

- It also mixes with the food preparation for prevention their oxidation.

- **Chapter -4**

- **Size Reduction:-**

- It is the process of reducing drugs size in smaller particles, or fine powder. The term size reduction is applied to ways in which particles of solids are cut or broken into smaller pieces. Size reduction is necessary if the starting material is too coarse, and final product needs to be a fine powder.

- **Importance of size reduction.**

- To improve the stability of certain pharmaceutical dosage forms such as suspension the rate of sedimentation decrease to a large extent by reducing the particle size of the drug.
- To help in the process of separation of the solid from liquids by filtration by the rate of filtration depend upon the particle size.
- To increase the rate of absorption of a drugs the smaller particle size the greater is the rate of absorption.
- To increase the rate of solution is case of chemical substance become reduction of the particle size increases the surface area for the action of solvent.
- Due to size reduction, we are design the different type of drug dosages form (tablets, capsules, suspension and emulsion etc).

- **Factor affecting size reduction**

- **Hardness:-** The hardness of the material affect the process of production it is easier brakes soft material to a small size then hard

material. Due to the hardness of any material it affects the drug solubility and modification of any drug dosages form.

- **Toughness:-** The crude drugs of fibrous nature, it is not easily break down in smaller particle and shows the tough nature. In the toughness, materials
 - fibrous are attached to each other in the layering form and affect the solubility of materials.
- **Material structure:-** Material structure is one of the major problem during the size reduction because special size and shape materials are easily break down by special machine or by special method.
- **Moisture content:** - The presence of moisture in the material influences a number of its properties such as hardness stickiness which in its turn effect the particle size reduction.
 - The material having 5% moisture in case of drying grinding and 50% moisture in wet grinding does not create the problem.
- **Stickiness:-** Stickiness cause a lot of difficulty in size reduction this is due to the fact the material adhere to the grinding surface or sieve surface of the mill. Due to stickiness of material it affects the material weighing accuracy.
- **Softening temperature:-** Waxy substance (Stearic Acid, or drugs containing oil or fat) because softened during the size reduction process if a heat generated then the material not easily breakdown and sticks on the mill. If more the temperature generate in the machine, it affects the material stability and change their activity.
- **Purity required:-** Various mill are used for size reduction often cause the grinding surface to wear off and thus impurities come in the power

if a high degree purity is required such mill must be avoided.

- **Physiological effect:-** Some drugs are very potent during their particle size reduction in a mill dust is produced which may have an effect on their operator in such cases the enclosed mill may be used avoid dust.
- **Bulk density:-** The output of the size reduction of material in a machine depends upon the bulk density of the substance.
- **Ratio of feed size to product size:-** To get a fine powder in a mill. It is required to fairly small feed size should be used hence it is necessary to carry out the size reduction process in several stage using different equipment.
- **Example:-** Preliminary crushing following by coarse powder and then fine grinding.
- **Methods of Size Reduction.**
 - Cutting
 - Compression
 - Impact
 - Attrition
 - Combined impact and attrition
- **Cutting:-** The material is cut on a small scale by means of a sharp blade knife, root cutter or other any sharp instruments on a large scale a cutter mill is used cutting of the drug is usually done to hasten the drying of drugs.
- **Compression:-** In this method the material is crushed by the application of pressure on a small scale using mortar and pestle where as on a large

scale roller mill is used.

- **Example: Roller mill,**

- **Impact:-**

- Impact occurs when the material more or Less stationery and is hit by an object moving at high speed or when the moving particles strikes a stationary surface either case the material break into small pieces there is no apparatus which can be used on a small scale to effect size reduction by impact but on a large scale hammer mill and disintegrator are used.
- Example: Hammer Mill, Ball Mill

- **Hammer Mill**

- **Principal:-** It work on the principle of impact.

- **Construction:-**

- It consists of metal causing inclosing a control shaft to which four or more swinging hammer are attached the lower part of the mill, consists of a screen through which material can pass in a suitable receiver when the discrete of size reduction is reached.

- **Working:-**

- The material is put into the hopper.
- Which is connected with the drum the material is powered to the desire size due to fast rotation of hammer and is called under the screen this mill has the advantage of continuous operation because the chance of jamming is less as the hammer are not fixed the material can product

coursed to moderately fine powder.

- Due to the high speed of operation heat is generated which may affect themselves drugs are material more ever high speed of operation.

