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# PHARMACEUTICAL ENGINEERING

# UNIT 3

TOPIC :

- **Mixing :** 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,

# Mixing

- Mixing is the process of combining two or more materials (solid–solid, solid–liquid, liquid–liquid, or semisolid) to form a homogeneous product with uniform composition, properties, and dose distribution.
- In pharmaceutical manufacturing, mixing is a critical step to ensure that the active pharmaceutical ingredient (API) and excipients are evenly distributed in each dosage form.

## Objectives of Mixing

1. **Uniform Distribution** – ensures equal distribution of API and excipients.
2. **Dose Accuracy** – guarantees that each unit dose (tablet, capsule, suspension, etc.) contains the correct amount of API.
3. **Enhancement of Bioavailability** – uniform dispersion improves drug solubility and absorption.
4. **Improved Physical Properties** – enhances flow, compressibility, and appearance of powders.
5. **Prevention of Separation** – avoids segregation of ingredients during processing or storage.
6. **Product Consistency** – maintains uniform texture, taste, and stability.

## Applications of Mixing

- **Tablets & Capsules** → ensures uniform drug distribution in powders and granules.
- **Liquid Formulations** → dissolves API in solvent to prepare syrups, solutions.
- **Suspensions & Emulsions** → prevents separation of dispersed phase and ensures stability.
- **Ointments, Creams, and Gels** → ensures smoothness and homogeneity of semisolid products.
- **Dry Powder Inhalers (DPI)** → uniform blending of drug with carrier particles (like lactose).

# Factors Affecting Mixing

1. **Particle Size**
    - Smaller particles mix more efficiently due to greater surface area.
    - Large differences in particle size can lead to segregation.
2. **Density of Materials**
    - Heavier particles may settle, while lighter ones float.
    - Large density difference reduces mixing efficiency.
3. **Viscosity (in liquids/semisolids)**
    - High viscosity → more difficult mixing.
    - Low viscosity → easier mixing and dispersion.
4. **Shape of Particles**
    - Spherical particles mix more uniformly.
    - Irregular shapes cause poor flow and uneven mixing.
5. **Speed and Intensity of Mixing**
    - Too slow → inadequate blending.
    - Too fast → risk of de-mixing or segregation.
    - Optimal mixing speed must be selected.

## Types of Mixing

Mixing is the process of combining two or more phases (solid, liquid, or semi-solid) to form a uniform product with consistent physical and chemical properties. In pharmaceutics, mixing ensures uniform drug distribution, stability, bioavailability, and accurate dosage.

Mixing is broadly divided into three types:

1. **Solid Mixing**
2. **Liquid Mixing**
3. **Semi-Solid Mixing**

# 1. Solid Mixing

Solid mixing refers to the blending of two or more solid materials (powders, granules, excipients, API, etc.) to achieve a uniform distribution.

### Mechanisms of Solid Mixing

There are three main mechanisms:

1. **Convective Mixing**
   - Large masses of material are transferred from one location to another by bulk movement.
   - Movement of powder occurs due to mixing equipment like ribbon blenders, planetary mixers, etc.
   - Particles are carried along in bulk, leading to better distribution.
2. **Shear Mixing**
   - Mixing occurs by application of shear forces.
   - Particles slide over each other due to mechanical action, breaking up clusters and distributing materials uniformly.
   - Common in mixers with high shear blades.
3. **Diffusive Mixing**
   - Individual particles undergo random movement due to differences in size, shape, or density.
   - Smaller particles diffuse through void spaces, resulting in homogeneous distribution.
   - Achieved by prolonged gentle tumbling or rotating drum mixers.

## 2. Liquid Mixing

Liquid mixing is the process of blending two or more liquids to obtain a uniform solution, dispersion, or emulsion.

**Mechanisms of Liquid Mixing**

1. **Turbulent Mixing**
   - Achieved by high-speed stirring or agitation.
   - The rapid and chaotic movement of liquid molecules ensures efficient blending.
   - Used in preparation of emulsions and suspensions.
2. **Laminar Mixing**
   - Occurs in viscous liquids or at low stirring speeds.
   - Layers of liquid slide smoothly over each other, leading to gradual mixing.
   - Common in liquid-liquid extractions and viscous syrups.
3. **Bulk Transport**
   - Large-scale movement of liquid caused by pumping, stirring, or shaking.
   - Ensures uniform distribution of solutes or suspended particles.

