Practical considerations in Powder mixing

- When mixing formulations where the proportion of active drug is low, a more even distribution may be obtained by building up the amount of material in the mixture sequentially (geometric dilution).
- The volume of powder mixture in the mixer should be appropriate. Both overfilling and underfilling may reduce mixing efficiency.
- The mixer should produce the mixing mechanism appropriate for the formulation:
  - Potent drugs: diffusion is necessary
  - Cohesive material: shear mixing

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Practical considerations in Powder mixing

1. In order to determine suitable mixing time, the mixing process should be checked by removing and analyzing representative samples after different mixing intervals.
2. Static charges may be generated during mixing that result in reduction in diffusive mixing.
3. This is enhanced by low humidity in atmosphere. The mixer should be suitably earthed to dissipate the static charge.
4. Vibrations may cause segregation in normal mixes and dislodging of adsorbed particles in ordered mixes.

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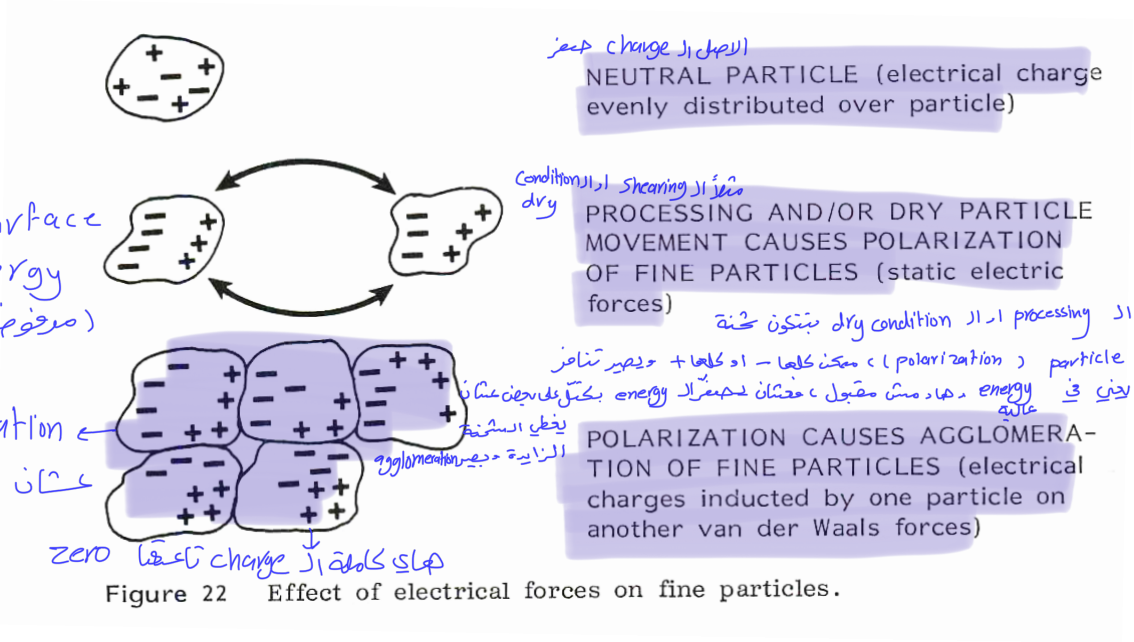


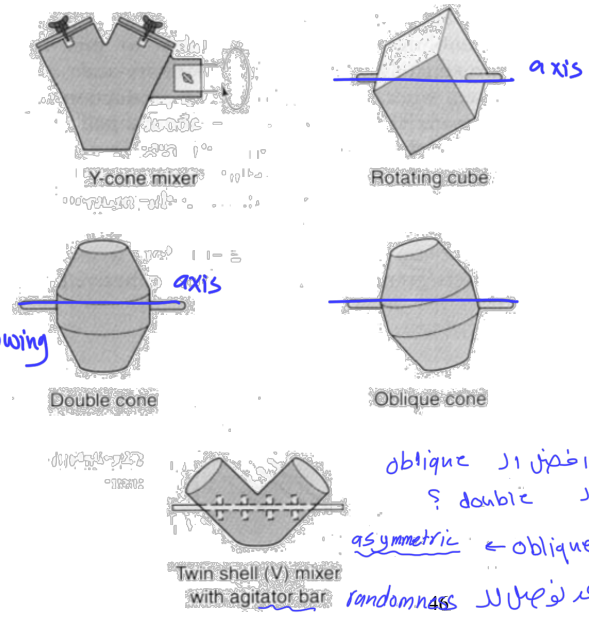
Figure 22 Effect of electrical forces on fine particles.