- **Advantage:-**

- It is used for production of intermediate grade of powder.
- It can be operated continuously.
- It is effecting in function and can grind different type of material.

- **Disadvantage:-**

- Due to high speed heat is generated.
- It is not suitable for heat sensitive material.
- **Attrition:-** the action or process of gradually reducing the strength or effectiveness of someone or something through sustained attack or pressure. The attrition mill is a device for mechanically reducing solid particle size by intense agitation of slurry of material being milled and coarse milling media.
- **Combined impact and attrition**—it is based on the impact and attrition principle. Example— Ball mill,
- It work on the principle impact and attrition.

- **Construction:-**

- It consists of a hollow cylinder which is mounted on a metallic frame.
- In such a way that it can be rotated on its clockwise (Longitudinal axis) the cylinder contains balls that occupy 30 to 50% of the mill.
- Volume the weight of the ball consists the ball size depends on the size of the feed and the diameter of the mill the cylinder and balls are made up of metal and are usually lined with chrome in pharmaceutical industry some time the cylinder of the ball mill is lined with rubber or porcelain.

- **Working:-**

- The drug to be put into the cylinder of the mill and is rotated the speed of rotation is very important at a low speed the mass of ball will slide or roll over each other and only a negligible amount of size reduction at a high speed the ball mill will be thrown out to the walls by centrifugal force and grinding but at about two-thirds of the speed the centrifugal force just occurs with the results that the balls are carried or most to be to the top of the mill and then fall by this way the mix size reduction is effected by attrition after a suitable time the material is taken out and passes through a sieve to get powder of the required size.

- **Advantages:-**

- It can produce very fine powder.
- It can be used for continuous operation.
- If sieves are classified classifier to attach to the balls.
- Suitable for both weight and drug grinding process.

- **Disadvantage:-**

- The ball mill is a very noise.
- Wear occurs from the ball as well as from the cassing which may result contamination.

Size Separation

- Definition: - Size Separation is a unit process that involved the separation of a mixture of various size particles into two or more portion by means of screening surface or by shifting. it is also known as sieving, sifting, and screening.
- Size separation technique is based on different physical properties of the separating mixture or substance like size, shape and density.
- Initially crude drugs (Nuxvomica, Rauwolfia, Ephedra, Ashoka etc.) are present in large size but involvement of size reduction and size separation we are obtain the desired size granules and particles and improve the pharmaceutical and pharmacological activity.
- **Applications/objectives of size separation:-**
- Size separation technique determines the particle size for the production of tablets capsules, suspension and emulsion etc.
- Due to separation, we obtain the desired granules or particles and ensure their flowability and uniformity.
- Undesirable substances are removed by the size separation technique.
- By obtaining the desired size particles we improve the mixing properties of the powders.

- To improve the solubility and stability of particles during production.
- Size separation technique optimize feed rate, agitation, screening during production.
- Quality control of raw materials.
- **Official standards for powders accoding to Indian pharmacopoeia.**
- The Indian Pharmacopoeia has defined the standard of powder for Pharmaceutical purpose. The Indian Pharmacopoeia specified five grade of powder.
- **Coarse powder:** - A powder of which all the particles pass through a No.10 sieve with nominal mesh aperture of 1.7mm and not more than 40.0 percent through a No.44 sieve with nominal mesh aperture of 355 μ m, this is usually referred to as a 10/44 powder or coarse powder.
- **Moderately coarse powder:** - A powder of which all the particle pass through a No.22 sieve with the nominal mesh aperture of 710 μ m and not more than 40.0 percent through a No.60 sieve with nominal mesh aperture of 250 μ m, this is usually referred as a 22/60 powder or moderately coarse powder.
- **Moderately fine powder:-** A powder of which all the particle pass through a No.44 sieve with the nominal mesh aperture of 355 μ m and not more than 40.0 percent through a No.85 sieve with nominal mesh aperture of 180 μ m, this is usually referred as a 44/85 powder or moderately coarse powder.
- **Fine powder:** - A powder of which all the particles pass through a No.85

sieve with nominal mesh aperture of $180\mu\text{m}$, it is called as fine powder.

- **Very fine powder:** - A powder of which all the particles pass through a No.120 sieve with nominal mesh aperture of $125\mu\text{m}$, it is called as fine powder.

