
welcome

MIXING

BY

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Outline of the lecture:

Mixing

Definition and objectives

Mixing equipment

Impellers for liquids

Introduction

- Almost every pharmaceutical product contains more than one component, and this necessitates mixing or blending stages in their manufacturing process

Definition:

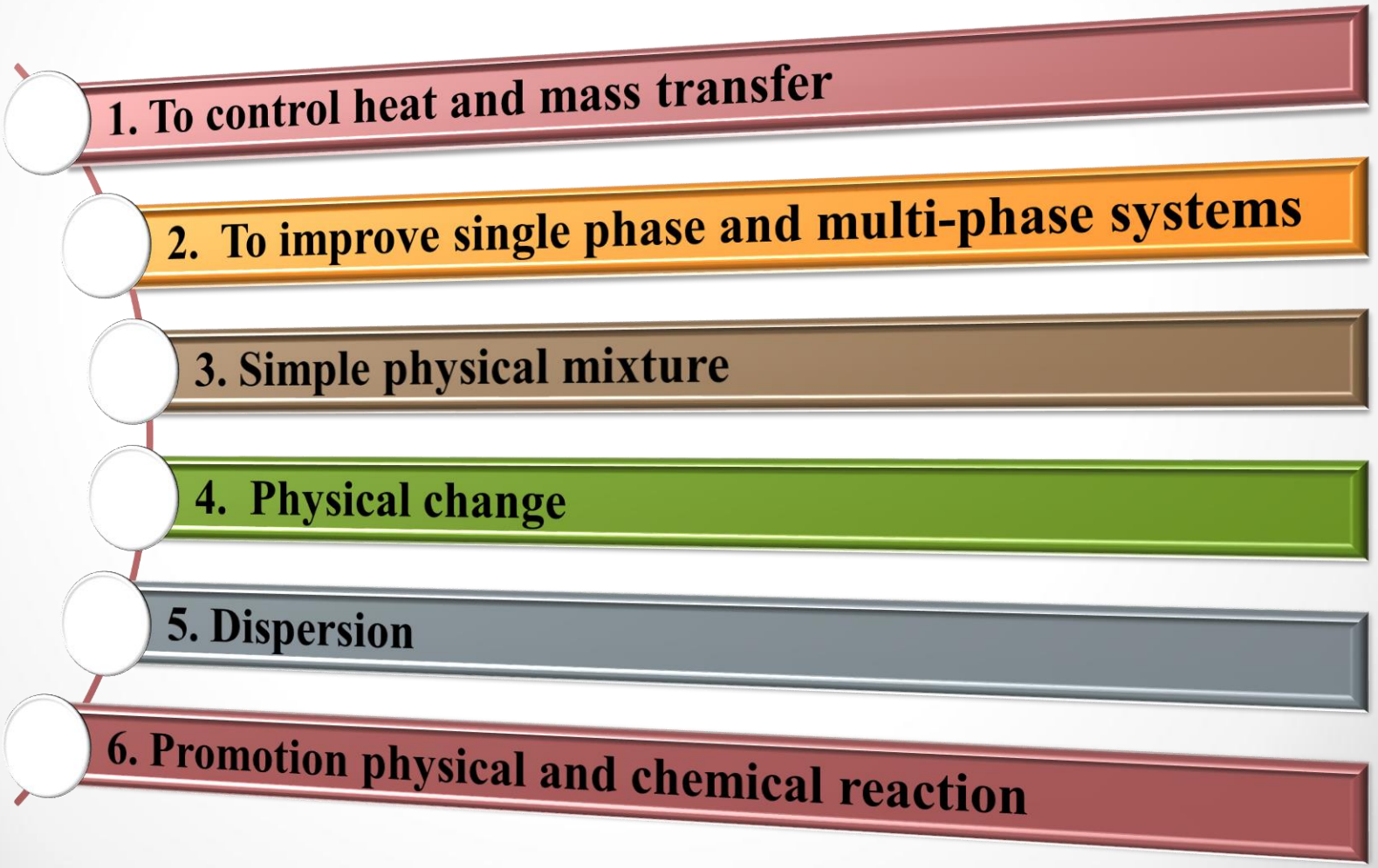
- Mixing is an operation in which two or more components (in a separate or roughly mixed condition) are treated so that each particle lies as nearly as possible in contact with a particle of each of the other ingredients. OR
- The process that tends to result in a randomization of dissimilar particles within a system.

→ This differs from an ordered system where particles are arranged according to an iterative تكرارية rule and follow a repetitive pattern.

- The term blending is synonymous with mixing, and segregation is the opposite
  - 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.

Objective of mixing

- Mixing is a fundamental step in most process sequences, and is normally carried out:



Objective of mixing

Dispersion

- Dispersion of two immiscible liquids (Emulsion and creams)
- Dispersion of a solid in liquid (Suspension or Paste).
- Good mixing is required to ensure stability.

Promotion of reaction

- Mixing activate, promote and and controls a chemical reaction, so ensuring uniform products.
- Such as dissolution, in which natural diffusion is supplemented by agitation.

Objective of mixing

Simple physical mixture

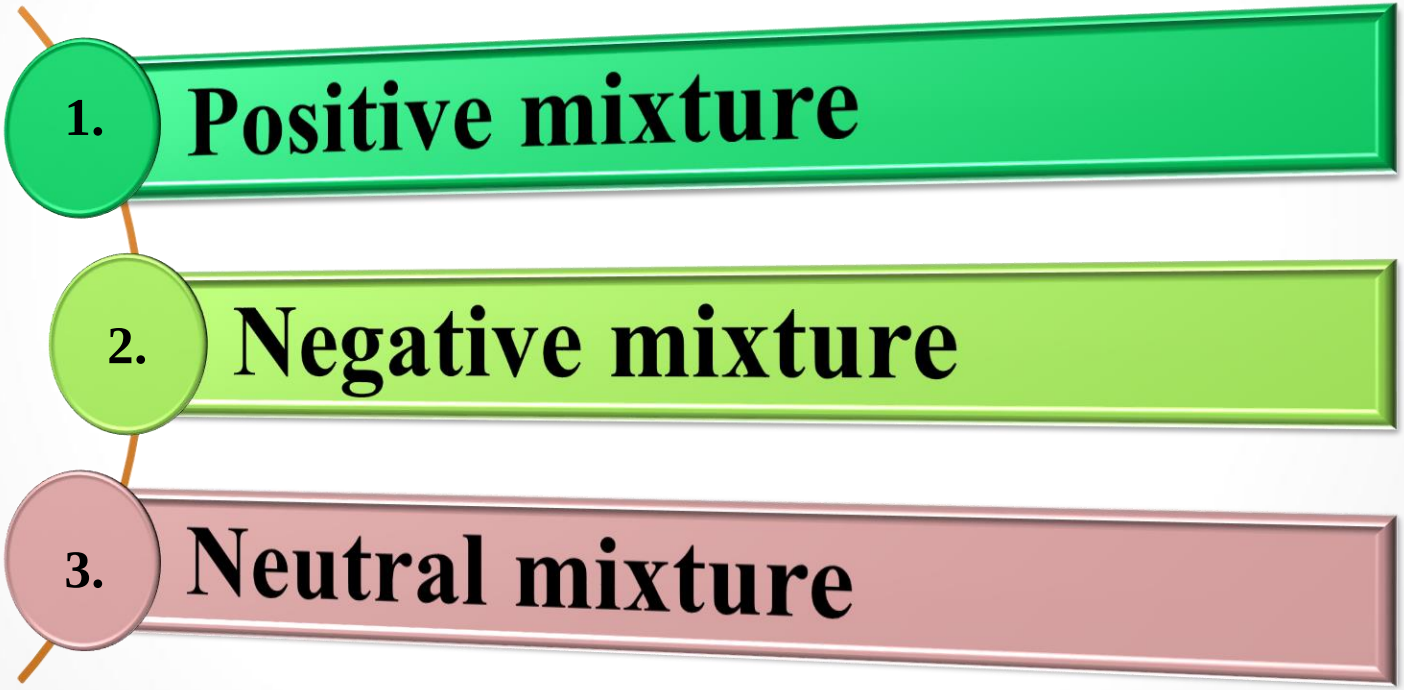
- This may be simply produced by blend two or more miscible liquids or two or more uniformly divide solids.
- In the production of tablets, capsules, sachets and dry powders.
- The degree of mixing must be high as much mixture are dilution of a potent substance and correct dosage must be ensured; so that small samples withdrawn from a bulk material represent the overall composition of the mixture.

