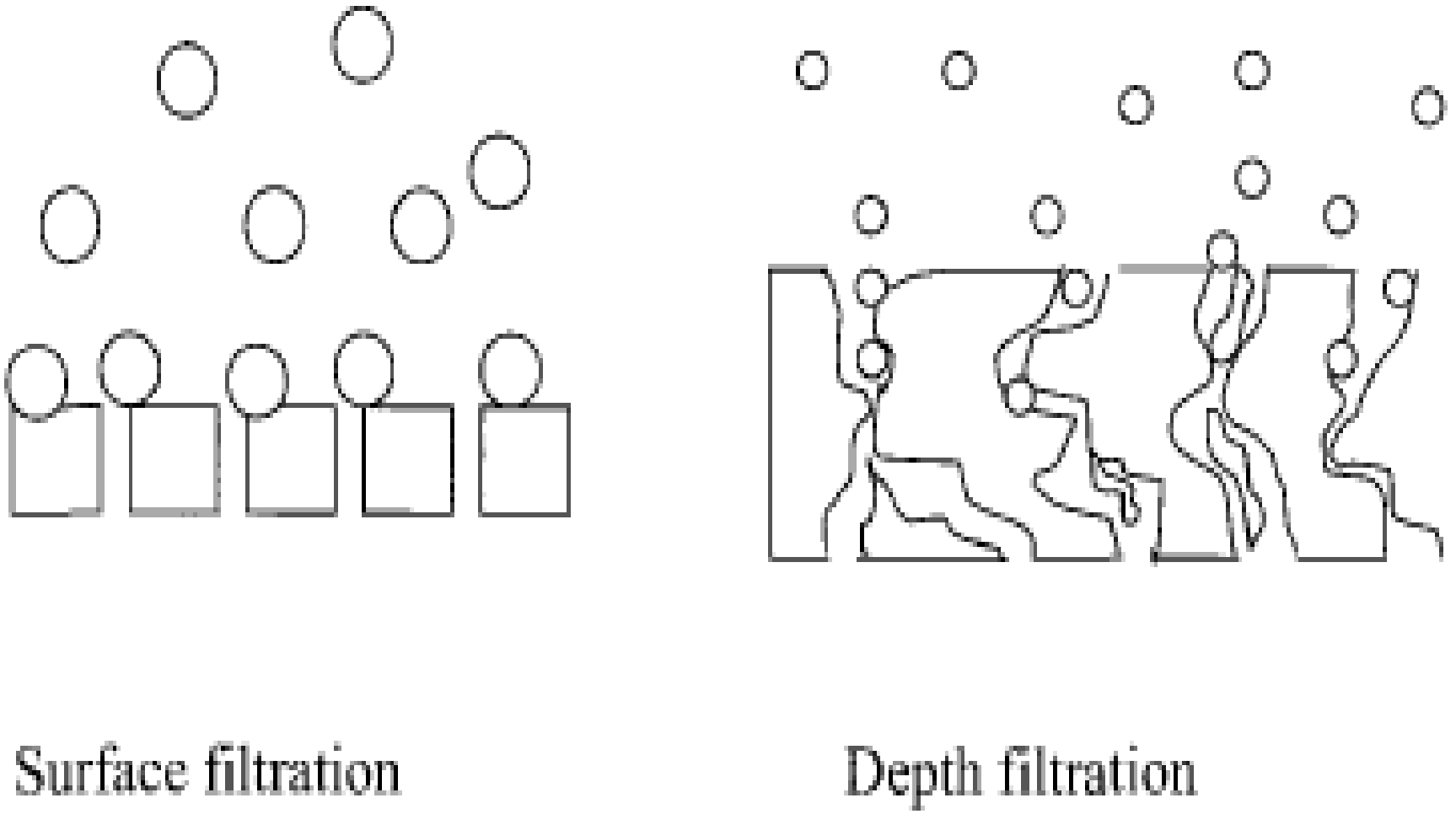
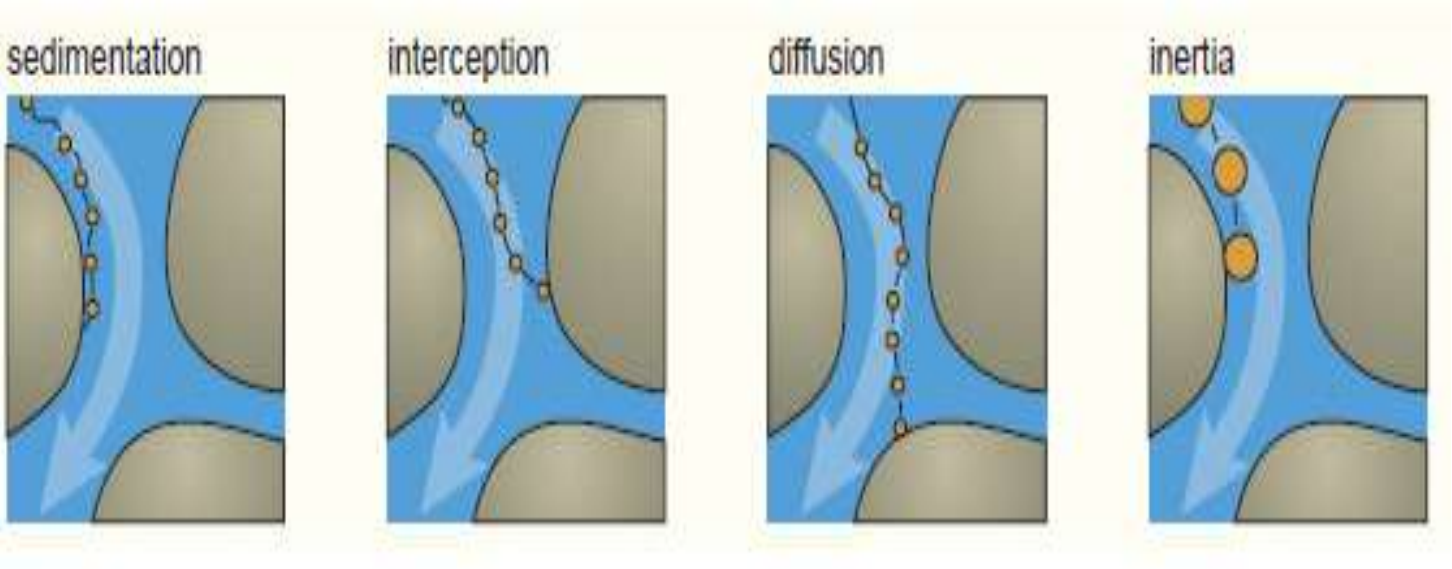



Fig 2- Mechanisms of filtration

**In depth Filtration, the mechanisms are:**

- Diffusion deposition
- Direct interception
- Inertial deposition
- Electrostatic deposition
- Gravitational deposition



# Theory of filtration

The mathematical model for flow through porous medium , cake filtration and granular bed filtration may differ, but all follow this basic rule. The energy lost in filtration is proportional to the rate of flow per unit area.

**rate = driving force/ resistance**

The rate can express by " **Poiseuilles equation**"

$$\frac{dV}{dT} = \frac{A\,P}{\mu(\alpha W/A + R)}$$

V= volume of filtrate . T= time , A = filter area

P= total pressure drop through cake and filter medium,

μ= viscosity of filtrate , α= average specific cake resistance

W= weight of dry cake , R= resistance of filter medium

# Rate of Filtration:

- the object of the operation is to filter the slurry as quickly as possible.
- The Previous equation can be simplified by another equation which summarized the factors affecting rate of filtration is known **as Darcy"s law** and may be expressed as:

$$dV / dt = K A P / u l$$

- where

V= volume of filtrate, t = time of filtration , K = constant for the filter medium and filter cake , A = area of filter medium , P = pressure drop across the filter medium and filter cake , u = viscosity of the filtrate , and l = thickness of cake.

k is proportional constant depend on porosity and specific area of particles.

- **Factors affecting rate of filtration :**

- **1- Permeability coefficient:** The constant (K) represents the resistance of both the filter medium and the filter cake. As the thickness of the cake increase, the rate of filtration will decrease. Also the surface area of the particles .the porosity of the cake, and rigidity or compressibility of the particles could affect the permeability of the cake.

- **2 - Pressure drop;** The rate of filtration is proportional to the pressure difference across both the filter medium and filter cake.

