BP 304 T. PHARMACEUTICAL ENGINEERING (Theory) UNIT III

B. PHARM. THIRD SEMESTER

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CONTENTS

DRYING

Outlines: ***Objectives, applications & mechanism of drying process, measurements & applications of Equilibrium Moisture content, rate of drying curve. principles, construction, working, uses, merits and demerits of Tray dryer, drum dryer, spray dryer, fluidized bed dryer, vacuum dryer, freeze dryer.***

Drying involves removal of water or another solvent by evaporation from a solid, semi-solid or liquid by application of heat and finally a liquid free solid product is obtained. In general, drying is accomplished by thermal techniques but non-thermal drying processes such as squeezing wetted sponge, adsorption by desiccant (desiccation) and extraction are also used. In bioproducts like food, grains, and pharmaceuticals like vaccines, the solvent to be removed is almost invariably water [1].

Table 1. Difference between Drying and Evaporation

Drying	Evaporation
Done to get a stable dry product.	Final product is either concentrated suspension or wet slurry.
Removal of less amount of moisture.	Removal of large amount of liquid.
Drying occurs below boiling point.	Evaporation occurs more at boiling point.
Emphasize on solid product.	Emphasize on reducing the volume.

OBJECTIVES OF DRYING

The main **objectives of drying** include to preserve foods and increase their shelf life by reducing the water content and water activity; avoid the need for use of refrigeration systems for transport and storage (expensive); reduce space requirements for storage and transport.
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 stability. 2. To improve or keep the good properties of a material like granules, e.g. Flowability, compressibility [2].

APPLICATIONS OF DRYING

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

1. Preparation of bulk drugs: In the preparation of bulk drugs, drying is the final stage of processing. A few examples are – dried aluminium hydroxide, spray dried lactose and powdered extracts.
2. Preservation of drug products: Drying is necessary in order to avoid deterioration. For examples protection of blood products, skin, tissues and crude drugs from microbial growth.
3. Improved characteristics: Drying produces materials of spherical shape, uniform size, free flowing and enhanced solubility.
4. Improved handling: To reduce the cost of transportation of large volume materials.
   To make the materials easy or more stable for handling. Drying reduces moisture content [3].
5. Drying as final step: Drying is the final step in evaporation, filtration, and crystallization.

MECHANISM OF DRYING PROCESS

Drying does not mean only removal of the moisture but during the process, physical structure as well as the appearance has to be preserved. Drying is basically governed by the principles of transport of heat and mass. When a moist solid is heated to an appropriate temperature, moisture vaporizes at or near the solid surface and the heat required for evaporating moisture from the drying product is supplied by the external drying medium, usually air or a hot gas. Drying is a diffusional process in which the transfer of moisture to the surrounding medium takes place by the evaporation of surface moisture, as soon as some of the surface moisture vaporizes, more moisture is transported from interior of the solid to its surface. This transport of moisture within a solid takes place by a variety of mechanisms depending upon the nature and type of the solid and its state of aggregation. Different types of solids may have to be handled for drying crystalline, granular, beads, powders, sheets, slabs, filter-cakes etc. The mechanism of moisture transport in different solids may be broadly classified into (i) transport by liquid or vapour diffusion (ii) capillary section, and (iii) pressure induced transport. The mechanism that dominates depends on the nature of the solid, its pore structure and the rate of drying. Different mechanisms may come into play and dominate at different stages of drying of the same material [4].

The following terms are commonly used in Designing of Drying Systems:

Bound Water: Moisture content of a substance which exerts as equilibrium vapour pressure less than of the pure liquid at the same temperature is referred to as bound moisture or bound wated.

Unbound Water: Moisture content of the solid which exerts an equilibrium vapour pressure equal to that of pure liquid at the given temperature is the unbound moisture or unbound water.

Free Moisture Content (FMC): The moisture content of solid in excess of the equilibrium moisture content is referred as free moisture. During drying, only free moisture can be evaporated. The free moisture content of a solid depends upon the vapour concentration in the gas.

Equilibrium Moisture Content (EMC): The moisture contents of solid when it is in equilibrium with given partial pressure of vapour in gas phase is called as equilibrium moisture content. The EMC of a hygroscopic material surrounded at least partially by air is the **moisture content** at which the material is neither gaining nor losing **moisture**. The value of the EMC depends on the material and the relative **humidity** and temperature of the air with which it is in contact.

Critical Moisture Content (CMC): Similarly, the moisture content at which the constant rate drying period ends and the falling rate drying period starts is called critical moisture content.

Constant Rate Drying Period: During the constant rate drying period, the moisture evaporated per unit time per unit area of drying surface remains constant.

Falling Rate Drying Period: In falling rate drying period the amount of moisture evaporated per unit time per unit area of drying surface continuously decreases.

Rate Relationships:

Percentage Moisture Content:

$$\%\ \boldsymbol{Moisture\ content} = \frac{\boldsymbol{Weight\ of\ water\ in\ sample}}{\boldsymbol{Weight\ of\ dry\ sample}} \times \mathbf{100}$$

Rate of Drying:

$$\boldsymbol{Drying\ Rate} = \frac{\boldsymbol{Weight\ of\ water\ in\ sample\ (kg)}}{\boldsymbol{Time\ (h) \times Weight\ of\ dry\ solid\ (kg)}}$$

Loss on Drying:

$$\textbf{\textit{Loss on drying}}\ (\%) = \frac{\textbf{\textit{Mass of water in sample}}\ (\textbf{\textit{kg}})}{\textbf{\textit{Total mass of wet sample}}\ (\textbf{\textit{kg}})} \times \mathbf{100}$$

RATE OF DRYING CURVE

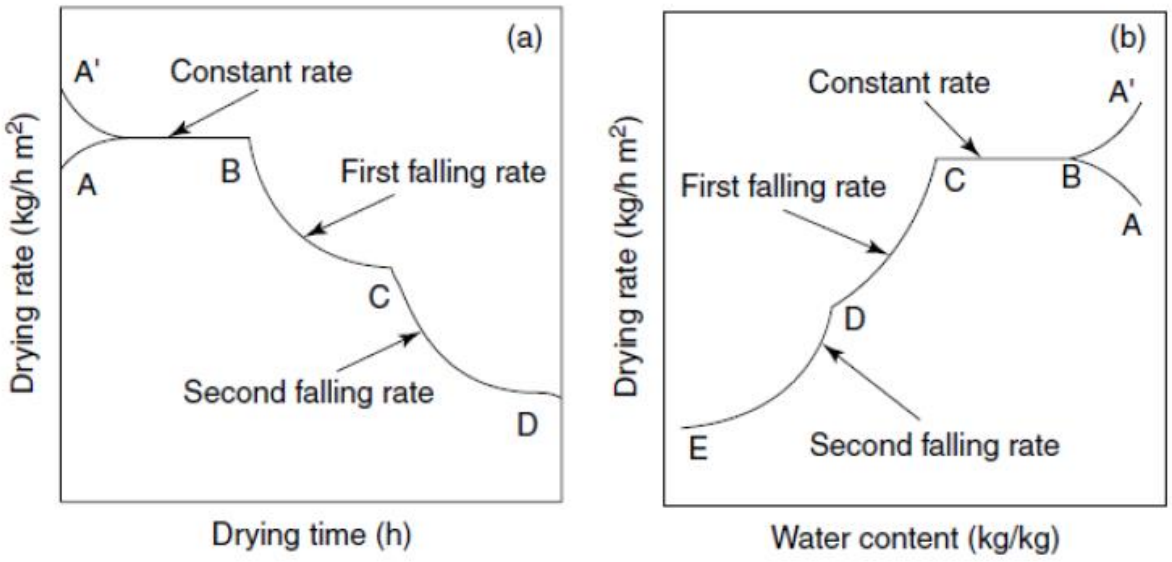


Fig. 1: Typical drying rate curves: (a) drying rate versus drying time and (b) drying rate versus water content

- Drying curve usually plots the drying rate versus drying time or moisture contents.
- Three major stages of drying can be observed in the drying curve [5].

1. **Transient early stage**, during which the product is heating up (transient period)
2. **Constant rate period**, in which moisture is comparatively easy to remove
3. **Falling rate period**, in which moisture is bound or held within the solid matrix

Critical moisture content: The moisture content at the point when the drying period changes from a constant to a falling rate.

The drying behaviours of food materials depend on the porosity, homogeneity, and hygroscopic properties.

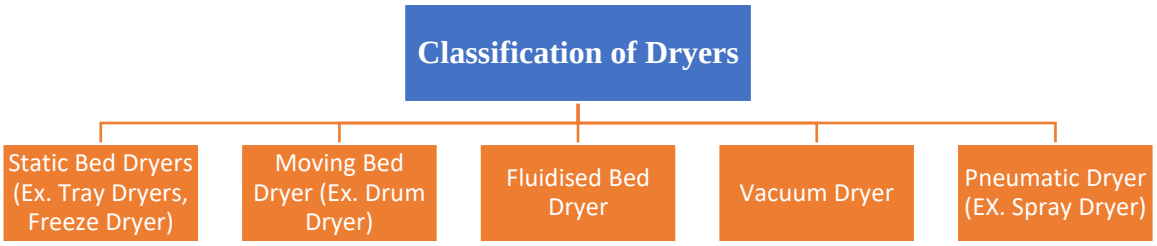
Hygroscopic food materials enter into the falling rate faster compared to non-hygroscopic food materials.

CLASSIFICATION OF DRYERS

Drying equipment is classified in different ways, according to following design and operating features. It can be classified based on mode of operation such as batch or continuous, In case of batch dryer the material is loaded in the drying equipment and drying proceeds for a given period of time, whereas, in case of continuous mode the material is continuously added to the dryer and dried material continuously removed. In some cases, vacuum may be used to reduce the drying temperature. Some dryers can handle almost any kind of material, whereas others are severely limited in the style of feed they can accept. Drying processes can also be categorized according to the physical state of the feed such as wet solid, liquid, and slurry. Type of heating system i.e. conduction, convection, radiation is another way of categorizing the drying process. Heat may be supplied by direct contact with hot air at atmospheric pressure, and the water vaporized is removed by the air flowing. Heat may also be supplied indirectly through the wall of the dryer from a hot gas flowing outside the wall or by radiation. Dryers exposing the solids to a hot surface with which the solid is in contact are called adiabatic or direct dryers, while when heat is transferred from an external medium it is

known as non-adiabatic or indirect dryers. Dryers heated by dielectric, radiant or microwave energy are also non adiabatic. Some units combine adiabatic and non-adiabatic drying; they are known as direct-indirect dryers [1], [2].

To reduce heat losses most of the commercial dryers are insulated and hot air is recirculated to save energy. Now many designs have energy-saving devices, which recover heat from the exhaust air or automatically control the air humidity. Computer control of dryers in sophisticated driers also results in important savings in energy.



TRAY DRYER

Principle of Tray Dryer:

The basic working **principle** of this incredible machine is the continuous circulation of hot air. In the **tray dryer**, moisture is removed from the solids that are placed in the **tray** by a forced convectional heating. The moist air is removed is partially but in a simultaneous fashion [6].

Construction of Tray Dryer:

Tray Dryer is used for the best drying results in conventional process. It is a double walled cabinet with Single or Two doors. The gap between two walls is filled with high density fibre glass wool insulation material to avoid heat transfer. Doors are provided with gaskets. Stainless steel trays are placed on the movable trolleys. Tray Dryer is provided with control panel board, process timer, Digital temperature controller cum indicator etc. Tray Dryer is available in capacities ranging from 6, 12, 24, 48, 96, 192 trays [1].