Physical change

- Producing a change that is physical as distinct from chemical
- Example: the solution of a soluble substance (mixing a solid with a solvent to produce a solution).
- Lower efficiency of mixing in case of dissolving a solid in a solvent will often acceptable because it take place by diffusion and the process will be just slow.
- In this case agitation makes the process rapid.

Type of mixtures

Dank wert classified mixtures in to three types



1. Positive mixture

- Applies to systems in which spontaneous, irreversible, and complete mixing occurs (and tends to approach a perfect mix) via diffusion.
- Mixing……..Without energy → No input of energy if time of mixing is unlimited, although time will be shortened if energy is supplied.
- Separation…..Requires energy
- Generally, these materials do not show any problems during mixing.
- Example:. Mixture of two or more gases or miscible liquids (water and milk)

2. Negative mixture

- Negative mixtures are generally more difficult to form and maintain and require a higher degree of mixing, along with the expenditure of energy that needs to be supplied to keep components adequately dispersed.
- **Mixing…….Requires energy**
- **Separation….. Without energy: i.e.:** materials have the tendency **to separate** out from each other unless they are continuously stirred.
- Some separate faster, while for others, the separation is slower.

❑ **For example:** <u>any two-phase systems such as →</u>

1. suspensions of **insoluble** solids in liquids (fast separation)
2. Emulsions of two immiscible liquid, creams and viscous suspension (a slow separation).

3. Neutral mixture

- Neutral mixtures are static in behavior. →
- i.e., the components of neutral mixtures have no tendency to spontaneously mix or segregate unless an outside force acts on the system.
- Both mixing and segregation occurs with consumption of energy.

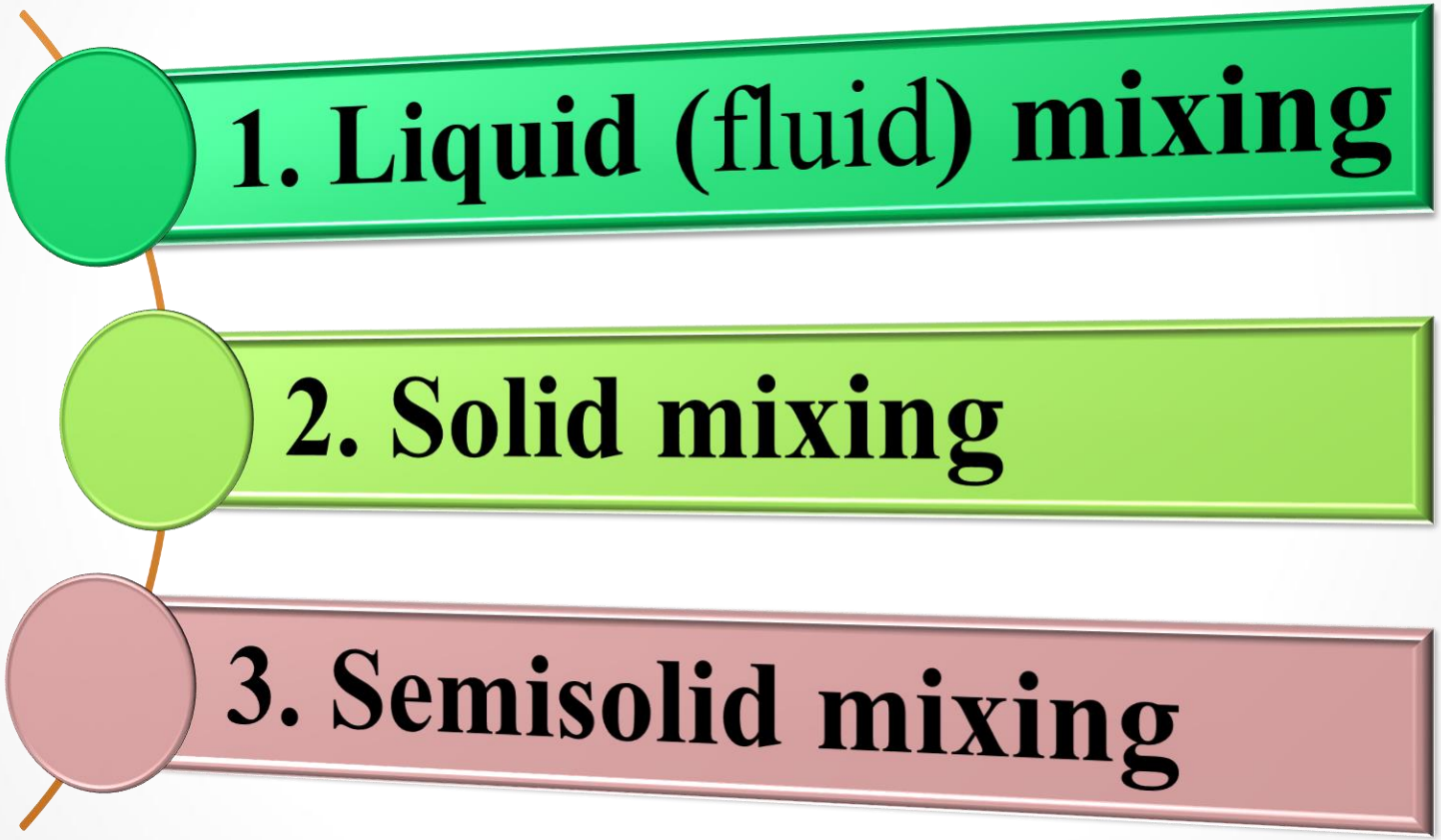
Examples are: → physical mixing

a) Mixed powders

b) Pastes

c) Ointments.

