
welcome

MIXING

BY

Ass. Prof. Dr. Mohamed Akl

Mixer Selection:

Equipment selection:

- Equipment selection is the most critical aspect of mixing.
- Factors that must be taken into consideration include:
  1. The physical properties of the materials to be mixed, such as density, viscosity, and miscibility.
  2. economic considerations regarding processing, e.g., time required for mixing and the power expenditure.
  3. cost of equipment and its maintenance.

❑ The equipment selection relies on the liquids' viscosity and the optimum way to generate high shearing forces.

Low Viscosity Systems

Monophase systems: it classified as +ve mixture

- if given time, → mix completely without external agitation
- Agitation reduces the time required for mixing, allowing for a rapid decrease in segregation intensity.
- In general, low viscosity liquids present no difficulties unless the operational scale is large.

Mixer Selection:

Equipment selection:

Low Viscosity Systems

Monophase systems:

- The flow and mixing mechanisms depend on the fluid(s)' viscosity and density.
- Mixing fluids with low viscosity required a methods that generate a high degree of turbulence, which can come from air jets, fluid jets, and different high-speed impellers.
- A viscosity of approximately 10 poises may be considered as a practical upper limit for the application of these devices (air jets, fluid jets, and impellers)
- Due to their high viscosity, thick creams, ointments, and pastes cannot induce turbulence during bulk or laminar mixing. Instead, molecular diffusion must be used. A turbine with flat blades can mix such fluids.

Mixer Selection:

Equipment selection:

Intermediate Viscosity Systems

- Mixing immiscible liquids (emulsions) or finely divided solids with a low-viscosity liquid (suspensions) depends on.
  - subdividing or deaggregating one or more phases and dispersing them throughout the material to be mixed.
- At low solid disperse phase concentrations the flow properties are Newtonian → propeller mixing is satisfactory as long as the dispersed components oppose settling.

  → in such cases, increase the impeller size and slow its speed.
- Emulsions and suspensions are too viscous to cause turbulence, thus laminar mixing and molecular diffusion must be used.

  → A turbine with flat blades can mix such fluids.

Mixer Selection:

Equipment selection:

High Viscosity Systems

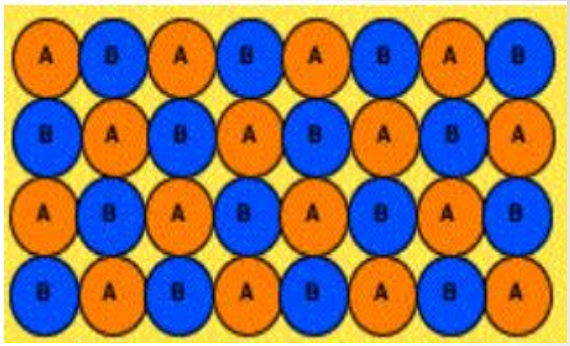
- viscous ointments is mixed efficiently by Shearing two surfaces moving at different velocities.
  - → This is achieved in paddle mixers, in which the blades clear the container walls by a small tolerance.
  - → These mixers provide enough shear to reduce globule size and sufficient circulation to ensure a uniform dispersion throughout the mixture.
- For thicker pastes and plastic masses, a kneading, stretching and folding action is employed.
  - → the commonly used mixers are sigma-blade mixer and muller mixer.

Mixing of solids

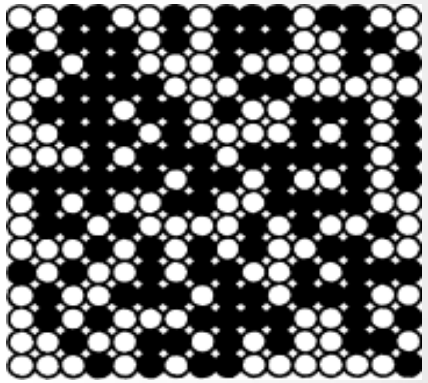
- It is an example of neutral mixture
- It is one the most common operation employed during preparation of different formulation like powder, tablets, capsules.
- Mixing is considered as a critical factor, especially in case of potent drugs and low dose drugs where high amounts of adjuvants are added.
- The diverse characteristics of particles such as size, shape, volume, surface area, density, porosity, and flow charge contribute to the solid mixing.

Degree of mixing:

Ideal Or Perfect Mixing



- When each particle lies as closely as possible in contact with a particle of the other component OR
- When quantity of materials in all part of a system is same (e.g., ABABAB) → it is perfect mixing.
- Even though a perfect mixture would have point uniformity, mixing equipment cannot practically achieve it.



Random mixing

- A mix where the probability of finding a one type of particle at any point in the mixture is equal to its proportion in the mixture
- Proportion is different in all parts a system. e.g., AB AA BA AB
- Powder mixing is a "chance" operation; hence → in practice a "random mix" is the best type of mix likely to be obtained.

Degree of mixing:

Special notes:

Scale of Scrutiny:

- It is the smallest amount of a drug that can be mixed well .
  - If the dose of the drug in the mixture is < the scale of scruting,

    → the normal mixing methods fail to attain efficient mixing.
    - In this case geometric ,i.e., dilution mixing must be adopted

      .