## 3. Semi-Solid Mixing

Semi-solid mixing involves blending viscous, thick materials such as ointments, creams, gels, and pastes to achieve uniform consistency and distribution of active and inactive ingredients.

**Mechanisms of Semi-Solid Mixing**

- **Shear Mixing** → High shear forces break up lumps and distribute ingredients.
- **Convective Mixing** → Movement of large masses of material within the container.
- **Diffusive Mixing** → Limited role due to high viscosity, but helps in micro-distribution.

## Difference Between Solid and Liquid Mixing

| Feature | Solid Mixing | Liquid Mixing |
| --- | --- | --- |
| **Phases** | Mixing of powders or granules (solid-solid) | Mixing of solutions, emulsions, suspensions |
| **Homogeneity** | Difficult to achieve (may form clusters) | Easier to achieve (true solution possible) |
| **Power Requirement** | Relatively less | Higher (especially for turbulent flow) |
| **Mechanisms** | Convective, Shear, Diffusive | Turbulent, Laminar, Bulk transport |
| **Complexity** | More complex (risk of segregation) | Generally simpler |
| **Examples** | Tablet granules, powder blends | Syrups, suspensions, emulsions |

# Double Cone Blender

## Principle

- The Double Cone Blender works on the principle of tumbling action. When the blender rotates, the material inside is continuously divided, intermingled, and recombined, ensuring uniform mixing of dry powders and granules.

## Construction

1. **Blender Body** – Consists of a double-cone shaped chamber, usually made of **stainless steel** or other non-corrosive materials.
2. **Inlet** – Provided at the top for loading powders or granules.
3. **Outlet/Discharge Valve** – Located at the bottom for unloading blended material.
4. **Support Frame** – Holds the blender body securely and allows rotation.
5. **Motor & Drive System** – Provides controlled rotational movement of the blender.
6. **Control Panel** – Used to operate and adjust the speed of blending.

**Working**

- Dry powders or granules are fed into the blender through the inlet port.
- The blender is rotated at a fixed speed.
- The conical shape causes powders to tumble and cascade in multiple directions, promoting homogeneous mixing.
- After sufficient blending time, the material is discharged through the outlet valve.

**Advantages**

- Provides uniform mixing.
- Low energy consumption compared to other mixers.
- Versatile – suitable for free-flowing dry powders and granules.
- Easy to clean and maintain.

**Disadvantages**

- Not suitable for materials with high moisture content or sticky powders.
- Time-consuming for achieving complete mixing.
- Not efficient for very fine cohesive powders.

**Applications**

- Mixing of dry powders in pharmaceutical formulations.
- Blending of granules for tablet and capsule production.
- Used in food industry for mixing flour, spices, etc.
- Applied in chemical and cosmetic industries for uniform mixing of ingredients.

# Twin Shell Blender (V-Blender)

## Principle

The Twin Shell Blender works on the principle of tumbling action and diffusion mixing.

- As the blender rotates, powders are repeatedly divided and recombined.
- The V-shaped design ensures movement of particles along multiple paths, leading to uniform mixing.

## Construction

1. **Blender Body** – Made of two stainless steel cylindrical shells joined at an angle (~75–90°), forming a V-shaped chamber.
2. **Inlet** – For loading the material, usually at the top with a lid.
3. **Outlet/Discharge Valve** – At the bottom of the V for unloading blended powder.
4. **Support Frame** – Holds the blender in position and allows rotation.
5. **Motor & Drive System** – Provides controlled rotation of the V-shell.
6. **Control Panel** – For adjusting speed and operational time.

**Working**

- Powders or granules are fed into the V-shaped chamber.
- The blender rotates around its horizontal axis.
- Due to the V-shape, the material continuously splits and recombines while sliding along the chamber walls.
- This promotes diffusion and convective mixing without applying strong shear forces.
- The blended product is discharged through the bottom outlet.

**Advantages**

- Produces uniform mixing for free-flowing powders.
- Gentle mixing action → suitable for fragile materials.
- Low energy consumption.
- Easy to clean and maintain.

**Disadvantages**

- Not suitable for materials with high moisture, stickiness, or cohesive nature.
- Time-consuming compared to high-shear mixers.
- Difficult to handle very fine or lightweight powders.