The **pressure drop** can be achieved in a number of ways:

- **Gravity:** A pressure difference could be obtained by maintaining a head of slurry above the filter medium. The pressure developed will depend on the density of the slurry.
- **Vacuum:** The pressure below the filter medium may be reduced below atmospheric pressure by connecting the filtrate receiver to a vacuum pump and creating a pressure difference across the filter.
- **Pressure:** The simplest method being to pump the slurry into the filter under pressure.
- **Centrifugal force:** The gravitational force could be replaced by centrifugal force in particle separation,

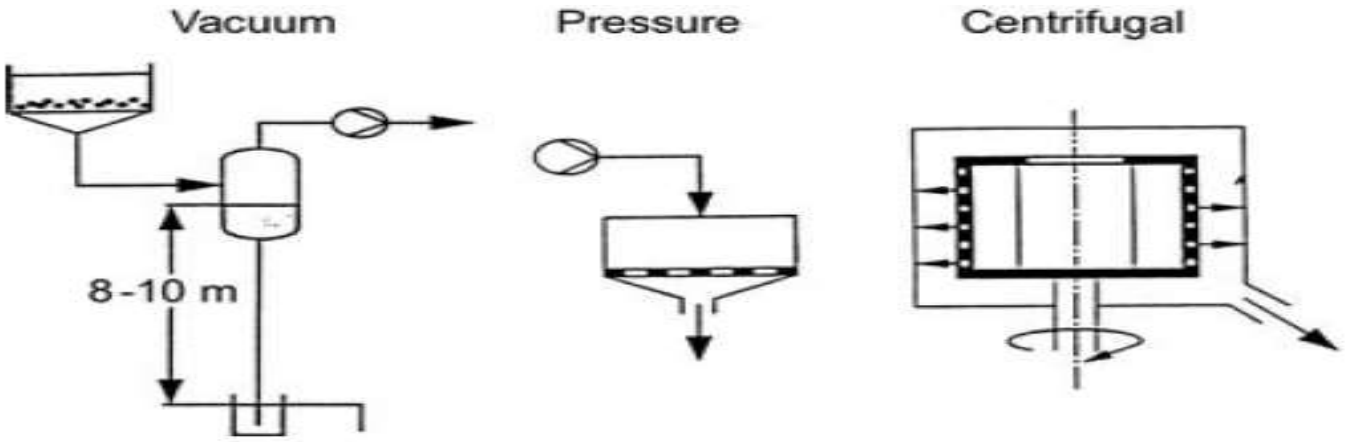



Fig- driving force in filtration.

- **3- Area of filter medium:** The total volume of filtrate flowing from the filter will be proportional to the area of the filter. The area can be increased by using larger filters. In the rotary drum filter, the continuous removal of the filter cake will give an infinite area for filtration.

- **4- Viscosity of filtrate:**

It would be expect that an increase in the viscosity of the filtrate will increase the resistance of flow , so that the rate of filtration is inversely proportional to the viscosity of the fluid.

- **5- Thickness of filter cake;**

The rate of flow of the filtrate through the filter cake is inversely proportional to thickness of the cake.

$$\text{rate of filtration} = \frac{\text{(area of filter) x (pressure difference)}}{\text{( viscosity) x ( resistance of cake and filter)}}$$

# Filter Media

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

- **Properties of ideal filter medium:**

- 1- It must be capable of delivering a clear filtrate at a suitable production rate.
- 2- It must withstand the mechanical stresses without rupturing or being compressed.
- 3- No chemical or physical interactions with the components of the filtrate should occur.
- 4- It must retain the solids without plugging at the start of filtration.
- 5- Sterile filtration imposes a special requirement since the pore size must not exceed the dimension of bacteria or spores.

# Classification of filter media

- 1- Woven filters: these include **a- natural.** Cotton, b- **synthetic**, nylon.
- **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 .
- Both cotton and nylon are suitable for coarse straining in aseptic filtration.
- **Monofilament nylon cloth** : strong , opening as small 10 micron
- **Teflon** superior for most liquid filtration
- **Wire screening** e.g. stainless steel is durable, resistance to plugging and easily cleaned
- 2- Non- woven filters:
- **Felt** are fibrous mass, give high flow rate with low pressure drop, function as depth media and recommended where gelatinous solution or fine particulate matter are involve
- **Bonded fabrics** are not found wide acceptance in production of dosage forms

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

- **white paper** preferred, can crinkled to produce large surface area.

A support of cloth or wire mesh is required in large filter pass to prevent rupture of paper with pressure.

- **Porous stainless steel filter** use in clarification. For example milk, syrup, sulfuric acid and hot caustic soda . Easy clean and repeatedly sterilized

**3-Membrane filters:** These are basic tools for **micro-filtration and ultrafiltration**, useful in the preparation of sterile solutions.

These filters are **made by casting** of various esters of cellulose, or from nylon, Teflon, polyvinyl chloride. Polyamide , polysulfone or silver

The filter is a thin membrane with millions of pores per square centimeter of filter surface.

The distinction between ultrafiltration and microfiltration lies in the nature of the filter medium. Ultrafiltration membranes contain pores of relatively narrow size distribution $10^{-3}$ to $10^{-2}$ microns (10 to 100 Å) and are formed by etching cylindric pores into a solid matrix. Ultrafiltration membranes are fragile and require supporting substrates because of the high-pressured differences required during filtration.

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. An approximate pore size reference guide can be set down as follows:

| *Pore Size (micron)* | *Particle Removed* |
|---|---|
| 0.2 (0.22) | All bacteria |
| 0.45 | All coliform group bacteria |
| 0.8 | All airborne particles |
| 1.2 | All nonliving particles considered dangerous in i.v. fluids |
| 5 | All significant cells from body fluids |

**4- Cartridge unit:** economic and convenient when used to remove small percent of solids range in particle size 100 - < 0.2 micron

- It may be ***surface*** or ***depth*** filter and consist of porous medium integral with plastic or metal structural hardware.
- synthetic and natural fibers, cellulose ester and fiber glass, fluorinated HC polymers, nylon, and ceramic are employed for manufacture of disposable cartilages.
- Porous materials for cleanable and reusable cartilages use stainless steel, monel, ceramic , fluorinated HC polymers and exotic metals

# Filter Aid

- Usually, the resistance to flow due to the filter medium itself is very low, but will increase as a layer of **solids** builds up , blocking the pores of the medium and forming a solid cake.

- The **object** of the filter aid is to prevent the medium from becoming blocked and to form an open, porous cake, so reducing the resistance to flow of the filtrate.

- The important characteristics for filter aids are:
  It should have a structure that permits formation of previous cake
  It should have a particle size distribution suitable for retention of solids
  It should remain suspended in liquid
  it should be free from impurities and should be inert to liquid being filtered

- The particles of filter aids must be inert, insoluble, incompressible, and irregular shaped.
- Types of filter aids are: a) fine filter aids " mean size range 4-6 microns"
  b) coarse filter aids " mean size range 20-40 microns"

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 slow 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.