- **SIEVE/SHIFTING.**

- Sieve for Pharmaceutical testing are constructed from wire cloth with square meshes woven from wire of brass, bronze, stainless steel or any other suitable material. The wire should be of uniform circular cross-section and should not be coated or plated these should not be any reaction between the material of the sieve and the substance which is being shifted from it.
 - Generally iron wire is used as screen material because it is cheap but their disadvantage and corrosive nature and chances of contamination by iron. This disadvantage can be overcome by coating iron with galvanizing agents which increase the strength and also make it corrosive resistant.
 - For separation of fine powder bolting cloth sieve are used. They are woven from twisted multi strand fibers made of silk, nylon and cotton. Nylon cloth is generally designated for their micrometer opening and also their availability in different grades.

- **Sieve Analysis:** - the International Standards Organization (ISO) fix lowest a sieve diameter $45\mu\text{m}$. powder are generally defined as particles having a maximum diameter of $1000\mu\text{m}$, so this is the upper limit. In practice, sieve analysis can be performed in a range of 5 to $125,000\mu\text{m}$.

sieve analysis used to monitor material quality based on particle size.

- **Standard for Sieve**

- Standards for sieves used to testing must specify the following:
- Holes in the screen are called mesh. Mesh number indicate number of holes included in a length of 1 inch. Aperture of screen is the clear space between wires of screen opening and screen number denotes number of meshes in a linear length of 25.4mm.
- Number of sieve: - Sieve number indicates the number of meshes in a length of 2.54 cm in each transverse direction parallel to the wires.
- Nominal size of aperture: - Nominal size of aperture indicates gap between two adjacent wires. It represents the length of the side of the square aperture. The I.P. has given the nominal mesh aperture size for majority of sieves in mm or in cm.
- Nominal diameter of the wire: - Wire mesh sieves are made from the wire having the specified diameter in order to give a suitable aperture size and sufficient strength to avoid distortion of the sieve.
- Approximate percentage sieving area: - This standard expresses the area of the meshes a percentage of the total area of the sieve. It depends on the size of the wire used for any particular sieve number. Generally the sieving area is kept within the range of 35 to 40 percent in order to give suitable strength to the sieve.
- Tolerance average aperture size: - Some variation in the aperture size is unavoidable and when this variation is expressed as a percentage, it is known as the 'aperture tolerance average'.

- **The working of mechanical sieving devices is based on any of the following methods.**
 - Agitation.
 - Brushing.
 - Centrifugal.
- **Agitation methods-** Sieves may be agitated in a number of different ways, such as:
- **Oscillation:** This sieve is mounted in a frame that oscillates back and forth. It is a simple method but the material may roll on the surface of the sieve.
- **Vibration:** The sieve is vibrated at high speed by means of an electric device. The rapid vibration is imparted to the particles on the sieve which helps to pass the powdered material through it.
- **Gyration:** In this method, a system is made so that sieve is on rubber mounting and connected to an eccentric flywheel. This gives a rotary movement of small amplitude to sieve which turn gives spinning motion to the particles that helps to pass them through a sieve.
- Agitation methods are not continuous methods but can be made so by inclination of the sieve and the provision of separate outlets for undersize and oversize particles.
- **Brushing methods-** In this case, a brush is used to move the particles on the surface of the sieve and to keep the meshes clear. The brush is

rotated in the middle in the case of a circular sieve but spiral brush is rotated on the longitudinal axis in case of a horizontal cylindrical sieve.

- **Centrifugal methods-** In this method, a high speed rotor is fixed inside the vertical cylindrical sieve, so that on rotation of rotor the particles are thrown outwards by centrifugal force. The current of air which is produced due to high speed of rotor helps in sieving the powder.

- **SIEVING METHOD**

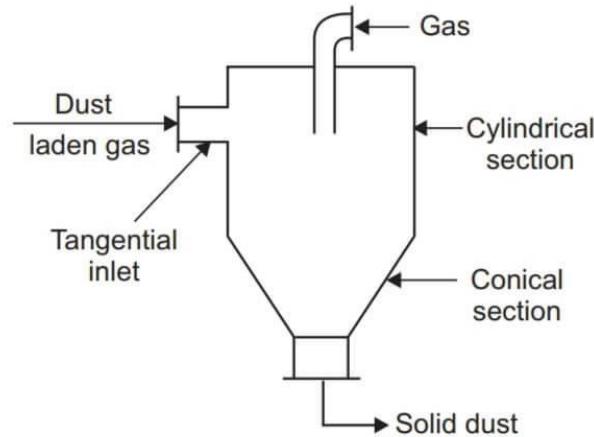
- In this method, the fine powder is separated from the coarse powder by using sieves of desired number. The degree of fineness of a powder is known with the help of sieve through which the powdered material is passed. Sieves are numbered in order to distinguish from each other.
- **Working & construction:** - Size separation of powder is done by passing the powdered material through a set of sieves. Sieves are arranged in descending order
- i.e. sieve of larger size is at the top and the smallest one at the bottom. The bottom sieve is attached to the receiving pan. The material is placed in the uppermost sieve. The sieves are shaken with the help of mechanical sieve shaker or electromagnetic devices. It helps the particles to pass through the sieves.

