PHB

Dr. Arvind Kumar Gupta
(M.Pharm, PDCR, PGDMM & Ph.D)
GATE 2003 Qualified with 97.2 percentile
Dr. S. N. Dev College of Pharmacy
Shamli (U.P.)

OFFICE:BUILDINGNo.3/314,OFFICE-1,GAUSHALAROAD,SHAMLIDISTRICTSHAMLI(U.P.)–247776
Mobile:+91-9719638415
Email:arvindrkgit@gmail.com

Course Name	**: D. Pharm**
Year	**: First Year**
SubjectName	**: Pharmaceutics**
Topic Name	**: Mixing**

4.3 MIXING

Mixing and Homogenization

MIXING is defined as the unit operation that combines two or more components together by agitation, shear or mixers. The final product of mixture contains uniform distribution of both components of mixture. **Example of mixers:** Blenders, Planetary mixtures, Propellers etc.
If this is achieved it produces a theoretical 'ideal' situation, i.e. a ***perfect mix***.

Objectives of mixing:

1. To make simple physical mixture: In the production of tablets, capsules, sachets and dry powders two or more powders or granules are mixed.
In linctuses two or more miscible liquids are mixed completely.
2. Physical change: Mixing may aim at producing a change that is physical, for example the solution of a soluble substance. In case of dissolving a solid in a solvent mixing will take place by diffusion but the process will be slow. In this case agitation makes the process rapid.
3. Dispersion: In case of emulsions and creams two immiscible liquids are mixed where one liquid is dispersed into other. In suspension and pastes solid particles are dispersed in a liquid by mixing.
4. Promotion of reaction: Mixing will usually encourage (and control at the same time) a chemical reaction, so ensuring uniform products.

Types of Mixtures

Mixtures may be divided into three types that differ fundamentally in their behavior:
1. Positive mixtures
2. Negative mixtures
3. Neutral mixtures

1. Positive mixtures: are formed from materials such as gases or miscible liquids, which mix ***spontaneously*** and ***irreversibly*** by diffusion and tends to approach a perfect mix.
There is no input of energy required.
e.g. Mixing of sodium chloride and sugar in water.
2. Negative mixtures: after mixing, the components will tend to separate out. If this occurs quickly, then energy must be continuously input to keep the components in dispersed state.
Negative mixtures are more difficult to form and a higher degree of mixing efficiency is required.
e.g. Calamine lotion.
3. Neutral mixtures: are static in their behavior, the components having no tendency to mix spontaneously, nor do they segregate when mixed.
e.g. Pastes, ointments and mixed powders.

Mechanism:

A. Mechanism of solid-solid mixing

Solids mixing proceeds by a combination of one or more of the following mechanisms:

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

B. Mechanisms of Liquid – Liquid mixing

The mechanism of mixing of liquids can be studied under four classes. They are:

1. Bulk transport
2. Turbulent mixing
3. Laminar mixing
4. Molecular diffusion

C. Mechanisms of Solid – Liquid mixing

D. Mechanisms of Semi Solid mixing

Double Cone Blender

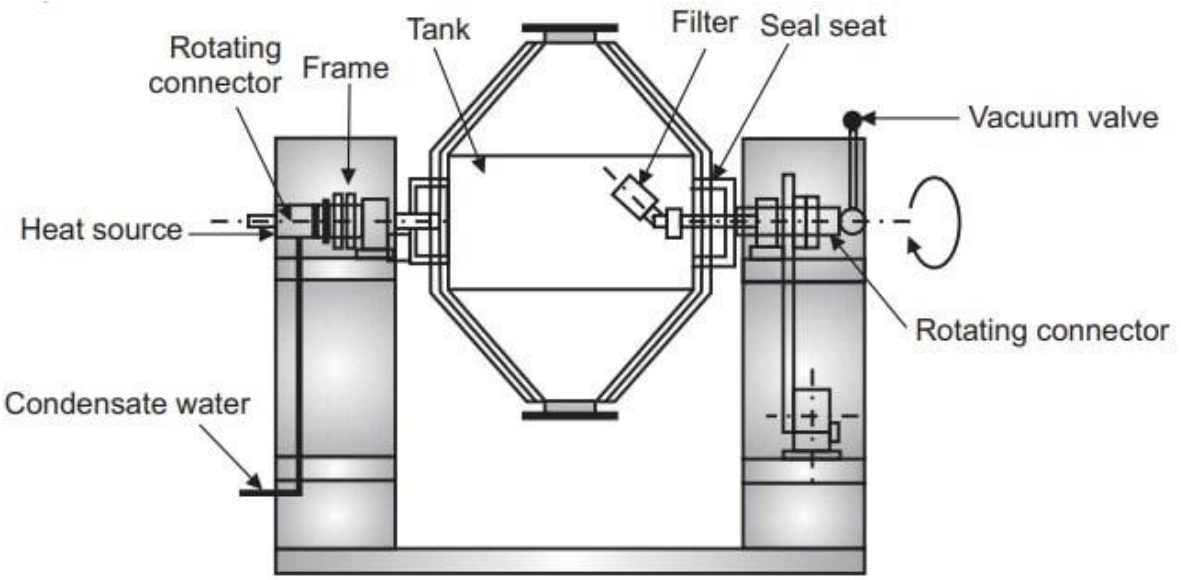
Mixing is one of the most common pharmaceutical operations. It is difficult to find a pharmaceutical product in which mixing is not done at one stage or the other during its manufacturing. **Double Cone Blender** is one of the commonly used equipment for mixing ingredients.