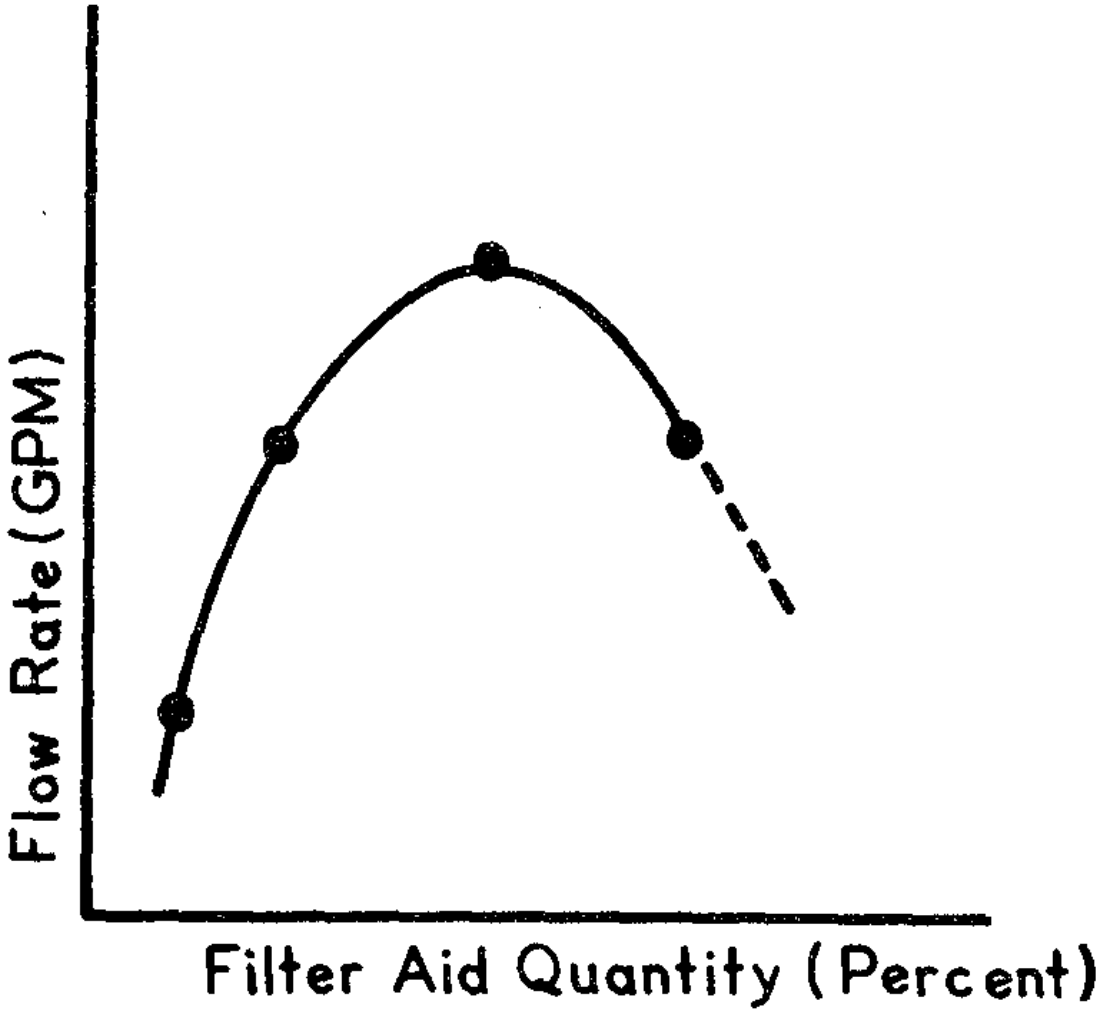



**FIG. 7-1.** *Experimental determination of flow rate as a function of filter aid quantity discloses correct operating level.*

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.

The following filter aids may be used:

- Diatomite ( diatomaceous earth ) , obtained from natural siliceous deposites.

Perlite , it is an aluminium silicate.

Cellulose

Asbestos

Non- activated charcoal

*Diatomite* (diatomaceous earth) is the most important filter aid. Processed from fossilized diatoms, it has an irregularly shaped porous particle that forms a rigid incompressible cake. Since diatomite is primarily silica, it is relatively inert and insoluble. *Perlite*, an aluminum silicate, forms filter cakes that are 20 to 30% less dense than diatomic cakes. Perlite is not a porous incompressible particle, but it has an economic advantage over diatomite.

*Cellulose, asbestos,* and *carbon* 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. It is available in high-purity material and has excellent chemical resistance.

**TABLE 7-2.** *The 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 of diatomites. | More soluble than diatomites in acids and 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 |

Filter aids are chosen by trial and error in either laboratory or plant.

Filtration efficiency also may be affected by changes in temperature, since there is an inverse relationship of flow rate to viscosity

# Filter Selection

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-micron 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.

# Nonsterile Operations

The question of time for a filtration cycle is resolved by determining total volume versus time during a test run at pressures approximating normal operating conditions. Flow rate decreases with time as the media plugs or as the cake builds up. Plotting log total volume per unit area versus log time usually gives a straight line suitable for limited extrapolation (Fig. 7-7). If the filter area of production equipment is fixed, the time to filter a given batch size may be estimated. Alternately, the filter area required to complete the process within an allotted time period may be established.

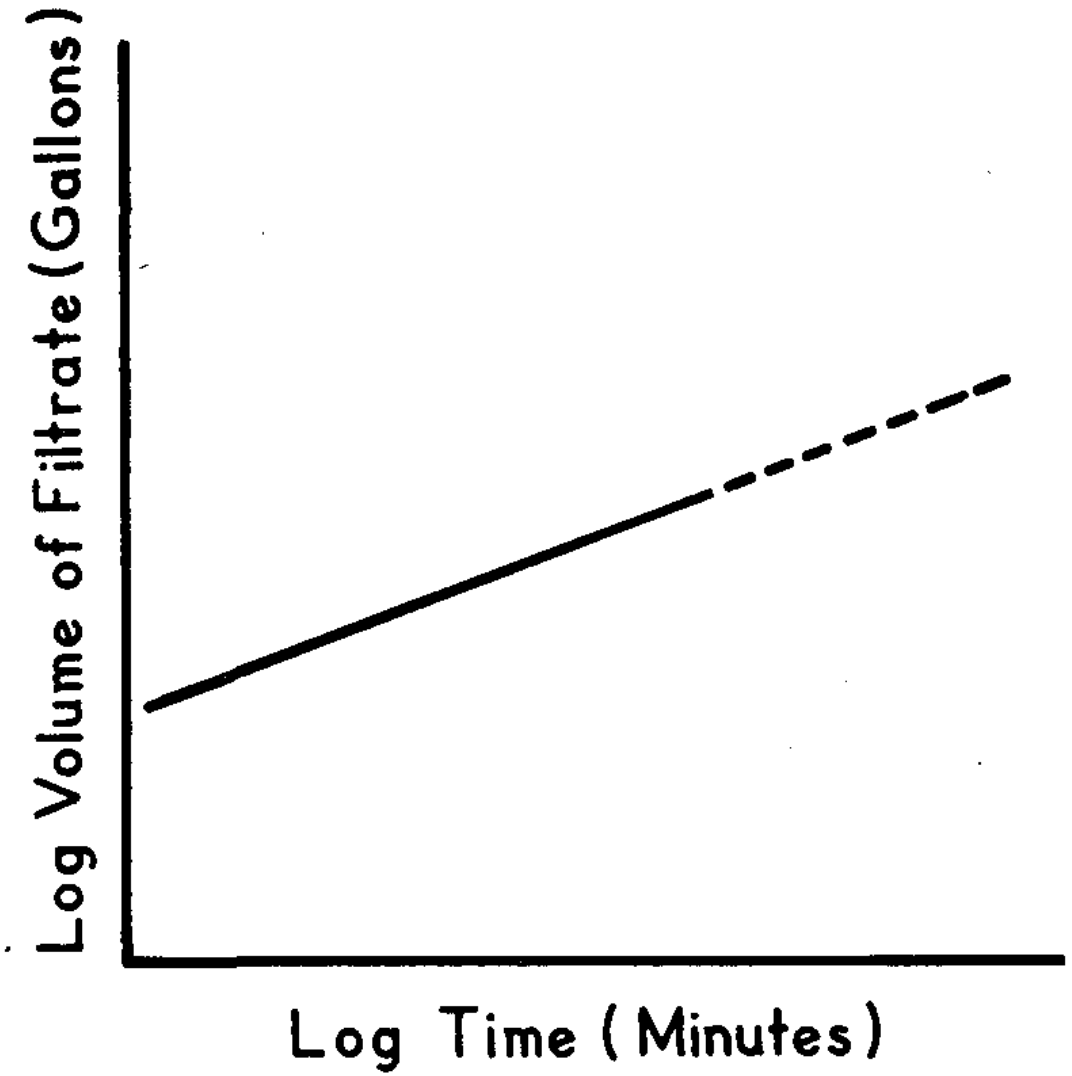



**FIG. 7-7.** *Extrapolation of filtrate volume produced in a given time can be made from log-log plots of experimental data.*

In semicontinuous operations, decisions must be made on length of the cycle prior to shutdown for replacement of media. If the goal is maximum output from the filter per unit of overall time, the graphic approach of Figure 7-8 is applicable. During productive time T, the filter discharges a clear filtrate at a steadily decreasing rate. Nonproductive time T′ is required to clean the filter and replace media. For graphic analysis, nonproductive time T′ is plotted to the left of the origin of a volume V versus time curve. When a line is drawn from T′ tangent to the curve, the value of V and T at the point of tangency indicates where the filtration should be

stopped. The time lost in cleaning is offset by a return to high filtration rates associated with the new media. This point also can be calculated from theoretic relationships for constant pressure or constant volume filtration.