- **CYCLONE SEPARATOR**

- **Principle:** - In cyclone separator, the centrifugal force is used to separate solids from fluids. The separation depends not only on the

particle size but also on density of particles. Hence depending on the fluid velocity, the cyclone separator can be used to separate all types of particles or to remove only coarse particles and allow fine particles to be carried through with the fluid.

- **Construction:** - It consists of a tapering cylindrical vessel which consisting of a top vertical section and lower conical/tapering section terminating in an apex opening - a short vertical cylinder which is closed by a flat plate on top and by a conical bottom. It is provided with a tangential feed inlet nozzle in the cylindrical section near the top and an outlet for the gas, centrally on the top. The outlet is provided with a downward extending pipe that extends inward into the cylindrical section to prevent the gas short-circuiting directly from the inlet to the outlet and for cutting the vortex.



- **Cyclone separator.**

- **Working:** - The suspension of a solid in gas (usually air) is introduced tangentially at a very high velocity, so that rotary movement takes place within the vessel. The fluid is removed from a central outlet at the top. The rotatory flows within the cyclone separator generate the centrifugal force on the particle. The solids are thrown out to the walls; thereafter it falls to the conical base and discharged out through solids outlet.
- **Uses:** - Cyclone separators are used to separate the suspension of a solid in a gas (air). It can be used with liquid suspensions of solids

Mixing

- **Mixing** is defined as a process that tends to result in a randomization of dissimilar particles within a system. Mixing refers to the random distribution into and through one another of two or more separate phases. Some of the mixing operations in the dispensing practice are spatulation, trituration, tumbling, geometric dilution etc.
- **Agitation**—Agitation refers to the induced motion of a material in a specified way, usually in a circulatory pattern inside a container.
- The term mix means to put together in one mass or assemblage with more or less through diffusion of the constituent elements among one another.
- The term blending means to mix smoothly and inseparably together.

During blending minimum energy is imported to the bed

- **Factor influencing mixing process—**

- Nature of surface.
- Density of the particles.
- Particle size and shape.
- Particle charge.
- Proportion of materials.

- **Mechanism of mixing in Solids—**

- **Convective mixing**—It is achieved by the inversion of the powder bed using blades or paddles or screw element. A large mass of material moves from one part to another. Convective mixing is referred to as macro mixing.
- **Shear mixing**—In this type, the forces of attraction are broken down so that each particle moves on its own between regions of different composition and parallel to their surface.
- **Diffusive mixing**—It involves the random motion of particles within the powder bed, there by particles change their position relative to one another. Diffusive mixing is referred to as micro mixing.

- **In Solid-solid mixing operation four steps are involve—**

- Expansion of the bed of solids.
- Application of three dimensional shear forces to the powders.

- Mix long enough to permit true randomization of particles.
- Maintain randomization (no segregation after mixing).
- **Equipment used for solid Mixing**— V cone blender, Double cone blender, Ribbon blender, sigma blade mixer etc.
- **Mixing Of liquids.**
- **Liquid-liquid mixing** is considered as a simple operation compared to that of solid-liquid mixing. It involves the formulation of a homogeneous system.
- According to theories of solutions, liquid mixtures are classified as follows—
- **Miscible liquids**—Miscible in all proportion. Example- Ethyl alcohol and water.
- **Partially miscible liquids**—Miscible in one another at one particular proportion. Example- P-cresol and water.
- **Immiscible liquids**—these are not miscible. Example- vegetable oils and water.
- **Equipment used for liquid mixing**— Propellers, turbines, Airjet mixer.
- **Mixing of Immiscible liquids.**
- Mixing of immiscible liquids is carried in pharmacy mainly in the manufacturing of emulsions. The equipment used for preparation of an emulsion is known as emulsifier. Generally a fine emulsion can be obtained and therefore, equipment is also known as homogenizer.