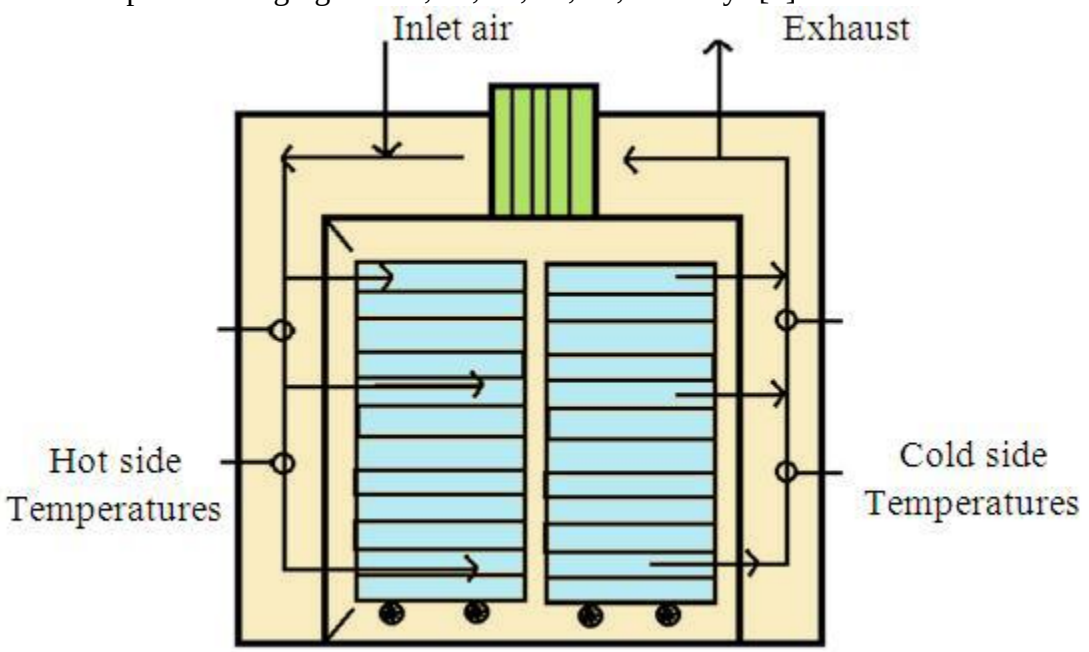


Fig. 2: Tray Dryer

Working of Tray Dryer:

- In tray dryer hot air is continuously circulated. Forced convection heating takes place to remove moister from the solids placed in trays.
- Simultaneously the moist air is removed partially.
- Wet solid is loaded in to the trays. Trays are placed in the chamber.
- Fresh air is introduced through in let, which passes through the heaters and gets heated up.
- The hot air is circulated by means of fans at 2 to 5 metre per second.
- Turbulent flow lowers the partial vapour pressure in the atmosphere and also reduces the thickness of the air boundary layer.
- The water is picked up by the air. As the water evaporates from the surface, the water diffuses from the interior of the solids by the capillary action.
- These events occur in a single pass of air. The time of contact is short and amount of water picked up in a single pass is small.
- Therefore, the discharged air to the tune of 80 to 90 % is circulated back through the fans. Only 10 to 20% of fresh air is introduced.
- Moist air is discharged through outlet. Thus, constant temperature and uniform air flow over the materials can be maintained for achieving uniform drying.
- In case of the wet granules as in tablets and capsules drying is continued until the desired moister content is obtained.
- At the end of the drying trays or trucks are pulled out of the chamber and taken to a tray dumping station.

Advantages of Tray Dryer:

- Each batch is handled as a separate entity.
- It is more efficient in fuel consumption.
- It is operated batch-wise.
- It is simple to use.
- It provides tendency to over-dry the lower trays.
- It requires little labour costs – merely load and then unload.

Disadvantages of Tray Dryer:

- The process is time-consuming.
- It requires extra cost.
- Not suitable for oxidizable and thermolabile substances.

Pharmaceutical Uses of Tray Dryer:

- Tray dryer is used in the drying of the sticky materials.
- It is used in the drying of the granular mass or crystalline materials.
- Plastic substances can be dried by the tray dryers.
- Wet mass preparations and pastes can be dried in a tray dryer.
- In the tray dryers the crude drugs, chemicals, powders and tablet granules are also dried to obtain free flowing materials.
- Some types of equipments can be dried in the tray dryers.

Variants:

Tray dryer may be operated under vacuum called vacuum tray dryers. Another is Tunnel dryer. In this type, trucks are loaded with wet materials at one end of the tunnel. The tunnel comprised of a number of units, each of which is electro-statically controlled. The solids get dried and the product is discharged at the other end of the tunnel.

DRUM DRYER OR ROLL DRYER

Principle of Drum Dryer:
In **drum drying**, the heated surface is the envelope of a rotating horizontal metal cylinder. The cylinder is heated by steam condensing inside, at a pressure in the range of 200 to 500 kPa bringing the temperature of the cylinder wall to 120–155°C [1].

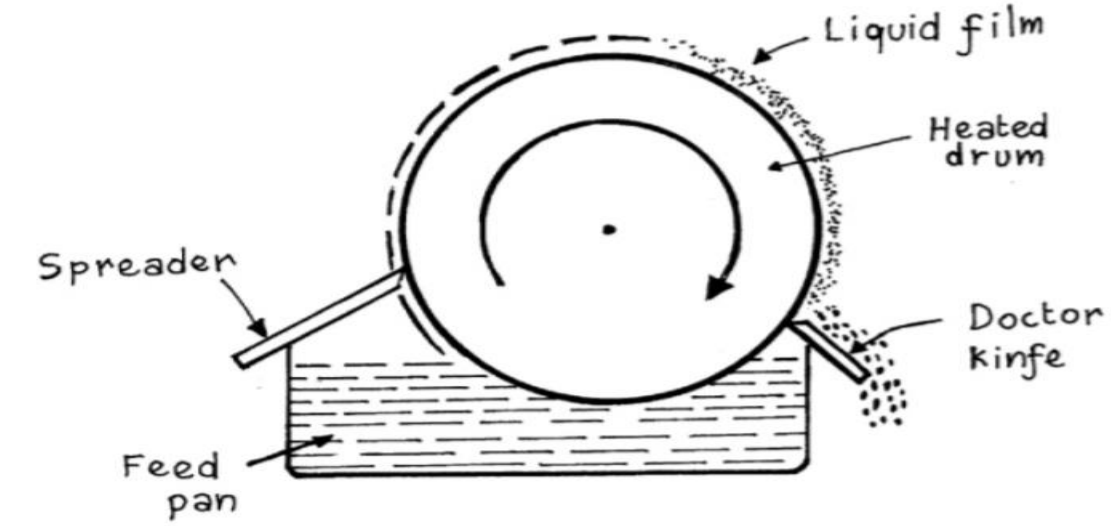


Fig. 3: Drum Dryer or Roll Dryer

Construction of Drum Dryer or Roll Dryer:
A **drum dryer** consists of one or two horizontally mounted hollow cylinder(s) or drums of about 0.75-1.5 m in diameter and 2-4 m in length, made of high-grade cast iron or stainless steel, a supporting frame, a product feeding system, a scraper, and auxiliaries. The drum is heated internally by steam, and rotated on its longitudinal axis. The external surface of the drum is polished. Liquid or slurry is placed as feed in a pan. The drum is partially dipped in pan. The spreader is used to spread liquid film evenly on roller. The rotation of the drum adjusted so that all of the liquid is fully vaporized. The drum is rotated continuously. The dried deposits can be scrapped off with the help of doctor knife.

Working of Drum Dryer or Roll Dryer:
As the drum rotates, the liquid material gets adhere to external surface of drum. The liquid is spread as film on to the surface. The drying of the material is done by process of steam when passed in to the drum. By the mechanism of conduction, the heat gets transferred in to drum and drying process takes place. The material is completely dried during whole process during its revolution. The dried material is scrapped by the knife and that fall in to the bin.

Advantages of Drum Dryer or Roll Dryer:

- Drying takes place in less time.
- It is suitable for thermosensitive drugs.
- It occupies less space.
- In order to reduce the temperature of drying the drum can be enclosed in a vacuum chamber.
- Rapid drying takes place due to rapid heat and mass transfer.

Disadvantages of Drum Dryer or Roll Dryer:

- Maintenance cost is high.
- Skilled operations are essential to control thickness of film.
- It is not suitable for less solubility products.

- The operating conditions are critical. It is necessary to introduce careful control on feed rate, film thickness, speed of drum rotation and drum temperature.

Pharmaceutical Uses of Drum Dryer or Roll Dryer:

- Drum dryer takes viscous liquids, slurries, suspensions, and pastes as input material to be dried and produces the output as powders or flakes.
- Drum dryers find application majorly in Food & Dairy industry and Chemical &Pharmaceutical Industries for drying various type of pasts and slurries.

Variants:

- A vacuum drum dryer encloses both drum and feed line in a vacuum chamber to facilitates drying of heat sensitive materials.
- In large scale, instead of one drum, two drums are set in parallel, rotating in opposite direction with a common feed inlet.

SPRAY DRYER

Principle of Spray Dryer:

Spray drying is an industrial process for dehydration of a liquid feed containing dissolved and/or dispersed solids, by transforming that liquid into a **spray** of small droplets and exposing these droplets to a flow of hot air [7], [8].

Construction of Spray Dryer:

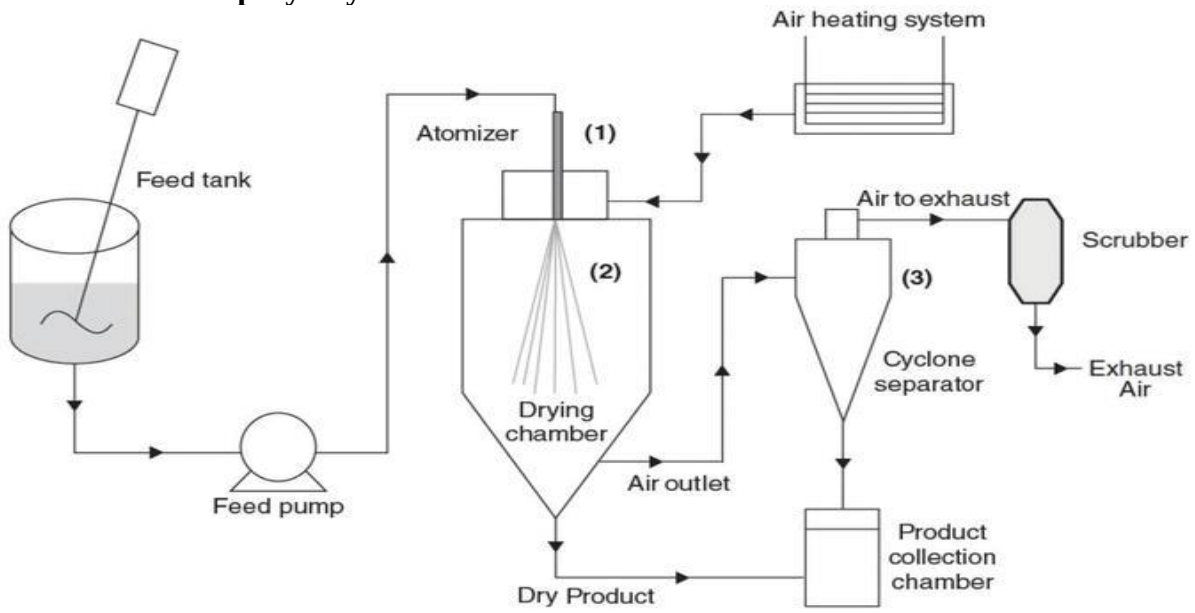


Fig. 4: Spray Dryer

A spray dryer is composed of a feed pump, atomizer, air heating unit, air dispenser, drying chamber (diameter of the drying chamber ranges between 2.5 to 9.0 m and height is 25 m or more) and also systems for exhaust air cleansing and also powder recovery/separator. The spray disk atomizer is about 300 millimetres in diameter and rotates at a speed of 3,000 to 50,000 revolutions per minutes. In the spray dryer the liquid to be dried is atomised into the good droplets, that are tossed radially into a relocating stream of warm gas [9].

