## Introduction:

Mixing is defined as a process that tends to result in a randomization of dissimilar particles within a system.

The term MIX means to put together in one mass.

The term BLENDING means to mix smoothly and inseparably together during which a minimum energy is imparted to the bed.

The terms MIXING and BLENDING are commonly used interchangeable in the pharmaceutical industry.

The law of mixing appears to follow first order:

$$M = A\,(1 - e^{-kt})$$

Where M = degree of mixing after time t

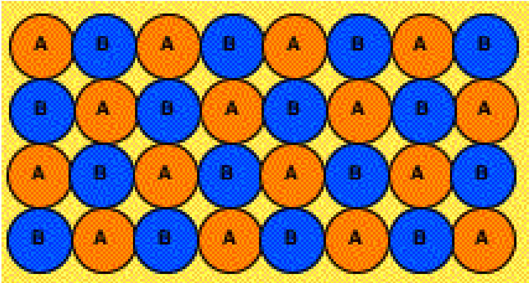
t = time

A and k = constants

- A and k depends on the:
  - ✓ Mixer geometry
  - ✓ Physical characteristics of the powders and
  - ✓ Proportion of the material being mixed.

**Degree of mixing:**

1- Ideal mixing or perfect mixing:




2- Acceptable mixing:

A- Random mixing.

B- Ordered mixing:

-Mechanical means of ordered mixing.

-Adhesion means of ordered mixing.

-Coating means of ordered mixing.

**Classification of mixing:**

A. Mixing of liquids

B. Mixing of solids

C. Mixing of immiscible liquids

D. Mixing of semisolids

**Mixing of Fluids**:

**Mechanism:**

**1. Bulk transport:** Movement of large portion of a material from one location to another location in a give system. Rotating blades and paddles are used.

**2.Turbulent mixing:** Highly effective, mixing is due to turbulent flow which results in random fluctuation of the fluid velocity at any given point within the system. Fluid velocity at a given point changes in 3 directions (X, Y and Z).

**3.Laminar mixing:** Mixing of two dissimilar liquids through laminar flow, i.e., applied shear stretches the interface between them. Suitable for liquids which require moderate mixing.

**4. Molecular diffusion:** Mixing at molecular level in which molecules diffuse due to thermal motion.

**5. Scale and intensity of segregation:** The quality of mixtures must ultimately be judged upon the basis of some measure of the random distribution of their components. Such an evaluation depends on the selection of a quantitative method of expressing the quality of randomness or "goodness of mixing ".

Bulk transport, turbulent flow, and laminar flow all result in the intermingling of "lumps" of the liquids to be mixed. The shape and size of these lumps largely depend on the relative contribution of each of these mechanisms to the overall process and on the time over which mixing is carried out. Unless molecular diffusion occurs, however, the composition of the lumps varies discontinuously from one to the next. In other words, each lump retains a constant and uniform internal composition. This can be altered only if molecular diffusion in the case of liquids and gases, or interparticulate motion in the case of powders, tends to eliminate concentration gradients between adjacent lumps. On this basis, Danckwerts defined "two quantities to describe the degree of mixing-namely the scale of segregation and the intensity of segregation. "

The scale of segregation is defined in a manner analogous to the scale of turbulence discussed earlier, and may be expressed in two ways: as a linear scale or as a volume *scale*. The linear scale may be considered to represent an average value of the diameter of the lumps present, whereas the volume scale roughly corresponds to the average lump volume. The intensity of segregation is a measure of the variation in composition among the various portions of the mixture. When mixing is complete, the intensity of segregation is zero.

**6. Time, dependence:** In any given case, the mechanisms that are active in bringing about mixing are time-dependent in their relative importance as the process of mixing proceeds. For example, consider the mixing of two miscible liquids of different densities contained in a vertical tank of cylindric form. The denser liquid is placed in the bottom of the tank, and an approximately equal volume of the less dense fluid is layered on top.

If the propeller is operated at a speed sufficient to produce turbulent flow in its discharge region, mixing occurs initially, to any significant degree, only by mechanisms that reduce the scale of segregation. Until such time as both fluids are present in the region of turbulence, created by the impeller, only bulk transport is effective in the mixing process. The convection results from the flow generated by the pumping action of the propeller. When the scale of segregation has been reduced to the point at which both fluids are present in the turbulent zone, turbulent mixing becomes an important means of further reduction in scale.