1. Principle:

- The mixing occurs due to tumbling motion.
- The **Double Cone Blenders** design is most often used for the intimate dry blending of free-flowing solids.
- 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 conical shape at both ends enables uniform mixing and easy discharge.

2. Construction:

- All parts of equipment including mixing tank and blades are made of stainless steel.
- The equipment consist of two cones joined as a cylindrical section which is rotated about an axis on the shaft.



3. Working:

1. The powder is filled up to two third of volume of blender to ensure proper mixing.
2. The rate of rotation should be 30-100 revolutions per minute.
3. On rotation mixing occurs due to tumbling motion. The product can be discharged from the bottom of the equipment.
4. The mixing tank can be slanted freely at the angle of 0° to 360° degrees for discharging and cleaning purposes.

4. Advantages:

1. Easy to maintain and clean.
2. Large amounts can be handled easily.
3. There are no chances of clogging of material into corners.
4. It is efficient for mixing powders of different densities.

5. Disadvantages:

1. Not suitable for fine particles.
2. Not suitable for particles with greater particle size difference due to less shear.

6. Applications of Double Cone Blender

1. **Double Cone Blender** is efficient and versatile equipment for the homogeneous mixing of dry powders and granules. Dry powder mixing for tablets and capsule formulations.
2. **Double Cone Blender** can be used for pharmaceutical, food, chemical and cosmetic products etc.

Triple Roller Mill

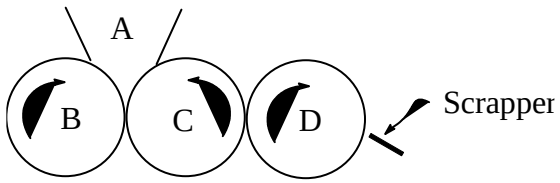
Triple Roller Mill is one of the equipment used for mixing purposes in various industries. It is also known as three roll mill.

1. Principle:

A three roll mill or **triple roller mill** is a machine that uses shear force created by three horizontally positioned rolls rotating in opposite directions and at different speeds relative to each other, in order to mix, refine, disperse, or homogenize viscous materials fed into it.

2. Construction:

- Triple roller mill consists of three rollers which are made up of hard abrasion-resistant material.
- These rollers are arranged in such a way that they come very close to each other.
- These rollers are rotated at different rates of speed. The material coming between the rollers is crushed depending on the gap between them and the difference in rates of movement of the two surfaces.



Cross-section of three roll mill

3. Working:

- The material after passing through the hopper comes between roller 1 and 2 and is reduced in size in the process.
- The gap between rollers 2 and 3 is usually less than that between 1 & 2, further, crush and smooth the mixture which adheres to the roller two.
- A scrapper is arranged in such a way that it can remove the mixed material from roller no.3. and does not allow the material which has not passed between both sets of the rollers to reach the scrapper.

4. Applications:

- It is used to disperse material within a semi-viscous material such as cream.
- It is used in the homogenization during preparation of ointments, creams, pastes, doughs and other viscous preparations.
- It is used for mixing pharmaceutical, herbal and alternative medicine, chemicals and fine chemicals, food, agriculture, cosmetics and detergents, pigments, etc.
- It can also be used in mixing of coating compositions, composites, adhesives, sealants and foods.