- Sometimes, the above equipment directly gives fine emulsion. Otherwise, coarse emulsion is subjected to homogenization in the second stage to get fine emulsion by using one of the following- Silverson emulsifier, colloid mill, rapisonic homogenizer.

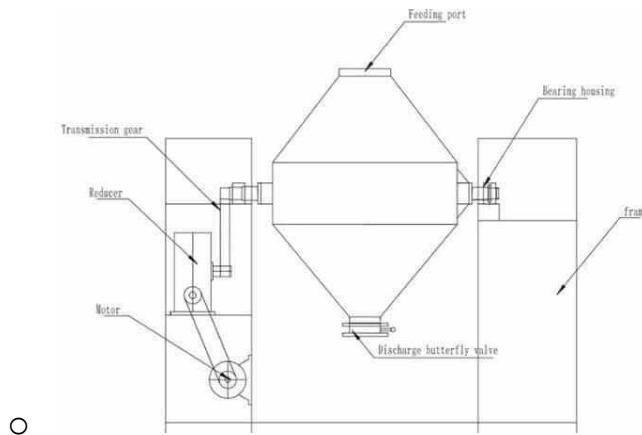
- **Mixing of semisolids.**

- Semisolid dosages forms include ointments, pastes, creams, jellies etc. while mixing such dosages forms, the material must be brought to the agitator or the agitator must move the material throughout the mixer.
- The mixing action includes combination of low speed shear, smearing, wiping, folding, stretching and compressing. Mixing equipment are also used for preparing tooth paste, pill mass and wet mass for granulation.
- Some semisolids exhibit dilatants property that is viscosity increase with increase in shear rates. Therefore, mixing must be done at lower speeds. The speed must be changed accordingly to thixotropic, plastic and Pseudo plastic materials.
- Equipment used for mixing of semisolid— Sigma mixer and planetary mixer (Solid-solid mixer), triple roller mill, colloidal mill.

- **Double cone blender.**

- **Principle**—It is an efficient design for mixing of powder of different densities. It is usually charged and discharged through the same port. These are used mostly for small amounts of powders.

- The rate of rotation should be optimum depending on the size and shape of the tumbler, nature of materials to be mixed. Commonly the range is 30 to 100 R.P.M.
- **Construction—**



- The conical shape at both the end enable uniform mixing and easy discharge.
- The cone is statically balanced which protects the gear box and motor from any excessive load.
- Powder is loaded into the cone through a wide opening and discharged through a butterfly or a slide valve.
- Depending upon the characteristic of the products, paddle type baffles can be provided.
- **Working—**The material is loaded approximately 50% to 60% of its total volume. As the blender rotates, the material undergoes tumbling motion. This motion dividing and recombination continuously yields ordered mixing by mechanical means. Blender speed is the key for mixing

efficiency. At high speed, more dusting or segregation of fines is possible, while at low speeds, not enough shears may be applied.

- **Uses/Applications**—It is an efficient and versatile machine for mixing of dry powders and granules homogeneously.

- **Advantage**—

- It is suitable for fragile granules because of minimum attrition.
- Easy to clean, load and unload.
- They handle large capacities.
- This equipment requires minimum maintenance.

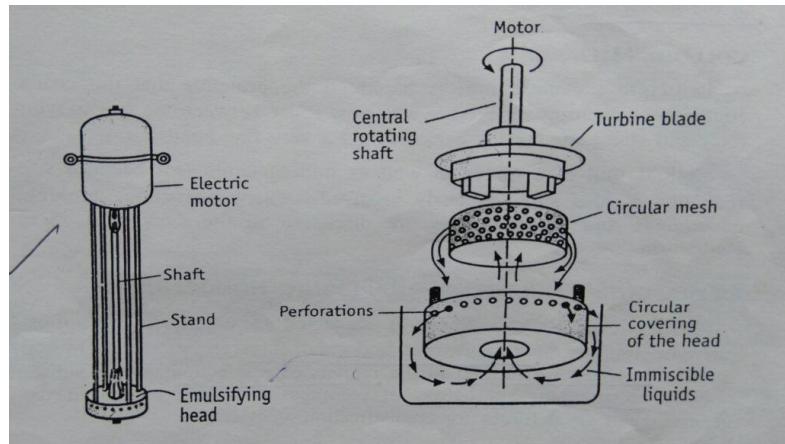
Disadvantage—

- Need high head space for installation.
- It is not suitable for fine particulate system or ingredients of large differences in the particle size distribution because not enough shears is applied.