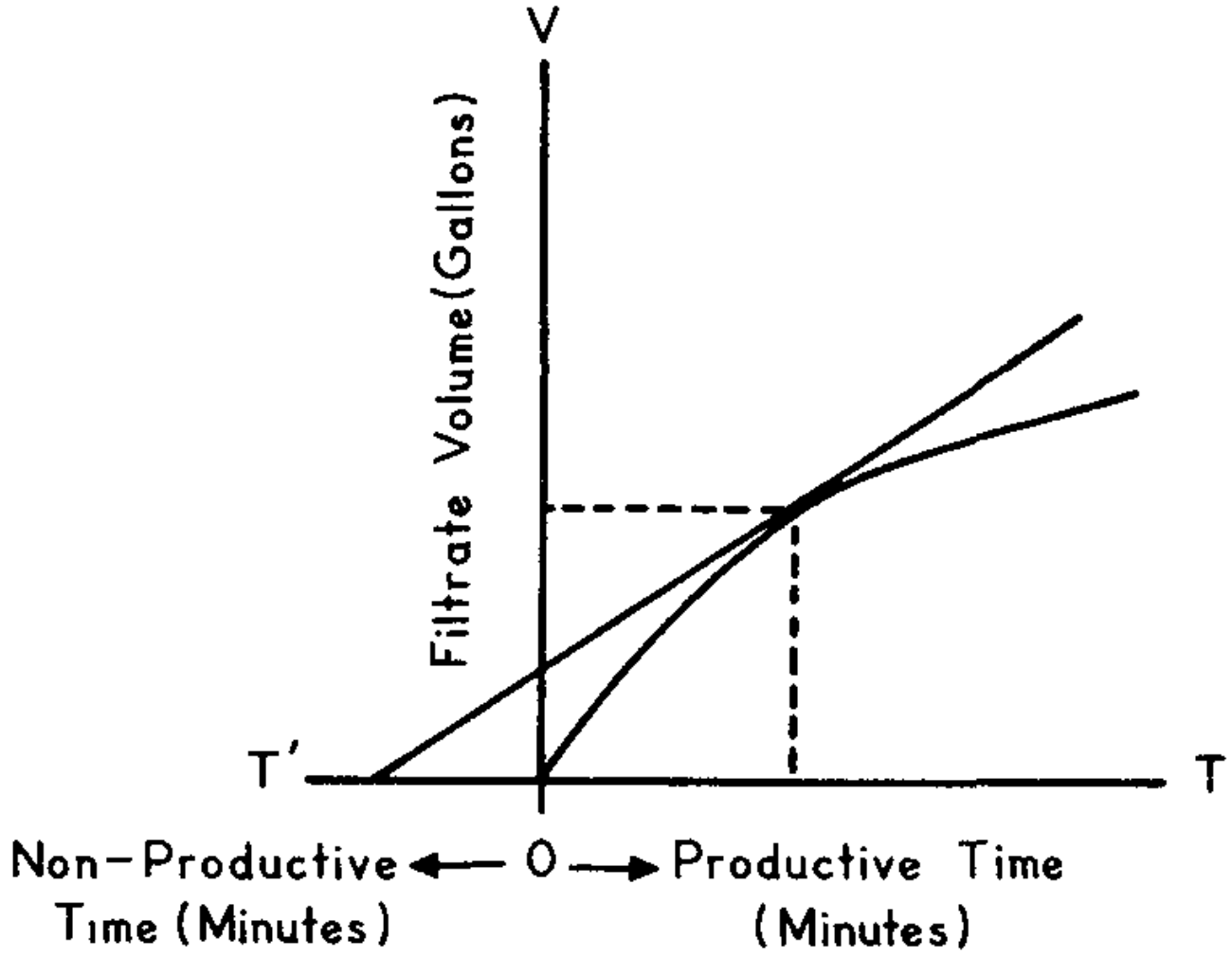



**FIG. 7-8.** *The optimal filtration cycle prior to cleaning can be determined by a graphic technique.*

# Sterile Operations

Filtration may be used to clarify and sterilize pharmaceutical solutions that are heat-labile. Until the introduction of membrane media, unglazed porcelain candles and the asbestos pad were the accepted standards.

Membranes with porosity ratings of 0.2 or 0.45 microns 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-micron filters only in cases of colloidal solutions in which 0.2-micron filters have been shown to clog very rapidly.

Most pharmaceutical liquids are compatible with one or more of the membrane filters now available. 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. Oil and viscous aqueous menstruums are therefore heat-sterilized whenever possible. These solutions are usually clarified through coarser, nonsterilizing membranes, preferably prior to heat sterilization. Paraffin oils, however, may be successfully filtered through 0.2-micron membranes after heating to reduce viscosity.[15]

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 sterilizing filtration. The objective is removal of gross contamination that would rapidly plug the finer membranes. Difficult materials, such as blood fractions, demand serial filtration through successively finer membranes. The cost of multiple filtration may seem excessive, but it is often the only way to achieve sterility.

# Filter evaluations & testing

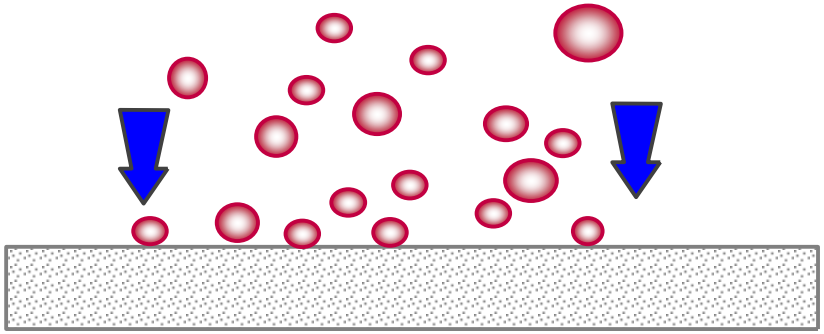
Integrity testing: Integrity testing sterilizing filters is fundamental requirement of critical process filtration applications in the pharmaceutical industry.

Two classifications of integrity testing are destructive and nondestructive. There are three types of non-destructive testing which are available to show that the system has no leaks and is correctly assembled. These are referred to as the **bubble point test**, **the diffusion test**, and **the forward flow test** .

# What is Membrane Integrity?

## Integral Membrane

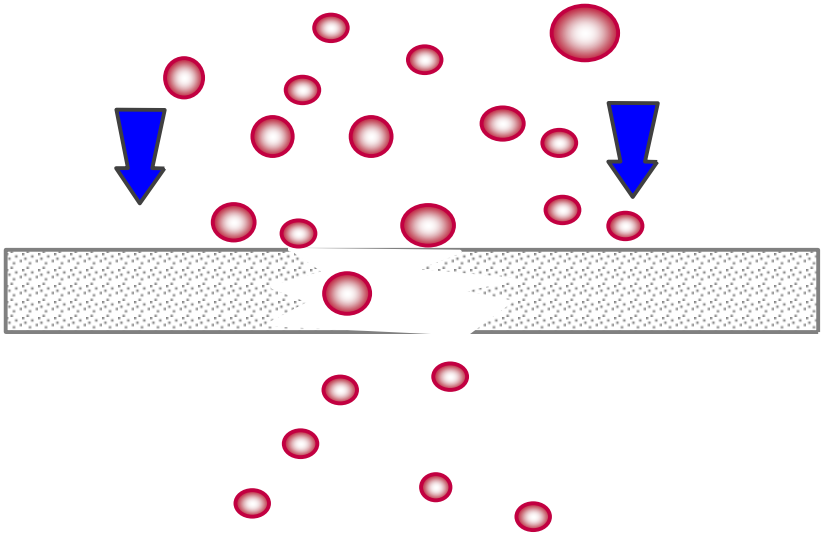
Contaminants larger than pores upstream



No downstream contamination

## Non-Integral Membrane

Contaminants larger than expected pores upstream



Downstream contamination

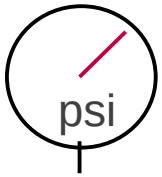
Bubble point test: The bubble point is a direct measure of the largest pore in the filter. The membrane or cartridge is first wetted and has aliquid above(liquid is held inside the channel by surface tension) and agas below.Since the pors are full of liquids,there will be no passage of gas at zero pressure.(The minimum pressure required to force the liquid outside the capillary shoud 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**,asmall bubble forms at the largest opening** .As the pressure is further increased ,rapid bubbling begins to occure.**Bubble point pressure** for agiven membrane is different for different liquids.

