

Mixing Process (S/L)



Prepare by:
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Definition of Mixing:

- ❖ A process of intermingling of two dissimilar proportions of materials to attain a desirable uniformity either physical or chemical in the final product.
- ❖ Mixing may be defined as a unit operation in which two or more components, in an unmixed or partially mixed state, are treated so that each unit (particle, molecule etc.) of the components lies as nearly as possible in contact with a unit of each of the other components.
- ❖ Mixing the random distribution, into and through one another, of two or more initially separate phases.

Objectives of mixing :

- ❖ To secure uniformity of composition and to ensure correct dose .

- ❖ To promote chemical and physical reactions by increasing the contact surface such as in dissolving, absorption, extraction.

❖ **To make the following products:**

- Solutions
- Emulsions
- Syrups
- Suspensions
- Pastes
- Creams
- Ointments
- Suppositories
- Capsules
- Tablets

Types of Mixtures:

1- Positive mixtures

2- Negative mixtures

3- Neutral mixing

TYPES OF MIXTURES AND ENERGY REQUIREMENTS

There are 3 types of mixtures:

1- Positive mixtures:

- Formed from materials such as, gases or miscible liquids.
- The materials mix spontaneously and irreversibly by diffusion
- No input of energy if time of mixing is unlimited, although time will be shorten if energy is supplied.
- Generally, these materials do not show any problems during mixing.

2- Negative mixtures:

- materials have the tendency to separate out from each other.
- Energy needs to be supplied to keep components adequately dispersed.
- Some separate faster, while for others, the separation is slower.
- **Examples:**
 - a) In a suspension, there is the dispersion of solid in the solution (fast separation)
 - b) Emulsions, creams and viscous suspension have a slow separation.
 - c) Are more difficult to be formed and require high degree of mixing efficiency.

3- Neutral mixtures:

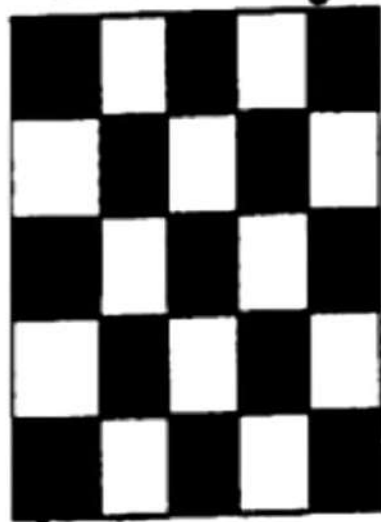
- Are static in behavior
- Neither mixing nor de-mixing occurs, unless acted upon by an external system of forces.
- **Examples are:**
 - a) Mixed powders
 - b) Pastes
 - c) Ointments.

Mixing of Powders

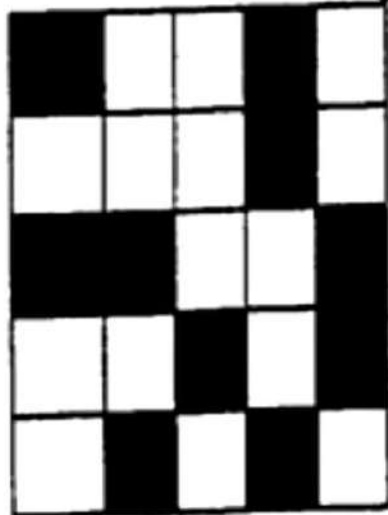
Degree of mixing :

Perfect mixing indicates that each particle of one component lies as nearly as possible in contact with a particle of each of the other ingredients.

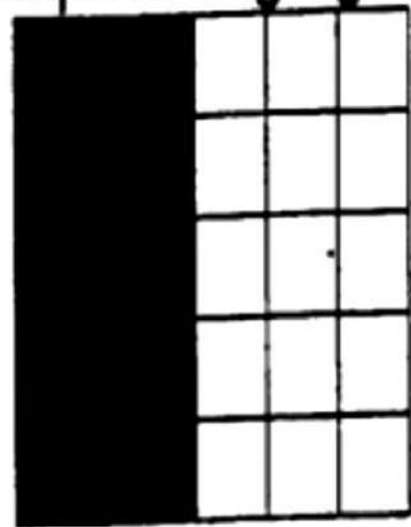
Ideal Mixing



Random Mixing



complete segregation



Scale of scrutiny :

- The term state of scrutiny was introduced to describe the minimum size of the regions of segregation.
- It is the smallest amount of a drug that can be mixed well .If the dose of the drug in the mixture is less than the scale of scrutiny, the normal mixing methods fail to attain efficient mixing. In this case geometric ,i.e., dilution mixing must be adopted .
- e.g. Tablet containing 100 mg of A and 100 mg of B, powders must be sufficient mixed so that on withdrawing any sample from the mixture, will contain the correct ratio of A & B (1:1).

Types of mixing

1- Solid-Solid mixing (S/L)

2- Liquid-Liquid mixing (L/L)

Factors affecting mixing of solids :

1- Particle size:

large or small particle size of the same or different materials tend to segregates the large particles will roll and flow over one another while the small particles will be dusted out or coat the surface of large particles: particles with no uniformity in size will segregate.

To overcome this:

- 1- Slow rotating of mixers to prevent aerated mixing.
- 2- Operate the mixer under vacuum.
- 3- Use powders of the same particle size.

2- Density difference: Heavy particles settle to the bottom of the mixer and light ones rise and dust out (minimizing by keeping particle size uniform and small)

3-Electrostatic charge:

It produced by friction of particles and present on the surface of particles will result in unblending.

It can be prevented :

A- stop mixing when satisfactory blend has been obtained

B- Add SAA if permissible to wet particles and neutralize the surface charges.

C- Add small amount of water.

Why addition of H₂O isn't acceptable?

1- drying is required.

2- aggregation occur → size reduction is required also.

1- Solid-Solid Mixing

Mechanisms of S-S mixing:

Solid mixing proceeds by the combination of one or more mechanism.

1. Convective mixing
2. Shear mixing
3. Diffusive mixing

1- Convective mixing:

- ❖ It is the transfer of a group of adjacent particles from one location in the mass to another. If a spatula is inserted into a heap of powder on a tile then a small pile may be withdrawn on the blade and deposited elsewhere in the mass of powder
- ❖ This type of mixing predominates in (horizontal ribbon mixer)
- ❖ Mechanism is analogous to bulk transport in fluid mixing.
- ❖ Convective mixing can occur by
 - a. An inversion of the powder bed
 - b. Blades or paddles
 - c. Revolving screw
 - d. Any method of moving relatively large mass of material from one part of the powder bed to another.

2- Diffusive mixing:

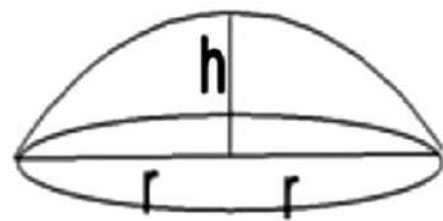
- ❖ By tilting the bulk of the material beyond its angle of repose \rightarrow slipping of the upper layers which lead to mixing of the powders.
- ❖ This type of mixing predominates in (tumbling mixers).

N.B :

The angle of repose gives an indication of the flowability of powders. Flowability increase as the angle decrease. $\Theta = h/r$ (h: height, r: radius).

If $\Theta < 30 \rightarrow$ good flowability.

If $\Theta > 30 \rightarrow$ poor flowability.



3- Shear mixing:

- ❖ **By causing shear forces in the material by using agitator arm.**
- ❖ **Depending on flow characteristic these can occur singly or in such a way to give rise to laminar flow.**
- ❖ **When shear occurs between regions of different composition and parallel to their interface, it reduce the scale of segregation by thinning the dissimilar layers.**
- ❖ **It thus reduces the scale of segregation.**

PROBLEMS RELATED TO MIXING.

Segregation

- ❖ Particles tend to segregate due to differences in the size, density, shape, and other properties of the particles of which they are composed.
- ❖ Powders that are not free-flowing or that exhibit high forces of cohesion or adhesion b/w particles are difficult to mix due to agglomeration.
- ❖ Clumps can be broken by use of mixers that generate high shear forces.
- ❖ However these are less susceptible to segregation due to high interparticulate forces that resist interparticulate motion leading to unmixing

PROBLEMS RELATED TO MIXING.

Segregation

- ❖ Problem of segregation is worse when one is working with free flowing, cohesion less, or nearly cohesion less particulate matter.
- ❖ Segregation has been also attributed by mixers.
- ❖ Those that generate principally convective motion have been classified as non-segregating.
- ❖ While those producing shear or diffusive mixing are classified as segregating.

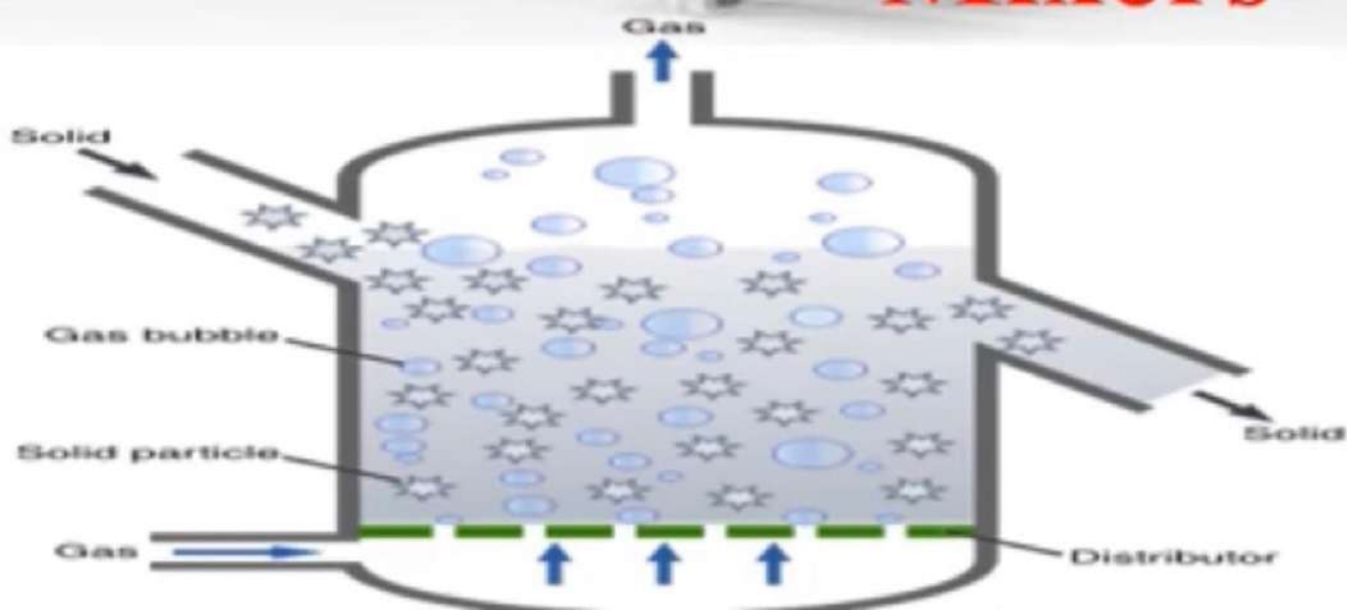
Evaluation of blend of powder:

Samples are taken using **sample thieves** → take samples without vibration of the powder.