- **Turbine Mixer.**

- **Principle**—A turbine mixer is a mechanical device that is used in mixing different types of liquids. The turbine mixer works mainly on the principle of shearing action.

- **Construction**—



- A turbine consists of a circular disc to which a number of short blades are attached. The diameter of the turbine ranges from 30% to 50% of the diameter of the vessel.
- It rotates at a lower speed than propeller (50-200 R.P.M).
- The blades may be straight, curved, pitched or vertical.
- **Working**—A flat bladed turbine produces radial and tangential flow, but as speed increase radial flow dominates. A pitched blade turbine produces axial flow.
- Near the impeller, the zone of rapid currents high turbulence and intense shear is observed. The shear produced by turbines can be further enhanced using a diffuser ring.
- A diffuser ring is a stationary perforated or slotted ring, which surrounds the turbine. It increase shear forces, the liquid passes through the perforations reducing rotational swirling and vortexing.
- **Uses/Applications**—Turbines are effective for high viscous solutions

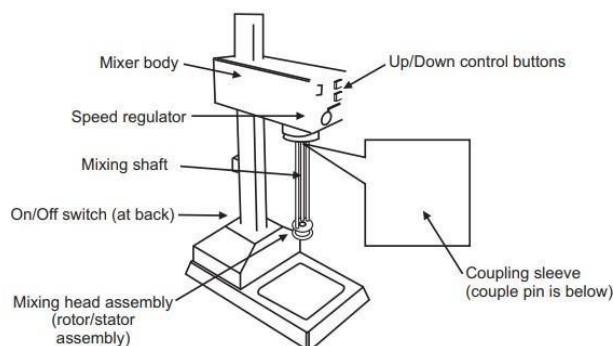
with a very wide range of viscosities up to 700 Pascal/seconds (syrups, liquid paraffin, glycerin etc). They can handle slurries with 60% solids. Turbines are suitable for liquids of large volume and high viscosity, if the tank is baffled.

- **Advantage**—Turbine gives greater shearing forces than propellers, though the pumping rate is less. Therefore, turbines are suitable for emulsification.
- **Disadvantage**—Turbine has less pumping rate.

- **Silverson Mixer.**

- **Principle**—Silverson mixer produces intense shearing forces and turbulence by the use of high speed rotors. This turbulence causes the liquids to pass through fine interstices formed by closely placed perforated metal sheets. Circulation of material takes place through the head by the suction produced in the inlet at the bottom of the head. Circulation of the material ensures rapid breakdown of the dispersed liquid into smaller globules.

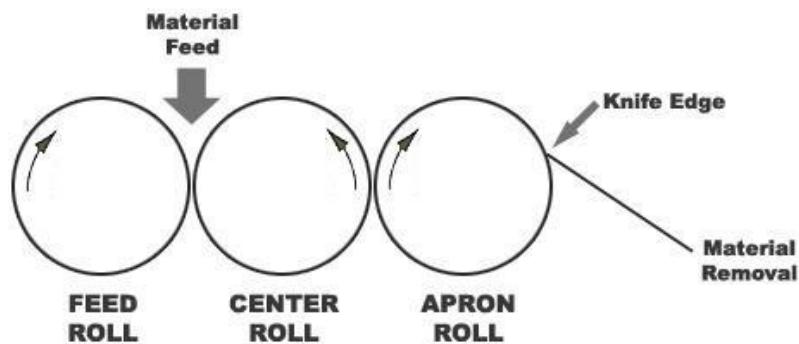
- **Construction—**



- It consists of long supporting columns connected to a motor which give support to the head. The central portions contain a shaft, one end of which is connected to the motor and the other end is connected to the head.
- The head carries turbine blades. The blades are surrounded by a mesh, which is further enclosed by a cover having openings.
- **Working—**
- The emulsifier head is placed in the vessels containing immiscible liquids in such a way that it should get completely dipped in the liquid.
- When the motor is started, the central rotating shaft rotates the head. This in turn rotates turbine blades at a very high speed.
- This creates a pressure difference; as a result liquids are sucked into the head from the center of the base and subjected to intense mixing action.
- The intake and expulsion of the mixture set up a pattern of circulation to ensure rapid breakdown of the bigger globules into smaller globules.
- **Uses/Applications**—Silverson mixer is used for the preparation of emulsions and creams of fine particle size.
- **Advantage**—Silverson mixer is available for thousand liter of mixing.
- **Disadvantage**—Occasional there is a chance of clogging of pores of the mesh.