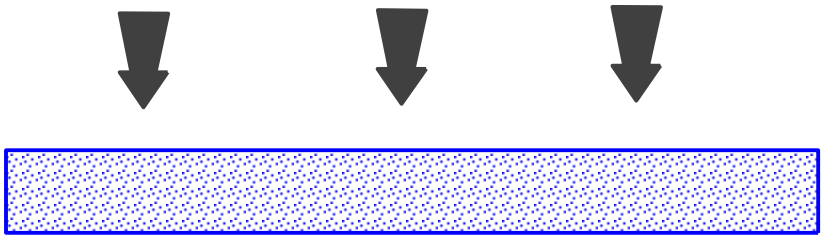
- **Diffusion test:** This test is usually recommended for high volume system ,e.g.,multicartridge or other systems with high filtration areas. When pressure is applied to a wetted membrane filter, air dissolves in the liquid, diffuses through the film, and is released on the low pressure side .The diffusion 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.
- The pressure is increased until reach bubble point pressure at an increment of 2 psi. 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.

# What is Pressure Hold/Bubble Point?

## Water Wet
## Integral Membrane

Air pressure upstream greater than specification

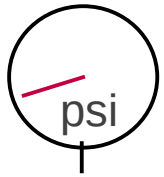


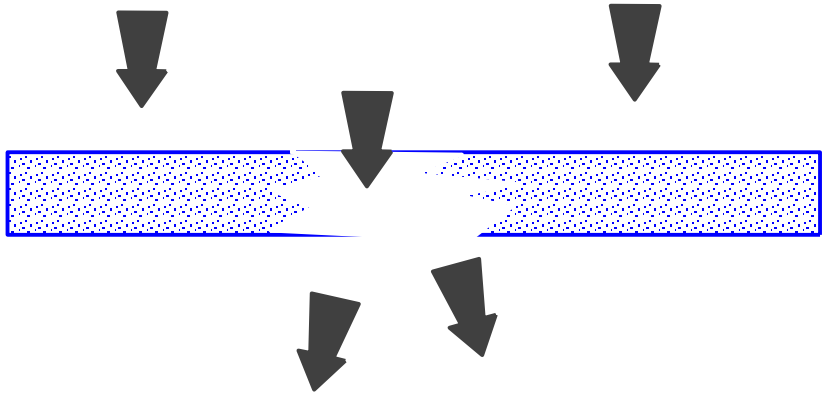



Water in pores is a barrier to gas flow: No gas flow observed downstream until upstream pressure exceeds critical value

## Water Wet
## Non-Integral Membrane

Air pressure upstream less than specification



Gas will flow through large opening and is easily observed downstream

**Forward flow test :**

Is based upon measurement of the diffusion rate of air flow through water in a wetted filter at a pressure below the bubble point pressure.

The forward flow test is done before , during and after filtration.

The integrity test detect a damage membrane ,system leak, ineffective sealing.

The test performed after filtration conforms that the system is remaining leak-free through out the run.

# Filtration Equipments

Commercial equipments are classified according to:

- Driving force:

  gravity, pressure , vacuum and centrifugal

- Method of operating :

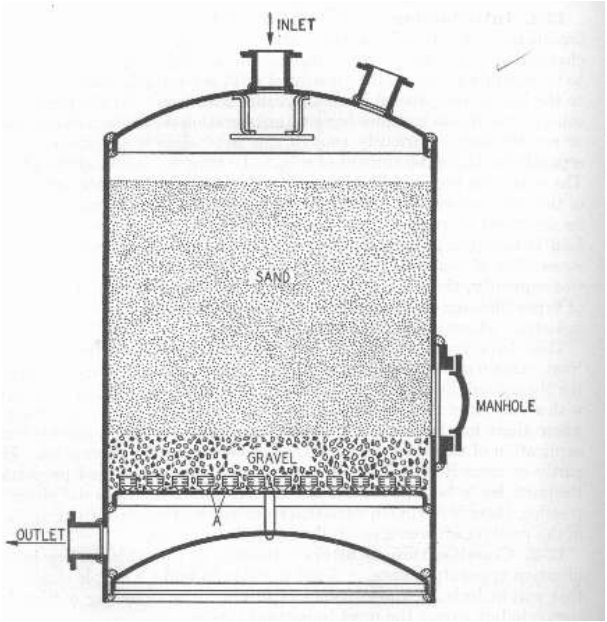
  batch and continuous

- End product desired:

  filtrate and cake solid

# Filtration Equipment and systems

## -gravity filters:




- Employing thick granular beds

  are widely used in water

  filtration prior to distilation or deionization

  e.g: Sand Filter or cake bed

- gravity bag filters is applied to concentration

  of magmas, such as milk of magnesia

## - vacuum filters:

- Are employed on a large scale ,but rarely used for collection of crystalline precipitates or for sterile filtration.
- Continuous drum filter system , it is a cheap method and we can collect large quantity in a short time.

# Rotary Vacuum Filter:

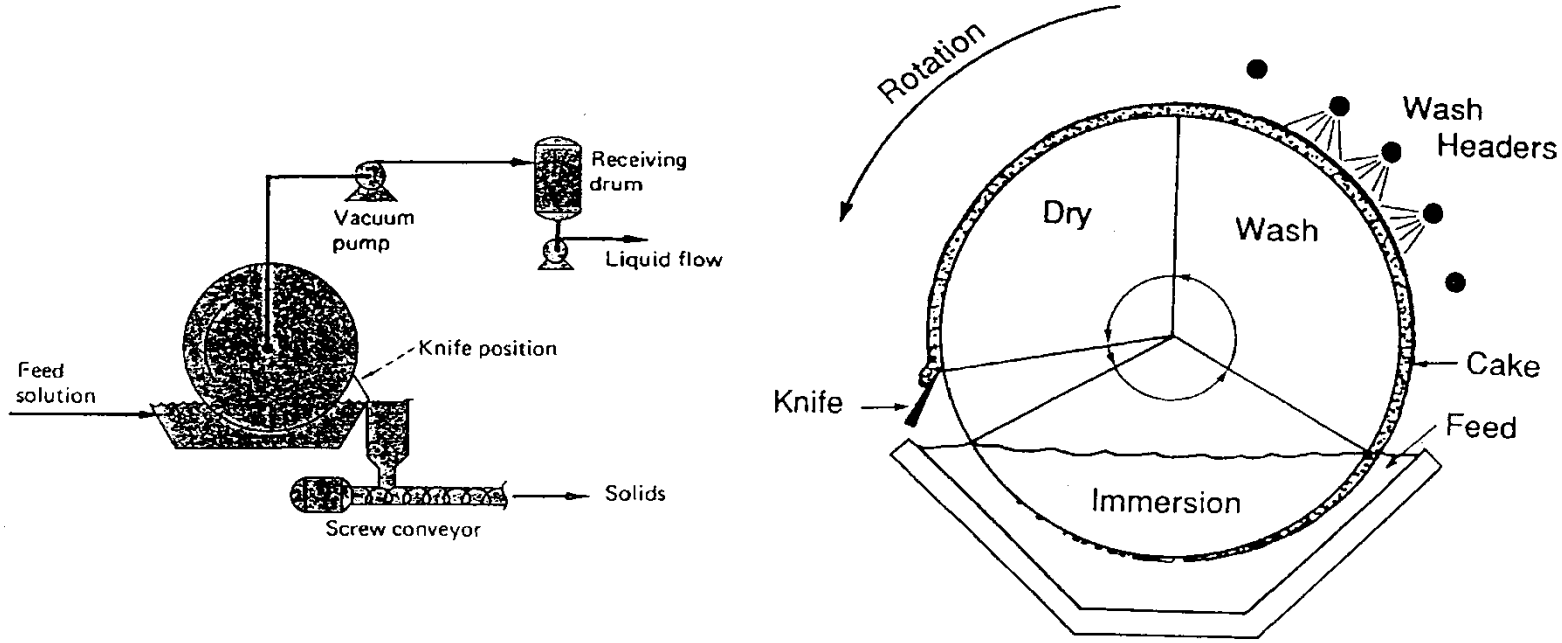



**Figure 2.1-2.** Rotary vacuum filter. This continuous cylindrical filter, shown from the end, is the workhorse for bioseparations. The filtrate is removed from the end of the cylindrical drum. The times shown are typical values.