45

Powder mixing equipment

① Tumbling mixers

- Mixing containers are mounted so that they can rotate about an axis.
- Commonly used for mixing of free flowing powders and are not suitable for cohesive powders.
- Commonly used for mixing granules with lubricant, glidant and external disintegrant.



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① oblique عشان ازيد ال Randomness

② agitation bar بخلي ال particles تخبط ببعض وما يصير regular movement وبرع انه تخيرا اتجاهها تغير الـ بعمل Randomness

③ يكون في بال mixer ← baffles على ال walls تخلي ال powder تخبط فيها ويرجع فبتتغير الـ randomness

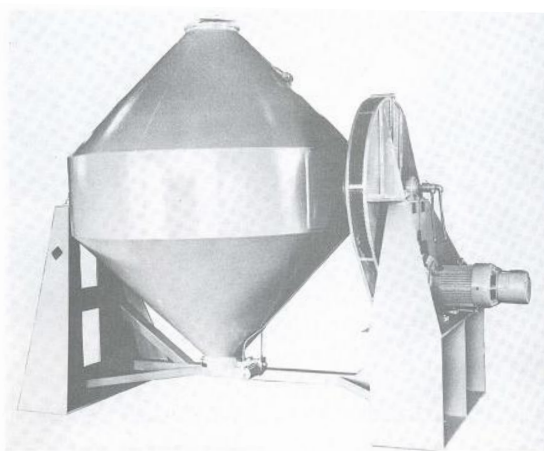


Figure 28 Double-cone blender. (Courtesy of Patterson-Kelley Company, Division of HARSCO Corporation, East Stroudsburg, Pennsylvania.)

Figure 29 Slant double-cone mixer. (Courtesy Gemc Jersey.)

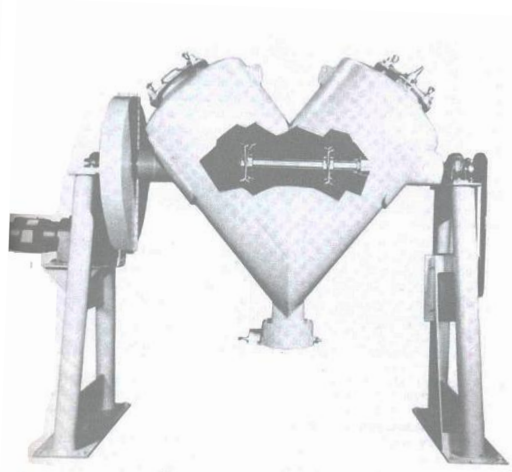
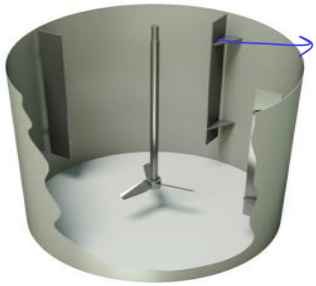


Figure 31 V-shaped blender with agitator mixing assembly. (Courtesy of Gemco, Middlesex, New Jersey.)

Powder mixing equipment

Tumbling mixers

- The shear mechanism occurs because of velocity gradient produced while diffusion occur through voids produced during powder flow.
- The addition of prongs, baffles or rotating bars helps convective mixing.
- Care about segregation is necessary.