Working of Spray Dryer:

A spray dryer takes a liquid stream and separates the solute or suspension as a solid and the solvent into a vapor. The solid is usually collected in a drum or cyclone. The liquid input stream is sprayed through a nozzle into a hot vapor stream and vaporized. Solids form as moisture quickly leaves the droplets [10].

The three stages that occur in a spray dryer before drying is accomplished include:

- Atomization
- Spray-air mixing and moisture evaporation.
- Dry product separation from the exit air [9].

The nature of the final product obtained after drying in a spray dryer depends on;

- The design and operation of the spray dryer.
- The physicochemical properties of the feed.

Advantages of Spray Drying:

- Product quality and properties can be effectively controlled and maintained through the entire drying operation.
- Thermolabile products/ pharmaceuticals can be dried at atmospheric pressure and low temperature.
- Spray dryer permits high- tonnage production in continuous operation adaptable to conventional PLC control (Programmable Logic Controller) and it is relatively simple to operate.
- Feedstock in solution, slurry, emulsion, paste, and melt form can be dried if pumpable.
- Corrosion problem is minimal and the selection of materials of construction of spray dryer is simplified since the dried material comes in contact with the equipment surfaces in an anhydrous condition.
- Spray dryer produces dry powder particles of controllable particle size, shape, form, moisture content, and other specific properties irrespective of dryer capacity and heat sensitivity.
- Spray dryer handles a wide range of production rates and provides extensive flexibility in its design that is product specification are readily met through the selection of appropriate spray dryer design and its operation from a wide range of available design.
- It is energy-intensive equipment because specific heat of evaporation can be supplied in a short time. The temperature difference across the drying chamber is relatively small and an appreciable amount of heat is lost with exhaust air.

Disadvantages of Spray Drying:

- Spray dryer is bulky and also expensive to install.
- It is difficult to clean after use.
- It has a low thermal efficiency that is a lot of heat is wasted during operation.
- Solid materials cannot be dried using spray dryers.
- Product degradation or fire hazard may result from product deposit on the drying chamber.

Pharmaceutical Uses of Spray Dryer:

- Spray dryer is used in drying pharmaceuticals like penicillin, blood products, enzymes, vaccines, etc [10], [11].
- It is used in the production of excipients and co-processed excipients with increased flowability, compatibility, and tablet disintegration.
- To improve drug compressibility and reduce capping tendencies in crystals.
- It is equally used in the preparation of matrix microcapsule containing drug substances and a biodegradable polymer in order to obtain controlled drug release formulation.
- It is employed in enhancing solubility and dissolution rates of poorly soluble drugs by formation of pharmaceutical complexes or via the development of solid dispersion thus increasing bioavailability.

- It is used in the production of dry powder formulation/dry powder aerosol and thermolabile materials.
- Apart from its applications in the pharmaceutical industries, spray dryers also find use in; Chemical industries, Ceramic industries, Food industries, etc.
- Biochemical industries e.g. algae, fodder antibiotics, yeast extracts, enzymes, etc.
- Environmental pollution control e.g. flue gas desulfurization, black liquor from paper-making etc.

Variants:

- Spray dryer can be constructed in such a way as to suit sterile products.
- It can be operated under closed conditions to recover solvents.
- It can be operated under oxygen free environment.
- The same equipment can be used for spray congealing.
- It is useful for encapsulation (coating) of solid and liquid particles.

FLUIDIZED BED DRYER (FBD)

Principle of Fluidized Bed Dryer (FBD): The equipment works on a principle of fluidization of the feed materials. In fluidization process, hot air is introduced at high pressure through a perforated bed of moist solid particulate. The wet solids are lifted from the bottom and suspended in a stream of air (fluidized state) [4], [8], [12].

Construction of Fluidized Bed Dryer (FBD):

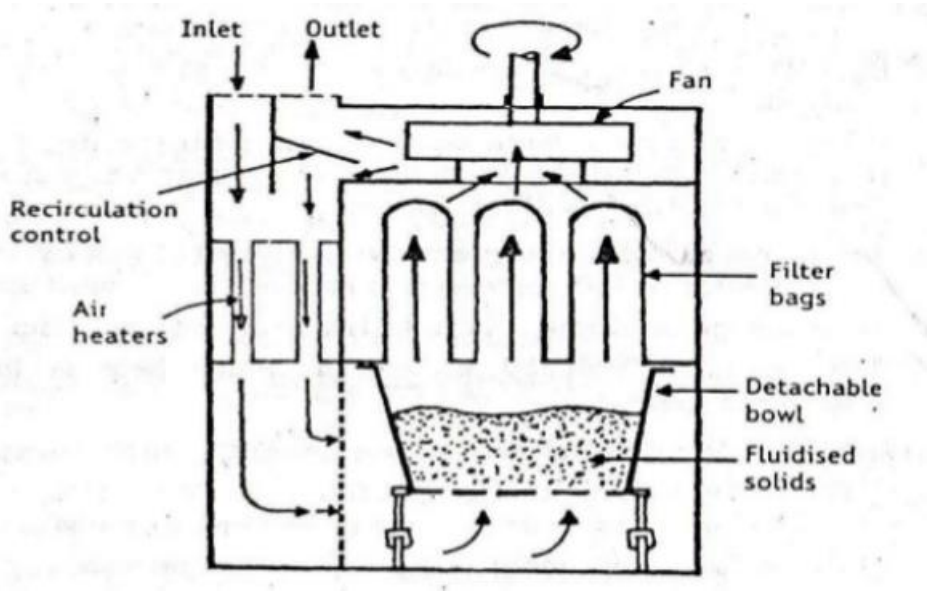


Fig. 5: Fluidized Bed Dryer

- The dryer is made up of stainless steel or plastic.
- A detachable bowel is placed at the bottom of the dryer, which is used for charging and discharging.
- The bowel has a perforated bottom with a wire mesh support for placing materials to be dried.
- A fan is mounted in the upper part for circulating hot air.

- Fresh air inlet, prefilter and heat exchanger are connected serially to heat the air to the required temperature.
- The temperature of hot air and exit air are monitored.
- Bag filters are placed above the drying bowl for the recovery of fines.

Working of Fluidized Bed Dryer:

- The wet granules to be dried are placed in a detachable bowl. The bowl is inserted in the drier.
- Fresh air can pass trough a prefilter, which is then heated when passing trough a heat exchanger.
- Hot air flows through the bottom of the bowl.
- At the same time, fan start to rotate.
- The air speed increases gradually.
- When the velocity of air is greater than the sedimentation rate of the granules, the granules remain suspended in the gas stream.
- After specific time, a pressure point is reached in which the friction drag on a particle is equal to the force of gravity.
- The granules rise in the container due to high gas velocity of 1.5 to 7.5 meter per minute and then fall back. This state is known as fluidized state.
- The gas surround to each granule do dry them completely.
- The air comes out of the dryer passing through the filters in the bag.
- The entrained particles remain adhered to the interior surface of bags.
- Periodically bags are shaken to remove entrained particles [13], [14].

Advantages of Fluidized Bed Dryer:

- It takes less time to complete drying as compared to other dryer.
- Drying is achieved at constant rate.
- Handling time is also short.
- It is available at different sizes with different drying capacity.
- The equipment is simple and less labour cost required.
- More thermal efficiency.
- Drying capacity is more than other dryer.
- It facilitates the drying of thermolabile substances since the contact time of drying is short.
- It is batch type or continuous type process.

Disadvantages of Fluidized Bed Dryer:

- Many organic powders develop electrostatic charge during drying. To avoid this efficient electrical grounding of the dryer is essential.
- Chances of attrition of some materials resulting in production of fines.

Pharmaceutical applications of Fluidized Bed Dryer:

- It is used for drying of granules in the production of tablets.
- It is used for coating of granules.
- It can be used for three operations such as mixing, granulation and drying [12].

Variants:

Plug flow dryer: It is a rectangular fluid bed dryer having different compartments for fluidisation. The material is made to move from inlet through different compartments to outlet. Different drying condition can be maintained in the compartments. Often the last compartment is fluidised with cold gas to cool the solids before discharge.

VACUUM DRYER

Principle of Vacuum Dryer:

Vacuum drying is generally used for the drying of substances which are hygroscopic and heat sensitive, and is based on the principle of creating a vacuum to decrease the chamber pressure below the vapour pressure of the water, causing it to boil. Hence, water evaporates faster. The heat transfer becomes, i.e., rate of drying enhances substantially.

Construction of Vacuum Dryer:

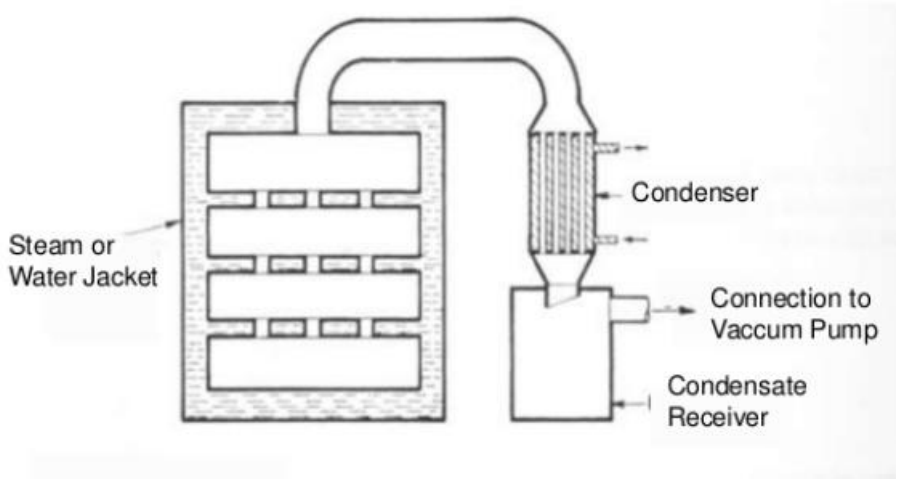


Fig. 6: Vacuum Dryer

The oven is divided into hollow trays which increases the surface area for heat conduction. The oven door is locked air tight and is connected to **vacuum** pump to reduce the pressure. The materials to be dried are kept on the trays inside the **vacuum dryer** and pressure is reduced by means of **vacuum** pump.

The enclosed space (aproximately 1.5 meter cube) is devided in to a number of portions by means of 20 hollow shelves, which are part of the jacket. These shelves provide larger surface area (about 45 to 50 meter square) for conduction of heat. Over the shelves, metal trays are placed for keeping the material. The oven door can be locked tightly to give an air tight seal. The oven is connected to a vacuum pump by placing condenser in between.