**Applications**

- **Pharmaceutical industry** – blending powders for tablets and capsules.
- **Food industry** – mixing of spices, flour, and dry food ingredients.
- **Chemical and cosmetic industries** – uniform mixing of dry powders and granules.

# Ribbon Blender

## Principle

The Ribbon Blender works on the principle of convective mixing**.**

- A set of inner and outer helical ribbons rotates inside a U-shaped trough.
- The outer ribbons move material in one direction (towards the center), while the inner ribbons move material in the opposite direction (towards the ends).
- This counter-flow action ensures uniform and quick mixing of powders and semi-solid materials.

## Construction

1. **Trough/Body** – U-shaped chamber made of stainless steel.
2. **Ribbons** – Double helical ribbons (inner and outer), mounted on a horizontal shaft.
3. **Shaft & Bearings** – Support and rotate the ribbons inside the trough.
4. **Drive System** – Motor and gearbox for controlled speed of rotation.
5. **Inlet (Hopper/Lid)** – For feeding powders or materials.
6. **Outlet (Discharge Valve/Port)** – At the bottom for unloading the blended material.

## Working

- Materials are loaded into the U-shaped trough.
- As the shaft rotates, outer ribbons push the material inward, while inner ribbons push it outward.
- Simultaneously, material moves radially and laterally, creating a three-dimensional mixing effect.
- After achieving uniform mixing, the blended product is discharged through the bottom valve.

## Advantages

- Provides fast and efficient mixing.
- Suitable for large-scale blending.
- Can handle powders, granules, and semi-solid materials.
- Can be fitted with jacketed troughs for heating/cooling if required.

## Disadvantages

- Not suitable for liquid mixing.
- Not ideal for materials that are sticky, gummy, or have high moisture content.
- May cause segregation in case of large differences in particle size or density.

## Applications

- Pharmaceutical industry – blending powders for tablets, granules, and dry syrups.
- Food industry – mixing flour, spices, and bakery ingredients.
- Cosmetic industry – mixing of powders and creams.
- Chemical industry – uniform mixing of chemicals, detergents, and fertilizers.

# Sigma Blade Mixer

## Principle

The Sigma Blade Mixer works on the principle of shear mixing and kneading.

- It consists of two counter-rotating Z-shaped blades (sigma blades).
- These blades apply high shear and compressive forces to the material, ensuring thorough mixing, kneading, and homogenization of highly viscous and sticky masses.

## Construction

1. **Mixing Chamber (Trough)** – A heavy-duty, jacketed trough made of stainless steel for heating/cooling if required.
2. **Sigma Blades** – Two Z-shaped blades mounted on shafts; rotate at different speeds (commonly in a 2:1 ratio).
3. **Drive Mechanism** – Motor, gearbox, and timing gears that control the blades' rotation.
4. **Discharge System** – A bottom discharge valve or tilting mechanism to remove the mixed mass.
5. **Cover** – Provided on top to prevent dusting or contamination.

## Working

- Material is loaded into the mixing chamber.
- The two sigma blades rotate toward each other at unequal speeds.
- One blade moves material from the sides of the trough to the center, while the other circulates material within the chamber.
- The combined effect produces intense shear, kneading, and folding action, ideal for cohesive and plastic materials.
- After uniform mixing, the final product is discharged through the bottom valve or tilting trough.

## Advantages

- Suitable for highly viscous, sticky, and plastic materials.
- Provides intense mixing and kneading.
- Can handle materials that are difficult to mix in ordinary blenders.
- Jacketed trough allows heating or cooling.

## Disadvantages

- High power consumption due to heavy mixing load.
- Cleaning is time-consuming.
- Not suitable for free-flowing powders or liquids.

## Applications

- Pharmaceutical industry – preparation of gum bases, ointments, and suppositories.
- Food industry – mixing dough, chewing gum, chocolates, and candies.
- Cosmetic industry – creams, gels, and pastes.
- Chemical industry – resins, adhesives, rubber compounds, and sealants.

# Planetary Mixer

## Principle

- The Planetary Mixer works on the principle of planetary motion.
- The mixing blade rotates on its own axis while simultaneously revolving around the central axis of the mixing bowl (like planets orbiting the sun).
- This motion ensures thorough mixing, kneading, and homogenization of semi-solid and viscous preparations.