- Mixing will be dealt with in 3 categories



1. Liquid mixing

- is the formation of homogenous system by the application of shear
- Mixing process may be easy for some fluid and difficult for others. Following three parameters gives necessary knowledge about basic requirement of fluid for mixing.

    A. Flow characteristics.

    B. Mixing mechanisms.

    C. Mixing equipment

1. Liquid mixing

- Liquid mixing may be divided into following two subgroups:

1. Mixing of liquids and liquids

a. Mixing of two miscible liquids (just stirring or shaking)

b. Mixing of two immiscible liquids (shear force is essential)

2. Mixing of liquids and solids

a. Mixing of liquids and soluble solids (just stirring or shaking)

b. Mixing of liquids and insoluble solids

1. Liquid mixing

A. Flow characteristics:

- The fluid may flow freely or flow with resistance.
- Depending on the relationship between their shear rates and the applied stress, fluids show different flow characteristics and may be classified as
  - **Newtonian**
  - **Non - Newtonian**

Remember that:

- Shear: is the movement of material relative to parallel layer. (shear are generated by interactions between moving fluids and the surfaces over which they flow during mixing)
- Shear stress (F, Dyne/ cm^2) is the force applied per unit Area required to move one layer of fluid in relation to another. i.e. to make liquid flow (Force/Area)
- Shear rate (G, S^{-1}) difference in velocity dv, between two planes of liquids separated by distance dr (i.e. dv/dr) (as the derivative of velocity with respect to distance measured normal to the direction of flow.)

1. Liquid mixing

A. Flow characteristics:

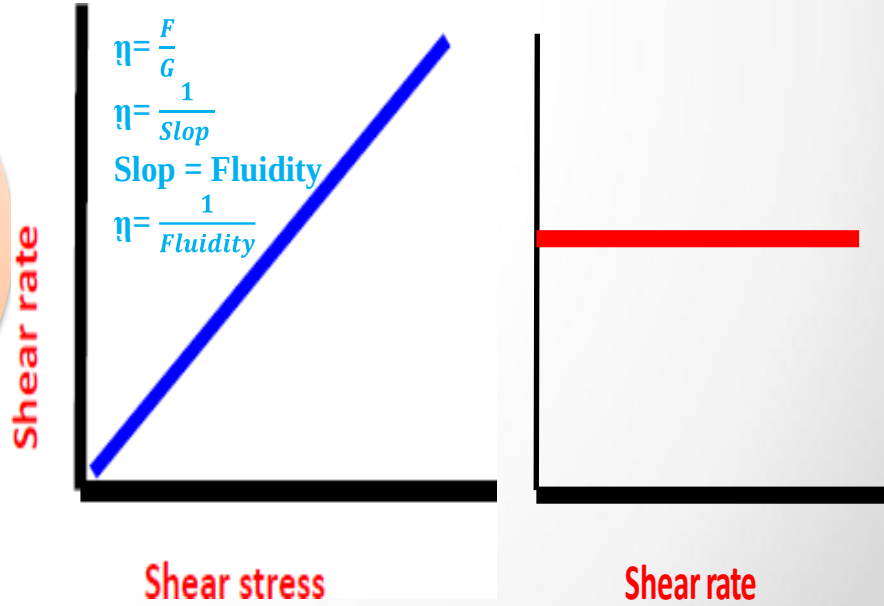
Newtonian fluids

- Such fluid flow like water and for them the rate of shear is directly proportional to the applied shear stress (force applied).
- Newtonian fluids are those whose have a dynamic viscosity dependent on T but independent of flow rate.

Remember that:

- **The viscosity is the ratio of shear stress to the shear rate (**the internal friction of a moving fluid**)**

  $(\eta = \frac{F}{G})$



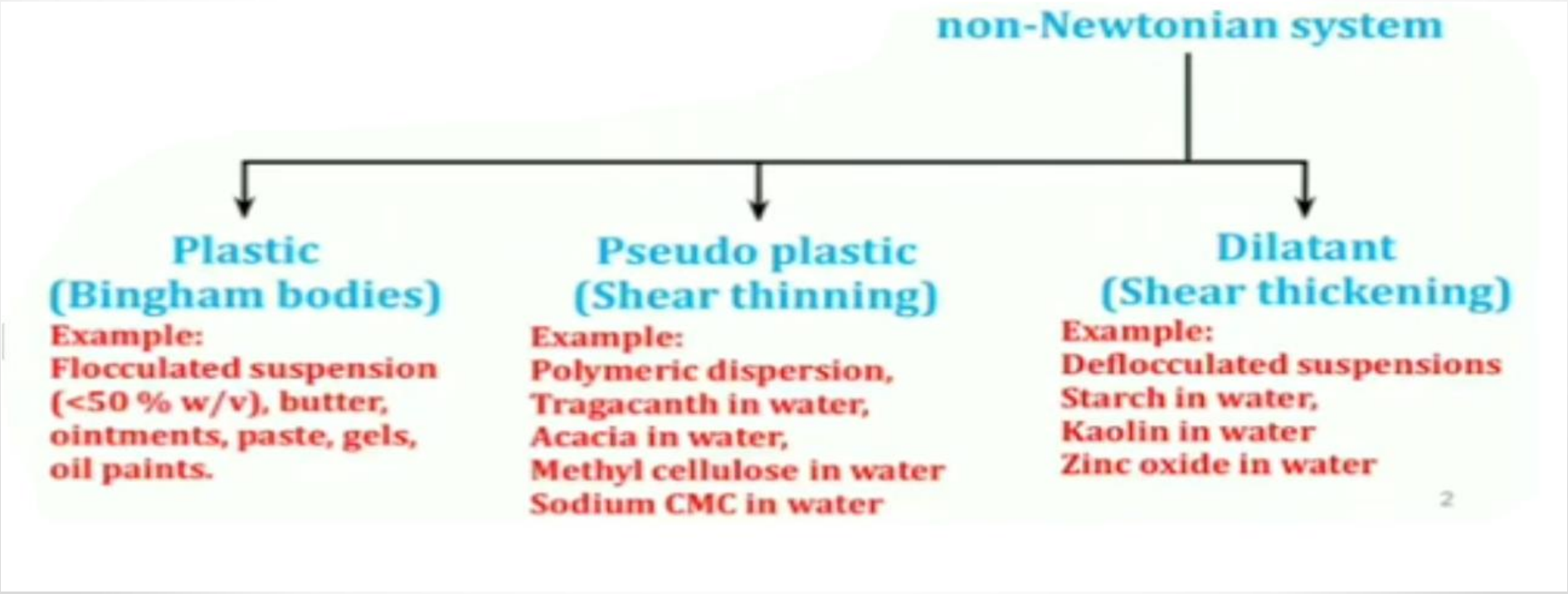
1. Liquid mixing

A. Flow characteristics:

non-Newtonian fluids

- Fluids whose apparent dynamic viscosity is a function of the shear stress (i.e. changes with the increase or decrease of shear stress).