Working of Vacuum Dryer:

- The tray that are present in the dryer are used to dry the material that are placed in the shelves and the pressure is reduced to 30 to 60 Kps by vacuum pump.
- The door closes firmly and steam passes through the jacket space and the shelves.
- So the heat transfer is carried out by the conduction mechanism.
- When evaporating under vacuum, the water is evaporated from the material at 25 - 30℃.
- The vapour goes to the condenser.
- After drying vacuum line is disconnected.
- Then the materials are collected from the tray.

Advantages of Vacuum Dryer:

- Material handling is easy.
- Hollow shelves which are electrically heated can be used.
- It provides large surface area. So the heat can be easily transfer through the body of the dryer and last drying action takes place.
- Hot water can be supplied through the dryer, which help in drying process at the desired temperature.

Disadvantages of Vacuum Dryer:

- Dryer is a batch type process.
- It has low efficiency.
- It is more expensive.
- Labour cost is too high.
- Needs high maintenance.
- There is a danger of overheating due to vacuum.

Uses of Vacuum Dryer:

Vacuum dryer can be used for drying of following:

- Heat sensitive materials, which undergo decomposition.
- Dusty and hygroscopic material.
- Drugs containing toxic solvents. These can be separated in to closed containers.
- Feed containing valuable solvents. These are recovered by condensation.
- Drugs which are required as porous end products.
- Friable dry extracts.

FREEZE DRYER

Principle of Freeze Dryer:

Freeze drying or lyophilisation is a drying process used to convert solutions or suspensions of labile materials into solids of sufficient stability for distribution and storage. The fundamental principle in freeze-drying is sublimation, the shift from a solid directly into a gas. Just like evaporation, sublimation occurs when a molecule gains enough energy to break free from the molecules around it. Drying is achieved by subjecting the materials to temperature and pressures below the triple point [1], [4], [15].

Construction of Freeze Dryer:

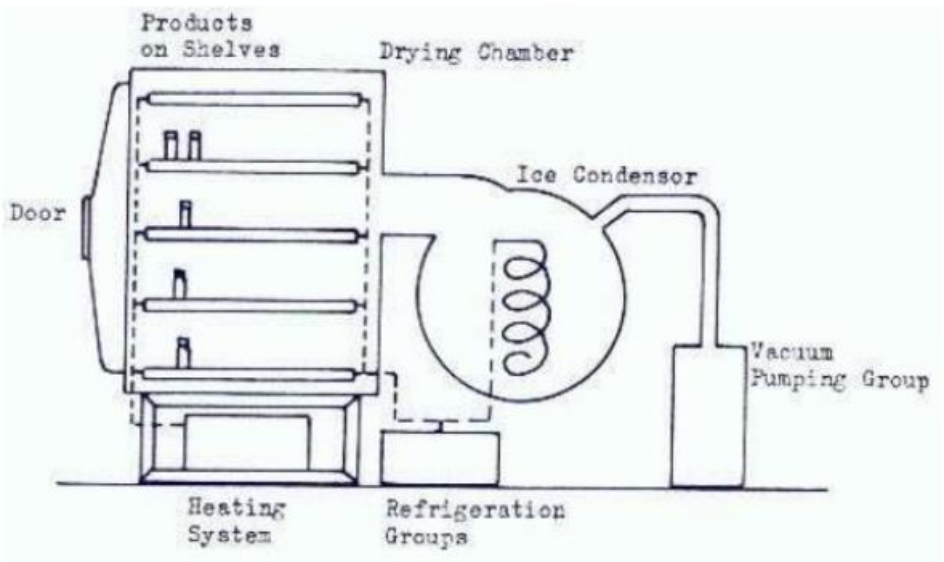


Fig. 7: Freeze Dryer

The construction of freeze dryer is shown in figure 7. It consists of

- Drying chamber in which trays are loaded.
- Heat supply in radiation source, heating coils.
- Vapour condensing or adsorption system.

- Vacuum pump or stream ejector or both.

The chamber for vacuum drying is generally designed for batch operation. It consists of shelves for keeping the material. The distance between subliming and condenser must be less than the mean path of molecules. This increases the rate of drying. The condenser consists of relatively large surface cooled by solid carbon dioxide slurred with acetone or ethanol. The temperature of condenser must be much lower than evaporated surface of frozen substance. In order to maintain this condition, the condenser surface is cleaned repeatedly.

Working of Freeze Dryer:

The following steps are involved in the working of freeze dryer

Pretreatment includes any method of treating the product prior to **freezing**. This may include concentrating the product, formulation revision (i.e., addition of components to increase stability, preserve appearance, and/or improve processing), decreasing a high-vapor-pressure solvent, or increasing the surface area. This reduces the actual drying by 8 to 10 times. The final product becomes more porous[1] [16].

During **pre-freezing**, the **freeze dryer** works as a **freezer** in that no vacuum is applied. Vials, ampoules or bottle in which the aqueous solutions are packed or frozen in cold shelves (about -50℃). During this stage, cabinet is maintained at low temperature and atmospheric pressure. The normal cooling rate is about 1 to 3 kelvin per minute so that large ice crystals with relatively large holes are formed on sublimation of ice. This is also responsible for giving a porous product.

Primary drying (sublimation of ice under vacuum): In this step, the material to be dried is spread as much large surface as possible for sublimation. The temperature and pressure should be below the triple point of water, i.e., 0.0098℃ and 0.533 Kilopascal, (4.58 mmHg) for the sublimation, when water alone is present.

When a solution of solid is dried, the depression of freezing point of water occurs. Hence it is essential that the temperature be brought bellow the eutectic point. The pressure and temperature at which the frozen solid vaporises without conversion to a liquid is referred to as the eutectic point. Depending on the drug substance dissolved in water, the eutectic point is determined. The usual range is from -10℃ to 30℃. The condition of 1 to 8 K bellow eutectic point is sufficient.

Vacuum is applied to the tune of about 3 mmHg (0.4 Kilopascals) on the frozen sample. The temperature is linearly increased to about 30℃ in a span of 2 hours.

Heat (about 2900 Kilojoules per kg) is supplied which transfers as latent heat and ice sublimes directly into vapour state. The heat controls the movement of ice layer inwards. It has to be controlled in such a manner so as to get highest possible water vapour at ice surface without melting the material. As soon as the vapour molecules are formed, these are removed. The overall driving force is the temperature difference (also vapour pressure difference) between evaporating surface and condenser.

As the drying proceeds, the thickness of frozen layer decreases and thickness of partially dried solids increases. Primary drying stage removes easily removable moisture. During this stage, about 98% to 99% water is removed. Till traces of moisture is present in the sample.

Secondary drying (removal of residual moisture under high vacuum): During this stage traces of moisture is removed. The temperature of solid is raised to as high as 50 to 60℃, but vacuum is lowered bellow that is used in primary drying (50 mmHg). The rate of drying is very low and it takes about 10 to 20 hours.

Primary drying is a top-down process with a well-defined sublimation front moving through the product as it dries. Above the ice surface interface is dried product, or "cake"; below the interface is product with ice crystals still remaining to be sublimed.

After primary freeze-drying is complete and all ice has sublimed, in the area where ice has been removed, desorption of water from the cake occurs. This process is called **secondary drying** and has started in the primary drying phase. The product appears to be **dry b**ut the residual moisture content may be as high as 7–8%.

Packing is done by replacing vacuum with inert gas, bottles and vials are closed.

Advantages of Freeze Dryer:

- It is suitable for drying heat sensitive products
- Freeze dried products is porous and easy to dehydrated and instantly dissolved.
- Drying takes place at very low temperature, so that enzyme action is inhibited and chemical decomposition, particularly hydrolysis, is minimized.
- Denaturation of protein does not occur.
- Loss of volatile material is less.
- Sterility can be maintained.

Disadvantages of Freeze Dryer:

- The process is very slow**.**
- Expensive process.
- It is not a general method of drying, but it is limited to certain type of valuable products that cannot be dried by any other means.
- The period of drying is high.
- The product is prone to oxidation, due to the high porosity and large surface area. Therefore, the product must be vacuum packed or with an inert gas or in container.

Uses of Freeze Dryer:

- It is used in production of injection, solutions, and suspension.
- It is also used for production of blood plasma and its fractionated products, bacterial and viral cultures, antibiotics and plant extracts, steroids, vitamins and enzymes.
- Food product like mushroom, meat products can be dried by this method.
- Coffee and tea concentrates and citrus fruit juices are also dried by this method.
- Pharmaceutical companies often use freeze-drying to increase the shelf life of products, such as vaccines and other injectable.
- By removing the water from the material and sealing the material in a vial, the material can be easily stored, shipped and later reconstituted to its original form for injection [6].

MIXING

Outlines: ***Objectives, applications & factors affecting mixing, Difference between solid and liquid mixing, mechanism of solid mixing, liquids mixing and semisolids mixing. Principles, Construction, Working, uses, Merits and Demerits of Double cone blender, twin shell blender, ribbon blender, Sigma blade mixer, planetary mixers, Propellers, Turbines, Paddles &Silverson Emulsifier.***

OBJECTIVES OF MIXING

The main objective of this mixing is to produce a bulk mixture which when divide into different doses, every unit of divided doses must contain the correct proportion of each ingredient. It is critical process because the quality of the final product and its attributes are derived by the quality of the mixing [4].

APPLICATIONS OF MIXING

- Mixing is an intermediate step in production of tablet or capsule. Mixing of powders in different proportion prior to granulation or tableting.
- Dry mixing of materials for direct compression in to tablets.
- Dry mixing of powder or composites powders in capsule and insufflations respectively.
- Blending of powders are also important in preparation of cosmetic products such as facial powder or dental powder.
- In case of potent drugs where dose is low, mixing is critical factor. Otherwise it will affect content uniformity of tablet [1], [8].

FACTORS AFFECTING MIXING

These factors include the following [2], [7]:

1. **Nature of product**: For effective mixing particle surface should be smooth.
2. **Particle size**: It is easier to mix powder of same particle size. Increasing the difference in particle size will lead to segregation.
3. **Particle shape**: Particle should be spherical in shape to get a uniform mixture.
4. **Particle charge**: some particle due to electrostatic charge exerts attractive force which leads to separation.
5. **Proportion of material**: It is easier to mix powders if available in same quantities.
6. **Relative density**: If the components have a different density, the denser material will sink through lighter material.
7. **Viscosity**: An increase in viscosity reduces the extent of mixing.
8. **Surface tension of liquids**: High surface tension reduces the extension of mixing.
9. **Temperature**: Temperature also affects the mixing because viscosity changes with increase in temperature.
10. **Mixture volume**: Mixing efficiency depends on mixture volume.
11. **Agitator type**: The shape, size, location and type of agitator also affect affects the degree of mixing.
12. **Speed/rpm of the impeller**: Mixing at less rpm is more homogenous than at higher rpm.
13. **Mixing time**: Mixing time is also very important for appropriate mixing.

DIFFERENCE BETWEEN SOLID AND LIQUID MIXING

The difference between solid and liquid mixing has been shown in Table 2.

Table 2. Difference Between Solid and Liquid Mixing

Solid Mixing	Liquids Mixing
In solid mixing two or more substances are intermingled by continuous movement of particles.	This is achieved by mixing elements of suitable shape to act as impeller to produce appropriate flow pattern in mixing vessel.
This is used for mixing of dry powders.	This is used in preparation of emulsion, suspension and mixtures.
Large sample size is required.	Small sample size is sufficient.
High power required for mixing.	Less power required for mixing.