- 1- **Microscopic Counting**: in case of small particle size and one particle differ from other.
- 2- **Analytical technique** : Such as dissolving and removing one of the constituents and with the residue.
- 3- **Screen analysis** : May be applicable in same cases when particle size of material mixed is different. Statistics method also may be used (variance and S.D)

Conditions for good mixing:

- 1- Optimum space:** to allow expansion and movement of powder, more space reduces mixing and increase time while over filling prevents mixing.
- 2- Suitable shear force:** to ensure that all the materials pass through the shearing zone.
- 3- Optimum mixing time :** depend on the scale of scrutiny.
- 4- After mixing :** the mixture must be handled carefully to avoid any vibrations to minimize segregation.



Types of powder mixers :

1- Tumbling mixers:

By tilting the material beyond its angle of repose.

- a. Barrel mixer,
- b. Cube mixer,
- c. Double cone
- d. V-mixer.

2- Agitator mixers:

Which shear is applied by means of agitating forces

e.g. Ribbon blender.

3- Special mixers:

- a. Nautamixer
- b. High shear mixer
- c. Impact wheel mixer

1- Tumbling mixers

- A. The mixer uses the gravity to give a flow and they operate by tumbling the material in a partially filled container rotating around a horizontal axis.**

- B. Diffusive mixing predominates: Used mainly for free flowing powder and granular material.**

1- Barrel mixer :

- ❖ Stainless steel.
- ❖ Shear force is low.
- ❖ End to end movement.
- ❖ baffles or helical plates may → interfolding of the material.

➤ Advantages:

- 1- easy cleaning.
- 2- easy design.
- 3- easy maintenance.



2- Cube mixer:

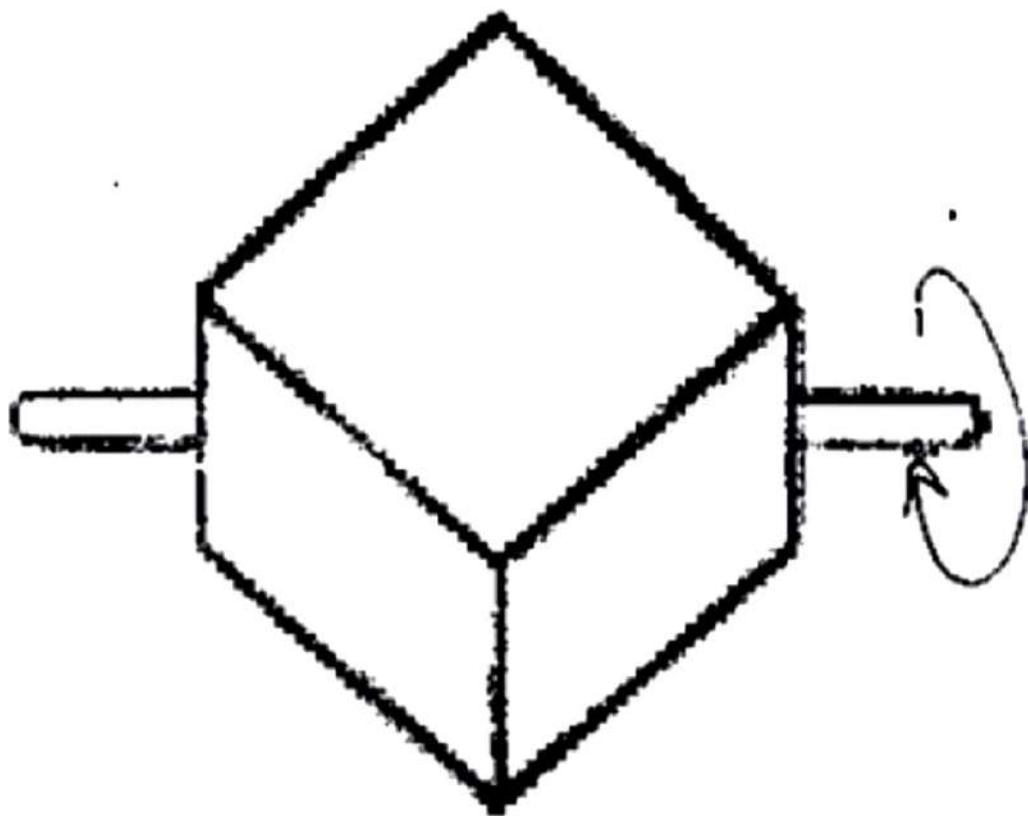
- High shear force due to corners.

Disadvantages:

- ❖ Has corners → difficult to clean.
- ❖ Has flat surface → powder reach its angle of repose.

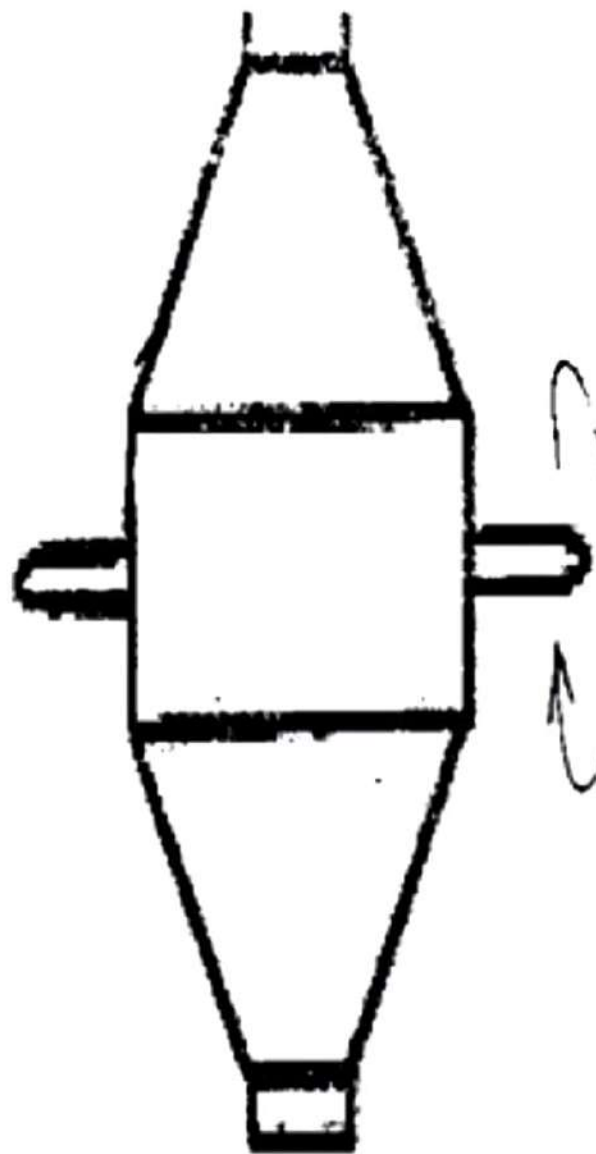
When 1 cone is added:

- 1- No flat surface → powder not reach its angle of repose.
- 2- No sharp corners → easily cleaned.



3- Double cone blender :

- 2 cones joined to each other to a relatively short cylindrical section
- and the axis of rotation is centrally located on the cylindrical portion. **Good cross flow is established by:**
 - 1- Constant changing flow cross- section as the vessel rotates.
 - 2- Inter folding of the material as it flow
 - 3- Easy to cleaned (no baffles)

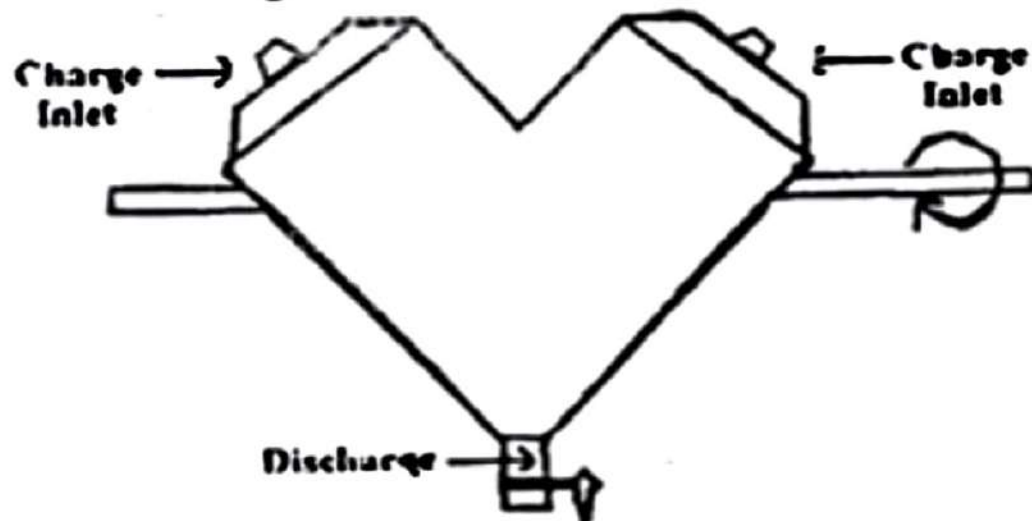


4- Twin - Shell Blender: (V-Shaped blender)

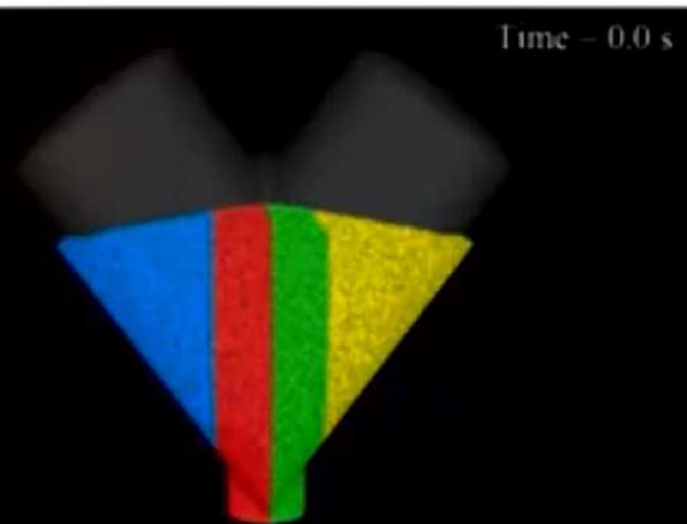
- ❖ The V-shaped blender provides a non symmetrical shape about the axis of rotation.
- ❖ Efficient blending occurs when the two inclined cylinders combine.
- ❖ Internal baffles may be provided to increase mixing efficiency.