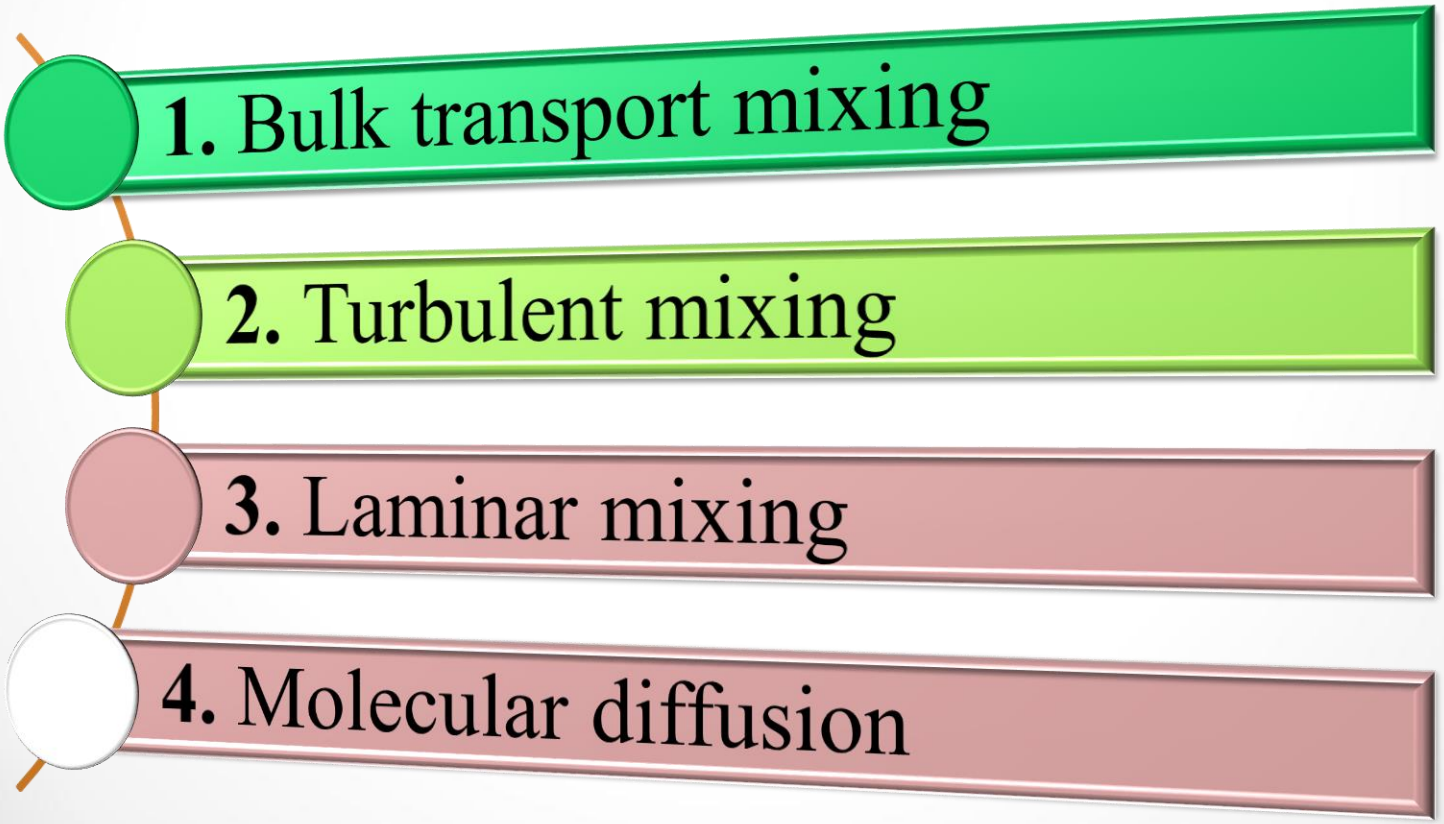
Remember that:



1. Liquid mixing

B. Mixing mechanisms.

- Four types of mechanism are involved in mixing of fluids.
- Usually, more than one of these mechanisms is operative in practical mixing situations. أكثر من الية واحدة تكون فعالة فى العملية الواحدة



1. Liquid mixing

B. Mixing mechanisms.

1. Bulk transport mixing → The movement of a relatively large portion of the material being mixed from one location in a system to another location in a given system.

- Simple circulation of material Does not result in efficient mixing
- It is made effective by means of rotating blades and paddles or shuffling خلط of system in three dimensions.

2. Turbulent Mixing → Highly effective, mixing is due to turbulent flow which results in a random fluctuation of the fluid velocity at any given point within the system

- Fluids move in 3-D directions; movement may be dominant in one direction.
- يمكن تصور التدفق المضطرب بسهولة باعتباره مركبًا من الدوامات
- https://www.youtube.com/watch?v=qzS01USNlAU.

1. Liquid mixing

B. Mixing mechanisms.

3. **Laminar الرقائقي (streamline) Mixing** → Mixing of two dissimilar liquids through laminar flow, → i.e., shear that is generated stretches يمتد the interface between them.

- In this mechanism, layers fold back on themselves. → Layers increase. → Therefore, mixing decreases fluid layer thickness.
- Suitable for highly viscous liquids or which require moderate (gentle) mixing.

https://www.youtube.com/watch?v=AGDVup5RotE.

4. **Molecular Diffusion** → mixing at the molecular level in which molecules diffuse as a result of their thermal motion.

- This type of mixing occurs whenever there is a concentration gradient (According to Fick's law)

1. Liquid mixing

C. Mixing equipment

- A system for liquid mixing commonly consists of two primary components:
  - a tank or other container suitable for holding the material being mixed,
  - a means of supplying energy to the system to bring about reasonably rapid mixing.
- Power may be supplied to the fluid mass by means of an
  - impeller, ▪air stream, or ▪ liquid jet.
- Besides supplying power, these also serve to direct the flow of material within the vessel.
- Baffles, vanes, and ducts are also used to → direct the bulk movement of material in such mixers, thereby increasing their efficiency

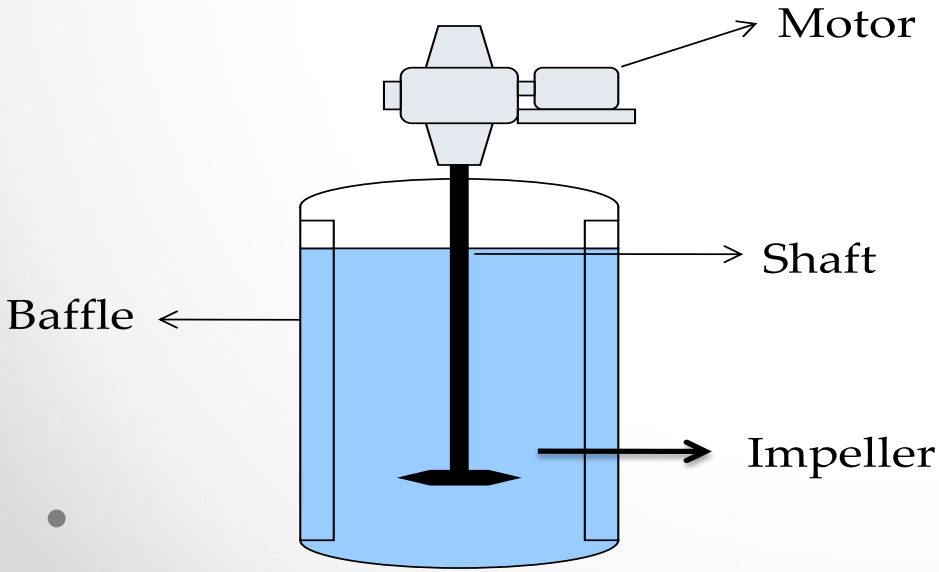
❑ **Batch mixing :** Mixing a specific and limited quantity of material
  - batch mixing is usually more feasible, أكثر جدوى