MECHANISM OF MIXING

Mechanism of Solid Mixing:
Mechanism in involved in solid mixing are
Convective mixing, In which group of particles move from one position to another. It also referred to as macromixing.
Shear mixing, In this, shearing force is created within the mass of material by the use of a stirring arm or a burst of air.
Diffusive mixing, During this mixing, gravitational forces cause the upper layers of material to slip and random motion of individual particles take place on newly developed surfaces. Also known as micro mixing [1].
Mechanism of Liquid Mixing:
Mechanism of liquid mixing are
Bulk transport: It is the movement of large portion of material from one location to another location. The movement is done by rotating blades or paddles.
Turbulent mixing: In this mixing is due to turbulence. Turbulence is a function of velocity gradient between two adjacent layers of a liquid.
Laminar mixing/Streamline mixing: When two dissimilar liquid are mixed through a laminar flow, the shear that is generated stretches the interface between them. In this mechanism layers folds on themselves. As a result, the number of layers, and therefore interfacial area between them, increases exponentially with time.
Molecular diffusion: The mechanism responsible for mixing at molecular level is the diffusion resulting from thermal movement of molecules.
Primary mechanism responsible for mixing at the molecular level is the thermal motion of molecules. Governed by Fick's fist law of diffusion,
$dm/dt = - DA\ dc/dx$
Where,
dm/dt – rate of transport of mass across a surface area
D – Diffusion Co-efficient
A – Area across which diffusion is occurring
dc/dx – Concentration gradient
Mechanisms of Semi-Solid Mixing:
The mechanisms involved in mixing semi solids depend on the character of the material

which may show considerable variation. Many semi solids form neutral mixtures having no tendency to segregate although sedimentation may occur. Three most commonly used semi solid mixers are

(a) Sigma blade mixer – Contains two blades which operate in a mixing vessel which has a double trough shape, the blades moving at different speeds towards each other. Used for products like granulation masses and ointments.

(b) Triple-roller mill – The differential speed and narrow clearance between the roller develop high shear over small volumes of material. The roller mills are generally used to grind and complete the homogeneity of ointments.

(c) Planetary mixers – it utilizes a mixing arm rotating about its own axis and also about a common axis usually the centre of the mixing wheel. The blades provide the kneading action, while the narrow passage between the blades and the wall of the can provides shear.

MIXER SELECTION

Factors to be taken into consideration while selecting a mixing equipment include,
(a) Physical properties of materials to be mixed such as density, viscosity and miscibility
(b) Economic considerations – operating efficiency, cost and maintenance
One of the first things to determine is if the process is intended to be a batch or a continuous process, each of which can have its advantages and drawbacks depending on the load to be used. Size is considered keeping in mind the optimal working volume, fill level and residence time. The optimal working volume would depend on the construction of the mixer. It generally lies between 50 to 70 percent of the maximum. Similarly, too much of fill would lead to low mixing and hence fill level becomes important. Residence time which is defined as the amount of time ingredients are in the mixer and is a particularly important determinant of the size of a continuous mixer [4]. Choice of agitators determines the efficiency in breaking up lumps/agglomerates and serves to add shear aiding the final dispersion. A brief table showing various agitator types and their respective uses in shown below-

1. **Ribbon** - For Powders, granules, some slurries, mainly free flowing
2. **Paddle** - For Powders, granules, some slurries, free flowing, light pastes
3. **Sigma** - For Sticky materials, thick pastes and slurries

MIXING INDICES

The selection of a mixer depends on the mixing index or degree of mixing. Mixing index involves the comparison of standard deviation of sample of a mixer under study with estimated standard deviation of a completely random mixture [1].
Mixing index is expressed by Lacey. Two of them are

$$Mixing\ index, M = \frac{Standard\ deviation\ of\ random\ blend}{Standard\ deviation\ of\ the\ sample\ blend} = \frac{\sigma_R}{\sigma}$$

$$Mixing\ index, M = \frac{\sigma_0 - \sigma}{\sigma_0 - \sigma_R}$$

Where $\sigma_0 = standard\ deviation\ of\ unmixed\ powde.$
The ratio will be less than 1. The higher the M value, the greater the homogeneity. The above equations are used to determine homogeneity in a mixture depending on the objectives at hand. The selection of a particular equation is essential when the mechanism of mixing is being results of practical use can be achieved by using statistical analysis.

The differences may indicate poor or inadequate sampling, inappropriate mixing operation, improper handling of the powder sample, unsuitably of the mixer, operational condition etc.

Before mixing has begun, the material in the mixer exists in two layers, one of which contains no tracer material and one of which is tracer only. Under these conditions, the standard deviation at zero time σ_0 may be expressed as:

$$\sigma_0 = \sqrt{a(1-a)}$$

Where$a = overall\ fraction\ of\ tracer\ in\ the\ mixture.$

DOUBLE CONE BLENDER

Principles of Double Cone Blender:

The Double Cone Blenders design is most often used for the intimate dry blending of free flowing solids. The solids being blended in these units can vary in bulk density and in percentage of the total mixture. Materials being blended are constantly being intermixed as the Double Cone rotates. Normal cycle times are typically in the range of 10 minutes; however, they can be less depending on the difficulty of blending. The slant double cone design eliminates dead spots which occasionally occur in conventional double cone mixer. The conical shape at both end enables uniform mixing and easy discharge.

Construction of Double Cone Blender:

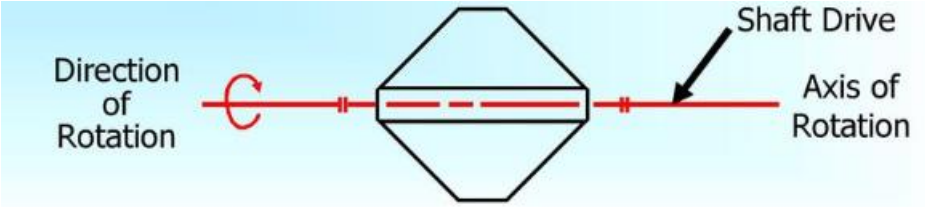


Fig. 8: Double Cone Blender

- The conical shape at both ends enables 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 product, paddle type baffles can be provided on the shaft.
- Flame proof electricals can be provided as optional.
- 'Slant' design (off centre) CLIN CONE BLENDER are also used.
- Dust free bin charging system ensures minimum material handling.
- Mixing, uniform blending and de-agglomeration.

Working of Double Cone Blender:

- **Double Cone Blenders** are most often used for dry blending of free flowing solids. The solids being blended in these units can vary in bulk density and in percentage of the total mixture.
- Materials being blended are constantly being intermixed as the **Double Cone** rotates.

Uses of Double Cone Blender:

- **Double cone blender** is used to produce homogeneous solid-solid mixture.
- It is used for effective mixing of powder and granules.

- The double cone blender machine is of canonical shape at both ends that provide uniform mixing of granules in bulk.

Merits of Double Cone Blender:

- If fragile granules are to be blended, double cone blender is suitable because of minimum attrition.
- They handle large capacities.
- Easy to clean, load, and unload.
- This equipment requires minimum maintenance.

Demerits of Double Cone Blender:

- Double cone blender needs high head space for installation.
- It is not suitable for fine particulate system or ingredients of large difference in particle size distribution, because not enough shear is applied.
- If powders are free flowing, serial dilution is required for the addition of low dose active ingredients.

TWIN SHELL BLENDER OR V CONE BLENDER

Principle of Twin Shell Blender:

The mixing occurs due to tumbling motion.

Construction of Twin Shell Blender:

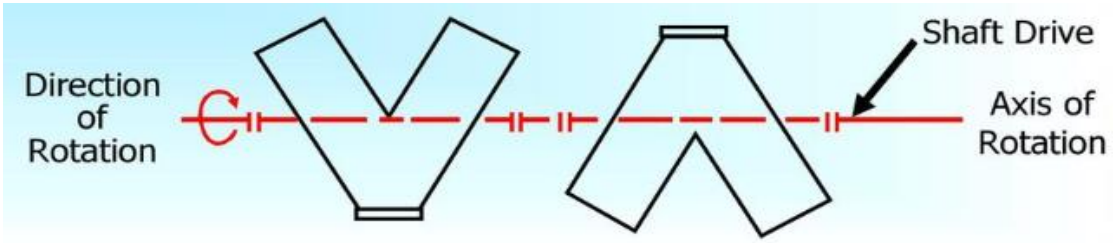


Fig. 9: Twin Shell Blender

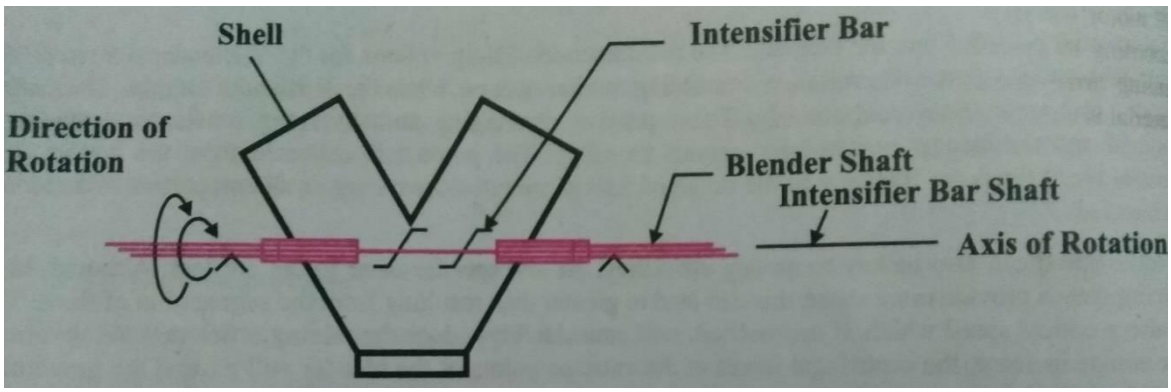


Fig. 10: V Blender with Intensifier Bar

- **Twin shell blenders** have two connected blending **shells** that are connected to form a V-shape. Intensifier bars are designed to break up clumps of solids while the product is separated in the two ends of the V (when the **twin shell blender** is upside down).
- It consists of horizontal shaft rotated about an axis causing the particles within the mixer to tumble over each other onto the mixture surface.
- The charging of materials into the V-Blender is through either of the two ends.

- Batches from 20 kg to 1 tonne can be loaded for mixing depending upon the size of the equipments.

Working of Twin Shell Blender:

- The V-**Blender** (also known as a **twin shell blender**) is one of the most commonly used tumbling **blenders**.
- The material is loaded into the blender.
- As the V-**blender** tumbles, the material continuously splits and recombines, with the mixing occurring as the material free-falls randomly inside the vessel.
- Tumble **blenders** rely upon the action of gravity to cause the powder to cascade within a rotating vessel.
- The recommended filled-up volume for the V-Blender is 50 to 60% of the total blender volume.
- The product is collected from the bottom of V.
- Normal blend times are typically in the range of 5 to 15 minutes depending on the properties of materials to be blended.