Scale and intensity of segregation

- Segregation is the opposite effect to mixing, i.e. components tend to separate out.
- Segregation is the main problem with mixing and handling solid particles, both during and after mixing.

Reason of segregation→ Solids tend to segregate due to

- differences in the **size, density, shape,** and other properties of the particles of which they are composed
- The Earth's gravitational field or a processing-generated centrifugal, electrical, magnetic field can satisfy the second segregation criteria.
- Segregation has been also attributed by mixers.
  - →Mixer producing shear or diffusive mixing are classified as segregating
  - →Mixer generate principally convective motion have been classified as non-segregating.

Scale and intensity of segregation

- Segregation of constituents in blending plays a very important role in powder blending.
- In order to characterize the homogeneity and structure of the blend at the output, it is important to understand and assess the performance of the blender based on the intensity and scale of segregation.

– **intensity of segregation** is a measure of the spread of the concentration of the component of interest in the mixture.

– **Scale of segregation** reflects the correlation of the composition of that component in that mixture (as a function of time for continuous systems and as a function of space for batch systems).

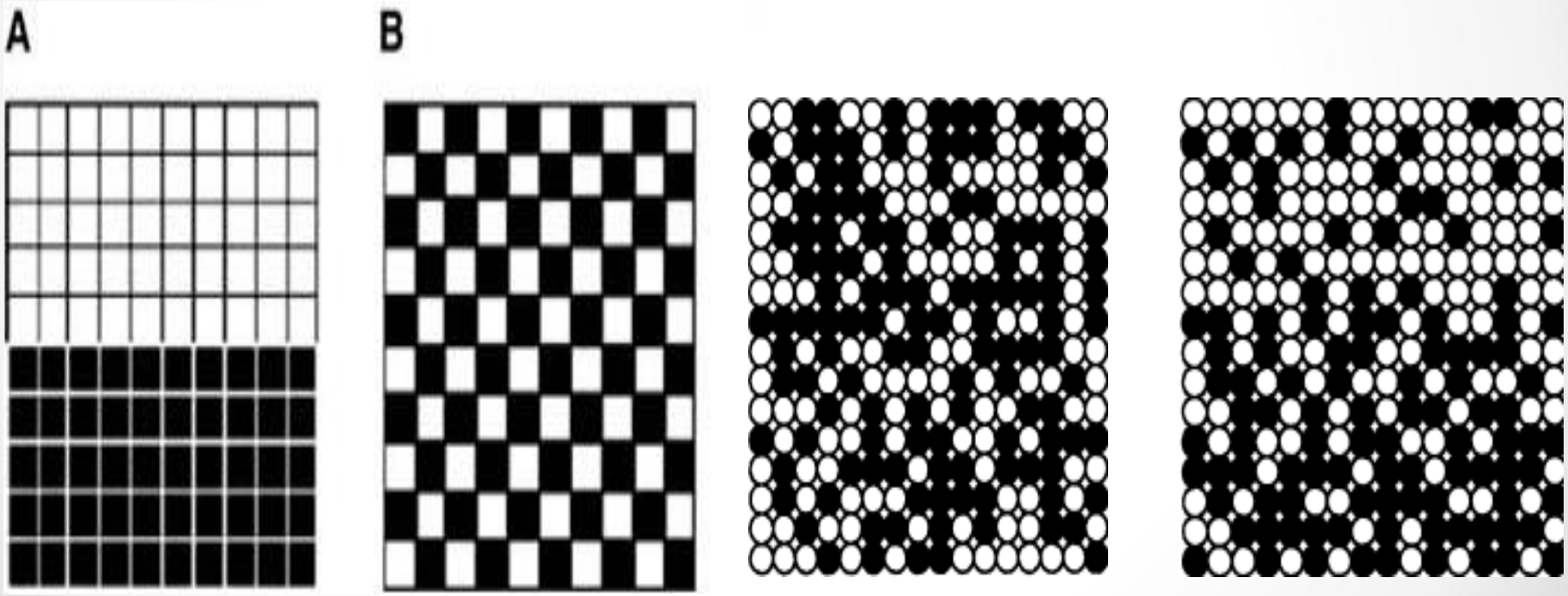
→ Therefore, scale and intensity of segregation describe the amount of unmixed material within the mixture.

→ A good mixture → will have a small scale of segregation and a low intensity of segregation.

❑ The role of a mixer is to reduce the scale of segregation and to lower the intensity of segregation

Scale and intensity of segregation

- In practice the best type of mixture that can be achieved by any physically realizable blender is the random mixture
- → In randomized mix the ratios of the components in the entire mixer is same.



Perfect mix Random mix Segregated mix

❖Factors affecting Demixing of solids

1. Particle Size and Size Distribution

3. Particle shape

4. Particle charge

2. Particle Size and Size Distribution

- a difference in the particle sizes of components of a formulations the main cause of segregation in powder mixes.