*** Rotate at a low speed during the operation.**

*** Pressure inside the drum is a partial vacuum.**

**Liquid is sucked through the filter cloth and solids are retained on the surface of the drum.** ☞

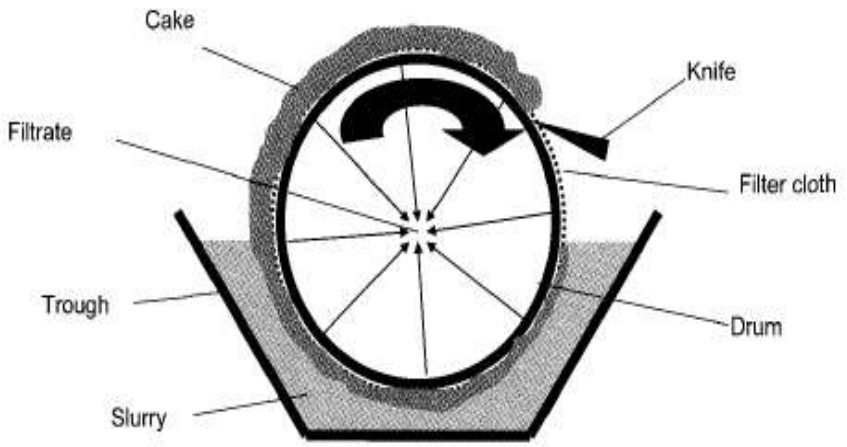
# Rotary vacuum filter (Rotary filter)

- 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 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

**Uses:**

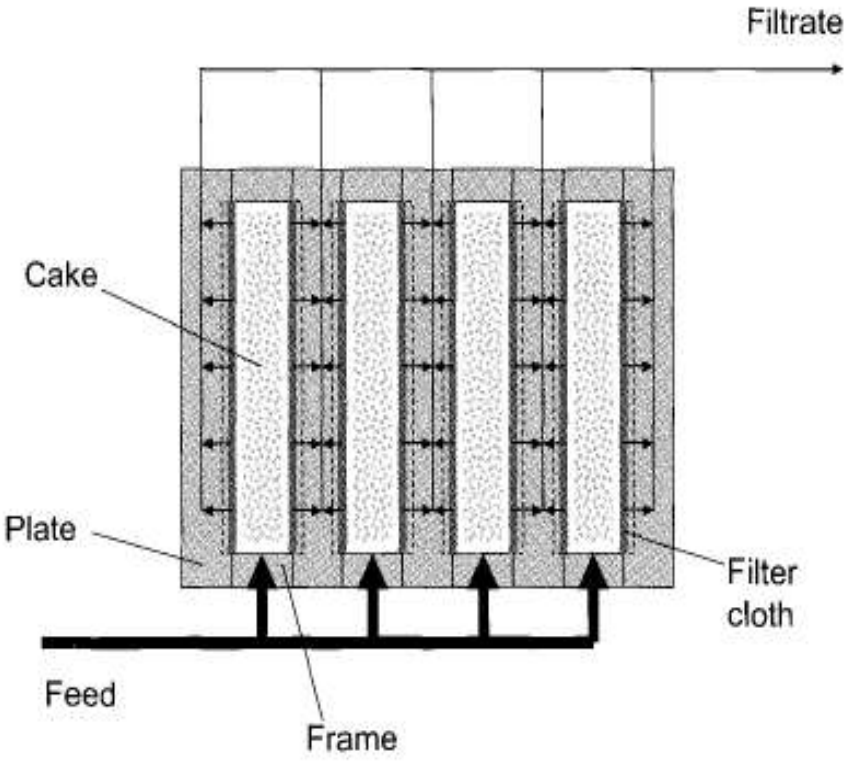
1- The rotary filter for continuous operation on large quantities of slurry.

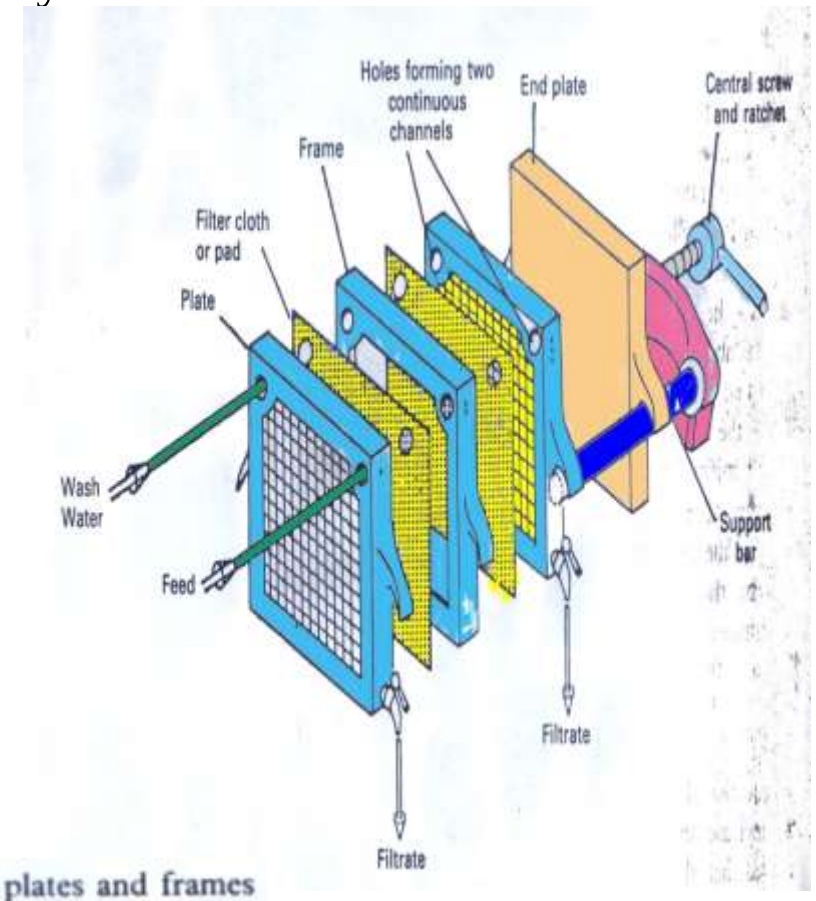
2- Suitable for slurry contains considerable amounts of solids in the range 15-30%.




Cycle of rotary-drum filter.

- **- Pressure Filters:**
- Example is plate and frame filter press.
- The most common type, but less common for bioseparations.
- * Used where a relatively dry cake discharge is desired.
- * Cake removal: open the whole assembly




Filter press. Assembly of plates and frames

# Plate and Frame Filter Press

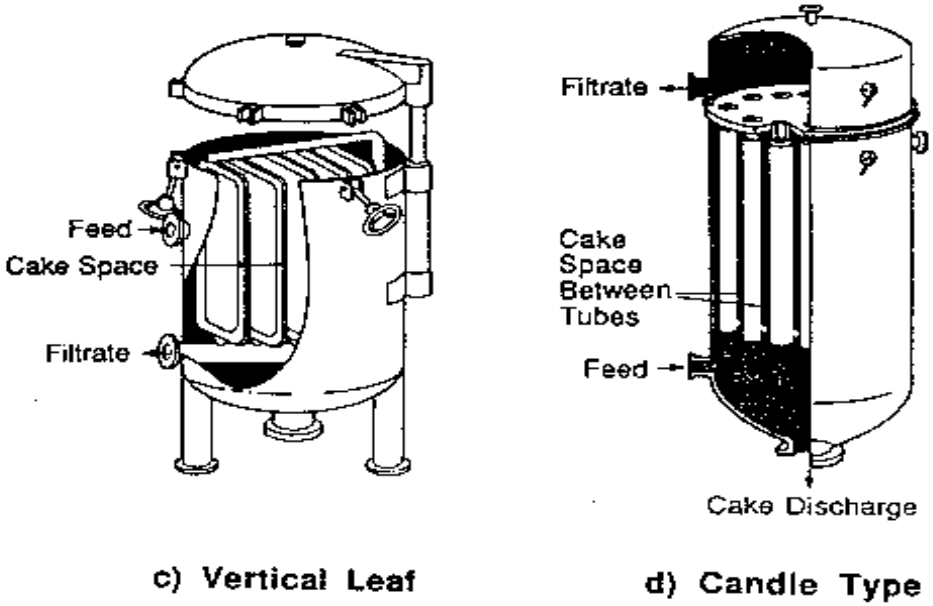
- This press is made up of **two units,** known respectively as **plates and frames**, with a filter medium, usually filter cloth, between the two.
- The frame is **open,** with an inlet for the slurry, while the plate has grooved surface to support the filter cloth, and with an outlet for the filtrate.