- **Triple Roller Mill.**

- **Principle—** The differential speed and narrow space between the rollers develop high shear over the materials. This shear causes crushing of aggregates particles and also distributes the drug uniformly throughout the semisolid base.
- **Construction—**



- It consists of three parallel rollers of equal diameters. These are made up of hard abrasion resistant material, normally stainless steel.
- The pressure and gap between the rollers are independently adjustable. A hopper is arranged between the first two rollers. A scrapper is attached to the last roller.

- **Working—**

- The rollers are rotated at different speeds. In practice, the first roller (receiving roller) rotates at a slower speed compared to the second roller. Similarly second roller speed is less than that of third roller (discharged roller).

- The feed is passed through the gap between the first and second roller. The aggregates and particles are crushed and then abraded by the rubbing action of the roller, which is developed due to different speed of rotation.
- A film of appreciable thickness of the feed is produced. The material passes from slow rotating to fast rotating roller.
- Between second and third roller, the gap is small and produces a thinner film of feed. The speed of the third roller is increased to compensate the reduction of cross-sectional area. In the thinning film, more crushing and more abrasion are developed.
- Finally the scrapper removes the material completely from the last roller which can be collected immediately into the receiver or transported through a suitable conveyor.
- **Uses/Applications**—It is used for production of fine or thinner film, on by large particle feed.
- **Advantage**— Triple roller mill is suitable for continuous process extremely uniform dispersion obtained.
- **Disadvantage**—Roller may cause the abrasion and speed maintain is key tasks.

- **Pharmaceutics | Chapter-4.**

- **Unit- 4 — Filtration.**
- **Filtration**— It is defined as a process of separation of solid from fluids

by passing mixture through a porous medium that retain the solid but allows the fluids to pass through. The mixture or suspension to be filtered is known as slurry. The porous medium used to retain the solids is known a filter medium. The accumulated solid on the filters are referred to as filter cake, while the color liquid passing through the filter is filtrate.

- When solids are present in a very low concentration that is not exceeding 1.0% w/v the process of its separation from liquid is called clarification.
- **Application of Filtration.**
- **Production of sterile products**— Air is filtered through HEPA filters (high efficiency particulate air filters) or laminar air bench to obtain sterile air, which maintain good environment prior to and during manufacturing of sterile products.
 - A solution is passed through a bacteria proof filter in order to obtain sterile solution, particularly when heat sterilization is not suitable on account of the thermolabile nature of the contents. In case of sterile products particle as small as $0.2\mu\text{m}$ should be removed, which includes the bio- burden of fungi, bacteria etc.
- **Production of bulk drugs**—solids of intermediates and finished products are separated from the reaction mixture by filtration techniques by the method, impurities can be removed.
- **Production of liquid oral formulation**—Filtration is an essential steps in the production of liquid oral for obtaining clear solution.
- **Affluent and waste water treatment**—Waste solid must be separated

from the waste liquid prior to its disposal. Sometimes, the soluble components are precipitated and the separated by filtration.

- **Factor influencing filtration.**

- A simple straining process does not provide a complete description of how particles are removed from a suspension. The particles are exposed to a number of forces including gravity or electrical fields. Some of the factors influencing the filtration rate-

- **Properties of the liquids**—Density, viscosity, and corrosiveness.
- **Properties of the solids**—Particle shape, particle size, particle charge, particle density, rigidity or compressibility of the solid under pressure and tendency of particle to flocculate or adhere together.
- **Temperature of the suspension.**
- **Filter cake formation rate.**
- **Surface area of the filter medium.**
- **Gravity forces.**
- **Appling pressure.**
- **Viscosity of filtrate.**
- **Centrifugal forces**— Centrifugal force could replace the gravitational force and is used to increase the rate of filtration.