❖ On mixing large particles with small particles → segregation where
  - large ones flow one another.
  - while Smaller particles tend to dust out or fall through the voids between larger particles, and thus move to the bottom of the mass

- Segregation problem due to particle size difference can be reduced by:
  a. Selection of a particular sized fractions (e.g. by sieving to remove fines or lumps) to achieve drug and excipients of the same narrow particle size range.
  b. Milling of components to either reduce the particle size range or to ensure all that particles are below approximately 30 μm, at which size segregation does not tend to cause serious problems.
  c. Granulation of the powder mix (size enlargement) so that large numbers of different particles are evenly distributed in each segregating unit/granule.

2. Particle shape

- ❖ spherical is the ideal particle shape → it exhibit the greatest flowability, and are therefore more easily mixed, but they also segregate more easily than non-spherical particles
- ❖ Particle shape is important because as the shape of a particle deviates more significantly from this spherical form, → the free movement it experiences along its major axis → the greater the difficulty of mixing.
  - The irregular or needle-shaped particles can become interlocked, → decreasing the tendency of segregation once mixing has been achieved.
  - Controlled crystallization during production of the drug/excipients to give components of a particular crystal shape or size range → reduces the tendency to segregate.

3. Particle Charge (attraction)

- The mixing of particles whose surfaces are non-conducting (electrically) often results in the generation of surface charges as evidenced by a tendency of the powder to clump following a period of agitation.
- These charges are formed due to constant friction among the mixed particles → electrostatic charge → decrease the process of inter-particulate "diffusion." → de-mixing.
- The effect increase as particle size decrease.
- Similar charges repel particles from each others leading to segregation.

- This can be overcome by:

1. Stopping the mixing equipment (no increase in time of mixing)
2. Adding wetting agent or S.A.A to wet particles and neutralize the similar developed charges on the particles.
3. Adding some water and evaporate it after the mixing operation is completed (if water do not affect stability of components)

Mixing mechanisms

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

Powder Mixing mechanisms

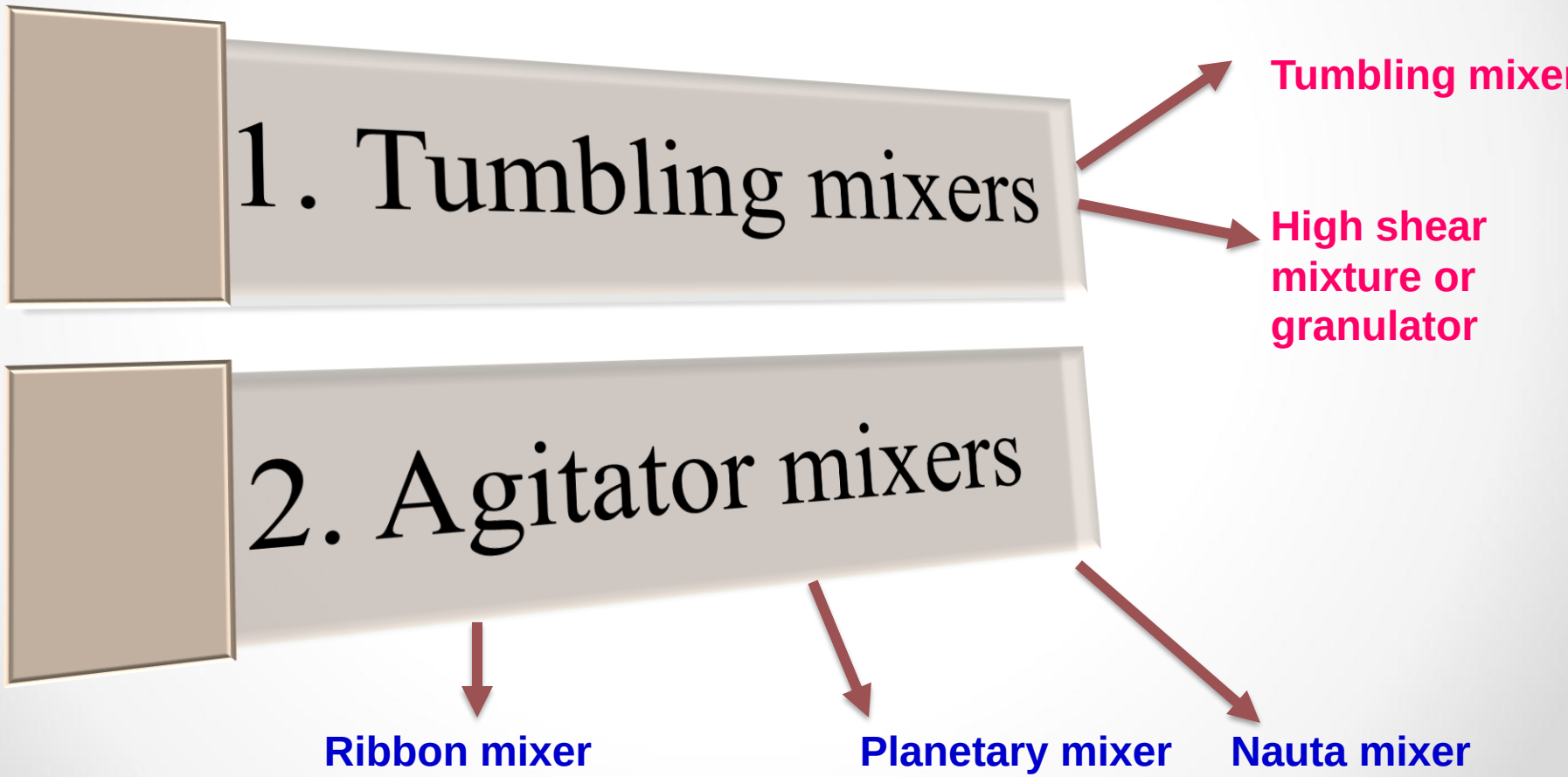
1. **Convective mixing/Macro mixing (bulk transport):**