❑ **Continuous mixing :** for larger volumes

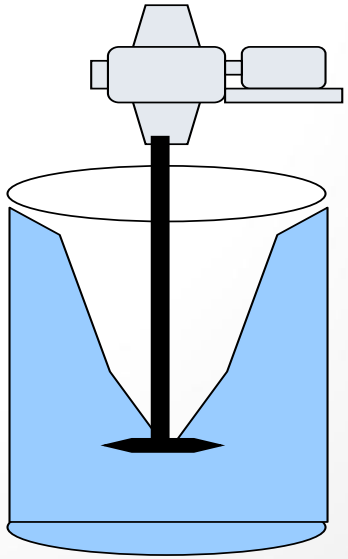
1. Liquid mixing

- **Impellers:** Liquids are most mixed by impellers rotating in tanks.
  - These impellers are classified as
    - Propellers
    - turbines
    - paddles
  - Distinction between impellers is made on the basis of :
    a. Type of flow pattern they produce
       - Radial flow
       - Axial flow
       - Tangential flow
       - These may occur singly or in various combinations
    b. Shape and pitch of blades

Baffled tank: no vertex

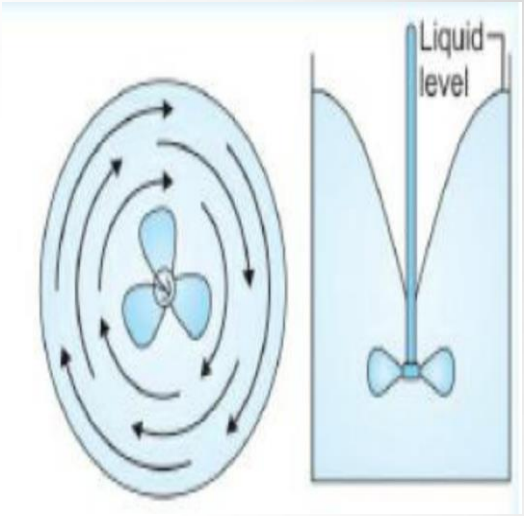


Un baffled tank: vertex formation



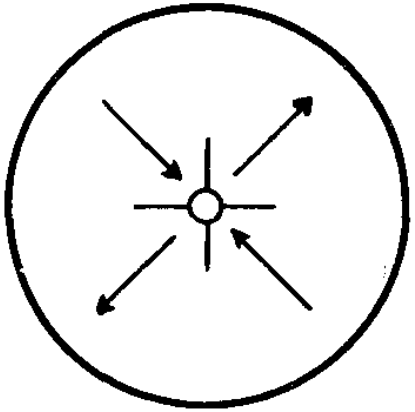
Flow pattern of impeller mixers

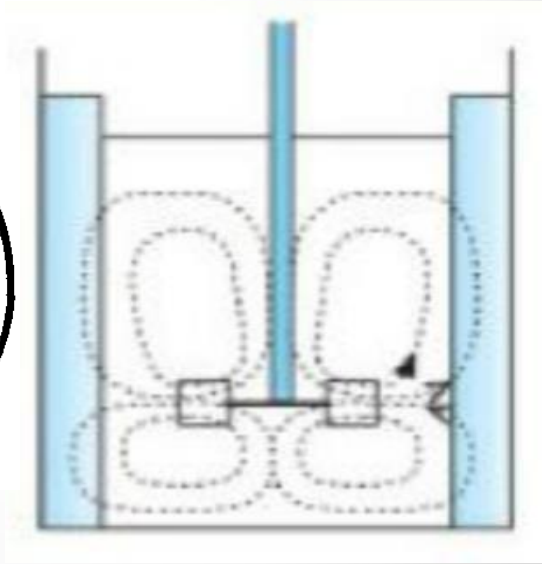
1. Tangential or rotational flow:



- Direction: The liquid flows tangentialمماسي to the circle of rotation around the impeller shaft.
- Effect: If shaft is placed vertically & centrally, tangential flow follows a circular path around the shaft & creates a vortex in the liquid

2. Radial flow: → perpendicular to the impeller shaft



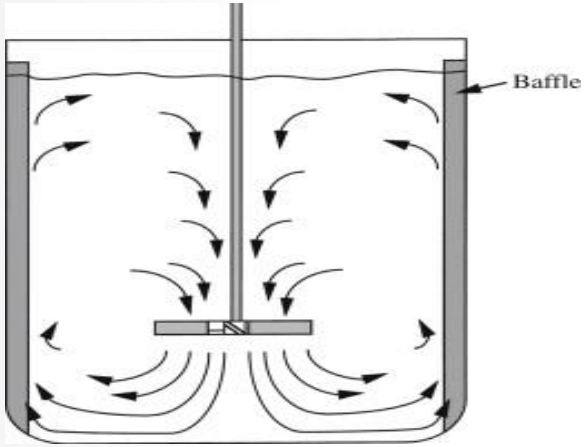


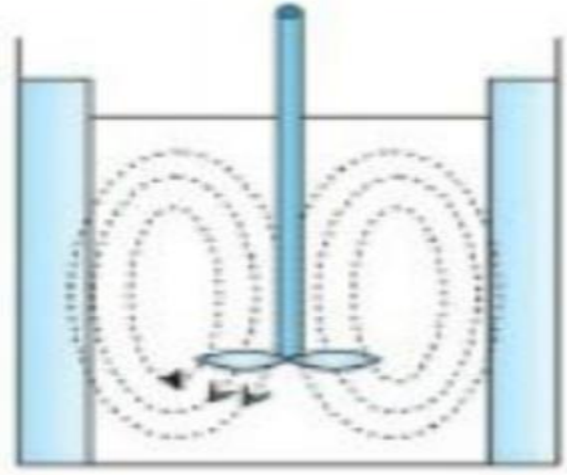
- Direction: The liquid drawn from above and below the impeller and discharged it toward the wall of the tank, perpendicular to the impeller shaft.
- dual recirculation loops above and under the impeller.