Advantages:

- Can be easily cleaned.
- Easy maintenance.



Mixing



- Efficiency is dependent on speed of rotation.
- Optimum rotation is 30-100 rpm.

Factors to be considered in operating Tumbling mixers

1- Optimum speed should be used :

* Too low speed cause sliding only

* Too high speed leads to centrifugation hence segregation.

2- The mixer should be **charged** not more than **50%** of its total capacity to provide the required space for the expansion for the powder bed movement of particles

3- A perfect **method of charging** the powder into the mixer e.g. adding the components together as is the V-shaped mixer.

➤ **Advantages of tumbling mixers:**

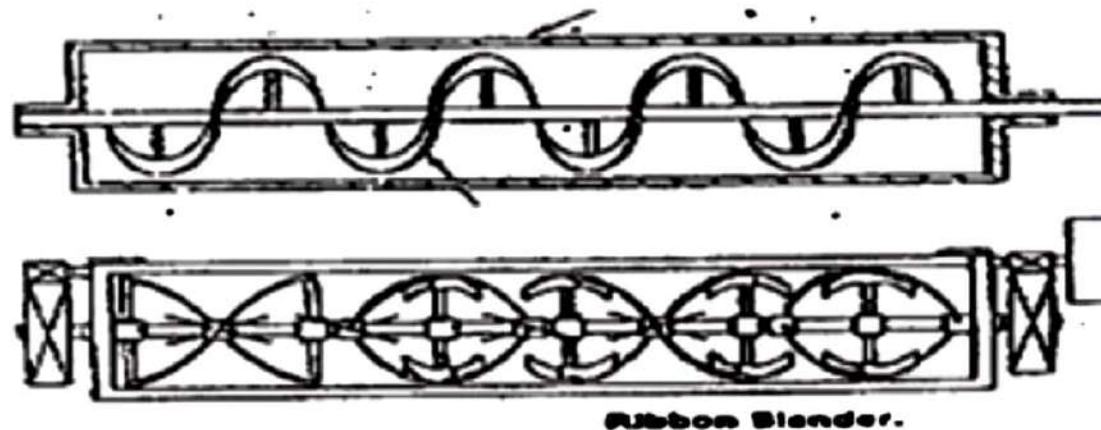
Suitable for mixing **friable materials** because of the mild forces involved

A- Agitator mixers : (ribbon mixer)

- It is a trough in which spiral ribbons or helical arm rotates to produce shear. Mixing is mainly convective mixing in addition to shear.
- The outer ribbon moves the material in one direction while the inner ribbon moves it in the opposite direction.

❑ Disadvantages of ribbon mixer :

- 1- Mixing is not highly efficient.
- 2- High power consumption.
- 3- It makes some grinding action
- 4- Can not be used for mixing fragile material.

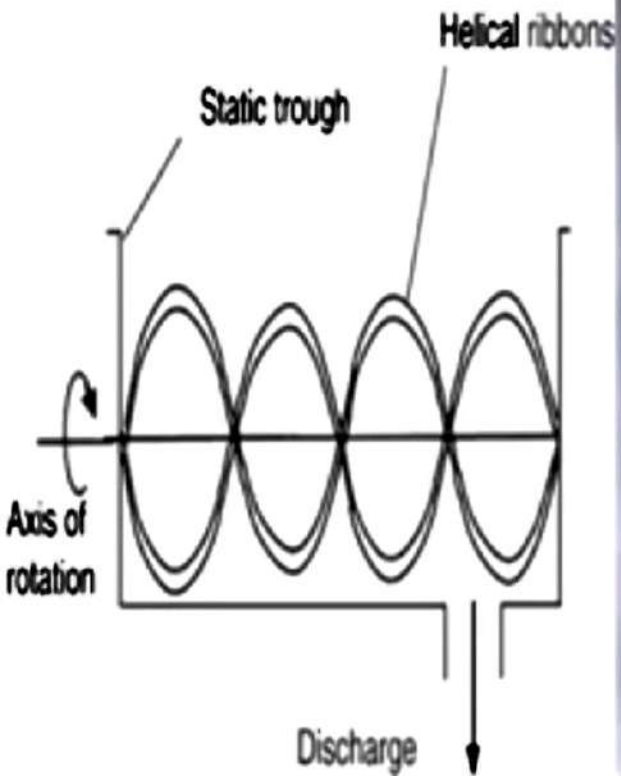


* Agitator mixer (ribbon or U- trough or double arm mixer) :

- ✓ Used in hot and cold ointment mixing (semisolids) and also used in wet granulation

	Volume in liter	Working capacity	Optimum space
Ut 10	18	10	10/18
Ut 20	42	25	25/42

Ribbon mixer



3- Special mixers for solid powder:

A- Entolator (Impact wheel blender)

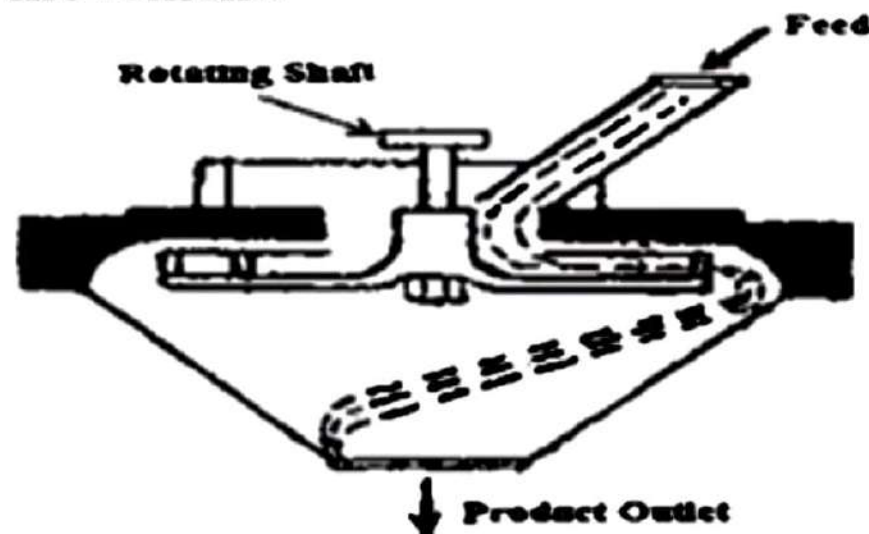
- Rotating Disc rotates at 1750-3500 rpm.
- Pd. Is introduced from the hopper to the center of the disc which make rotation under centrifugation force.
- Pd will come to mixing vessel in a spiral movement.

Advantages :

Suitable for continuous operation.

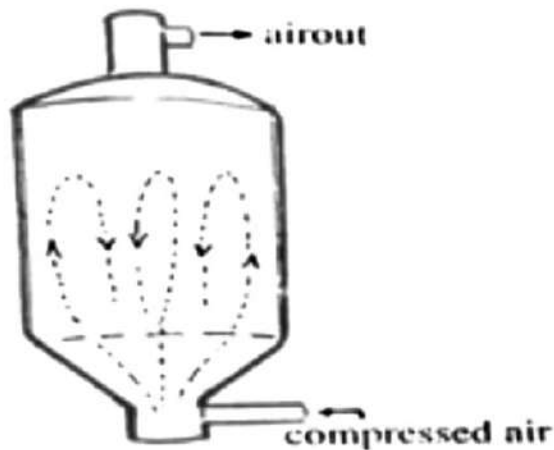
Disadvantages :

The powder needs premixing



B- Pneumatic mixer : (Airmix mixer)

- Here, the driving force is the compressed air which is introduced through nozzles present at the lower part.
- These nozzles are arranged in a manner that escaped air stream in a vertical motion gives a chance for powder to settle.





GORUN 1010



GORUN

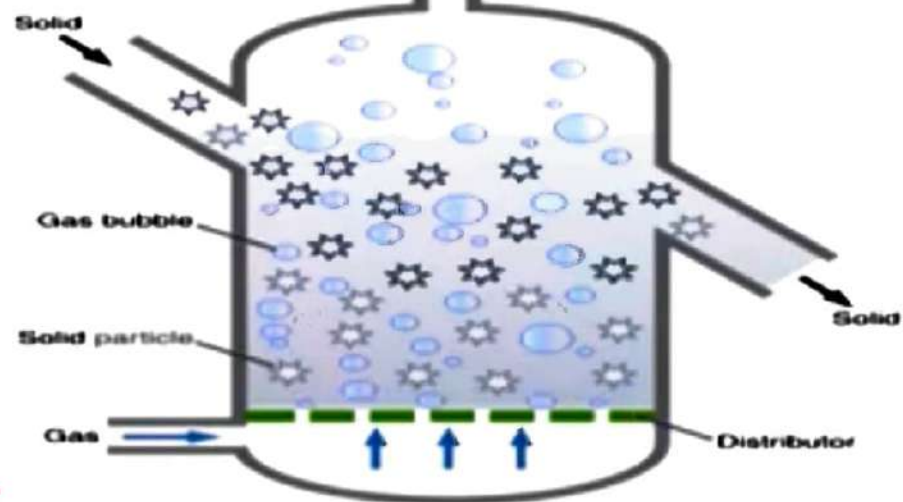


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CBC

Pneumatic mixer

C- Nautamixer :

It combines the 3 different mechanisms for mixing:

- 1- Diffusive (conical vessel).
- 2- Convective (helical conveyer).
- 3- Shear mixing (rotating arm).