- It takes place by transferring large mass of material from one location to another location of the system via
  - inversion of the powder bed
  - Using of blades or paddles or revolving screw of the equipment
  - rotation of container
  - This mechanism predominates in ribbon mixer.

2. **Shear mixing:**
   - In this type, forces of attraction are broken down so that each particle moves on its own between regions of different components and parallel to their surface.
   - By creating shear force in the powder by using agitator arm.

3. **Diffusion mixing/Micro mixing:**
   - Involves the random motion of particle within the powder bed, → thereby particles change their position relative to one another.
   - occur at the interfaces of dissimilar regions that are undergoing shear.
   - This mechanism predominates in tumbling mixers.

Powder mixing equipment



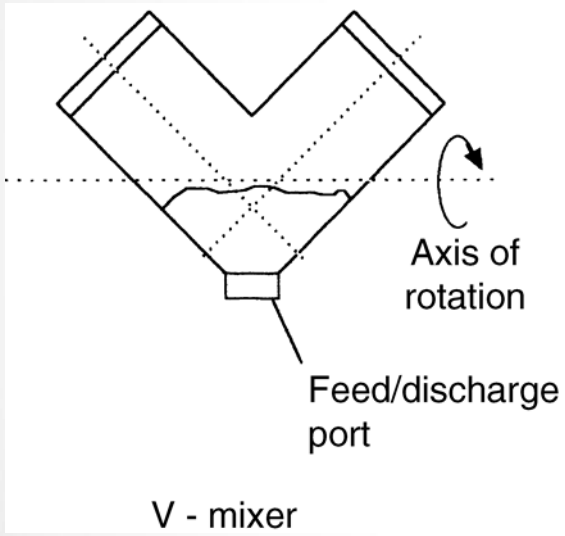
1. Tumbling mixers

- In this type of mixer, the movement of the whole mixer is responsible for the mixing action of solid → i.e. the movement of particles occurs by tilting the material beyond angle of repose using gravity to impel flow
- Mechanism: **is diffusive mixing.**
- used for mixing of granules and **free flowing powders.**
- It gives light movement so it is suitable **for friable particles.**

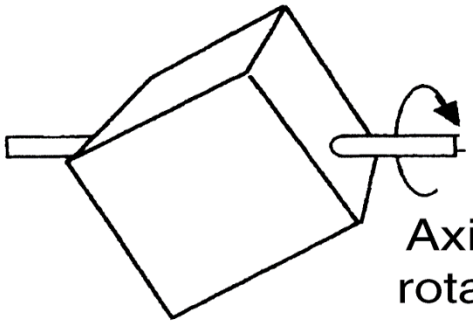
❑ Construction of Simple tumbling mixer

- It consist of closed cylindrical vessel made of stainless steal which are rotated on their horizontal axis at optimum speed by means of motor.
- To increase the efficiency, put the mixer inclined.
- The resulting tumbling motion is enhanced by baffles, lifter blades, or simply by virtue of the container's shape.

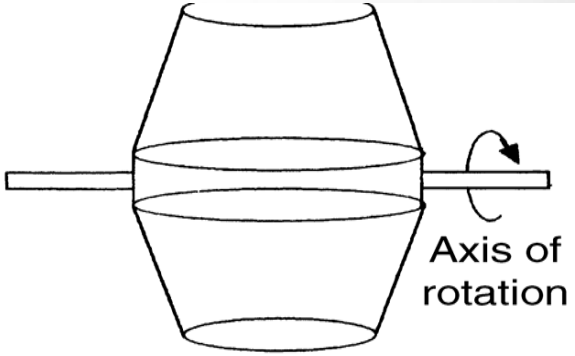
- Tumbling mixture are available in variety of geometric shapes and sizes these include
  - Y-cone blender
  - Cubical blender
  - V-shaped mixer
  - Double cone drum
  - Twin shell
- It may be rotated about almost any axis depending on the manufacturer



V - mixer



Rotating cube



Double cone

Shapes of tumbling mixers

- **4. Twin -shell or V -shaped mixer:**
  - popular
  - a cylinder that has been cut in half at approximately a 45-degree angle with its long axis, and then rejoined to form a "*V*" shape
  - This is rotated so that the material is alternately collected at the bottom of the "*V*" and → then split into two portions when the "*V*" is inverted.
  - It gives more efficient and precise mixing because the bulk transport and high shearing forces that occur in tumbling mixers, generally, are accentuated by this design.