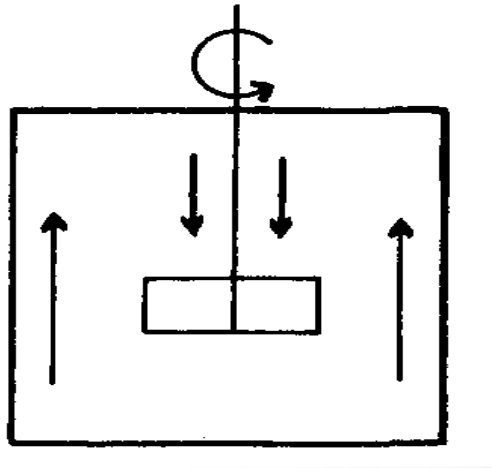
Flow pattern of impeller mixers

3- Axial or longitudinal flow: → parallel to the impeller shaft

- Direction: Fluid flow axially directed along the mixer shaft from top to bottom (down pumping) or from bottom to top (up-pumping).







N.B.

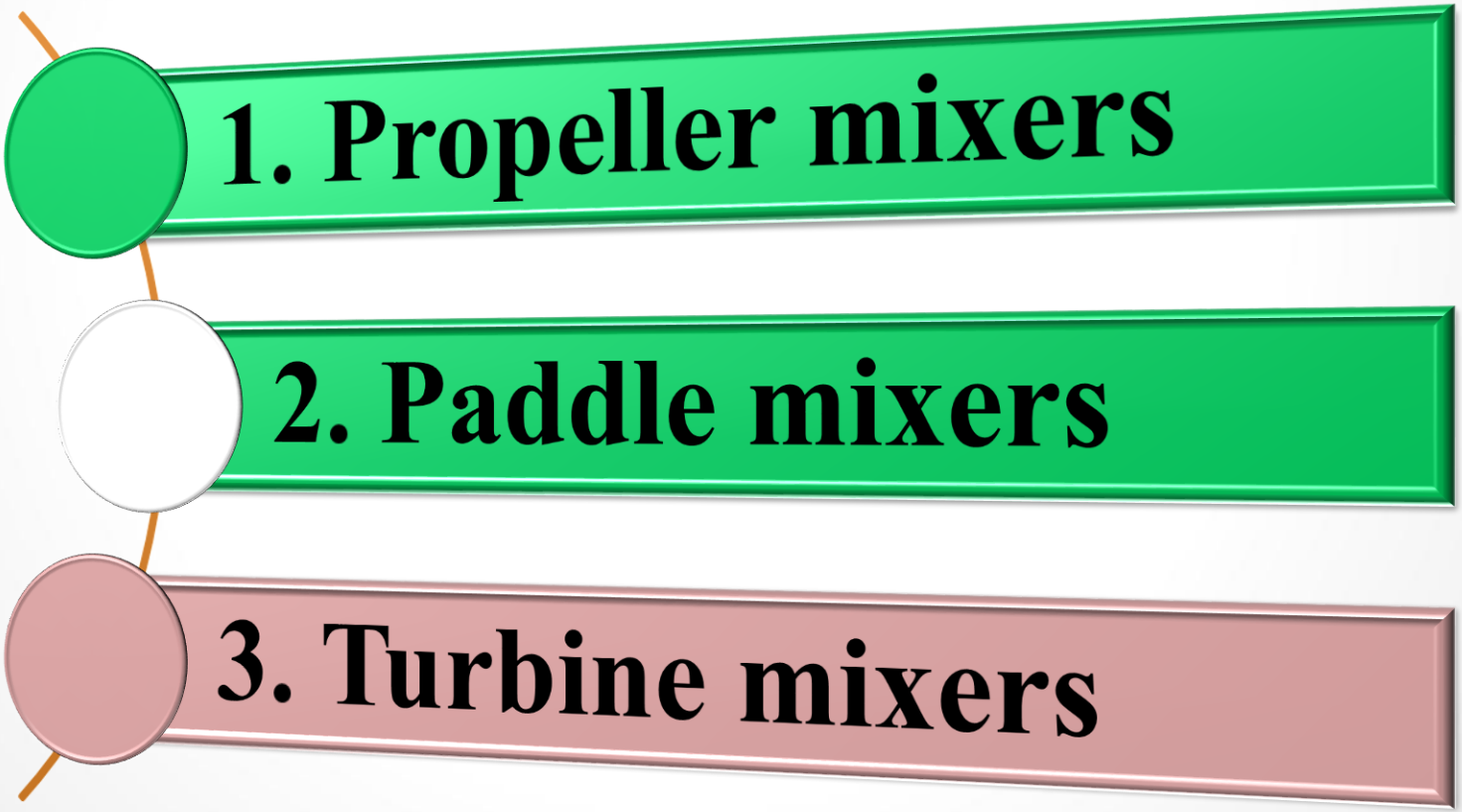
- Good mixing of liquids depends on the correct balance of the three types of flow
- https://www.youtube.com/watch?v=wzooJoF8A9M&list=PPSV
- https://www.youtube.com/watch?v=GqBOuD1ibDM

❑ Factor affecting flow pattern:

1. Type and position of impeller.
2. Size and Shape of the container.
3. Presence of baffles and agitator in the container.
4. Liquid properties

Types of impellers for mixing liquid dosage forms:

- Based on the shape of the blades and flow pattern produced by them, these impellers are classified as

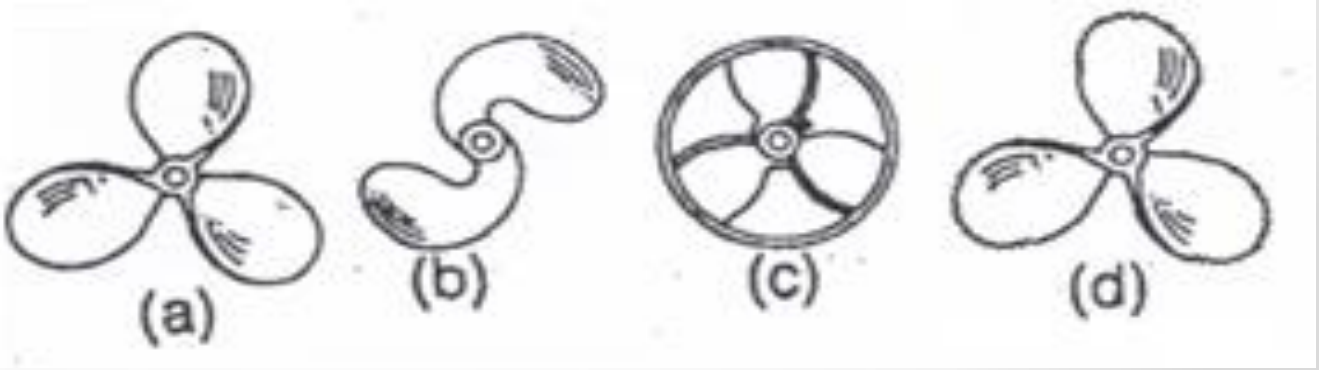


1. Propeller mixers

Construction

- Consist of angle blades attached at the end of the shaft, rotated by means of motor.
- The blades may be set at any angle or pitch, but for most applications, the pitch is approximately equal to the propeller diameter
- Any number of blades may be used but three-blades design is most common.
- It may be right or left-handed depending upon the slant of their blades
- The blades of the propeller, unlike those of a turbine, do not have a constant pitch throughout their length.

❑ **Revolution:** rotates at a high speed 400 – 1750 rpm/min (up to 8000 rpm).