## Construction

1. **Mixing Bowl** – A stainless steel bowl that holds the material to be mixed. It may be jacketed for heating or cooling.
2. **Agitator (Beater/Blade)** – Mounted on a vertical shaft; can be flat, spiral, or hook-shaped depending on the application.
3. **Planetary Gear System** – Provides dual motion: rotation around its own axis and simultaneous revolution around the bowl.
4. **Drive Mechanism** – Electric motor connected through a gearbox to control speed and torque.
5. **Discharge System** – Tilting bowl or bottom discharge valve for easy removal of product.
6. **Cover** – With ports for ingredient addition, preventing dust and contamination.

## Working

- Ingredients are placed in the mixing bowl.
- The agitator starts rotating around its own axis while revolving around the bowl.
- This dual action produces intense mixing and kneading, especially suitable for sticky, semi-solid, and viscous materials.
- After the desired mixing time, the product is discharged manually or by automatic mechanisms.

## Advantages

- Ensures thorough and uniform mixing due to planetary motion.
- Versatile – can handle powders, semi-solids, and pastes.
- Easy to operate with variable speed control.
- Can be used for both small-scale and large-scale production.
- Hygienic design with stainless steel construction.

## Disadvantages

- Not suitable for free-flowing liquids or dry powders.
- Higher maintenance cost compared to simple mixers.
- Cleaning can be time-consuming for very sticky materials.

Applications

- Pharmaceutical industry – preparation of ointments, creams, pastes, tablet granulations.
- Cosmetic industry – creams, gels, lotions.
- Food industry – dough, cake batter, sauces.
- Chemical industry – adhesives, sealants, and lubricants.

# Propeller Mixer

## Principle

- Propeller mixer works on the principle of fluid flow and turbulence.
- A high-speed rotating propeller impeller creates axial flow, which circulates liquid throughout the vessel, producing uniform mixing.
- Suitable for low to medium viscosity liquids.

## Construction

1. **Mixing Vessel** – Cylindrical tank, usually stainless steel, sometimes jacketed for heating or cooling.
2. **Propeller Impeller** – 2–4 blades made of stainless steel, fixed on a vertical or inclined shaft.
3. **Shaft** – Connects impeller to the motor, positioned centrally or off-center.
4. **Drive Mechanism** – Electric motor with speed control, often 400–1500 rpm.
5. **Baffles** – Fixed inside the tank to prevent vortex formation and improve mixing efficiency.

## Working

- Liquid is filled in the vessel.
- The motor rotates the propeller at high speed.
- The impeller blades push the liquid axially (up–down flow), generating turbulence and circulation.
- Continuous movement ensures proper mixing, dissolution, and homogenization of liquids.

## Advantages

- Efficient for liquid–liquid and solid–liquid mixing.
- Simple design and easy to operate.
- Produces rapid circulation in large tanks.
- Can be used in both small-scale and large-scale operations.

## Disadvantages

- Not suitable for highly viscous liquids or semi-solids.
- Vortex formation may occur without baffles.
- Limited use in solid mixing.

## Applications

- Pharmaceutical industry – preparation of syrups, suspensions, and solutions.
- Chemical industry – mixing dyes, chemicals, and liquid fertilizers.
- Food industry – juices, beverages, liquid foods.
- Cosmetic industry – lotions, shampoos, and liquid formulations.

# Turbine Mixer

## Principle

- Turbine mixers work on the principle of agitation and turbulent mixing.
- A flat-bladed turbine impeller rotates at moderate speed, producing radial and tangential flow, which creates strong shear forces for mixing.
- Suitable for medium to high viscosity liquids.

## Construction


1. Mixing Vessel – Usually cylindrical, made of stainless steel, with baffles to improve flow.
2. Turbine Impeller – Flat or curved blades (4–8 blades) mounted on a disc.
   - Diameter: 30–50% of tank diameter.
3. Shaft – Connects turbine impeller to motor.
4. Motor & Gearbox – Provides power and speed control (50–200 rpm).
5. Baffles – Prevent vortex and improve mixing efficiency.

**Working**

- The liquid is filled into the vessel.
- The turbine impeller rotates at moderate speed.
- Flow pattern:
  - Radial flow (outward from impeller).
  - Tangential flow (around the vessel).
  - Creates high turbulence and shear, improving mixing of viscous fluids.
- Solid particles can also be suspended uniformly.