V – cone tumbling mixer

Octagonal blender

❑ Factors for good mixing in tumbling mixers:

The efficiency of tumbling mixers is highly dependent on

1. **The speed of rotation** → optimum speed of the mixer is critical:.
   - Too low speed will cause sliding only and insufficient tumbling or cascading motion and will not produce rapid shear rates.
   - ↑ the speed (rotation that is too rapid) cause adhesion of powder on the walls (sides) of the mixer due to centrifugal force→↓ mixing efficiency → which leads to segregation.
   - Correct speed (30-100 rpm), cascading taking place across the diameter of the mixer.
2. **Capacity of the mixer** must not more than 75 % of its capacity.
3. **Optimum time of mixing.**
4. **The method of charging the powders,** addition of substances is side by side
   - The materials must not be placed in layers. If placed in layers, the diffuse movement will affect the upper layer only and no mixing will take place for some time.

2. Agitator mixers

- These are the mixers in which a stationary (fixed) container is used to hold the material
- Mixing is done by means of moving screws, a blade or a paddle
- they are useful in mixing solids that have been wetted, and are therefore in a sticky or plastic state
- The main mechanisms of mixing is **convection and shear.**

1. Ribbon blender

- Mechanism:
  - **Shear** that transferred by moving blades → high shear forces are effective in breaking up lumps and aggregates
  - **convective mixing**, as the powder bed is lifted and allowed to cascade to the bottom of the container. .

Construction

- Stationary horizontal cylindrical trough usually open at the top.
- It is fitted with two helical blades (ribbons), which are mounted on the same shaft by struts دعامات through the horizontal axis of the trough.
- Blades are connected to fixed speed drive
- The two helical blades are twisted in opposite directions to allow material to flow in both directions along the tank's axis→ (There is an outer spiral ribbon to move the material in one direction and an inner spiral ribbon to move the material in the opposite direction.)

1. Ribbon blender

Uses:

1. It is used for blending powders that tend to aggregate or don't flow freely
2. used for mixing of wet solid mass, liquid solid mixing.

❖ Disadvantage:

1. It is not suitable for heat sensitive materials or fragile materials.
2. blending cycle are quit long and more power consumption.

N.B.: mixtures with high homogeneity can be produced by prolonged mixing even when the components differ in particle size, shape, or density,

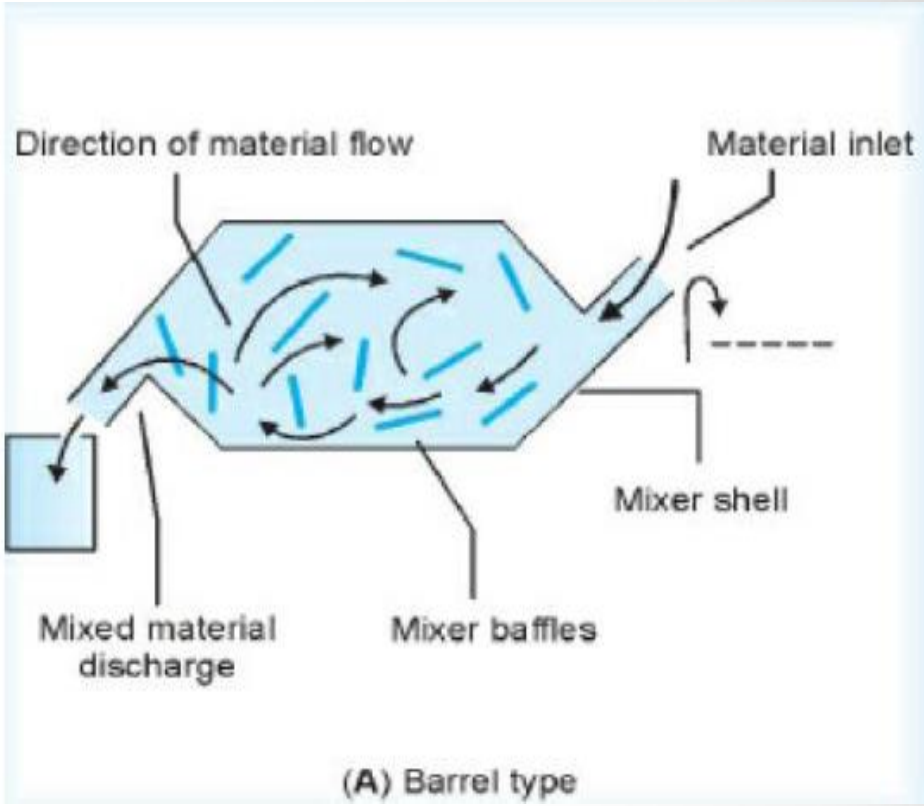
Continuous Mixers

- Large mixers produce mixtures with greater composition variation than small mixers. This is significant when little amounts of the combination must fall inside a restricted composition range.
- This is important when small amounts of the mixture are required to fall within a narrow composition range.
- Continuous mixing resembles fluid mixing. A device reduces segregation by impact or shearing metered amounts of powders or granules.