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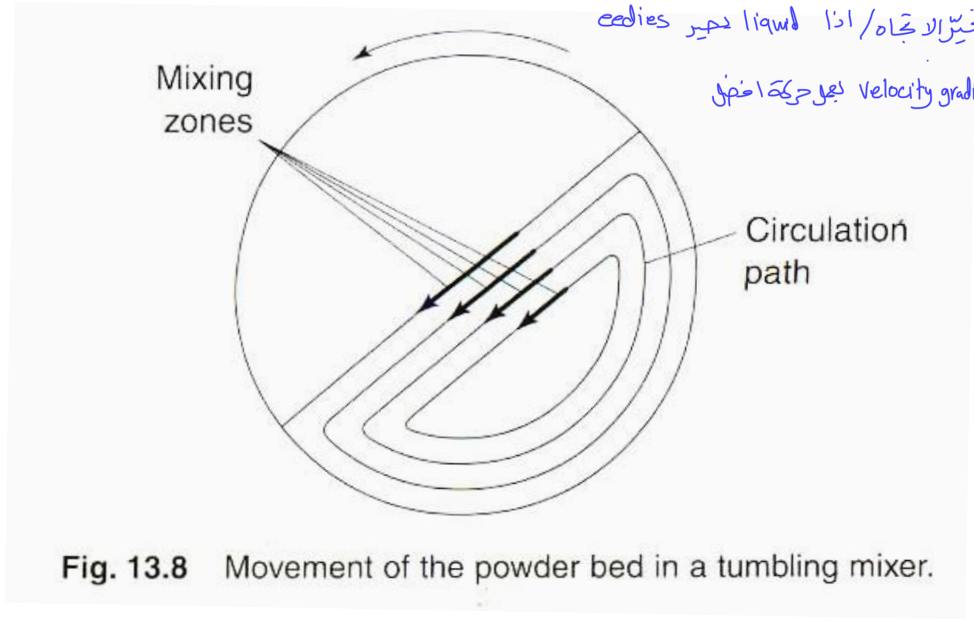

Fig. 13.8 Movement of the powder bed in a tumbling mixer.

50

Powder mixing equipment

Tumbling mixers

- Capacity ranges from 50 g to 100 kg.
- The material typically occupies 1/2 to 2/3 of the mixer volume.
- The mixing efficiency depends on speed of rotation. Speed of rotation should be suitable:
  - Very high speed will cause the powder to be held on the mixer walls by centrifugal force.
  - Very low speed will generate insufficient bed expansion and little shear mixing.

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Table 9 Effect of Powder Fill on Blending Time of Double-Cone Blenders[a]

Volume percent of blender filled with powder charge	Approximate blend time (minutes) in production-size blenders
50	10
65	14
70	18
75	24
80[b]	40[b]

[a] Blending done in double-cone blenders and times measured to obtain comparable blends.

[b] Uniform blend not attainable with this fill level.

Source: Sweitzer, G. R., Blending and Drying Efficiency Double Cone vs. V-Shape, GEMCO, Newark, New Jersey.

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Powder mixing equipment

Tumbling mixers

- ***Intermediate bulk containers (IBCs)*** are containers used both as mixing bowl and to either feed the hopper of a tablet or capsule machine or as the hopper itself.

- ***The Turbula shaker mixer (WAB, Switzerland)*** is a more sophisticated form of tumbling mixer that uses inversional motion in addition to the rotational motion leading to more efficient mixing.