❑ Advantages:

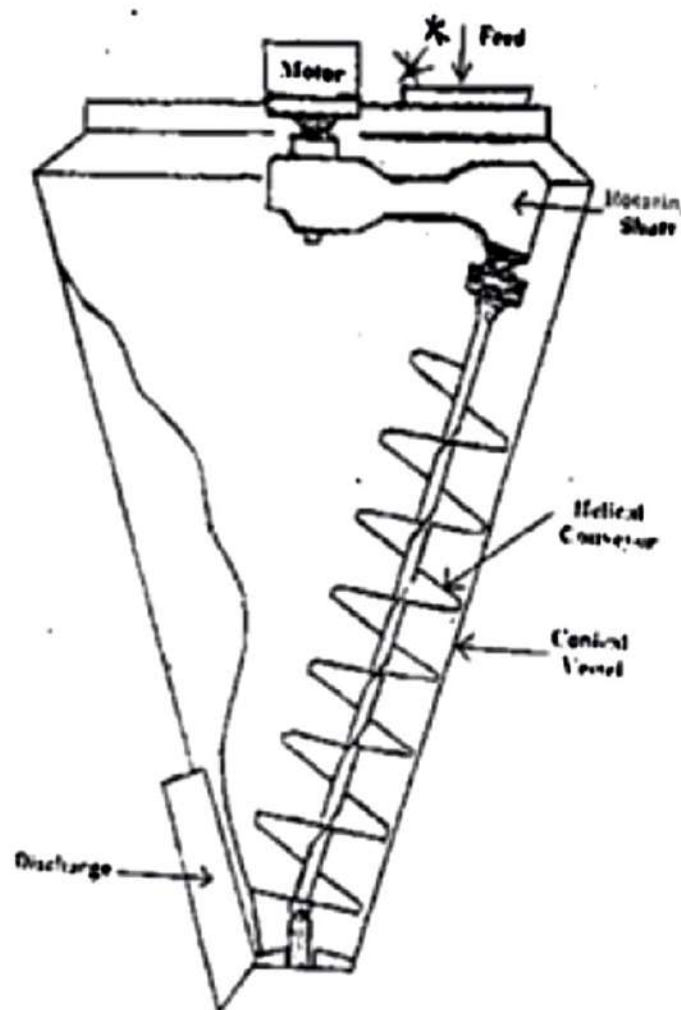
- ❖ No dead points.
- ❖ Can be used for drying under vacuum
- ❖ Development of Nautamixer

→ Saturn conical screw mixer:

- Double jacketed.
- Can be used as hopper for tablet machine.

❑ Disadvantage:

- expensive





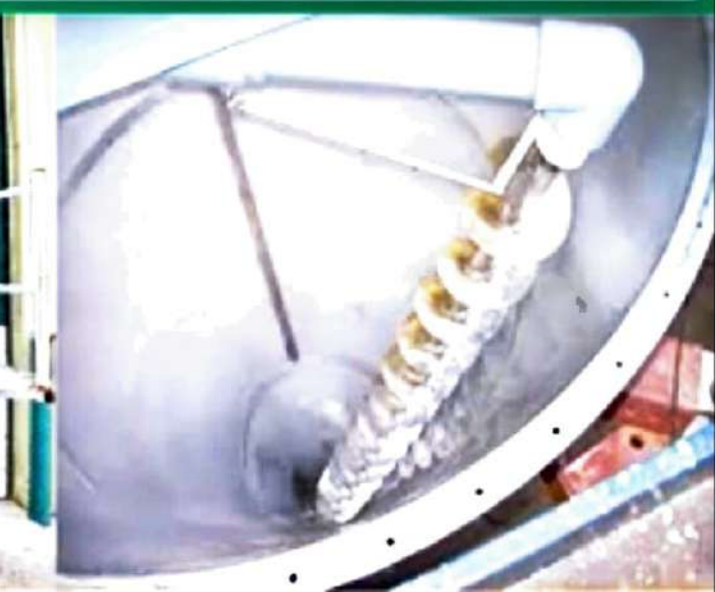
Nautamixer



mixing tank en. alibabacom



A conical twin screw mixer



D- High Shear Mixer:

- ❖ It is called **Diosna Mixer**
- ❖ It can be used for **mixing, granulation and drying** →
 - Decrease waste and
 - Decrease workers.

1- mixing

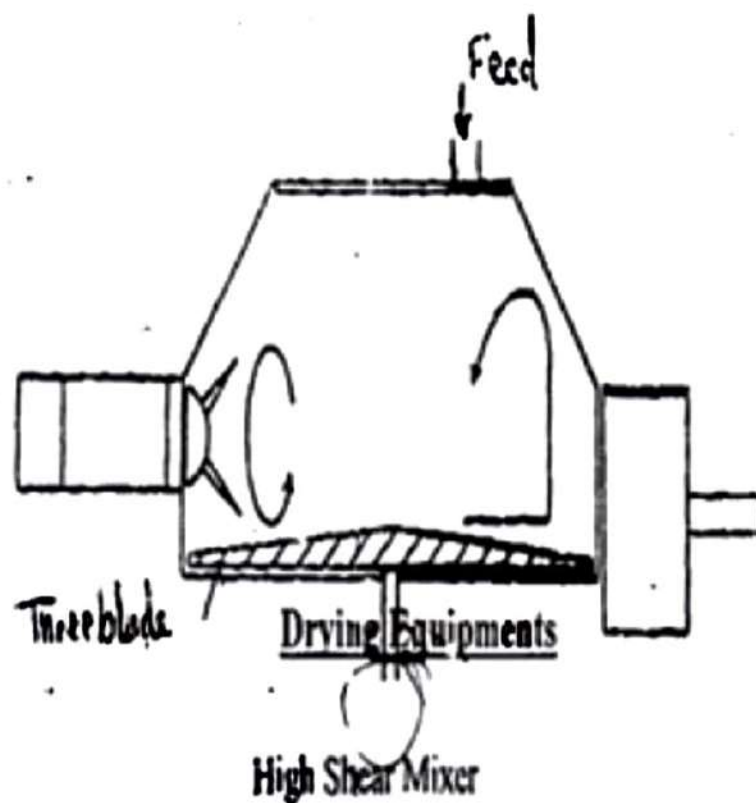
2- Granulation by adding binder → wet mass

Replace ! Motor
with chopper to cut ! Mass
into granules

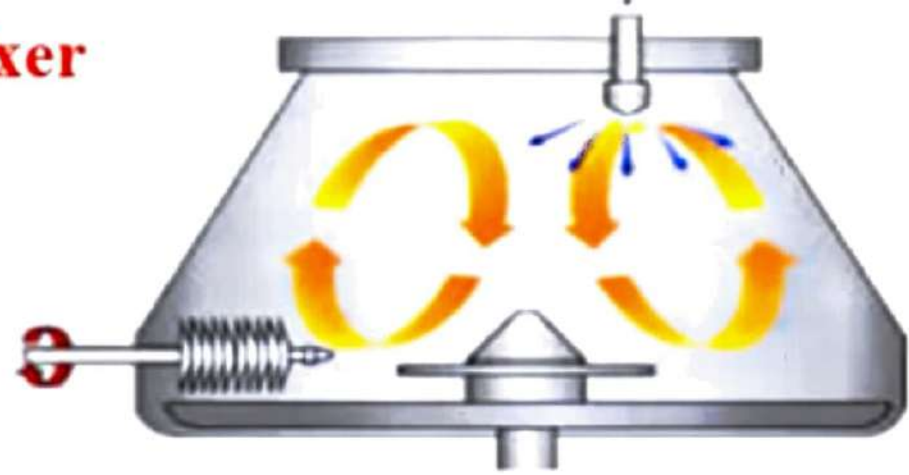
3- Drying: A- hot air B- heated jacket

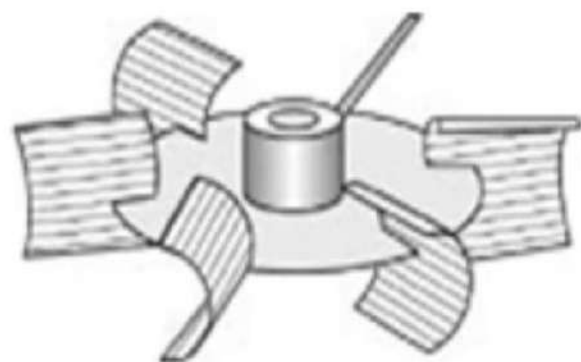
❑ High shear mixer:

- 1- Called **Diosna** → mixing, drying, granulation
- 2- Called **Zanchetta** → mixing, drying, granulation and size reduction
(as upon drying → aggregation occur and size reductions is required).

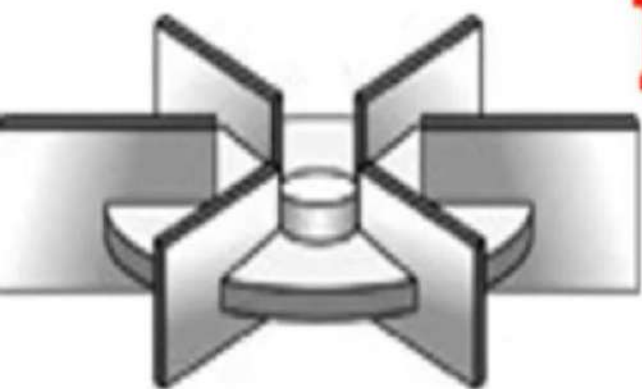


Diosna Mixer





II- Liquid-liquid Mixing L/L



Prepare by:
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PURPOSES OF AGITATION

1. Suspending solid particles
2. Blending miscible liquids
3. Dispersing a gas through the liquid
4. Dispersing a second liquid to form an emulsion or suspension
5. Promoting heat transfer

Mixing of Liquids (impeller mixers)

- ❖ The rotating part of a centrifugal pump, compressor, or other machine designed to move a fluid by rotation is called **Impeller**.