Barrel Type Continuous Mixer

❖ Construction:

- Resembles large cement mixer.
- Baffles are fitted to the inner surface of the shell → further enhances the mixing
- Shell is fixed to a shaft, which is allowed to rotate using electrical power.
- Side openings are provided on each side for charging and discharging of the material



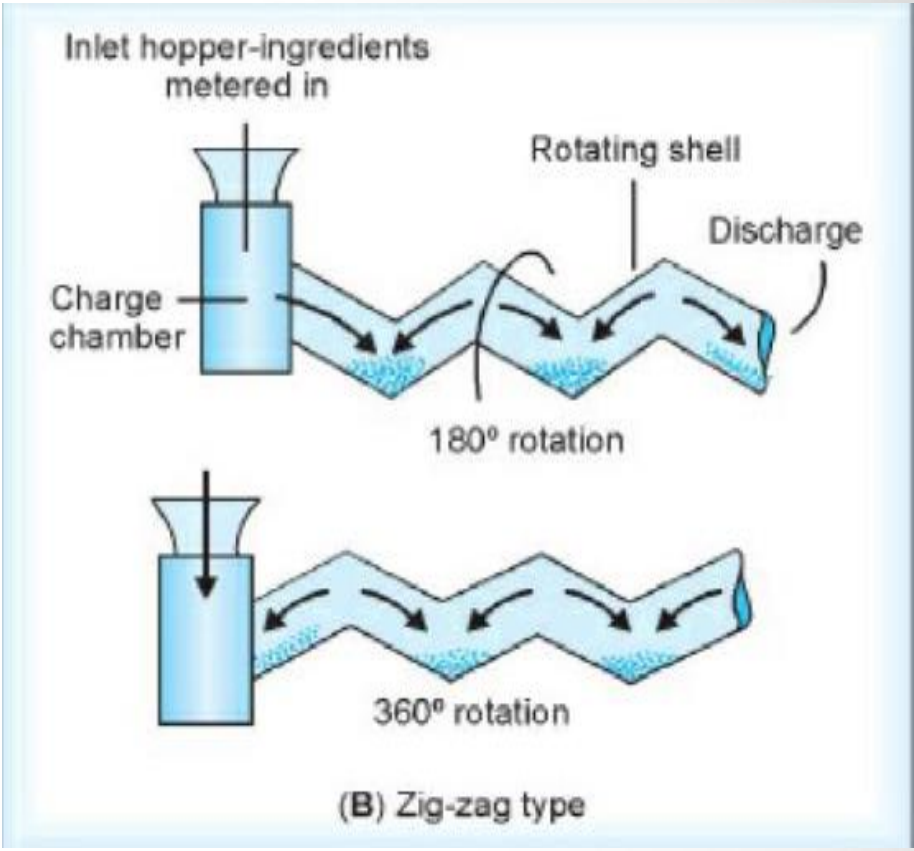
❖ Principle:

- Rotating shell keeps the material under tumbling motion.
- When the material approach the mid-point of the shell, a set of baffles causes a part of the material to move towards the direction of inlet end (backwards) allowing the remaining part to move forward.
- This process continuous up to discharge end, while another set of baffles guide the material to the discharge port.

Zig-zag Continuous Blender

Construction:

- It consists of a long rotating shell, which takes the shape of several V shaped blenders connected in series.
- At one end of the shell, a chamber for feeding is attached. While the other end allows the discharge of material
- The shell is inclined towards to discharge end



Principle:

- Material undergoes tumbling motion.
- When V section is inverted the material splits into two portions;
  - one half moves backward while another half moves forward.
- In each rotation, a part of the material moves towards the discharge end
- As the first V section clears the charge, a fresh feed enters, hence used for continuous blending.

Mixer Selection:

Equipment selection:

- Equipment selection is the most critical aspect of mixing.

Mixer Property

- An ideal mixer should be:
  - dust-tight,
  - easily cleaned and discharged,
  - require minimal maintenance and power consumption.
  - should produce a complete blend rapidly with as gentle mixing action as possible to avoid product damage.
- Special consideration:

❑ Rotating shell mixers suffer from poor cross-flow along the axis.

Overcome by:

- addition of baffles or inclining the drum on the axis increases cross-flow and improves the mixing action

❑ In cubical and polyhedron-shaped blenders, due to their flat surfaces, → the powder is subjected more to a sliding than a rolling action, a motion that is not conductive to efficient mixing.