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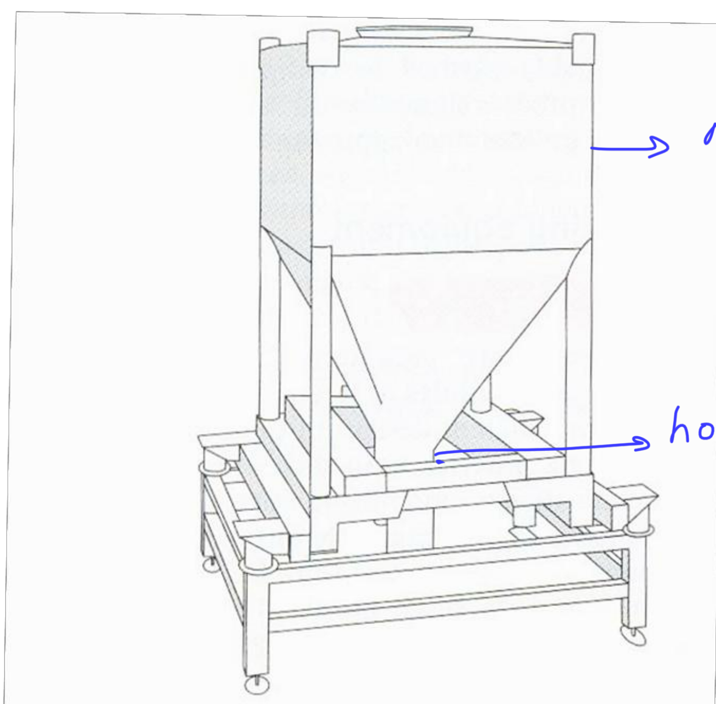

Fig. 13.7 Typical intermediate bulk container.

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Powder mixing equipment

High speed mixer granulators

- They are used both for mixing and granulation.
- It contains centrally mounted impeller blade that rotate at high speed throwing the material towards the mixing bowl.
- The side-mounted chopper blade helps in granulation.
- Care if material fractures easily.
- Not normally used for blending lubricants.

55

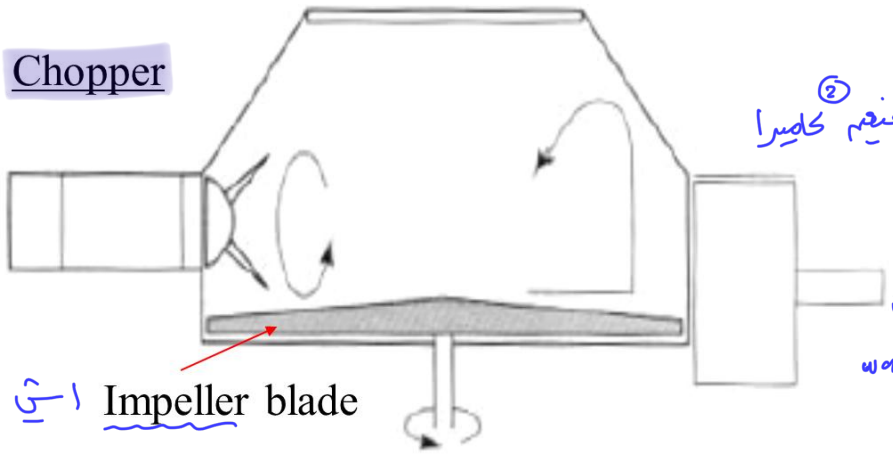

Fig. 13.9 Diagrammatic representation of a high-speed mixer–granulator.

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Powder mixing equipment

Agitator mixers

- These types of mixers depend on the motion of a blade or paddle though the product, and hence the main mixing mechanism is convection.

- There are three main designs of agitator mixers:
  - Ribbon mixer
  - Planetary (Orbital) mixer
  - Nautamixer

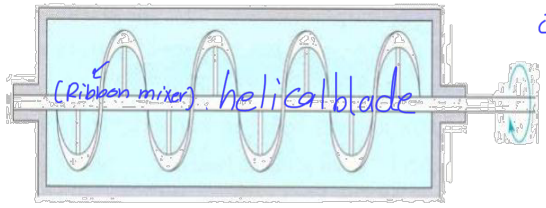

Fig. 12.10 Ribbon agitator powder mixer.

Powder mixing equipment

Ribbon mixers

- Mixing is achieved by the rotation of helical blades in a cylindrical tank.

Advantages

- Suitable for mixing of poorly flowing materials.
- Segregation is less likely to occur than in tumbling mixer

Disadvantages

- Dead spots are difficult to eliminate.
- The shearing action caused by movement of the blades may be insufficient to break up drug aggregates.