As pointed out earlier, diffusion is necessary for the effective reduction of the intensity of segregation to zero, at which time mixing is complete.

The increase in scale observed in the latter part of the mixing process, as shown in Figure 1-1, results from molecular diffusion, which equalizes the composition of adjacent portions of fluid, resulting in large regions with an intermediate composition. At the completion of mixing, the composition becomes uniform throughout the fluid, and the linear scale of segregation increases in value to a number equal in magnitude to the dimension of the mixing tank.

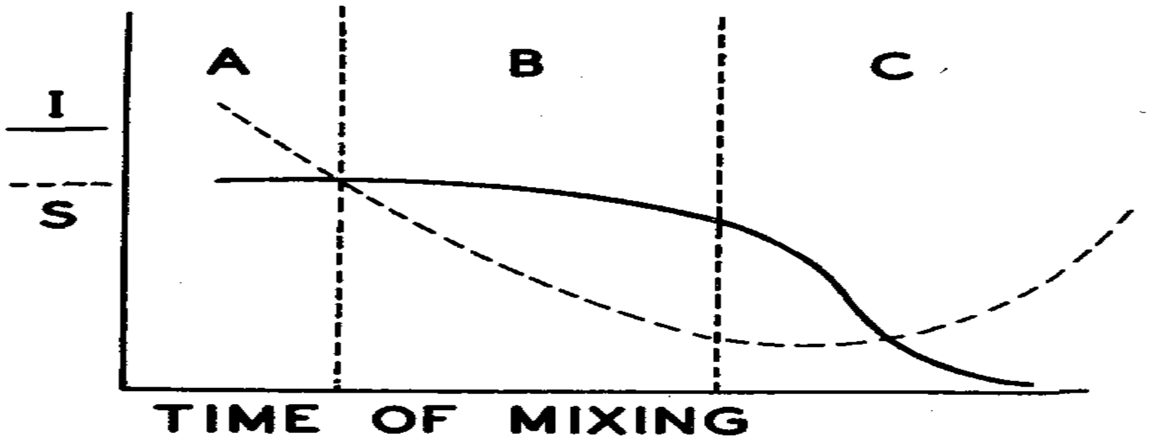



**FIG. 1-1.** *The intensity of segregation, I, and the scale of segregation, S, as a function of time. Bulk transport, turbulent mixing, and molecular diffusion are predominant over the time periods A, B, and C, respectively. The linear scale of segregation may be seen to increase at the end of the mixing operation. The final mixture will be uniform in composition and may be considered a single lump with a linear scale equal to the linear dimensions of the mixer.*

**Equipment:**

**Batch Mixing**, A system for batch mixing commonly consists of two primary components: (1) a tank (container) to hold the material being mixed, and (2) supplying energy to the system by an impeller, air steam, or liquid jet. Baffles, vanes, or ducts are used to direct the movement of material.

**Impellers, Air jets, Fluid jets, and Baffles:**

1- **Impellers**. The distinction between impeller types is often made on the basis of type of flow pattern they produce, or on the basis of the shape and pitch of the blades. Three basic types of flow may be produced: radial, axial, and tangential. These may occur singly or in various combinations. Figure 1-2 illustrates these patterns as they occur in vertical cylindric tanks. Propellers characteristically produce flow parallel to their axes of rotation, whereas turbines may produce either axial or tangential flow, or a combination of these.