**Advantages**

- Suitable for medium to high viscosity liquids (creams, pastes).
- Creates strong turbulence and shear, ensuring uniform mixing.
- Can handle liquid–liquid, liquid–solid, and gas–liquid systems.
- More efficient than propeller mixers for thick liquids.

**Disadvantages**

- Higher power consumption than propellers.
- May cause foaming if used with some liquids.
- Not ideal for very delicate materials (due to high shear).

**Applications**

- Pharmaceuticals – suspensions, viscous syrups, emulsions, creams, ointments.
- Food industry – sauces, dairy products, viscous beverages.
- Cosmetics – gels, shampoos, lotions.
- Chemical industry – paints, adhesives, polymer dispersions.

# Paddle Mixer

## Principle

- Works on the principle of agitation and bulk movement of materials.
- The flat blades (paddles) rotate slowly in a tank, causing radial and tangential flow.
- Suitable for highly viscous liquids, pastes, and semi-solids.

## Construction

1. Mixing Vessel – Cylindrical tank, usually stainless steel, sometimes jacketed for heating/cooling.
2. Paddle Shaft – Central shaft fitted with flat blades (paddles).
    - Paddles may be flat, inclined, or pitched.
    - Blade clearance is small, close to the vessel wall.
3. Motor & Gear System – Provides low-speed rotation (20–100 rpm).
4. Baffles – Sometimes used to prevent vortex and improve mixing efficiency.

## Working

- The viscous material (paste or thick liquid) is filled into the vessel.
- The paddles rotate slowly, pushing material radially and tangentially.
- This creates bulk circulation and kneading action.
- Effective mixing occurs by dragging material along vessel walls and folding layers.

## Advantages

- Effective for highly viscous liquids and semi-solid materials.
- Simple design and easy to operate.
- Gentle mixing → suitable for shear-sensitive materials.
- Can be jacketed for heating/cooling.

## Disadvantages

- Not efficient for low-viscosity liquids.
- Mixing is slower compared to propeller or turbine mixers.
- May require high power for very viscous materials.

## Applications

- Pharmaceuticals – ointments, creams, emulsions, gels, suspensions.
- Food industry – pastes, dough, sauces, jams, jelly.
- Cosmetics – thick lotions, creams, gels.
- Chemical industry – paints, adhesives, heavy slurries

# Silverson Emulsifier

## Principle

- Works on the principle of high shear mixing.
- A high-speed rotor rotates inside a stationary stator → creates intense shearing, tearing, and turbulence.
- Large globules of dispersed phase are broken into fine droplets, forming a stable emulsion or suspension.

## Construction


1. Mixing Head (Emulsifier head):
    - Consists of a rotor (impeller) inside a stator (perforated stationary housing).
    - Rotor speed: 3000–8000 rpm.
2. Stator:
    - Cylindrical metal casing with holes or slots.
    - Holds material while allowing sheared liquid to pass through.
3. Rotor:
    - High-speed impeller fitted inside stator.
    - Creates suction, drawing materials into mixing head.
4. Motor & Shaft:
    - Provides high-speed rotation to rotor.
5. Vessel/Tank:
    - Holds liquid or slurry to be emulsified.
    - May be jacketed for heating/cooling.

## Working

- Liquid (continuous phase) and another immiscible liquid (dispersed phase) are placed in vessel.
- Rotor rotates at high speed → draws materials into emulsifying head.
- Materials are subjected to intense shear forces as they pass through narrow gaps of rotor–stator.
- Large droplets are broken down into uniform fine globules.
- Final product: stable emulsion, suspension, or dispersion.

## Advantages

- Produces fine, stable emulsions.
- High efficiency due to strong shear.
- Suitable for heat-sensitive materials (short processing time).
- Can handle both small lab scale and large industrial batches.

## Disadvantages

- High energy consumption.
- Not suitable for extremely viscous materials.
- Generates heat (may need cooling).
- High maintenance cost (due to wear of rotor-stator).

## Applications

- Pharmaceuticals – emulsions, suspensions, ointments, creams, syrups.
- Food industry – sauces, dressings, ice creams, dairy emulsions.
- Cosmetics – lotions, gels, emulsified creams, shampoo.
- Chemical industry – paints, varnishes, polymers, emulsified resins.