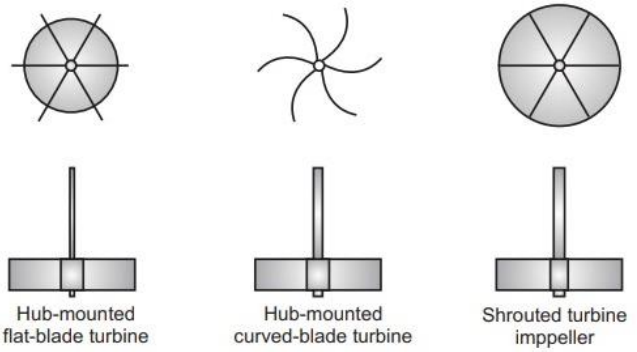
TURBINE MIXER

1. Principle:

Turbine mixer agitators can create a turbulent movement of the fluids due to the combination of centrifugal and rotational motion. These combined motions cause effective mixing of low to medium viscosity fluids.

2. Construction:

- A turbine consists of a circular disc impeller to which a number of short vertical blades are attached.
- The blades are surrounded by perforated inner and outer diffusing rings.
- Blades may be straight or curved.
- The diameter of the turbine ranges from 30-50% of the diameter of the vessel.



3. Working:

- Used in similar manner as that of impeller, however it is rotated at somewhat small speed than impeller (50- 200 rpm).
- Flat blade turbines produce radial and tangential flow but as the speed increases radial flow dominates. Pitched blade turbine produces axial flow.
- Near the impeller zone of rapid currents, high turbulence and intense shear is observed.
- Shear produced by turbines can be further enhanced using a diffuser ring (stationary perforated ring which surrounds the turbine).
- Diffuser ring increase the shear forces and liquid passes through the perforations reducing rotational swirling and vortexing.

4. Advantages:

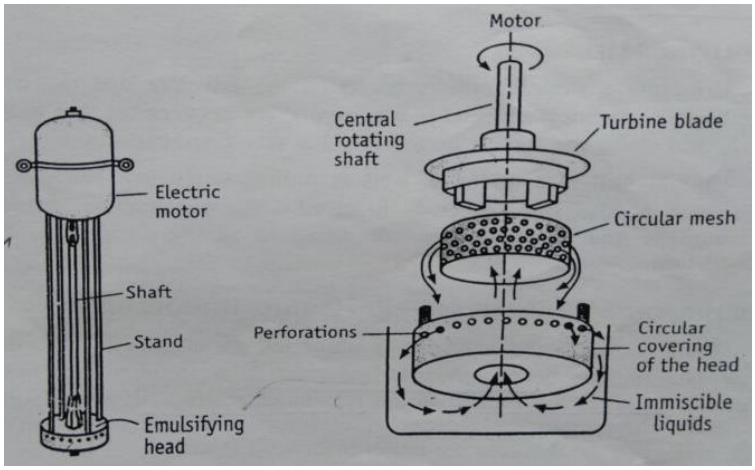
1. They can handle slurries with 60% solids.
2. Turbines are suitable for liquids of large volume and high viscosity, if the tank is baffled.
3. Effective for high viscous solutions with a wide range of viscosities up to 7.0 Pascal-Second.
4. In low viscous materials of large volumes turbine create a strong currents which spread throughout the tank destroying stagnant pockets.

Silverson Mixer Homogenizers

1. Principle:

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

2. Construction:



- ➢ It consists of long supporting columns connected to a motor that gives support to the head.
- ➢ The central portion contains a shaft, one end of which is connected to the motor and the other end is connected to the head.
- ➢ The head carries turbine blades.
- ➢ The blades are surrounded by a mesh, which is further enclosed by a cover having openings.

3. Working:

- The emulsifier head is placed in the vessel containing immiscible liquids (or coarse emulsion) in such a way that it should get completely dipped in the liquid.
- When the motor is started, the central rotating shaft rotates the head, which in turn rotates turbine blades at a very high speed.
- This creates a pressure difference. As a result, liquids are sucked into the head from the center of the base and subjected to intense mixing action.
- Centrifugal forces expel the contents of the head with great force through the mesh and onto the cover.
- As a result, a fine emulsion emerges through the openings of the outer cover.

- The intake and expulsion of the mixture set up a pattern of circulation to ensure the rapid breakdown of the bigger globules into smaller globules.

4. Advantages:

1. It can be used for batch operations. It is also used for continuous operation by incorporating into a pipeline, through which the immiscible liquids flow.
2. Silverson mixer is available in different sizes to handle liquids ranging from a few milliliters to several thousand liters.

5. Disadvantages:

Occasionally, there is a chance of clogging of the pores of the mesh.