- **Theories of filtration**

- The flow of a liquid through a filter follows the basic rules that govern the flow of any liquid through the medium offering resistance. The rate of

flow may be expressed as--

- **Rate = driving force/resistance.**
 - The rate of filtration may be expressed as volume/time.
 - The driving force is the pressure differential between the upstream and downstream of the filter.
 - The resistance is not constant .it increase with an increase in the deposition of solids on the filter medium.
- **Poiseuille's Equation—** Poiseuille considered that considered that filtration is similar to the streamline flow of a liquid under pressure through Capillaries.
 - $V = \pi \Delta P r^4 / 8 L \eta$.
 - Where $\rightarrow V$ = rate of flow, that is volume of liquid flowing in unit time m^3/s .
 - ΔP = Pressure difference across the filter. Pascal. r = radius of the capillary in the filter bed. Meter
 - L = Thickness of the filter cake (capillary length). Meter
 - η = Viscosity of the filtrate. Pascal/second.
- **Darcy Equation—**
 - $V = K A \Delta P / \eta L$.
 - K = permeability coefficient of cake m^2 .
 - A = Surface area of the porous bed (filter medium) m^2 .
 - The term k depends on the characteristics of the cake, such as

porosity, specific surface area and compressibility.

- **Kozeny-Carman Equation—**

- $V = A/\eta s^2 \times \Delta P/KL \times \epsilon^3/(1-\epsilon)^2$
 - Where $\rightarrow \epsilon$ = porosity of the cake (bed)
 - S = Specific surface area of the particles comprising the cake m^2/m^3 .
 - K = Kozeny constant (usually taken 5).

- **Membrane Filter.**

- **Principle**—Membrane filter consists of microsporous plastics films of specific pore sizes, therefore it is also known as screen, sieve or microsporous filter.
- Membrane present in these filters retains particles or microorganism (larger than the pore size) by surface capture. It act like sieve and the particulate matter is retained on the surface of membrane.
- **Construction**— Membrane filter consists of membrane of cellulose acetate, cellulose nitrate in mixed cellulose ester. The pores size of filter in micron or submicron range.
- A membrane filter is $150\mu m$ thick and contains about millions of microscopic pores. The diameter of these spores is uniform. Based on the requirement the size of these pores is adjusted, during the process of polymerization. The most widely accepted membrane filter possesses a pore size of $0.22\mu m$ and $0.45\mu m$.
- **Working**—The membrane filter functions like a sieve and thus removes particle. The filter of $0.010 - 0.10 \mu$ pore sizes remove even viruses from

water or air and filter of $0.30 - 0.65 \mu$ pore sizes remove bacteria. Filter with largest pore sizes is used in aerosol radioactivity and particle sizing applications.

- For sterile filtration, the membrane is autoclaved in the holder and to prevent curling they are packed between thick filters. Some membrane filters which are pre-sterilized (by ethylene oxide or ionizing radiation) are also available.
- A rigid base of perforated metal, plastic, or coarse sintered glass is used to support the membrane filter during filtration process (as in the case of fibrous pad filters).

- **Uses/Applications—**

- It is used for sterilization and clarifying aqueous and organic solvents including buffers, microbiological and tissue culture solution.
- It is suitable for filtration of enzyme solution.
- It is used for diagnostic cytology and receptor binding studies.

- **Advantages—**

- It does not allow any cross contamination.
- Its filtration rate is rapidly.
- It can be easily disposed off.
- Since absorption is negligible, it does not import any fibers or alkali into the filtrate.

- **Disadvantages—**
 - It may get clogged
 - It ordinary, it is less resistant to solvents like chloroform.
- **Sintered glass filter.**
 - **Principle**—It is works on the principle of Reducing pressure. During the filtration high pressure exerts on the sintered glass disc and lower pressure exert on the base of funnel. Due to pressure difference filtration is performing.
 - **Construction**—It consists of the glass funnel and sintered glass disc. These filters have as a filtering medium a flat or convex plate of Jenna glass powdered and shifted to produce granules of uniform size that are molded together. The variation in porosity depending on size of granules used in the plate. A vacuum attachment is necessary to facilitate the passage of liquid through the filter plate.
 - **Working**—the sintered glass filters are available in different pore size. Hence the funnel with a sintered filter is numbered according to the pore size. The filtration is carried out under reduced pressure. These funnel are used for bacterial filtration.
 - **Uses/Applications**— Sintered filters are also available in stainless steel which has a greater mechanical strength. However these are very much liable to attack by the solutions passing through them.
 - **Advantage—**
 - It is easy to clean and labor requirement is very low. Its shows low