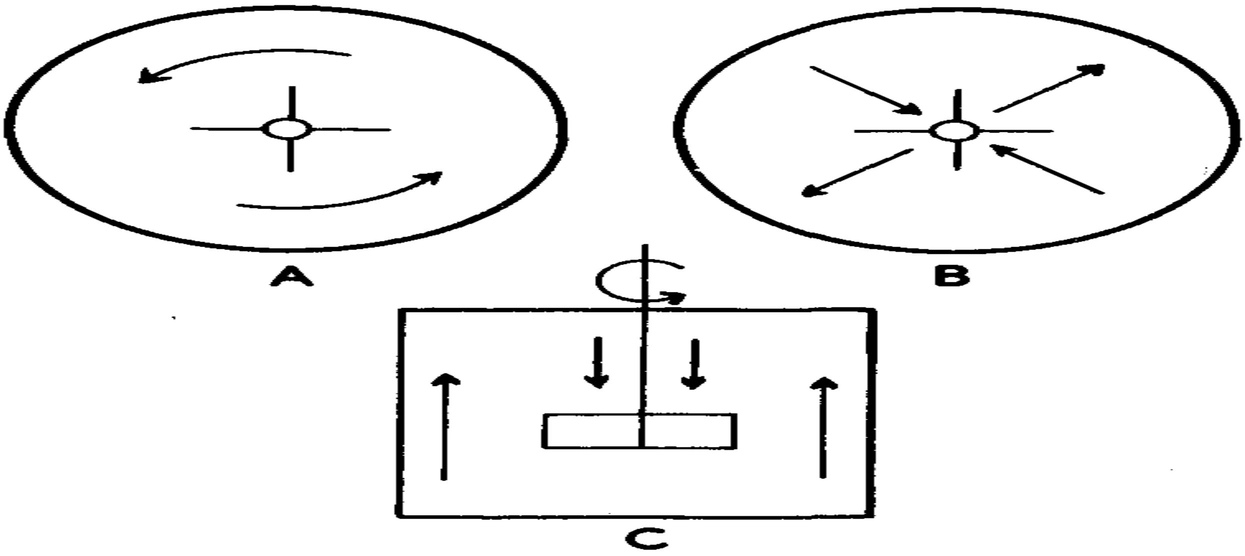
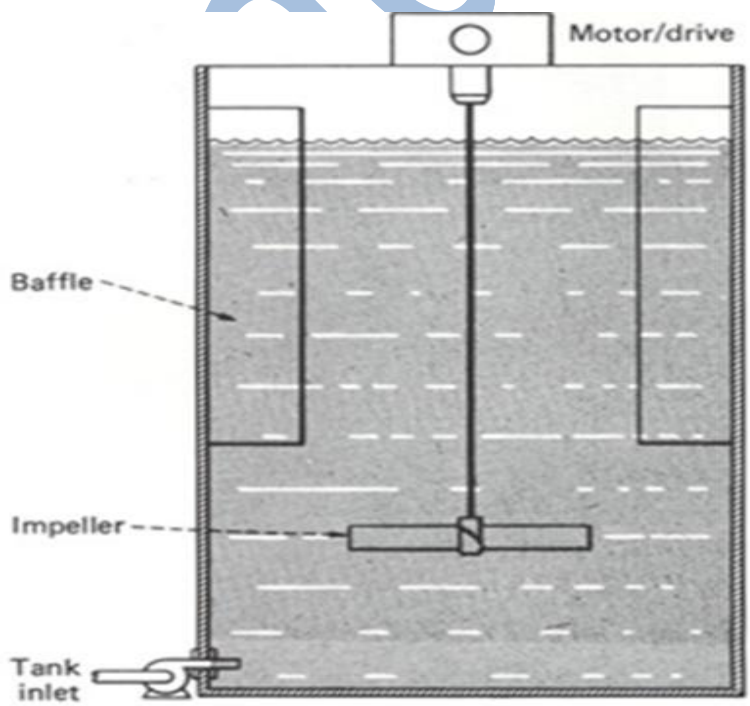



FIG. 1-2. A and B, Diagrammatic representation of cylindric tanks in which tangential and radial flow occur, respectively. C, Side view of a similar tank in which axial flow occurs. These diagrams represent systems in which only one type of flow occurs, in contrast to the usual situation in which two or more of these flow patterns occur simultaneously.

**Mixing Apparatus for fluids:**




Based on **shape** and **pitch**, impellers can be classified into 3 types:

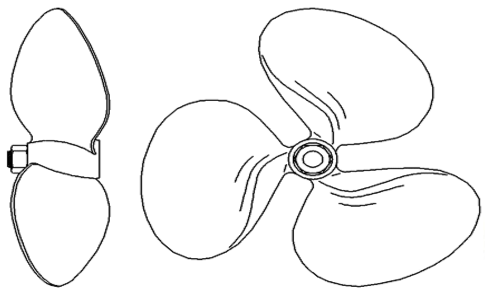
1- Propellers 2- Turbines 3- Paddles

**Propellers:** It consists of number of blades, generally 3 bladed design is most common for liquids. Blades may be right or left handed depending upon the slant of their blades.