Flow pattern depends on:

- 1- Properties of the liquid
- 2- Type of impeller
- 3- Size of the mixing tank
- 4- Baffles.

Flow pattern of impeller mixers:

1- Tangential flow:

The liquid follows a circular path around the shaft. It is the least effective type of flow.

2- Radial flow (better):

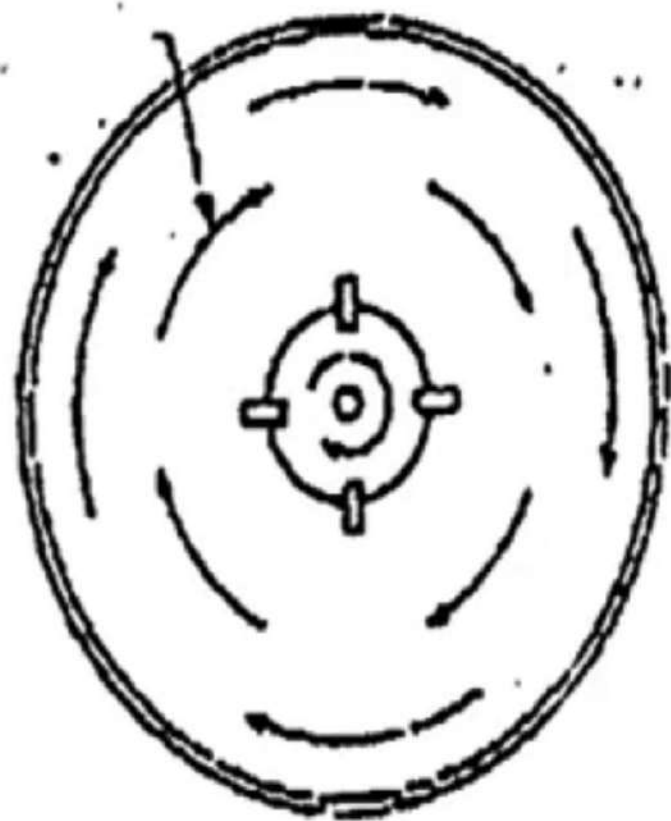
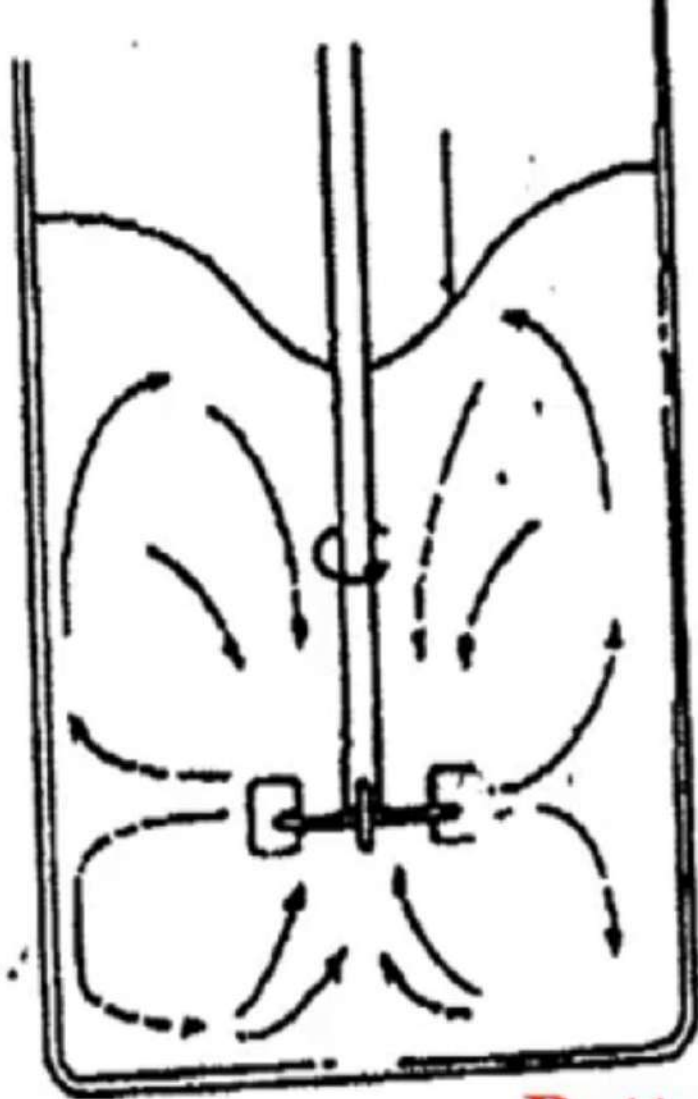
The liquid discharges from the impeller at right angle to its shaft

3-Axial or longitudinal flow :

The liquid discharges parallel to the shaft, either from the surface to the bottom or from the bottom to the surface.

N.B.:

Axial flow is necessary for liquid containing suspended



Pattern Flow of impeller mixers

Vortex formation:

When the shaft of the impeller is vertical or centrally located in the tank, the tangential flow predominates.

The liquid swirls around the vessel with little or no intermingling vortex at the surface of the liquid.

Disadvantages of vortex:

- 1- No good mixing due to swirling of the liquid layers.
- 2- If solid particles are present, they will settle by centrifugation.
- 3- Air is drawn into the mixed material which causes decomposition of oxidizable substances and foaming of others.

Suppression of vortex:

1- In small tanks:

The impeller is mounted

a- Off center or

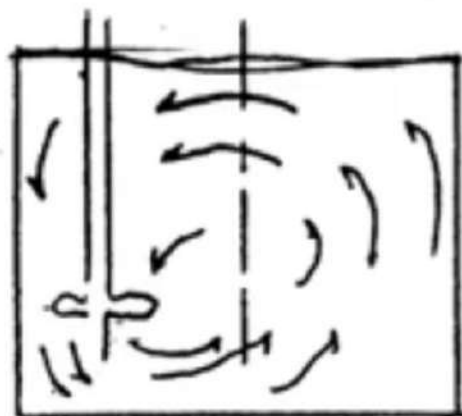
b- Tilted destroying the symmetry of the mixer thus the tangential flow is minimized.

2- In large tanks :

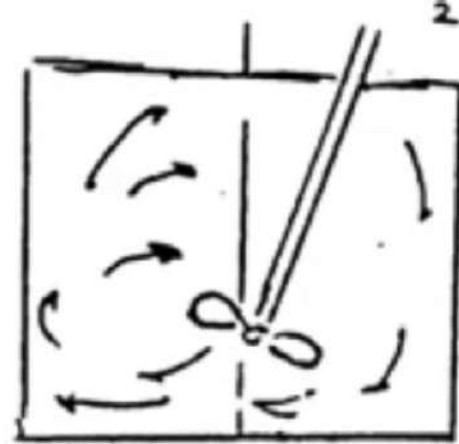
Baffles are added to the mixing tank.

3- In very large tanks :

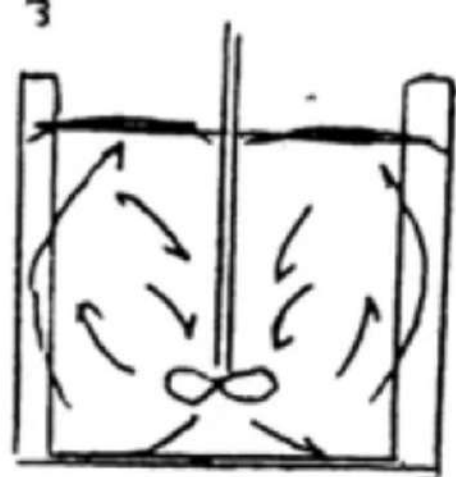
More baffles are used and the impeller is mounted in the side of the tank.



• (a) off center

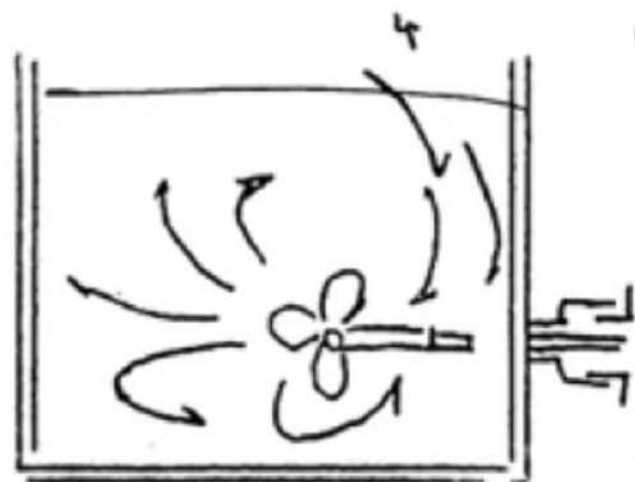


• (b) oblique



• large tanks & baffles

→ Top view



Side shaft in a very large tank

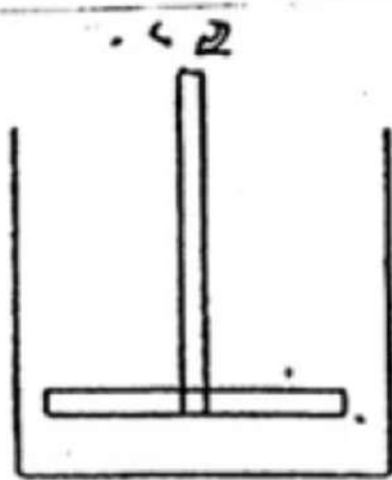
Types of mixers

- 1- Shaker mixer
- 2- Impeller mixers

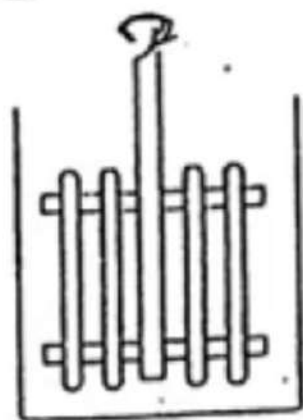
Impeller mixers for liquids classified into:

- 1- Paddle,
- 2- Turbine and
- 3- Propeller.