Marist of Twin Shell Blender or V Cone Blender:

V Cone Blender without Baffle-

- Have large capacities
- Easy handling
- Minimum maintenance

V Cone Blender with Baffle-

- Wet and dry mixing
- High shearing force
- Serial dilution is not required

Marist of Twin Shell Blender or V Cone Blender:

V Cone Blender without Baffle-

- High head space for installation
- Not suitable for fine particulate system
- Serial dilution is required

V Cone Blender with Baffle-

- Size reduction
- Cleaning problem
- Sealing problem

Uses of Twin Shell Blender or V Cone Blender:

- V blenders are used for dry mixing.
- It provides efficient blending in short time.
- This blender is often used for pharmaceuticals. But not suitable for very soft powders or granules.
- V blenders are generally used for the food products, milk products, dry flavors, pesticides and herbicides, animal feed, spice blends, baby foods and cosmetics.

RIBBON BLENDER

Principle of Ribbon Blender:

- The mechanism of mixing is shear which is transferred by moving blades (ribbon shaped) in a fixed (non-movable) shell.
- Convective mixing is the macro movement of large portions of the solids.

- Convection mixing occurs when the solids are turned over along the horizontal axis of the agitator assembly.
- High shear rates are effective in breaking lumps and aggregates. An equilibrium state of mixing can be achieved.

Construction of Ribbon Blender:

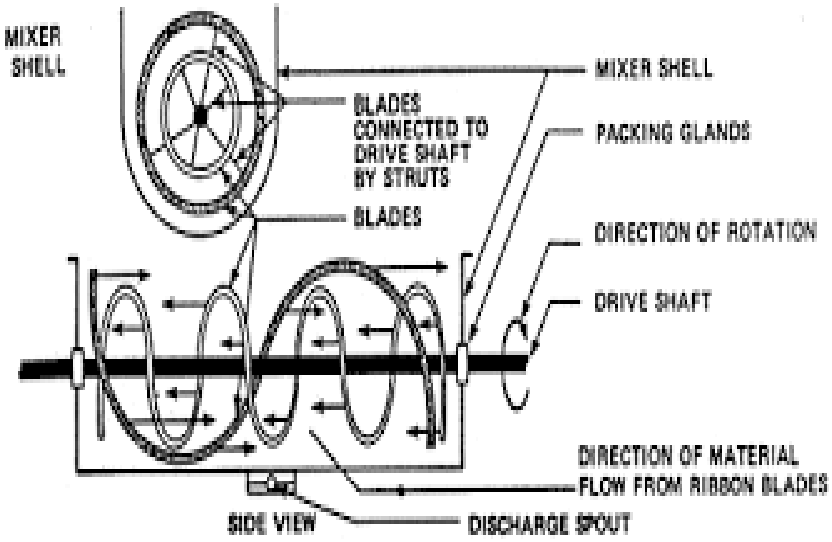


Fig. 11: Ribbon Blender

- A **ribbon blender** consists of a U-shaped horizontal trough (shell) containing a double helical **ribbon** agitator that rotates within.
- The agitator's shaft is positioned in the centre of the trough and has welded spokes on which the helical **ribbons** (also known as spirals) are welded.
- The blades have both right- and left-hand twists.
- The blades are connected to a fixed speed drive.
- The ribbon blender is top loading with a bottom discharge port.
- The trough can be closed with a lid.

Working of Ribbon Blender:

- Different powders are introduced from the top of the trough.
- The outer ribbon of agitator moves the material from the ends to centre while the inner ribbon moves the material from the centre to end.
- Through the fixed speed drive, ribbons are allowed to rotate.
- Radial movement is achieved because of the rotational motion of the ribbons.
- The difference in the peripheral speeds of the outer and inner ribbon results in axial movement, homogenous blending is achieved in short time.
- The powders are lifted by a centrally located vertical screw and allowed to cascade to the bottom of the container (tumbling action).
- The counter acting blades set up high shear and are effective in breaking up lumps or aggregates.
- Helical blades move the powders from one end to another.
- The blend is discharged from the bottom opening [17].

Merits of Ribbon Blender:

- The Ribbon mixer has price savings as a result of the thermal treatment is accomplished among a similar time and liner being utilized for combining step.

- Correct management of batch thermal treatment time. Low opportunity cost because the drying is accomplished within the same time and vessel getting used for transferring and combining.
- One of the most important benefits of using a ribbon mixer for any industrial project is that it blends nearly any material completely with nearly no flaws.
- This comes in handy for producing any material that must be mixed well like paint, concrete, and foods.
- These mixers are usually utilized in bakeries that require to blend large amounts of ingredients at only once. They will additionally mix materials fairly quickly, although the ribbons themselves inch.
- Finally, the common ribbon mixer features a very large trough, thus it's ideal for big projects.
- High shear is also applied by exploitation perforated baffles that create a rubbing and breakdown aggregates. Headroom needs less aera.
- Protect the motor and ribbon mixer from overload.
- Once the load is just too massive to the drum and rotates, the operating liquid is ejected from the liquid plug to separate the operating machine and therefore the load, in order that the motor and instrumentality won't be broken once beginning and overloading.
- The speed distinction caused by the impact is going to be mitigated by coupling.

Demerits of Ribbon Blender:

- The hydraulic mechanical device isn't loaded with the electrical converter generally, and may not modify the rotating speed of the ribbon mixer effectively, because the loading of hydraulic couplings is simple to make multiple transfer mechanical energy, leading to power consumption, thus it can't improve the start-up performance of the ribbon mixer.
- It is a poor mixer as a result of the movement of particles is two dimensional.
- Shearing action is a smaller amount than in planetary mixer.
- It has a set speed drive.
- Rate of mixing is greater at the surface, causing local differences in mixture composition.
- Attrition of particles may occur at the wall due to the higher forces present there.
- Prone to dead spots, especially near the discharge valve, and along the central axis.
- There aren't many downsides to using a ribbon mixer to combine ingredients. the sole major disadvantage that you simply may realize is that a ribbon mixer takes large amounts of power to work properly, thus you must positively detain mind your energy desires if you're about to use one in every of these machines.

Uses of Ribbon Blender:

- Ribbon blender is used to mix finely divided solids, wet solid mass, sticky and plastic solids.
- Uniform size and density material can be easily mixed.
- It is used for liquid-solid and solid-solid mixing.

SIGMA BLADE MIXER

Principle of Sigma Blade Mixer:

- The mechanism of mixing is shearing.
- The inter meshing of sigma shaped blades creates high shear and kneading actions.

- The mixing action is a combination of bulk movement, shearing, stretching, folding, dividing, and recombining as the material is pulled and squeezed against blades, saddle, and side walls.
- This is used for high viscosity material.

Construction of Sigma Blade Mixer:

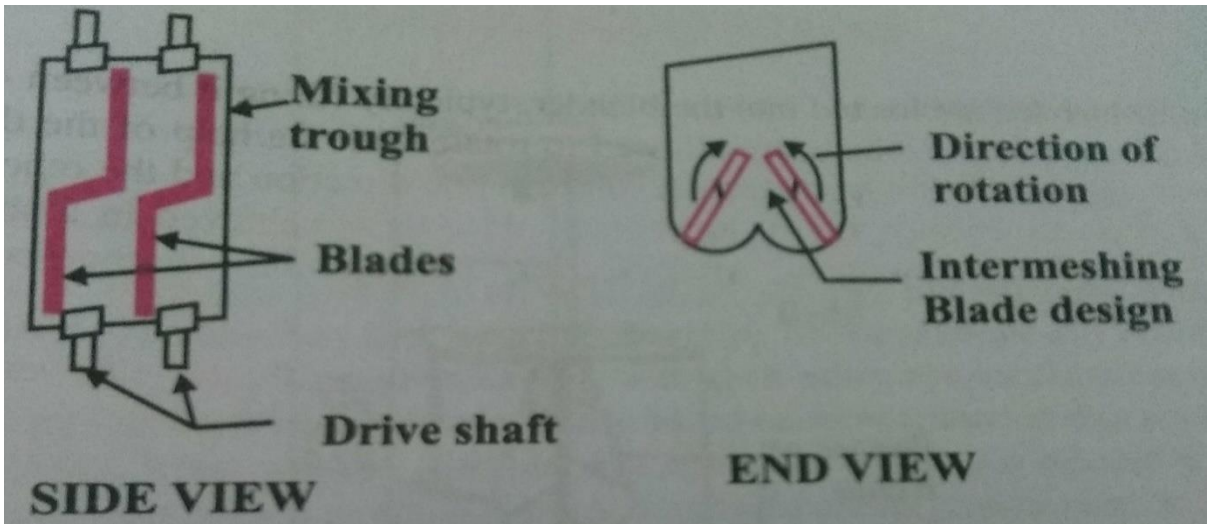


Fig. 12: Construction of Sigma Blade Mixer

- A ribbon blender consists of a u-shaped horizontal trough or shell containing a helical double ribbon agitator that rotates inside.
- The shaft of agitator is positioned in the centre of the trough on which the helical ribbons are welded.
- Since the ribbon stirrer consists of a set of internal and external helical ribbons, it is also called a double helical ribbon agitator.
- The ribbon blenders are powered by a drive system consisting of a motor, a gear box and couplings.
- These are powered by 10 HP to 15HP motor for 100Kg of product mass to be blended.
- The specific power ranges from 3 to 12 KW/M^3 according to the products to be mixed.

Working of Sigma Blade Mixer:

- Different powders are introduced from the top of the trough.
- The body is covered because considerable dust may be involved during dry blending and granulating solution may evaporate during wet granulation.
- Through the fixed speed drive, the sigma blades are allowed to rotate.
- The blade moves at different speeds.

Merits of Sigma Blade Mixer:

- Sigma blade mixture creates a minimum a dead space during mixing.
- Ideal for mixing, kneading of high viscous mass, sticky and dough like products.
- Extruding.
- These mixers and their variants are capable of handling viscosities as high as 10 centipoises.

Demerits of Sigma Blade Mixer:

- Sigma blade mixer works at a fixed speed.

- Power consumption in double arm kneader is very high compared to other type of mixer and range from 45 to 75 KW/m^3 of mix material.

Uses of Sigma Blade Mixer:

- The sigma blade mixer is a commonly used mixer for high viscosity materials.
- Sigma blade mixer is used for wet granulation process in manufacturing of tablets, pill masses and ointments.
- It is primarily used for solid-liquid mixing and also for solid-solid mixing.

PLANETARY MIXER

Principle of Planetary Mixer:

The principle of planetary mixers is very simple, which usually have two or three multi-hinged blades, when the paddles are revolution and rotation running at the same time, so that the material will flows up and down as well as around the inner cylinder, which can reach the mixing effect in a very short time. It is also known as change can mixer [4].

Construction of Planetary Mixer:

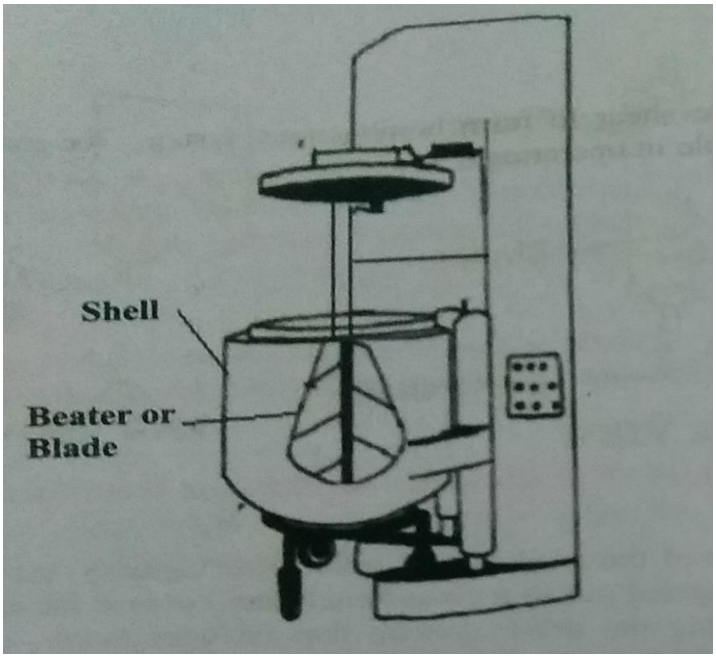


Fig. 13: Construction of Planetary Mixer

- It consists of a vertical cylindrical shell, which can be removed either by lowering it beneath the blade or raising the blade above the bowl.
- The mixing blade is mounted from the top of the bowl.
- The mixing shaft if driven by a planetary gear train.
- It rotates around the ring gear, which further rotates round the mixer blade.
- It is normally built with a variable speed drive.