1. Propeller mixers

- **Currents:** the primary effect of a propeller is due to Axial flow, although some tangential flow does occur
  - Also, intense turbulence usually occurs in the immediate vicinity of the propeller المجاورة مباشرة للمروحة.
  - Propellers are most efficient when they run at high speeds in liquids of relatively low viscosity

- **Used**

1. Effective for liquids which have maximum viscosity of 2.0 Pa.s or slurry up to 10% solids of fine mesh size.

- **Advantages of propellers:**

1. Used when high mixing capacity is required.

- **Disadvantages of propellers:**

1. Propellers are not normally effective with liquids of viscosity > 5 Pa.s, (such as glycerin or castor oil), due to absence of radial flow.
2. The centrally mounted vertical propeller produces vertex

3. Paddle mixers

Construction:

- Consist of a central vertical shaft to which 2 or 4 **long flat blades** are attached to it vertically).
- The blades sometimes pitched مائلة and may be dished or hemispherical.
- Their blades have a large surface area (Width of the blade is 1/6 - 1/10 its length) as compared to the tank in which they are employed, → that permits them to pass close to the tank walls and effectively mix viscous liquids and semisolids which tend to cling تشبث to these surfaces

Revolution : Paddle rotates at a lower speed of 50 rpm or less .

3. Paddle mixers

- **Current**: Circulation is primarily tangential flow, and somewhat radial flow but there is no axial (longitudinal) current unless blades are pitched.
  - concentration gradients in the axial and radial directions may persist in this type of mixer even after prolonged operation.

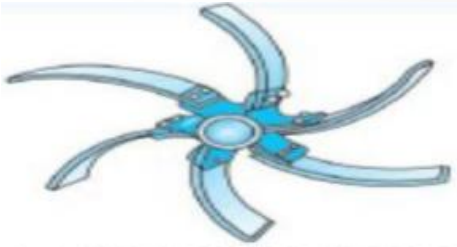
N.B: The ingredients should not be introduced to the mixing tank in layers.

- **Uses:**
  - Paddles are used in the manufacture of antacid suspensions,, 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:**

1. They are ineffective in suspending heavy solids because of absence of axial flow therefore baffled tanks are required.

3. Turbine mixers

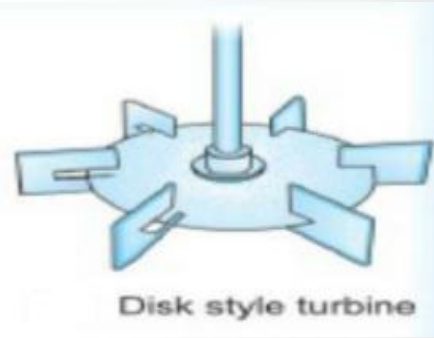
❖ Resemble paddles but the blades are more.


Curved blade turbine


Pitched blade turbir

Construction

- Turbines consist of a circular disk impeller to which a number of short, vertical blades (may be straight or curved) are attached.


Disk style turbine

Revolution: rotates at a lower speed (110-200 rpm/ min).

Diameter of the shaft: ranges from 30-50% of the inside diameter of the container.

Currents:

- Turbines having tilted (pitched) blades produce an axial discharge quite similar to that of propellers
- Turbines with blades (Flat) set at a 90-degree angle to their shaft → radial- and tangential flow but as the speed increases radial flow dominates (a radial flow is induced by the centrifugal action of the revolving blades)

3. Turbine mixers

❖ Advantages of Turbines:

1. Turbines give greater shearing forces than propellers through the pumping rate is less. Therefore, suitable for emulsification.
2. Effective for high viscous fluids with viscosities 1000 times more viscous than fluids in which a propeller of comparable size can be used.
3. Easy and cheap to manufacture and mostly with 4 blades. Hence it is highly applied in industry.
4. They can handle slurries with 60% solids.

❖ Disadvantages of turbines:

1. Not suitable for suspending heavy solid as propeller mixer, due to absences of marked vertical (axial) flow.

Over come: by using special heads

Vortex formation

Reasons:

A vortex develops at the center of the vessel:

- If the shaft of the impeller is placed vertical and centrally (symmetrically) in the tank.
- If the blades of the turbines are arranged perpendicular to the central shaft.
- At high impeller speeds, as velocity ↑→ the vortex ↑
- Unbaffled tank
- These impellers tend to induce tangential flow around the shaft with little or no mixing thus creates a vortex of the surface of the liquid.

❑ This is true except at very low impeller speeds or at very high liquid viscosities (>20,000 cps), neither of which is normally encountered in practice in the pharmaceutical industry.

Vortex formation

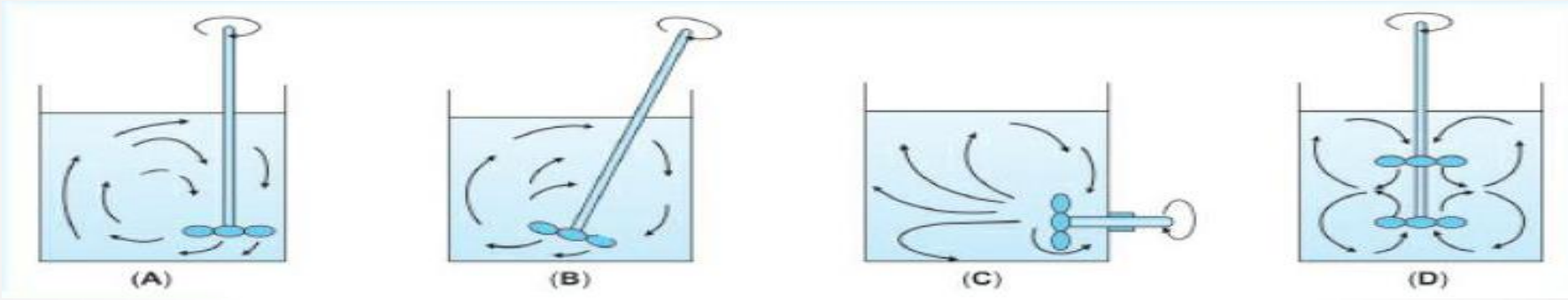
Disadvantages of vortex formation

1. When a vortex is formed, air is drawn into the impeller and is dispersed into the liquid, which is undesirable, as it may lead
   - foaming formation especially if surfactants are present → affecting accurate filling of the tank.
   - The entrapped air also causes → oxidation of the oxidizable substances.
   - → reduces the mixing intensity by reducing the velocity of the impeller relative to the surrounding fluid and because the full power of the impeller is not imparted to the liquid.