1.Paddles: Can be used for mixing liquids of low viscosity



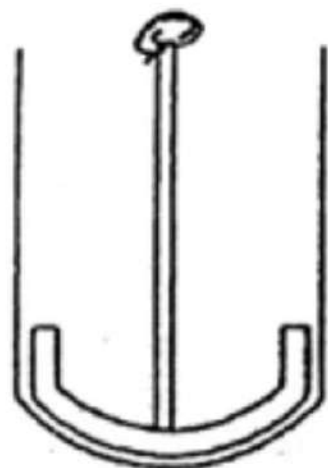
Single paddle suitable for mixing miscible liquids of low viscosity or solid in liquid.



Gate Agitator for mixing viscous liquids or & thin pastes due to shear force.



Multiple – Blade or Double – Acting paddle. For mixing viscous liquids & suppresses vortex formation



Anchor Paddle poor mixer but useful in preventing deposit on heat transfer surface (used during evaporation).

L – L Mixing (Mixers)

Impeller: Anchor (High Visc.)



Impeller: Anchor (High Visc.)



Prepared by Dr. Riad K. El Qidra

2- Turbines:



1-Straight –Blade Turbine

for majority of application



2-Curved – Blade Turbine

to facilitate starting up so it is suitable for viscous liq. , thin paste, emulsion.



3-Pitched – Blade turbine

to increase axial flow, to assist suspension of heavy solids.

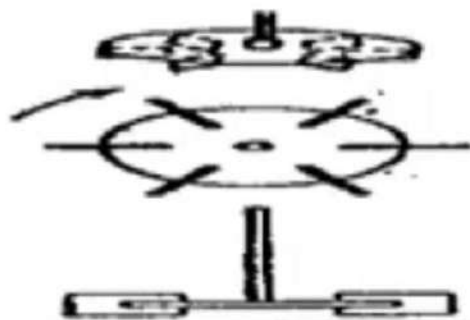
4-Shrouded Turbine

Curved blade turbine but rotates inside stator ring which has pins on the inside surface, to minimize tangential flow, suppress vortex formation. Used for emulsification.



5-Vaned-Disk Turbine (semiopen bladed disc)

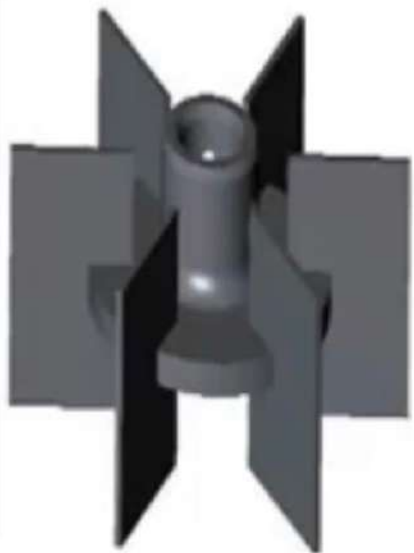
It has horizontal disc with straight vertical blades on its lower surface used for dispersing or dissolving a gas in liquid.



Radial-flow impellers



Disc turbine



Pitched-blade turbine The straight-blade turbine



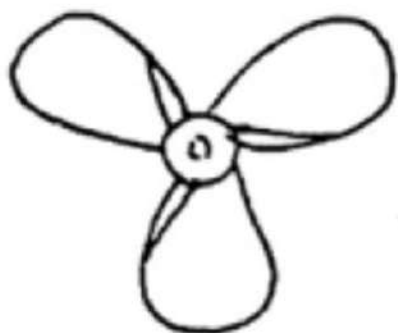
6- Concave blade CD-6 disc turbine

- It is also used for gas dispersion.
- Consists of six concave blades.



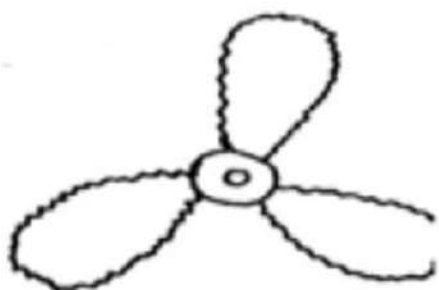
3- Propellers:

Mixing is achieved by combination of axial flow, turbulent flow and shear action produced by the propeller blades. They are used when solid particles are to be last in suspension.



Standard 3- Blade

For mixing of thin liq.



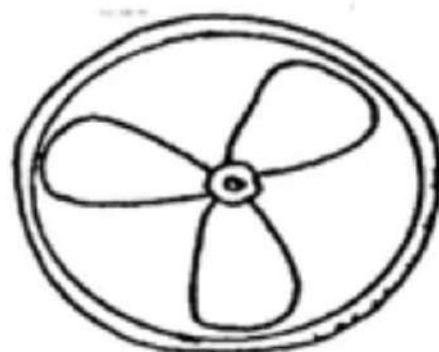
Saw – Toothed or Weedless

For mixing of viscous liquids



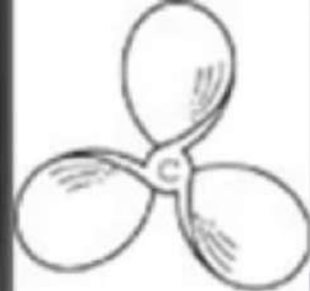
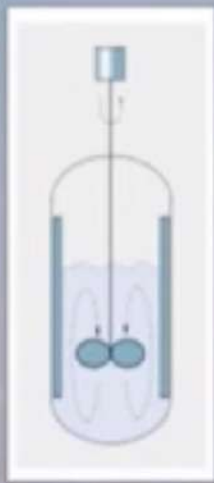
Guarded stator ring

has rotor blade to suppress vortex formation with thin liquid.



Axial-flow impeller

Axial Agitation



3-blade marine propeller

Types of impellers :

	Paddles	Turbines	Propellers
1-Speed of rotation	20-120 r.p.m. (low speed)	120-200 r.p.m. (moderate speed)	400 – 1750 r.p.m. (high speed)
2-Type of flow	Tangential and radial flow.	Radial and tangential flow	Axial and tangential flow
3-Viscosity	Up to 1000 centipoises	Up to 100.000 centipoises	Up to 5000 centipoises
4- Construction of impellers	2 bladed or 4 bladed, blades may be vertical or pitched	Multi – bladed up to 8 bladed, blades may be vertical or pitched and straight or curved	
	Length of paddle is 50-80% of inside diameter of vessel	Diameter of turbine 30-50% of inside diameter of vessel	Much smaller in diameter than paddles or turbine
			Suitable for suspensions of heavy solids due to axial flow.

Tank/Container



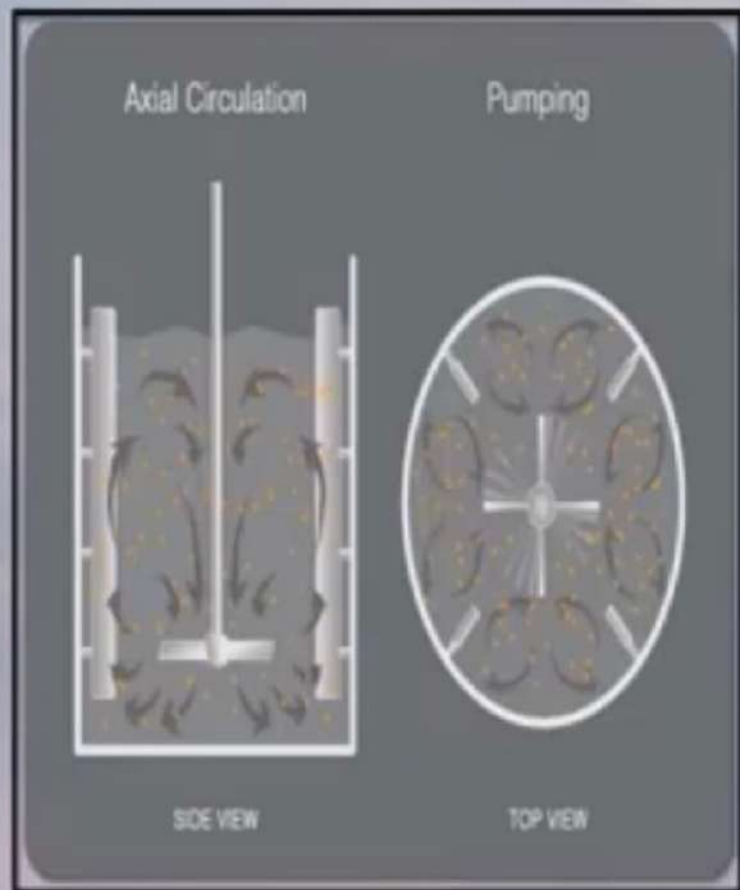
Tank/Container



Baffles



Baffles



Motor



Motor



D- Special Mixers for Liquids :

Cone mixer and Double cone mixer :