Working of Planetary Mixer:

- The material to be mixed is loaded in mixing bowl.
- The blade rotates on their own axis when they orbit the mixing bowl on a common axis. Therefore, there is no dead space in the mixing and high shear is applied for mixing.

- After mixing, the material is discharged through a bottom valve, or by manual scooping of the material from the bowl.

Merits of Planetary Mixer:

- Simple construction, operation, and relatively low cost.
- No dead spot in the mixing.
- Rotation speed of the blade can be varied.
- Used for wet granulation process.
- High mixing efficiency.

Demerits of Planetary Mixer:

- Requires high power.
- Heat build-up within powder mix.

Uses of Planetary Mixer:

- Planetary mixture produces precise blends in addition to breaking down of agglomerates rapidly.
- Low speeds are used for dry blending and kneading action is required in wet granulation.
- Steam jacketed bowls are used in manufacture of sustained released products and ointments.

PROPELLERS

Propellers are the mechanical device that are used to mix liquid materials using blades
A three bladed design is generally used for liquids [1].

Principle of Propeller Mixer:

- The propeller mixer mainly works on the principle of shearing force.

Construction of Propeller Mixer:

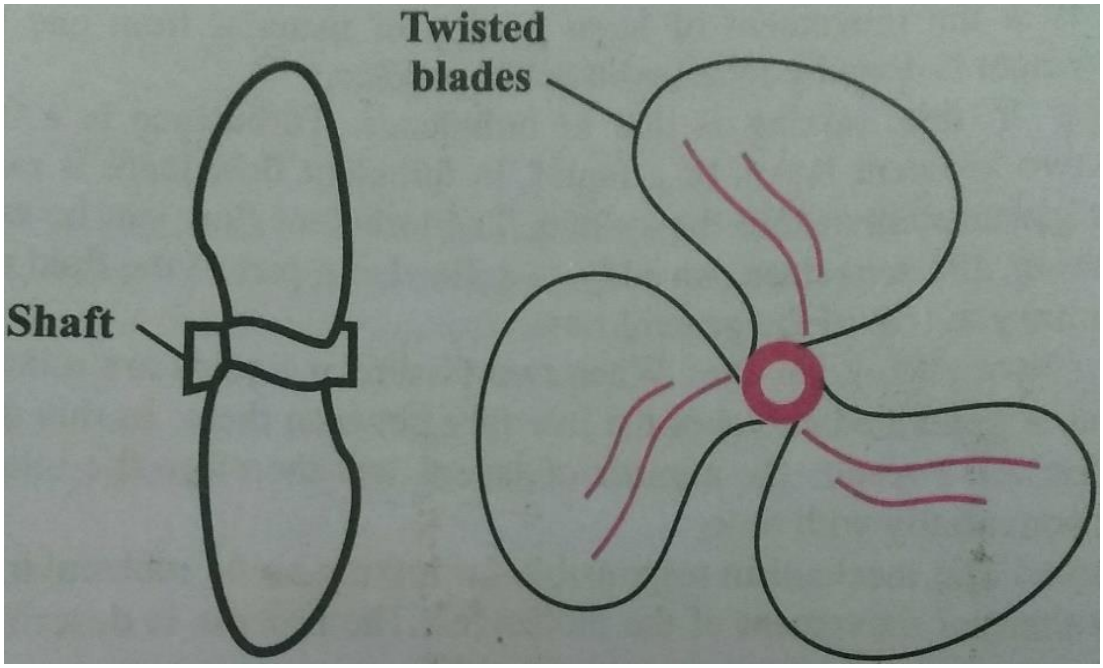


Fig. 14: Three Bladed Design Propeller

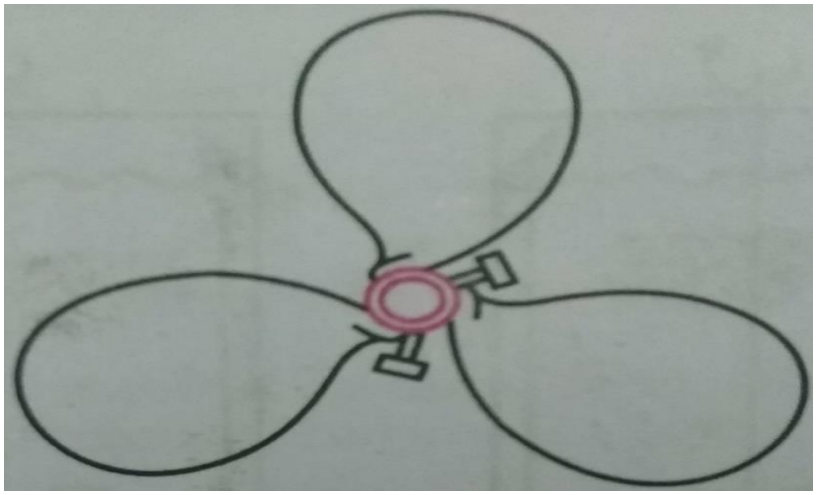


Fig. 15: Marine type Propeller

It consists of vessel and propeller.
A propeller has angled blades, which cause the fluid to circulate in both an axial and radial direction.
Size of the propeller is small and many increases up to 0.5meters depending on size of tank.
Small size propeller can rotate up to 8000 rpm.

Working of Propeller Mixer:

- A vortex forms when a centrifugal force is imparted to the liquid by the propeller blades cause it to backup ground the sides of the vessel and creates a depression at the shaft.
- As the speed of the rotation is increased air may be sucked in to the fluid by the formation of a vortex this causes frothing and possible oxidation.
- Another method supressing vortex is to fit vertical baffles in to the vessel.
- Installation of vertical propeller reduces the vortex to considerable extent.
- Vertical propeller mixer consists of three blades (4 ft long).
- **Horizontal or Inclined Propeller or Marine Propeller** are also used on side entry mixers.They are mounted with the impeller shaft inclined at an angle to the vessel axis to improve the process results.They provide good blending capability in small batches of low to medium viscosity.

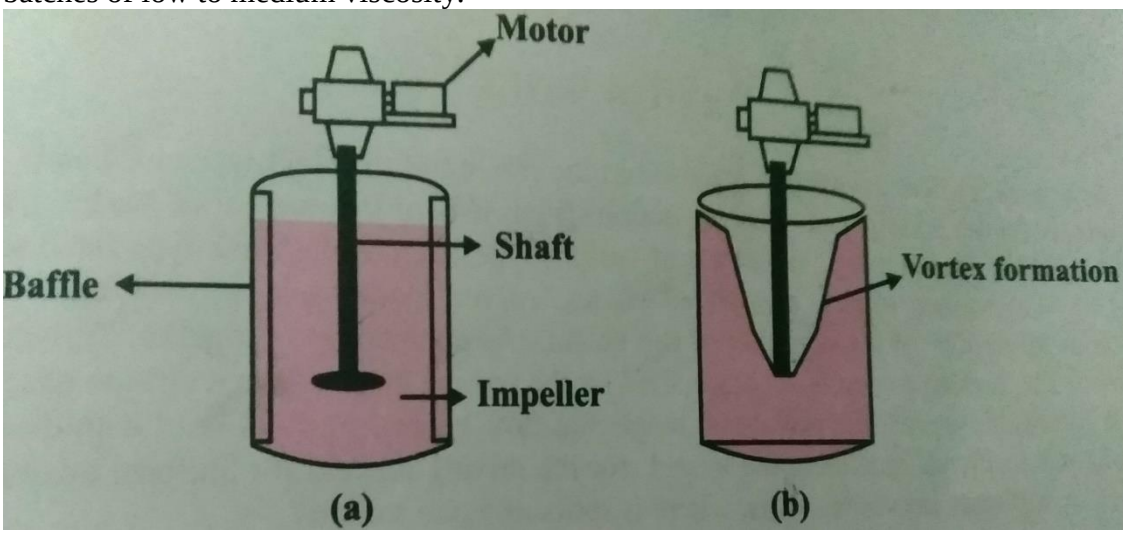


Fig. 16: (a) Baffled tank with no vortex formation; (b) Unbaffled tank having vortex formation

Merits of Propeller Mixer:

- Propeller is effective when high mixing capacity is required.

Demerits of Propeller Mixer:

- Propellers are not effective for liquids having viscosity greater than 5.0 Pascal second.
- Equipment cost is high.

Uses of Propeller Mixer:

- Propeller mixer used for mixing liquid having maximum viscosity of 2.0 pascal second, for mixing of low viscosity emulsions and also used in mixing suspensions with particle size up to 0.1 to 0.5 mm.

TURBINES

Principle of Turbine Mixer:

A turbine mixer is a mechanical device that is used in mixing different type of liquids.
The turbine mixer works mainly on the principle of shearing action.

Construction of Turbine Mixer:

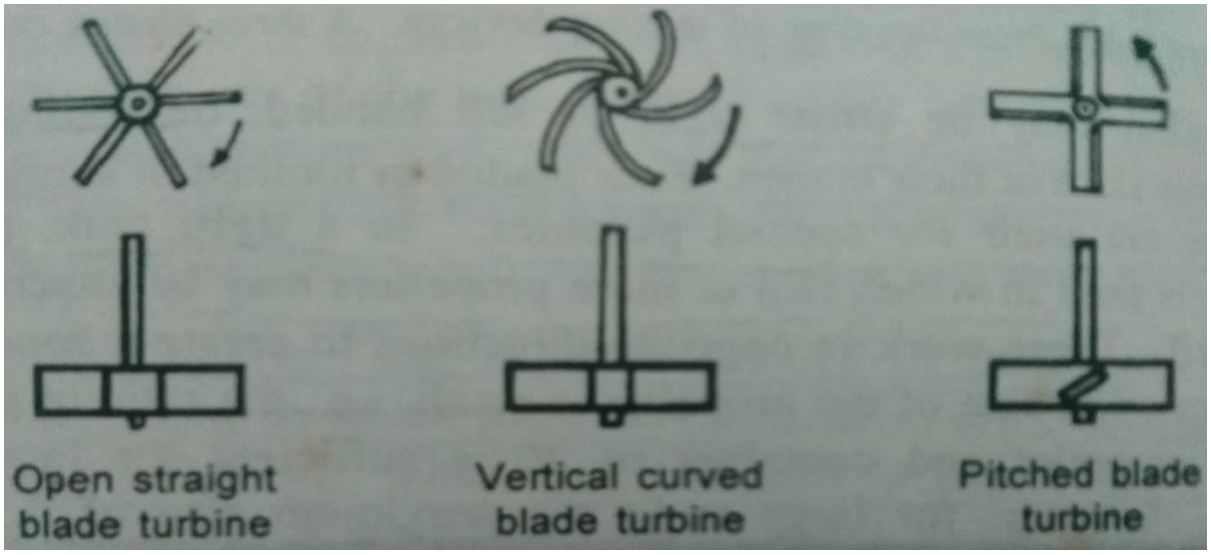


Fig. 17: Different types Turbines

- Turbine consists of number of blades attached to the circular disk.
- The blades used in the mixture are of various types: flat blades, disk-type flat blades, inclined blades, curved blades, arrow headed blades, and so on.
- The diameter of turbine varies from 30 to 50 percentage of the diameter of vessel.
- As compared to propeller turbines rotates at lower speed.