Two are more propellers are used for deep tank.

Size of propeller is small and may increased up to 0.5metres depending upon the size of the tank.

Small size propellers can rotate up to 8000rpm and produce longitudinal movement.



**Advantages of propellers:**

A- Used when high mixing capacity is required.

B- Effective for liquids which have maximum viscosity of 2.0pascals.sec or slurry up to 10% solids of fine mesh size.

C- Effective gas-liquid dispersion is possible at laboratory scale.

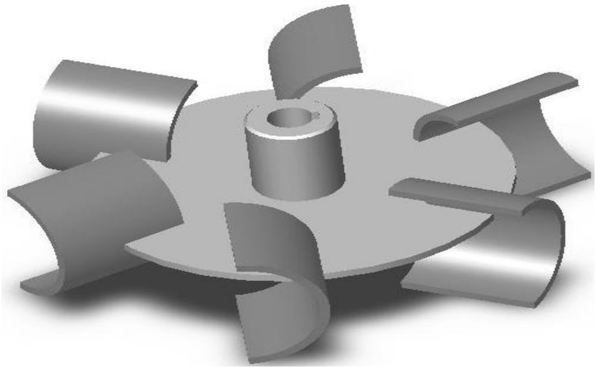
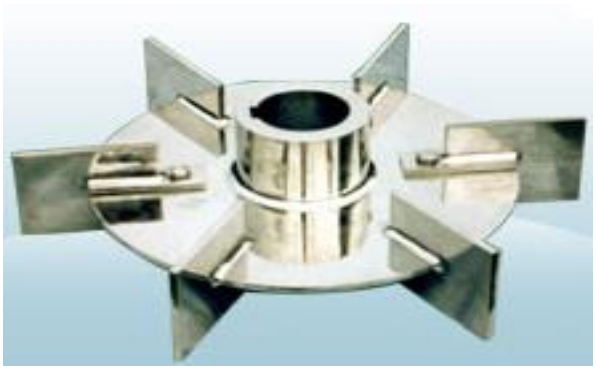
**Disadvantages of propellers:**

Propellers are not normally effective with liquids of viscosity greater than 5pascal.second, such as glycerin, castor oil, etc.

**Turbines:** consists of a circular disc to which a number of short blades are attached, blades may be straight or curved.

The diameter of the turbine ranges from 30-50% of the diameter of the vessel.

Turbines rotate at a lower speed than the propellers (50-200rpm).

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.

Advantages of Turbines:
A- Turbines give greater shearing forces than propellers through the pumping rate is less. Therefore suitable for emulsification.
B- Effective for high viscous solutions with a wide range of viscosities up to 7.0 Pascal. Second.
C- In low viscous materials of large volumes turbine create a strong currents which spread throughout the tank destroying stagnant pockets.
D- They can handle slurries with 60% solids.
E- Turbines are suitable for liquids of large volume and high viscosity, if the tank is baffled.

**Paddles:** consists of a central hub with long flat blades attached to it vertically.
Two blades or four blades are common. sometimes the blades are pitched and may be dished or hemispherical in shape and have a large surface area in relation to the tank in which they are used. Paddles rotate at a low speed of 100rpm. They push the liquid radially and tangentially with almost no axial action unless blades are pitched.
In deep tanks several paddles are attached one above the other on the same shaft. At very low speeds it gives mild agitation in unbaffled tank but as for high speeds baffles are

necessary.

**Uses of paddles:**

Paddles are used in the manufacture of antacid suspensions, agar and pectin related purgatives, antidiarrheal mixtures such as bismuth-kaolin.

**Advantages of paddles:**

Vortex formation is not possible with paddle impellers because of low speed mixing.

**Disadvantages of paddles:**

Mixing of the suspension is poor therefore baffled tanks are required.