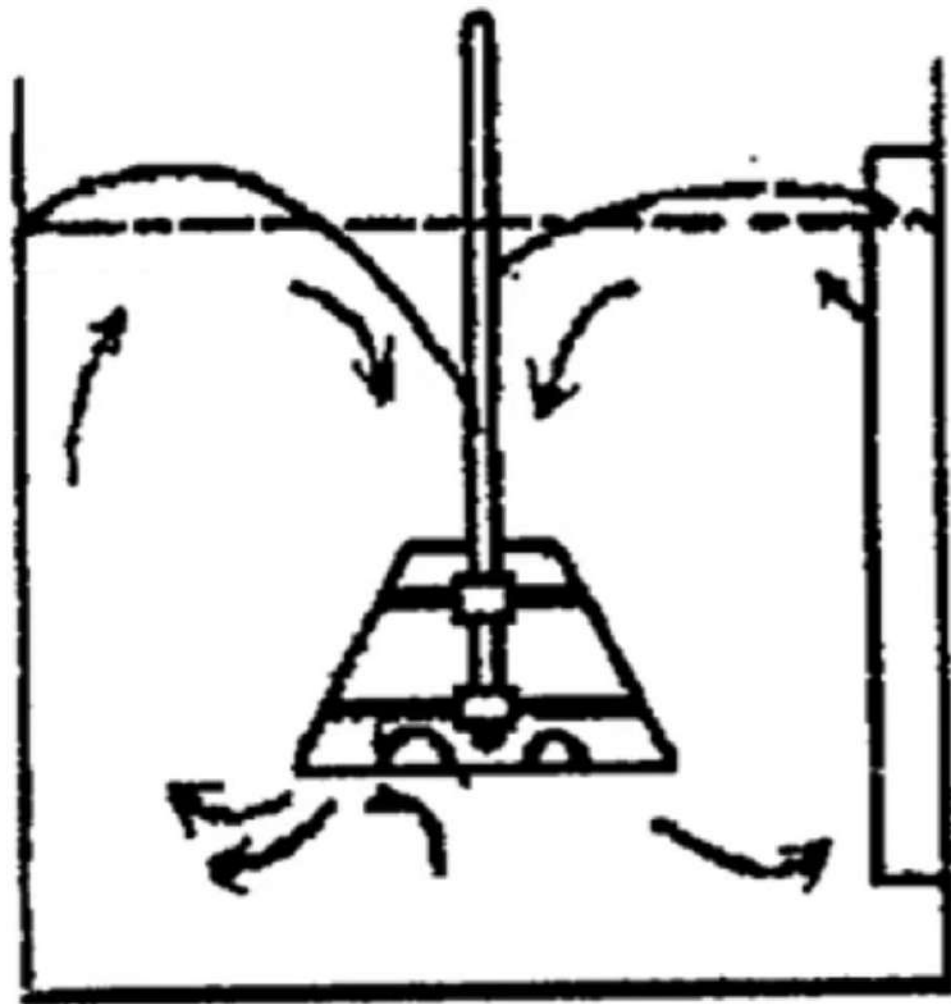
(axial flow)

- The liquid enters through narrow open end of the cone by suction.
- which is caused by the difference between the peripheral velocities.
- Due to the difference in diameter of the upper and lower surface of cone leads to gentle swirling motion.
- Then the liquid is then thrown outward by centrifugal action from wide surface of the cone.

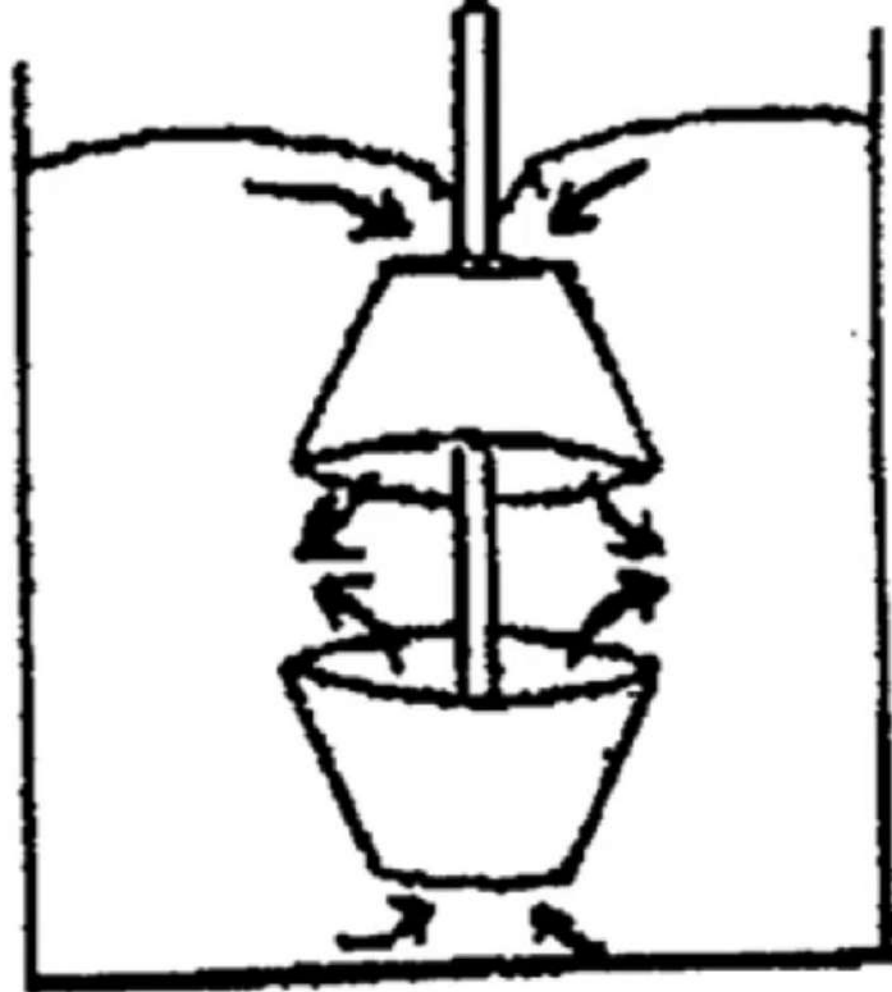
Uses

- Used to circulate dense slurry especially containing fibrous materials and require smooth uninterrupted flow path.
- To improve the flow we use double cone mixer.

* Baffles added to ↑ axial flow



Single Cone Agitator



Double Cone Agitator

Mixers for plastic materials (semisolid material)

- If the solid is not too coarse,
- the liquid is not too viscous and
- the percentage of solids is not too great, solids can be suspended in liquids by the use of a propellers or a flat bladed turbine in a cylindrical container.

Types of mixers:

- 1- Beaters
- 2- Kneaders
- 3- Mixer extruders
- 4- Roll meters .

1- Beaters:

e.g. A- Hobart's mixer:

- ❖ The agitator arm is designed to give **pulling and kneading** action.
- ❖ The arm visits all parts of the vessel (**planetary movement**) and scraps any material adhering to the wall or the bottom of the vessel (very narrow clearance) to:
 - 1- eliminate dead spots
 - 2- provide self cleaning action.
 - 3- remove any sticky substance
- ❖ Suitable for liquids, powders moistened with liquid as during tablet granulation.
- * **May be jacketed → for cold or hot process.**

B- Planetary Mixer

- ❖ The Planetary Mixer have two blades which rotate on their own axes, while they orbit the mix vessel on a common axis.
- ❖ The blades continuously advance along the periphery of the vessel, removing material from the vessel wall and transporting it to the interior.
- ❖ These mixers are ideal for mixing and kneading viscous pastes or putty-like materials.
- ❖ Planetary mixers are ideal for mixing of pharmaceutical creams, ointments, cosmetic creams, herbal creams etc.
- ❖ Planetary mixers are also ideal for mixing and kneading viscous pastes under atmospheric or vacuum conditions.
- ❖ Used in the mixing of viscous, heat sensitive and cohesive pastes, dough and moist etc.



Planetary mixer

Beaters



Hobart's mixer (Beater)

2- Kneaders :

E.g. double arm mixer (ribbon) (u-trough):

- ❖ It consists of two heavy arms rotating towards each other at different speeds (one operating at twice the speed of the other).
- ❖ Blades may be sigma, dispersion blades or double naben blade.
 - 1- As the material become cohesive, the blades continuous **stretch and kneading** the material.
 - 2- The stretched material is then folded over itself.
- ❖ The mixing tank can be cooled, heated or under vacuum

Design of Blades

❖ **Sigma blade:**

- ❑ Used for general purpose kneading
- ❑ Edges are serrated to give a shredding action

❖ **S-type Double-naben (fish-tail blade):**

- ❑ Effective with heavy plastic materials
- ❑ develop high shear force

❖ **Z-type Disperser blade:**

- ❑ Heavier and develop high shearing forces
- ❑ Disperse powders or liquids into rubbery masses

Kneader Design of Blades

Sigma blade



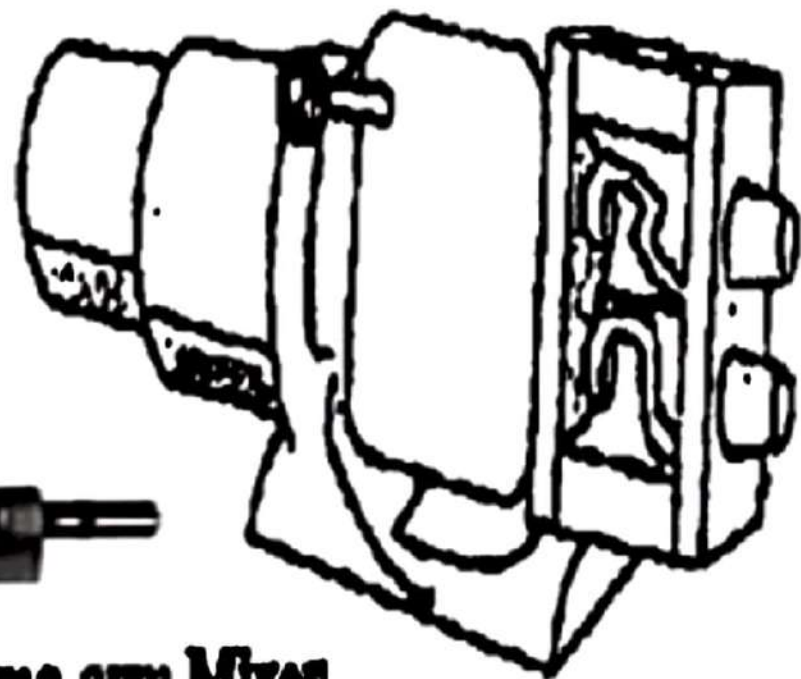
Double lobed blade



Dispersion blade



Sigma arm Mixer



E.g. Double arm mixer (ribbon) (u-trough)



2-Kneader (Sigma Blades)



3- Mixer extruders

E.g. Roto feed mixer

- It depends upon **cutting and folding** the material in a mixing chamber by means of special blades, and extruding it through a die, thereby subjecting the material to additional shear.
- A screw agitator **cuts and folds** the material as it flows towards the discharge end.
- Used for polymer mixing and transdermal therapeutic system.