Working of Turbine Mixer:

When turbine mixer operates at sufficiently at high rotational speeds, the radial tangential flow becomes pronounced with the formation of vortex.
It is necessary to install baffles in the vessel for the mixing process for uniform mixing.
The radial flow of the impeller impinges on vessel walls, where it slits in to two streams.

Merits of Turbine Mixer:

- Turbines give greater shearing force than propeller.
- Therefore, turbines are suitable for emulsification.

Demerits of Turbine Mixer:

- Turbines have less pumping rate.

Uses of Turbine Mixer:

- A turbine mixer suitable for viscous fluids (7.0 pascal-second).
- Turbines used for thin paste and emulsification.
- Turbines can also be used to handle slurries with 60 percentage solids.
- Mainly used for semisolid materials.

PADDLES

Principle of Paddles:

- Paddles consist of two long flat blades attached vertically to a shaft.
- IT rotates at low speed.
- Paddle mixer is suitable to mix viscous liquids or semisolids.

Construction of Paddles:

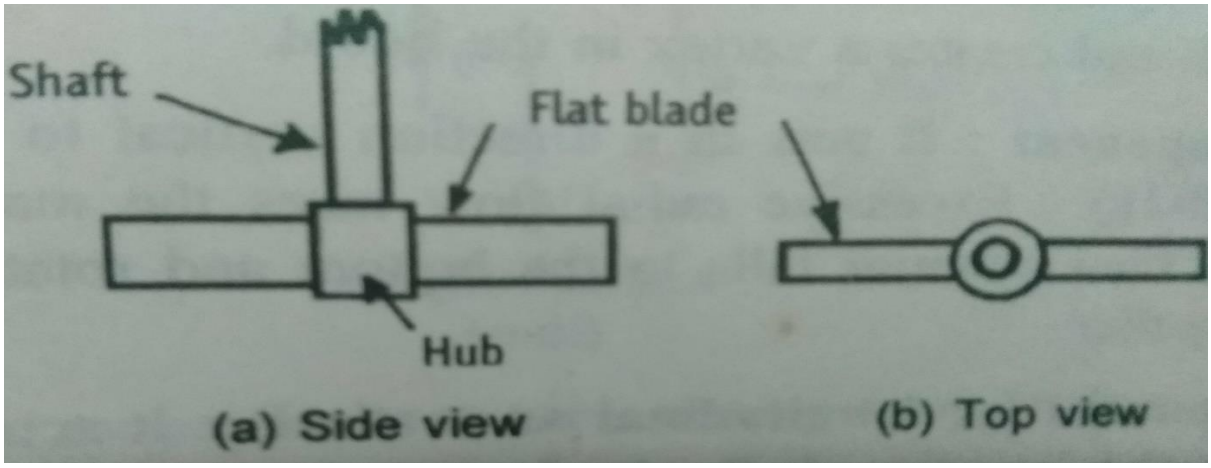


Fig. 18: Paddle type of Agitator or Impeller

- Blades used in this mixer are dished or hemispherical in shape.
- The diameter of paddle is 50-80 percentage of inside diameter of vessel.

Working of Paddles:

- Paddles push liquid radially and tangentially.
- There is no axial movement of flow during mixing.

Merits of Paddles:

- Vortex formation is not possible.
- It has low speed.
- Mixing efficiency is better.
- No dead spots and deposited solids.

Demerits of Paddles:

- Here suspension mixing is poor.
- Baffled tanks are required.

Uses of Paddles:

- Paddles are used in the manufacture of antacid suspensions (aluminium hydroxide gel and magnesium hydroxide), agar and pectin related purgative, antidiarroheal mixtures such as bismuth-kaolin.

SILVERSON EMULSIFIER

Principle of Silverson Emulsifier:

The silverson homogenizer works on the principle that the large globules in a course emulsion are broken in to smaller globules by intensive shearing forces and turbulence by high speed rotors [1].

Construction of Silverson Emulsifier:

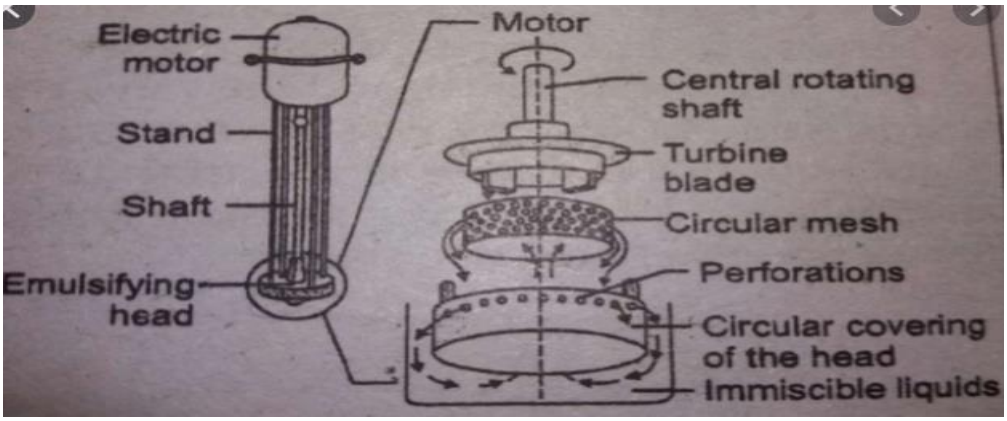


Fig. 19: Silverson Emulsifier

- It consists of emulsifier head.
- The emulsifier head consist of a number of turbine blades.
- The blades are surrounded by mesh which is enclosed by cover having perforations.
- The blades are rotated by using electric motor fitted at the top.
- There is also one shaft whose one end is connected to motor and other end is connected to head.

Working of Silverson Emulsifier:

- The emulsifier head is dipped in to the vessel containing immiscible liquids.
- When the motor is started, shaft rotates the head.
- Therefore, turbines blades also rotate at very high speed.
- The liquids are sucked trough the fine holes.
- The complex flow pattern can cause droplet break up under either laminar or turbulent conditions
- Centrifugal force expels the content through mesh and then to cover and subjects them to mechanical shear.
- This is followed by intense hydraulic shear.
- The oil is reduced in to globules quickly resulting in a homogenous uniform product.
- Then the fine emulsion emerge trough opening of cover.
- As a result, bigger globules rapidly break in to smaller globules [18], [19].

Merits of Silverson Emulsifier:

- Fast and efficient.
- They are used to get a fine droplet or particle size (2-5 microns).
- Process efficiency is good.
- Low operating cost.

Demerits of Silverson Emulsifier:

- Chance of chocking of pores of mesh.

Uses of Silverson Emulsifier:

- Used in preparation of creams, ointments, pharmaceutical suspension and emulsion of fine particle size.

REFERENCES

[1] C. V. S. Subramanyam, T. J. Setty, S. Suresh, and K. V Devi, " *Vallabh prakashan, Delhi*, vol. 9, pp. 70–120, 286-318, 2005.

[2] W. L. Badger, "Introduction to chemical engineering," pp. 469–519, 605-617,1955.

[3] H. Sabarez, "Advanced Drying Technologies of Relevance in the Food Industry," 2020.

[4] W. L. Mc Cabe, J. C. Smith, and P. Harriott, *Unit operation of chemical engineering*. McGraw-Hill, pp. 238-264, 773–810, 2018.

[5] N. Haque, S. V Jangam, and A. S. Mujumdar, "Life Cycle Assessment of Drying Systems," in *Handbook of Industrial Drying*, CRC Press New York, USA, 2015, pp. 1229–1238.

[6] K. Sambamurthy, *Pharmaceutical engineering*. New Age International, pp. 295–328, 279-396, 2007.

[7] L. Lachman, H. A. Lieberman, and J. L. Kanig, *The theory and practice of industrial pharmacy*. Lea & Febiger, pp. 3–30, 89-107, 2009.

[8] J. P. Remington, *Remington: The science and practice of pharmacy*, vol. 1. Lippincott Williams & Wilkins, pp. 453–757, 2013.

[9] S. K. Patel and M. H. Bade, "Energy targeting and process integration of spray dryer with heat recovery systems," *Energy Convers. Manag.*, vol. 221, p. 113148, 2020.

[10] A. F. McDonagh and L. Tajber, "The control of paracetamol particle size and surface morphology through crystallisation in a spray dryer," *Adv. Powder Technol.*, vol. 31, no. 1, pp. 287–299, 2020.

[11] M. B. Gonzatti *et al.*, "Nano spray dryer for vectorizing α-galactosylceramide in polymeric nanoparticles: A single step process to enhance invariant Natural Killer T lymphocyte responses," *Int. J. Pharm.*, vol. 565, pp. 123–132, 2019.

[12] C. Srinivasakannan and N. Balasubramanian, "An analysis on modeling of fluidized bed drying of granular material," *Adv. Powder Technol.*, vol. 19, no. 1, pp. 73–82, 2008.

[13] J. Burgschweiger and E. Tsotsas, "Experimental investigation and modelling of continuous fluidized bed drying under steady-state and dynamic conditions," *Chem. Eng. Sci.*, vol. 57, no. 24, pp. 5021–5038, 2002.

[14] W. Senadeera, O. Alves-Filho, and T. Eikevik, "Influence of drying conditions on the moisture diffusion and fluidization quality during multi-stage fluidized bed drying of bovine intestine for pet food," *Food Bioprod. Process.*, vol. 91, no. 4, pp. 549–557, 2013.

[15] R. Daoussi, S. Vessot, J. Andrieu, and O. Monnier, "Sublimation kinetics and sublimation end-point times during freeze-drying of pharmaceutical active principle with organic co-solvent formulations," *Chem. Eng. Res. Des.*, vol. 87, no. 7, pp. 899–907, 2009.

[16] D. Colucci, R. Maniaci, and D. Fissore, "Monitoring of the freezing stage in a freeze-drying process using IR thermography," *Int. J. Pharm.*, vol. 566, pp. 488–499, 2019.

[17] T. A. H. Simons, S. Bensmann, S. Zigan, H. J. Feise, H. Zetzener, and A. Kwade, "Characterization of granular mixing in a helical ribbon blade blender," *Powder Technol.*, vol. 293, pp. 15–25, 2016.

[18] C. J. U. Espinoza, F. Alberini, O. Mihailova, A. J. Kowalski, and M. J. H. Simmons, "Flow, turbulence and potential droplet break up mechanisms in an in-line Silverson 150/250 high shear mixer," *Chem. Eng. Sci. X*, vol. 6, p. 100055, 2020.

[19] S. Hall, A. W. Pacek, A. J. Kowalski, M. Cooke, and D. Rothman, "The effect of scale and interfacial tension on liquid–liquid dispersion in in-line Silverson rotor–stator mixers," *Chem. Eng. Res. Des.*, vol. 91, no. 11, pp. 2156–2168, 2013.