2- **Air jets**. Subsurface jets of air, or less commonly of some other gas, are effective mixing devices for certain liquids. Of necessity and for obvious reasons, the liquids must be of (1)low viscosity, (2)nonfoaming, (3)unreactive with the gas employed, and (4)reasonably nonvolatile. The jets are usually arranged so that the buoyancy of the bubbles lifts liquid from the bottom to the top of the mixing vessel. This is often accomplished with the aid of draft tubes. (Fig. 1-4). The overall circulation in the mixing vessel brings fluid from all parts of the tank to the region of the jet itself.

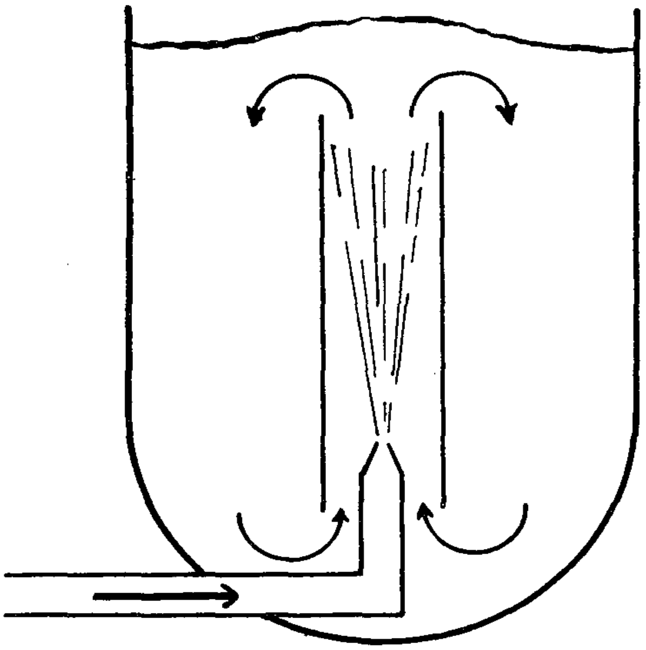


**FIG. 1-4.** *Vertical tank with centrally located air jet and draft tube. Bubbles confined within the draft tube rise, inducing an upward fluid flow in the tube. This flow tends to circulate fluid in the tank, bringing it into the turbulent region in the vicinity of the jet.*

3- **Fluid jets**. When liquids are to be pumped into a tank for mixing, the power required for pumping often can be used to accomplish the mixing operation, either partially or completely. In such a case, the fluids are pumped through nozzles arranged to permit good circulation of material throughout the tank. Fluid jets behave somewhat like propellers in that they generate turbulent flow in the direction of their axes. They do not in themselves, however, generate tangential flow, as do propellers.

4- **Baffles**. Bulk transport is important in mixing and is particularly desirable in the initial stages, when segregation may be present on a large scale. For bulk fluid flow to be most effective, an intermingling must occur between materials from remote regions in the mixer. To accomplish this, it is necessary to install auxiliary devices (Baffles, plates) for directing the flow. Baffle placement depends on the type of agitator used. Centrally mounted vertical shaft impellers tend to induce tangential flow, which is often manifested in the formation of a vortex about the impeller shaft. This is particularly characteristic of turbines with blades arranged perpendicular to the impeller shaft. The tangential motion does not in itself produce any mixing, except near tank walls where shear forces exist. Instead, swirl and the resultant vortex formation reduce the mixing intensity by reducing the velocity of the impeller relative to the surrounding fluid. If severe vibration occurs, and vortex reaches the impeller, this leads to uneven loading of the impeller blades and damaging it.

Sidewall baffles, when vertically mounted in cylindric tanks, are effective in eliminating excessive swirl and further aid the overall mixing process by inducing turbulence in their proximity. For these reasons, the power that can be efficiently applied by the impeller is significantly increased by the use of such baffles.