Mixer Selection:

Equipment selection:

Mixer Property

- In double cone blenders the mixing pattern provides a good cross-flow with a rolling rather than sliding motion
- in twin-shell blender → the uneven length of each shell provides additional mixing action when the powder bed recombines during each revolution of the blender
- Twin-shell and double-cone blenders are recommended for precision blending
- in agitator mixers → The shearing action that develops between moving blades and trough serves to breakdown powder agglomerates
- Ribbon mixers:
  - are not precision blenders
  - more difficult to clean than the tumblers
  - having a higher power requirement.
- Blendex provides efficient batch and continuous mixing for a wide variety of solids without particle size reduction and heat generation

Mixer Selection:

Equipment selection:

Mixer Property

- Special consideration:

❑ Sigma blade and planetary mixers:

- There are a mechanical heat build-up
- a relatively higher power requirement

Overcome by: the shorter time interval necessary to achieve a satisfactory blend may offset these factors.

Mixer Selection:

Equipment selection:

Material Property

- Powders that are not free-flowing or that exhibit high forces of cohesion or adhesion between particles of similar or dissimilar composition are often difficult to mix owing to agglomeration

Overcome by: the use of mixers that generate high shear forces or that subject the powder to impact → the clumps of particles can be broken down

→ Such as agitators mixer (preferably planetary and sigma blade)

- Strongly cohesive materials, → it is typically necessary to fragment agglomerates through the introduction of high shear, "intensification," devices such as agitators or mills that energetically deform grains on the finest scale.

III. Mixing of semi-solids:

- Mixing of semi solids is difficult compare to the liquids and powders. These materials will not flow easily, dead spots will remain there.
- So, the mixers with narrow clearances and high degree of shear mixing produce should select.

Semi-solids mixing equipment

Planetary mixers (chang-can)

❑ Construction:

- consisting of a rotating agitator arm and a stationary vertical cylinder shell that can be removed.
- The blade is mounted from the top of the bowl.
- The agitator arm consists of several vertical blades (slightly twisted) mounted from the top of the bowl on a rotating head and positioned near the wall of the can.

❑ Uses:

1. Ideal for mixing of pharmaceutical creams, ointments, (cosmetic creams, herbal creams etc).
2. Used in the mixing of viscous, heat sensitive and cohesive pastes.

Planetary mixers (chang-can)

Mechanism of mixing is shear.

- Shear is applied between moving blade and stationary wall.
- It imparts planetary mixing action, whereby the mixing arm rotates around its own axis and around the circumference of the mixer's container so that it reaches every spot of the vessel.
- The double rotation of the mixing element and its offset position reduces the dead zones and avoids vortex formation

Advantages:

1. Ease of cleaning
2. Ease of discharge
3. Semi-continuous operation
4. Capital cost
5. Energy savings

Mulling mixers

Different mixing action

- Mulling mixers provide forces that incorporate kneading, shearing, smearing, and blending of materials for a total uniform consistency.
- This method produces just enough pressure to move, mixes, and pushes particles without crushing, grinding, or distorting them. → produce a mixture that is chemically and physically uniform in consistency.

Uses:

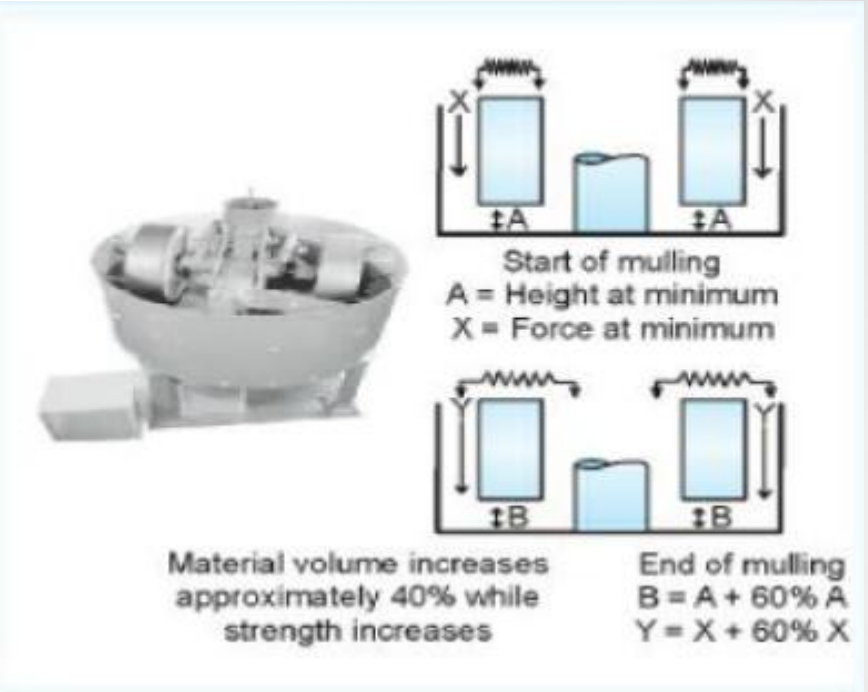
- These mixer are suitable for mixing previously mixed material of uniform composition, but containing aggregates of solid particles.
- Good mixer for batches of heavy solids and pastes
- Effective in coating the granular particles with liquid

N.B. In the event of segregation during mulling, a final remixing may be necessary.