**The operation**

- The slurry enters the frame from the feed channel,
- The filtrate passes through the filter medium on to the surface of the plate while the solids form a filter cake in the frame.
- The filtrate then drained down the surface of the plate , between the projections on the surface and escapes from the outlet.
- Filtration is continued until the frame is filled with filter cake, when the process is stopped , the frame emptied, and the cycle re-started.

- **Disc filter :**
- is applied to assemblies of felt or paper filter discs sealed into pressure case.
- The discs may be preassembly into self- supporting unit or each disc may rest on an individual screen or plate.
- Compactness, portability and cleanliness are obvious advantages of it.


## Vertical Leaf Filter and Candle Type Vertical Tank Filter :




c) Vertical Leaf  d) Candle Type

* Have a relatively high filtration area per volume.
  - ☞ Require only a small floor area.
* Filter cake is formed on the external surface of the tubes.
* The tubes are cleaned by backwashing.

## Cartilage filter:

- Used for filtration and sterilization for large scale, they are either disposal or permanent cartilage, also there is metalic edge filters with self- cleaning device.

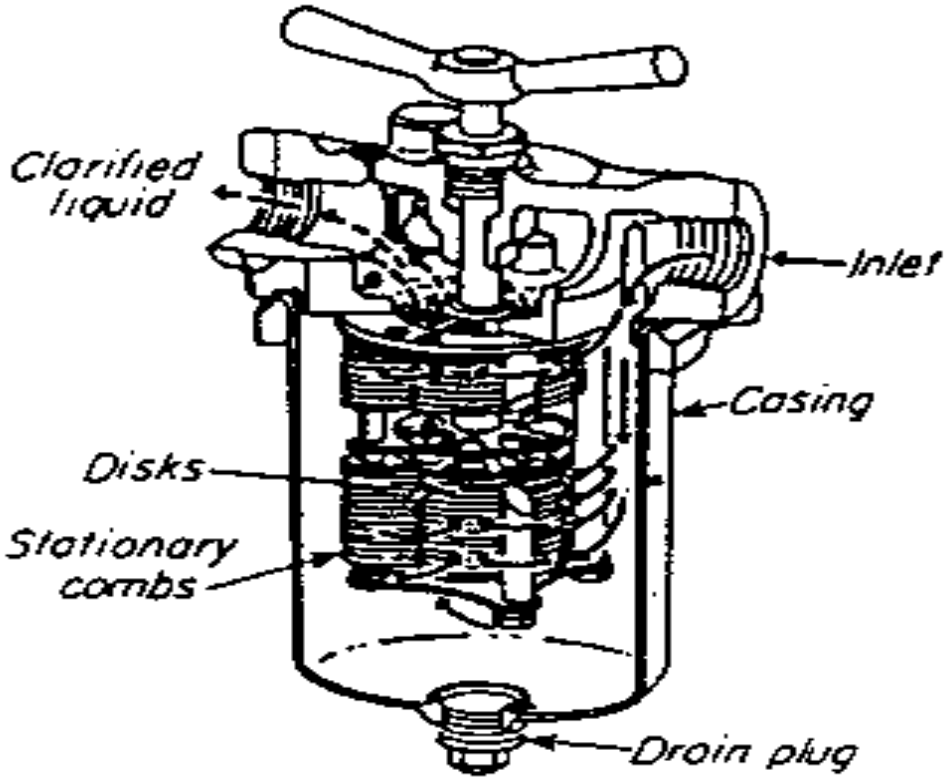



Figure 30–7 Cartridge filter.

## - Centrifugal Filters:

A centrifuge consists of a basket in which mixture of solid and liquid , or mixture of two liquids is rotated at high speed so that it is separated into its constituents by the action of centrifugal force.

- **Types of baskets**:

  **A**- ***Imperforated,*** in which the liquid is removed through a skimming tube , while the solid particles, sediment to the wall.

- In pharmacy, the centrifuge is commonly used for drying crystals and for separating emulsions into their constituent liquids.

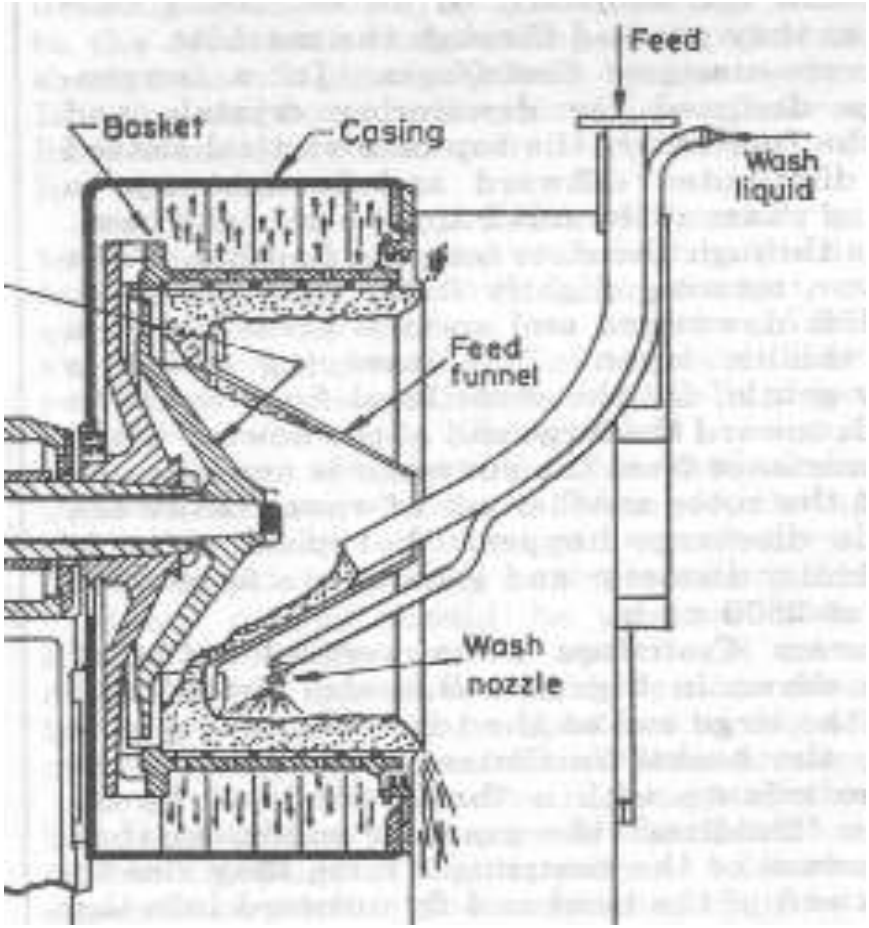
  ***B- Perforated basket***, in which the liquid passes out through the holes.

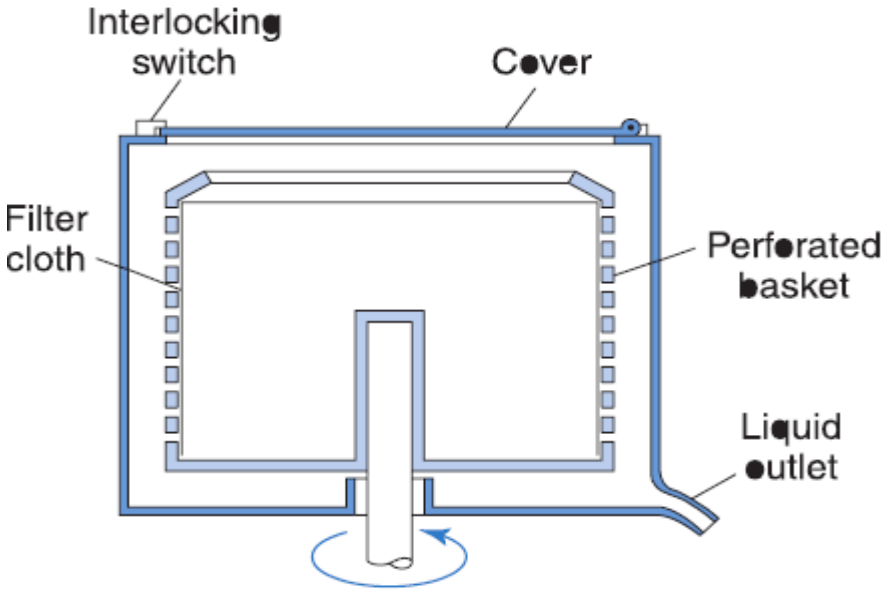
***-The perforated basket centrifuge:***

- A vessel about 1m. in diameter and its outer wall is perforated. It is mounted on a vertical shaft by means it can be rotated at a high speed. An outer casing with an outlet collects the liquid thrown out from the basket.