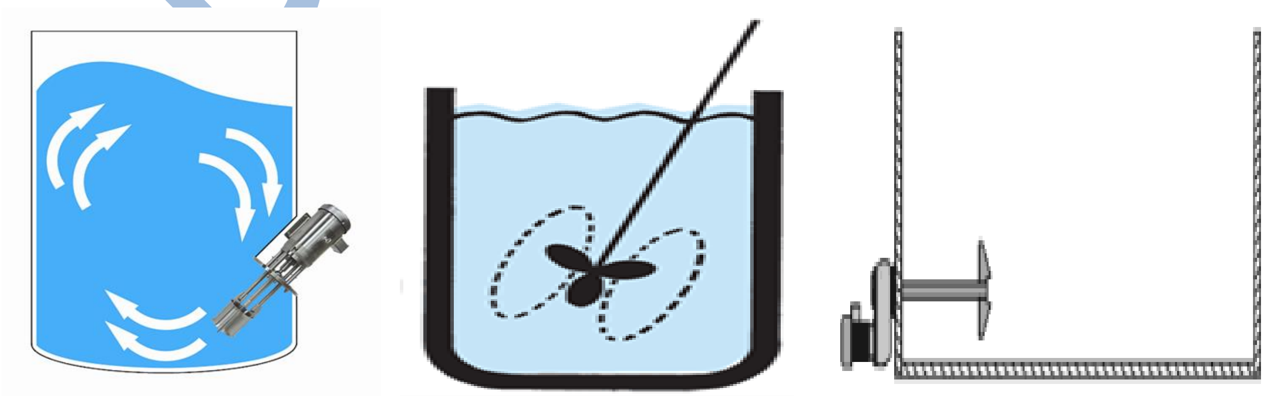
The best correction is by a change in impeller design so as to provide 'the desired general flow pattern. For example, a vertically mounted propeller in a cylindric tank, if set slightly to one side of the tank and canted a small amount in the direction opposite to its rotation, often can be operated efficiently without baffles.

An asymmetric tank geometry relative to the impeller may be used to produce an effect similar to that of baffles, and swirl prevention, but in many cases it is a time consumer due to the presence of regions within such tanks with poor circulation.

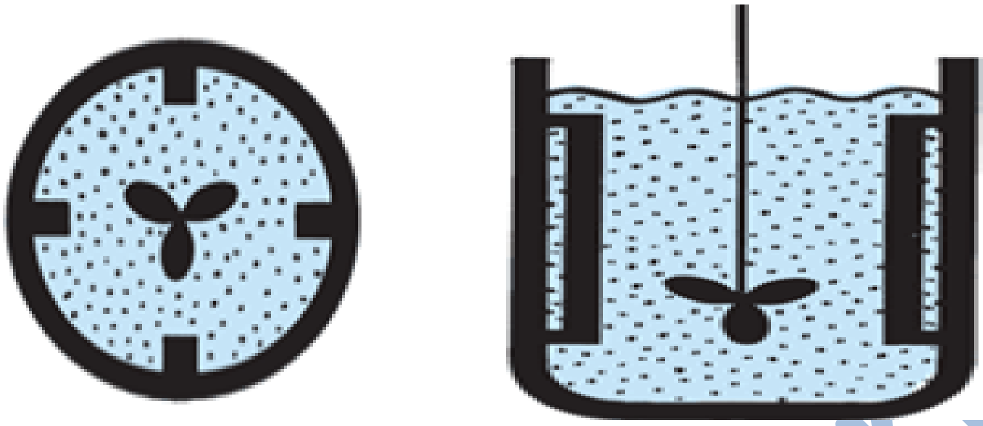
Side-entering propellers are often used with seldom swirling, as the tank geometry relative to the impeller provides a baffling effect and circulation of material from top to bottom. **Such a situation is also a source of contamination and may be difficult to clean.**

**Prevention of vortex formation:**

1-Impeller should in in any one of the position that can **avoid symmetry** such as off central, inclined, side entering, etc., and should be deep in the liquid.