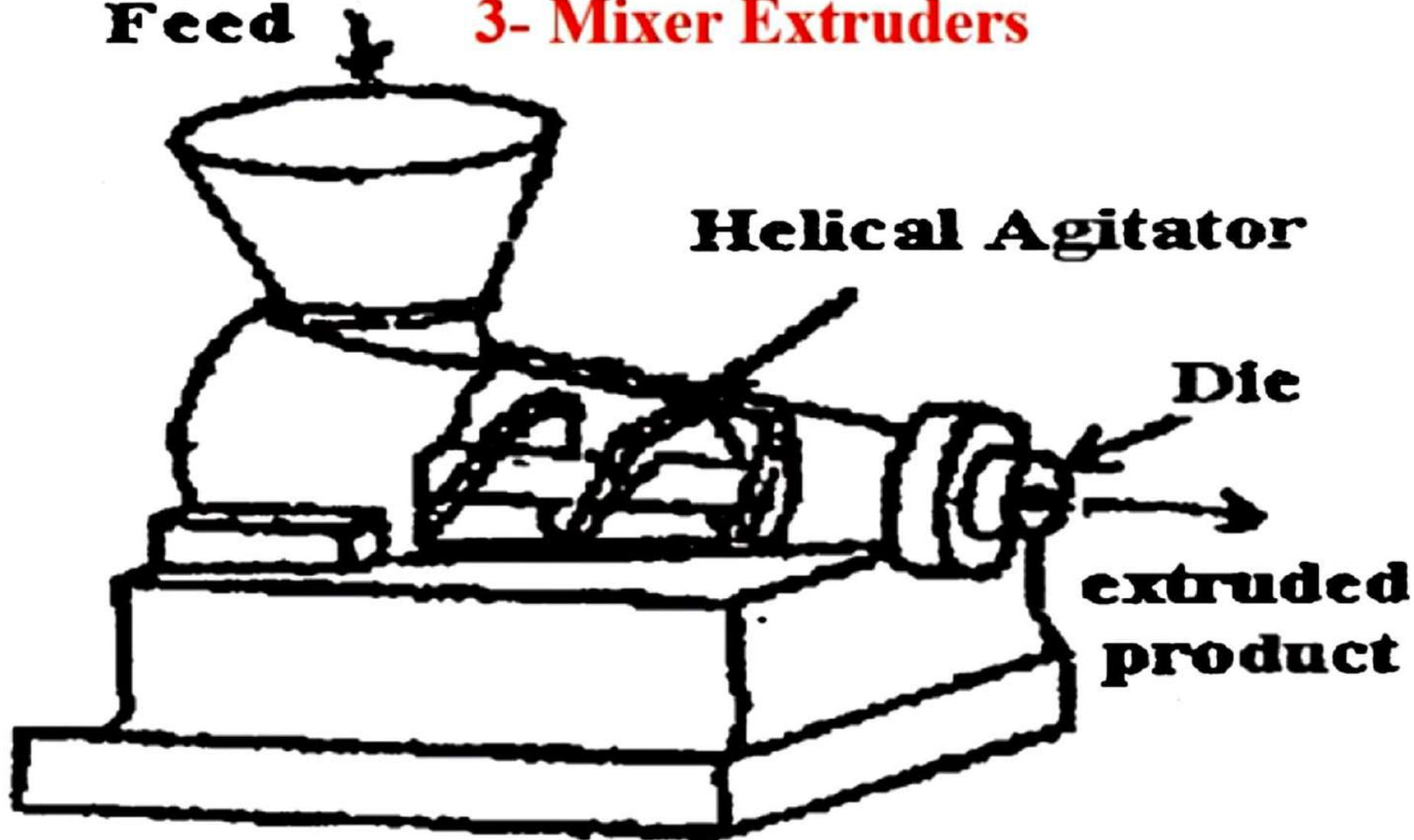
Feed

3- Mixer Extruders

Helical Agitator

Die

**extruded
product**



4- Mixing rolls:

E.g. Triple roll mill : (size reduction and mixing)

- ❖ The material is subjected to intense shear by repeated passage between smooth metal rolls tuning at different speeds.
- ❖ The gap between the rolls is adjusted for controlling the fineness of dispersion.
- ❖ The rolls can be cooled by passing water through the inside of the rolls.
- ❖ A scraper is used to remove the final ointment of smooth and uniform texture.
- ❖ The feed enters through a hopper

➤ Advantage:

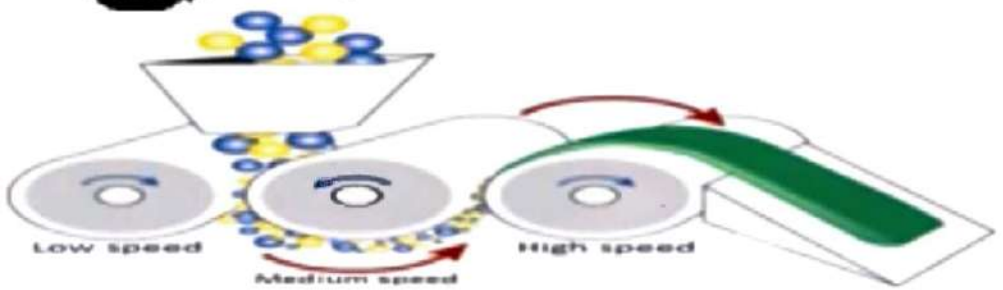
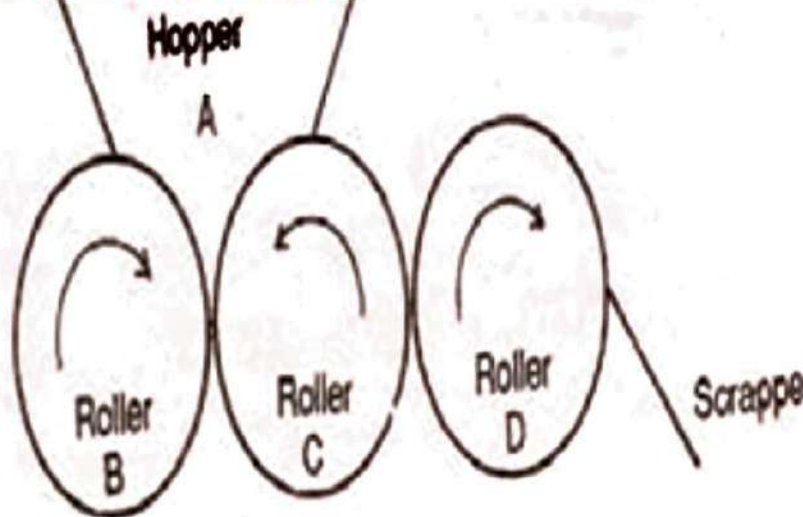
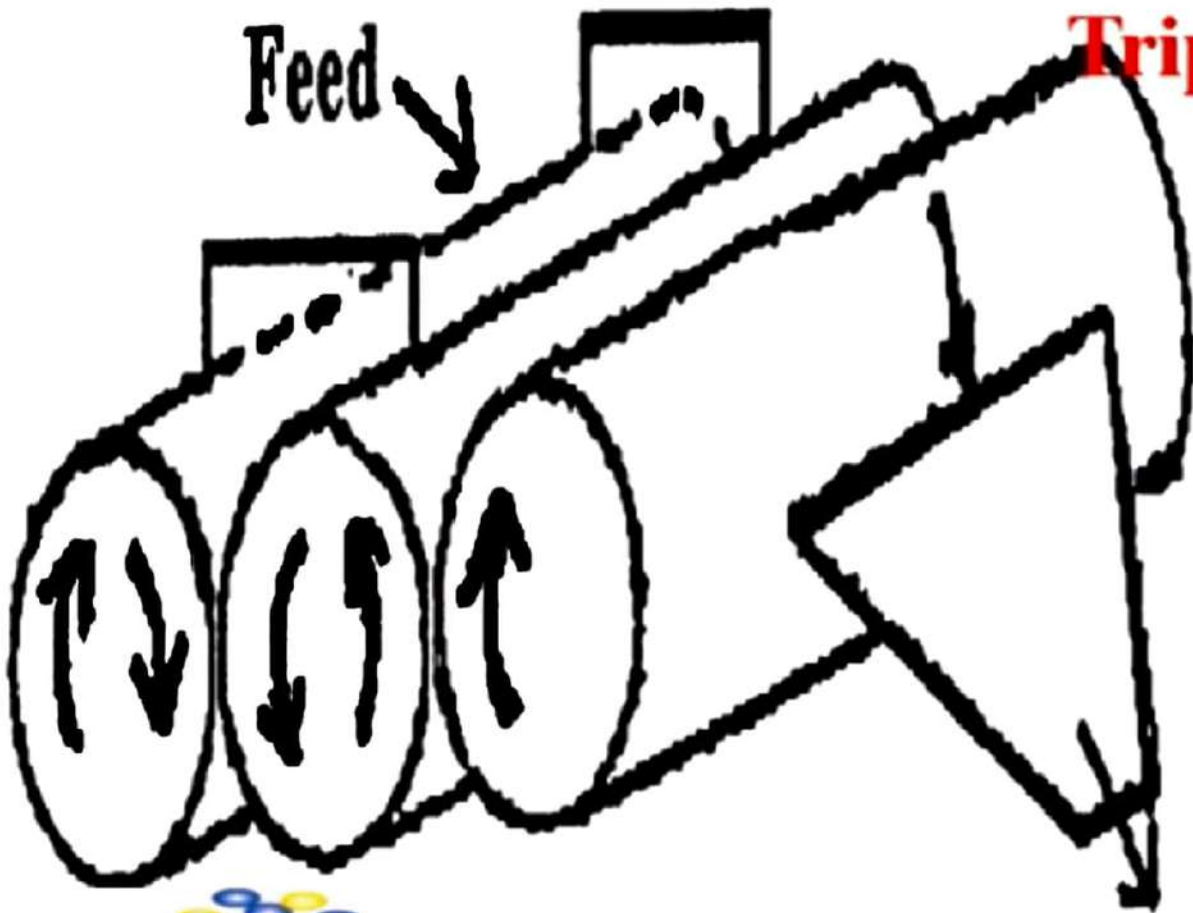
- 1- Produces a uniform dispersion and a
- 2- Continuous process

➤ Material used:

Stainless steel to prevent contamination

Feed

Triple roll mill



Product



Triple roll mill

Triple roll mill

is very effective for size reducing and dispersing solids in semi-solid media