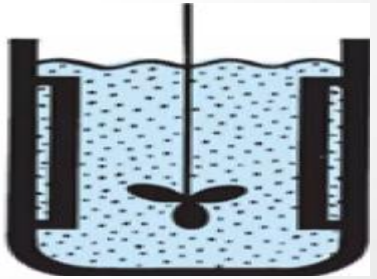
Vortex formation

Suppression of vortex:

1. changing arrangement of the impeller, → Impeller should be in any one of the following positions that can avoid symmetry such as;
   (A) off central (B) inclined (C) side entering, etc.,
   - It should be deep in the liquid



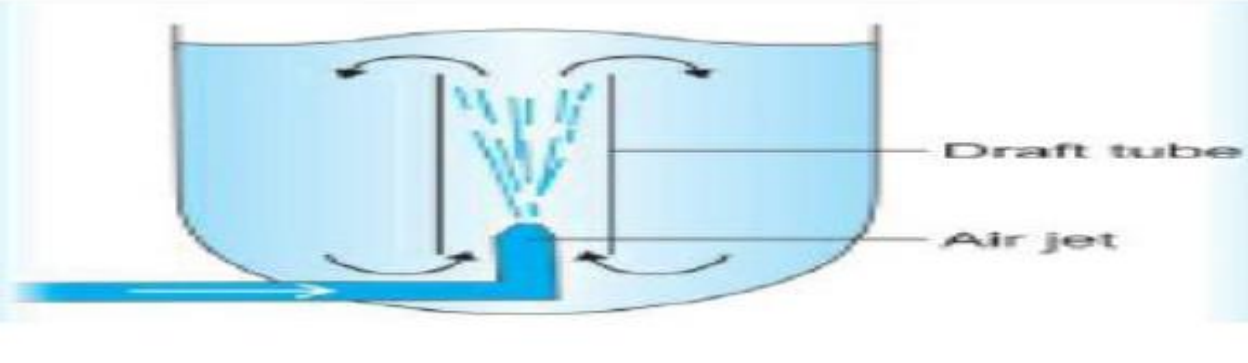
1. Using baffled containers (In large tanks). In such case impeller can be mounted vertically at the center
2. using diffuser ring
3. changing the tank geometry
4. using a push-pull propeller:



- Two or more propellers of opposite angles or pitch are placed on the same shaft to balance each other out → hence no vertex and no circulatory flow.
- The bottom impeller is positioned about one impeller diameter above the tank's base. It generates a zone of intense turbulence.

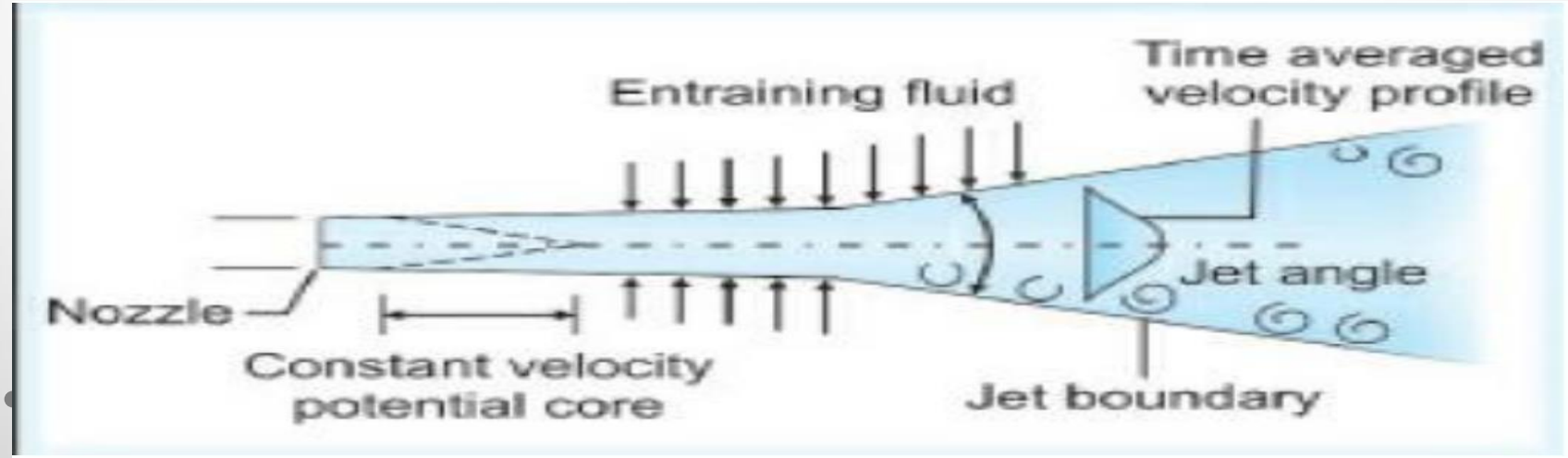
2-Air Jets

- Air jets devices involve sub-surface jets of air نفاثات الهواء تحت السطحية, or less commonly of some other gas, are effectively used for mixing purpose of certain liquids of the following characteristics;
  - Having low viscosity
  - Non-reactive with gas employed
  - Non foaming
  - Non-volatile in nature
- Principle
  - when compressed air jet or suitable gas is allows to pass at high pressure from the inlet provided at the bottom of the tank, air bubbles are formed in the liquid phase.
    → This causes buoyancy طفو of the bubbles which lifts the liquid from bottom to the top of the mixing vessel. → This is often accomplished with the aid of draft tubes انابيب السحب.
  - The overall circulation in the mixing vessel brings fluid from all parts of the tank to the region of the jet itself
  - The intense turbulence generated by the jet produces intimate mixing



3. Fluid Jets

- In this device, liquids pumped at high pressure into the mixing tank.
- The power required for pumping can often be used to accomplish the mixing operation, either partially or completely.
- Mechanism
  - In this case the fluids are pumped through nozzle which permits good circulation of material through the tank.
  - The fluid jets in this operation behaves like propeller in that they produce turbulent flow axially in the direction of their axis, while differ from propeller as they don't produce tangential flow themselves.
  - They may also operate simply by pumping the liquid from the tank and back into the tank through the jet



Continuous or In-line Mixers

- The process of continuous mixing produces an uninterrupted supply of freshly mixed material, and is often desirable when very large volumes of materials are to be handled.
- Continuous mixing may be accomplished in two ways.

1. By using tubes or pipes: the material flows through tube or pipe and there is very little back flow or recirculation.
2. By using mixing chamber: in which a considerable amount of holdup and recirculation occur.

– Mixing chamber is used as continuous mixing equipment, when there is difficulty in controlling the input rate and fluctuation.
– Fluctuation in the composition final mixture is greatly reduced by dilation effects of the material contained in the chamber

Continuous or In-line Mixers

- To ensure good mixing efficiency, devices such as vanes, baffles, screws, grids, or combinations of these are placed in the mixing tube.
- Mixing mainly takes place through bulk transport in the direction of primary flow.
- For effective mixing careful controlling the feed rate of raw materials is essential → uniform composition is to be obtained.
- The requirement of an exact metering in such a device results from the lack of recirculation, which would otherwise tend to average out concentration gradients along the pipe.
- Where suitable metering devices are available, → this method of mixing is very efficient.
- Little additional power input supplied over pump that required for simple transfer through a pipe is necessary to accomplish mixing.
- .

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.

Monophase systems

- The flow and mixing mechanisms depend on the fluid(s)' viscosity and density.
- Mixing fluids with low viscosity needs a lot of turbulence, which can come from air jets, fluid jets, and different high-speed 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.

Polyphase system.


Thank you
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