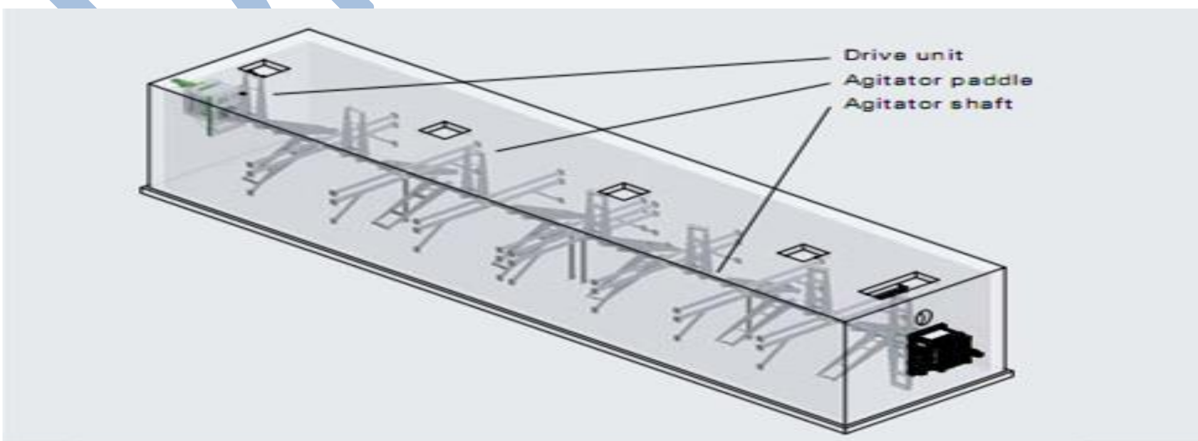


**2-Baffled containers should be used**. In such case impeller can be mounted vertically at the center.



**3-Two or more impellers are mounted on the same shaft** where greater depth is required. This system is known as push and pull mechanism. The bottom impeller is placed about one impeller diameter above the bottom of the tank. It creates zone of high turbulence.

**4-Tank other than cylindrical in shape** are used to prevent vortex formation. However, such shapes may facilitate the formation of dead spots.



**Continuous Mixing:** the process of continuous mixing produces an uninterrupted supply of freshly mixed material and is often desirable when very large volumes of material are to be handled. It can be accomplished in two ways: (1)in a tube or pipe through which the material flows and in which there is very little back flow or recirculation, or (2)in a chamber in which a considerable amount of holdup and recirculation occur. (Fig. 1-5).

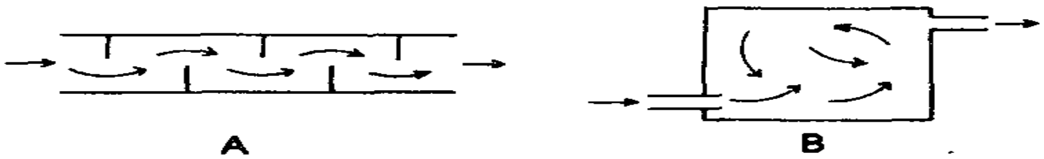



*FIG. 1-5. Continuous fluids mixing devices. A, Baffled pipe mixer; B, mixing chamber with flow induced recirculation. Both types induce turbulence in the fluid; however, recirculation is desirable when overall fluctuations occur in the material fed to the mixer, since these fluctuations will not be eliminated by simple transverse mixing in a pipe.*

## Mixer Selection:

**Equipment selection:** first and most important consideration in any mixing problem is equipment selection. 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.



**Monophase systems**. The viscous character and density of the fluid(s) to be mixed determine to a large extent the type of flow that can be produced and also, therefore, the nature of the mixing mechanisms involved. Fluids of relatively low viscosity are best mixed by methods that generate a high degree of turbulence (air jets, fluid jets, and the various high-speed impellers).

A viscosity of approximately 10 poise may be considered as a practical upper limit for the application of these devices.

Thick creams, ointments, and pastes are of such high viscosity that it is difficult if not impossible to generate turbulence within their bulk and laminar mixing, and molecular diffusion must be relied upon. Mixing of such fluids may be done with a **turbine of flat blade** design. A characteristic feature of such impellers is the relative insensitivity of their power consumption to density and/or viscosity.

**Polyphase system**. The mixing of systems composed of several liquid or solid phases primarily involves the subdivision or deaggregation of one or more of the phases present. The processes of homogenization, suspension formation, and emulsification may be considered forms of mixing.
Mixing of two immiscible liquids: (1)subdivision of one of the phases into globules, (2)then distributed throughout the bulk of the fluid.
The process usually occurs by stages during which the large globules are successively broken down into smaller ones. Two primary forces come into play here: the interfacial tension of the globules in the surrounding liquid, and forces of shear within the fluid mass. The former tends to resist the distortion of globule shape necessary for fragmentation into smaller globules.

**Reference text: The Theory and Practice of Industrial Pharmacy by Leon Lachman et al.**