***-The pusher-type centrifuge:***

- This type of centrifuge is used for the separation of suspensions, continuously operated apparatus, and is fitted with a perforated basket.




**Perforated basket centrifuge**

*The pusher-type centrifuge*

# Laboratory Filtration Equipment

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. Among the special types of laboratory filter paper for pharmaceutical industry are:

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

# Cake Filtration

Cake filtration in which solids recovery is the goal is an important pharmaceutical process.

The plate and frame press and precoat pressure filters used for clarification also are applied to solids recovery.

For large-scale operations, continuous vacuum filters are most widely used. *rotary-drum vacuum filter*

*Filtering centrifuges* are another general class of solids recovery devices.

# Membrane Ultrafiltration

ultrafiltration is a process of selective molecular separation.

The selectivity and retentivity of a membrane are characterized by its molecular weight cutoff.

Applications in the pharmaceutical industry are predominantly in the concentration of heat-labile 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.

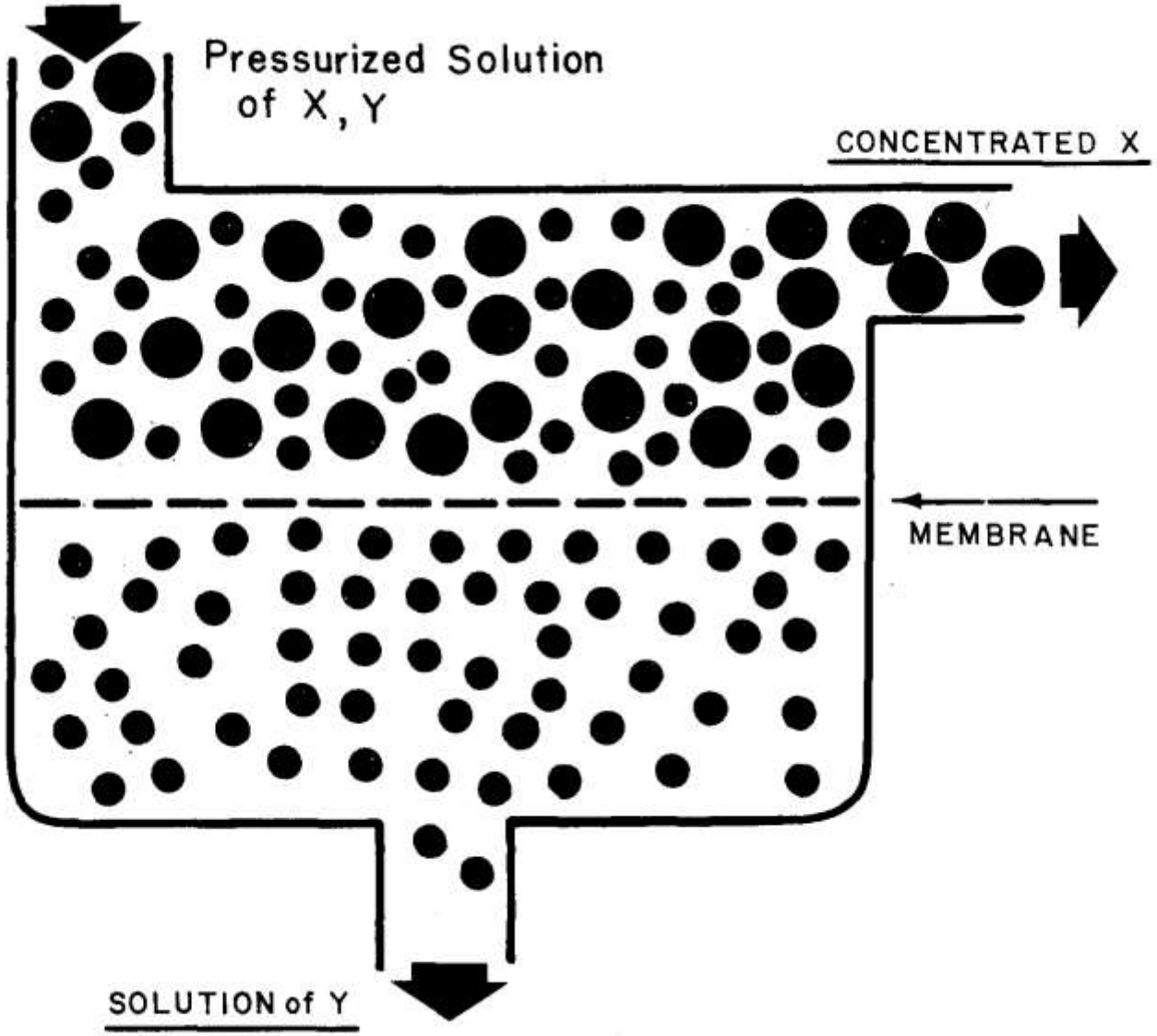



**FIG. 7-20.** *Schematic diagram of membrane ultrafiltration process.*

# Bubble point test

Membrane filters which have discrete uniform passage that penetrate from one side to the other side can be regarded as fine uniform capillary . The bubble point test base on when these capillary are full with liquid , the liquid is held by surface tension .

The minimum pressure required to force the liquid out of the capillary must be sufficient to overcome the surface tension. The capillary pressure is higher in the case of small pore than in that of large pore

The bubble point pressure is governed by the following equation

$P=K4\gamma Cos\Theta/D$

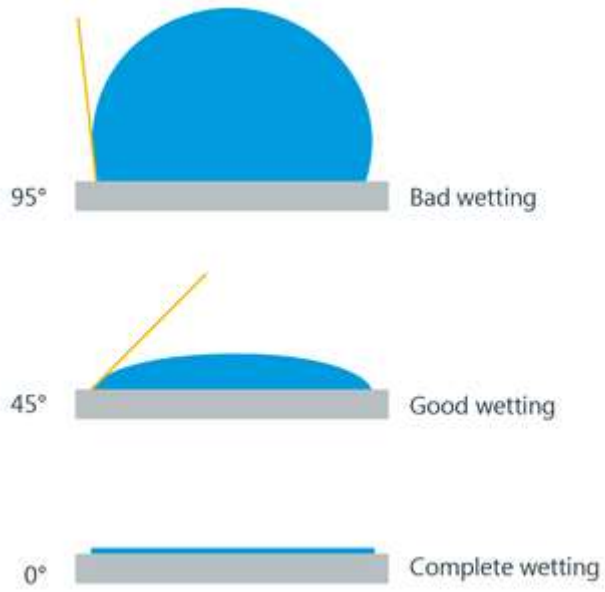
Where P=bubble point pressure

K=experimental constant

D=pore size

$\gamma$=surface tension of liquid

$\Theta$=liquid to membrane contact angle(angle of wetting)


95°
Bad wetting
45°
Good wetting
0°
Complete wetting

**Selection of filtration equipment**

The plate and frame press and precoat press used for both clarification and solid recovery, in general pressure filter is restricted to batch filtration and recovery of moderate weight of expensive material.

For large scale operation ,continuous vacuum filter are most widely used. The slurry is fed into a tank in which solid are held in a suspension by an agitator. As the drum is rotate the drum section passes through the slurry , and the vacuum draw the filtrate through the filter media at the drum surface.

The suspended solid deposit on the filter drum as cake . The cake is dried and washed as it moves towards the discharge point.

Filtering centrifuges are another general class of solid recovery. this type is advantageous for recovery of fine particles. this device is fitted with perforated basket , which support the filter media. The basket revolve inside the casing. Slurry is sprayed in the a basket in which centrifugal action force the filtrate through the media on which the cake deposit. Continuous discharge of solid is possible , but batch unit that require shutdown for removal of solid are also common.

# Membrane ultafiltration

It is define as process of removing dissolved molecules on the basis of membrane size and configuration by passing a solution under pressure through a very fine filter. Ultafiltration retain most macromolecules while allowing smaller molecules and solvent to pass through the membrane. The difference between

microfiltration

Remove particulate and bacteria

Ultra filtration

Separate the molecules

Separation of solvent and solute of different molecular size may be achieved by selecting a membrane that allow the solvent but not the solute to pass through.


Thank
You
Brooke Kroeger