Mulling mixers

Construction:

- It consist of two heavy rollers. The rollers moves on stationary bed. which is made of stone or iron
- Each roller has a central shaft carrying an arm supporting the wheels and revolve in a circular pan or tough (on its axis).



- Mulling mixers are efficient in deaggregation of solids
- Mulling mixers are are typically inefficient in distributing the particles uniformly throughout the entire mass.

Sigma blade mixer

Principle – shearing and convective in action. → Intermeshing تشابك of sigma blades creates high shear and kneading action.

❑ Construction:

- It is made up of a double tough-shaped stationary bowl with two heavy sigma-shaped blades installed horizontally in each tough and counter-rotating on parallel horizontal shafts.
- These blades are connected to fixed speed drive.
- Mixer is loaded from top and unloaded by tilting the entire bowl.

- ❑ The two blades rotate tangentially at different speeds, one about twice the speed of the other (a speed ratio of about 2:1.),
- ❑ The blade shape and difference in rotational speed resulting → in a lateral pulling of the material and impart kneading and rolling action on the material,
- ❑ Shear forces are also generated by the high viscosity of the mass and are thus effective in deaggregation as well as distribution of solids in the fluid vehicle.

Sigma blade mixer

- Advantages:

1. It creates a minimum dead space during mixing.
2. It has close tolerances between the blades and the sidewalls as well as bottom of the mixer shell.

- .Disadvantages:

1. Sigma blade mixer works at a fixed speed.
2. Problems of entrainment of the air and therefore lead to decomposition of oxidizable materials

- Uses:

1. Sigma blade mixer is a common form used to handle semi-solids of plastic consistency.

Mixing Rolls

- In mixing rolls, the materials subjected to intense shear by passing between smooth metal rolls turning at different speeds.
- Roller mills consist of one or more rollers and are commonly used. Of these, the three-roller types are preferred

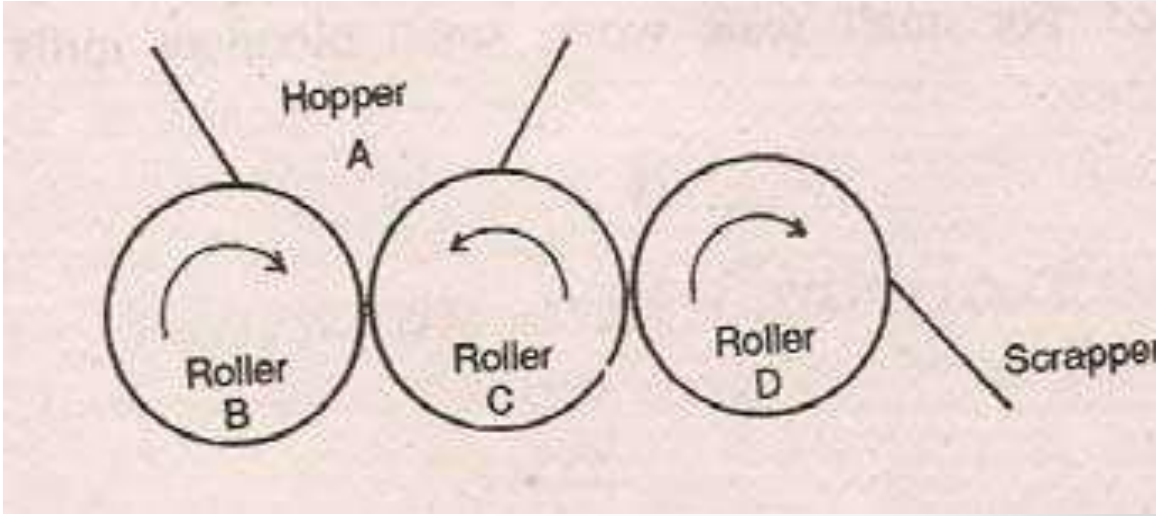
Triple-Roll Mill

- **construction and working principle:**
  - It consists of three rollers, made up of hard abrasion- resistant materials.
  - Rollers are fitted in such a way that they come in close contact with each other and rotate at different speeds.
  - Depending on the gap, the material that comes between the rollers is crushed, and also sheared by the difference in rates of movement of the two surfaces
  - A scraper is used to remove the final ointment of smooth and uniform texture.
  - The feed enters through a hopper.

Triple-Roll Mill

- **Note that:** The gap between rollers C and D is usually less than the gap between B and C.
- **Advantage:**
  - Produces a uniform dispersion and a continuous process
- **Applications:**

To mix paint, chemicals, glass coatings, pigments



Process of coating the solid particles with liquid

- It is an extreme case of solid-liquid mixing in which a small volume of liquid is to be mixed with a large quantity of solids.
  - This technique coats solid particles with liquid and transfers liquid between them.
  - In this type of mixing, the liquid is added slowly to reduce the tendency of the particles to form a lump.
- the process is not for fluids mixing, but for solids mixing.
  - When particles stick together due to the surface tension of the coating liquid, → the paste mixing equipment is utilized.
  - If the solids remain essentially free flowing, → solids mixing equipment is used.


THANK
YOU !