Powder mixing equipment

Kneader = زي العجانة

زي حركة الكوكب حولين نفسه وحول الشمس (محور) بتعمل محل الزوايا

planetary mixers

two in one < mixing / granulation

- The rotational path of paddle is similar to that of a planet.
- It is used:
  - for mixing powders and semisolids
  - Wet massing (granulation) (kneader)

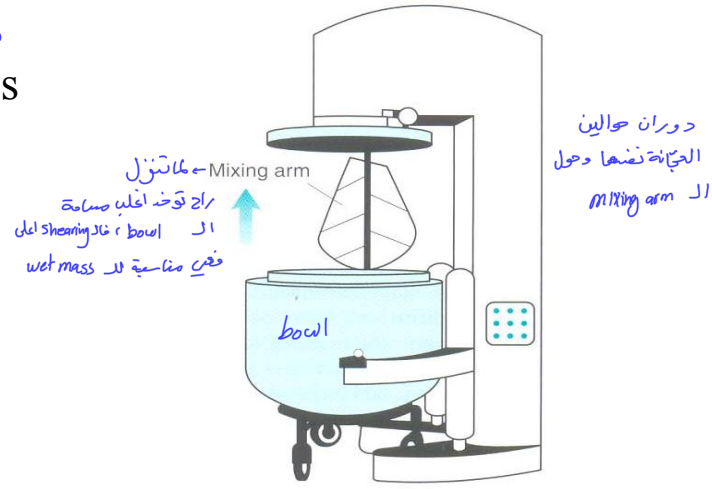

Fig. 12.11 Planetary mixer for powders and semi-solids.

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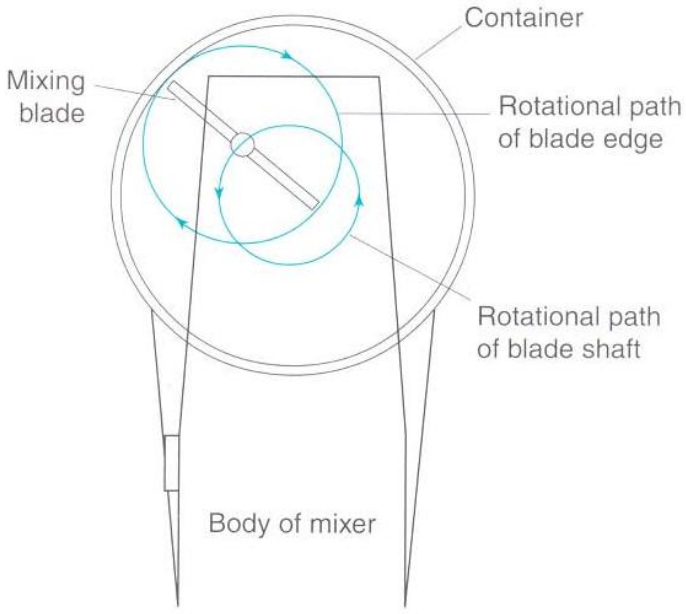

Fig. 12.12 Planetary mixer – top view, showing path of paddle.

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Powder mixing equipment

Nautamixer

- It consists of a conical vessel that contains inside a helical conveyor that conveys the material up to near the top where it cascades back into the mass.
- This mixer combines convective, shear and diffusion mixing

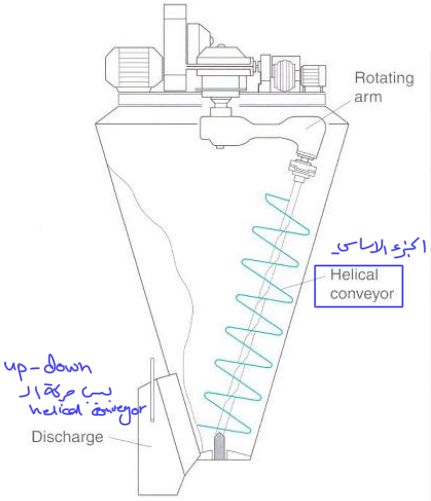

Fig. 12.13 Nautamixer (courtesy of Nautamixer Ltd).

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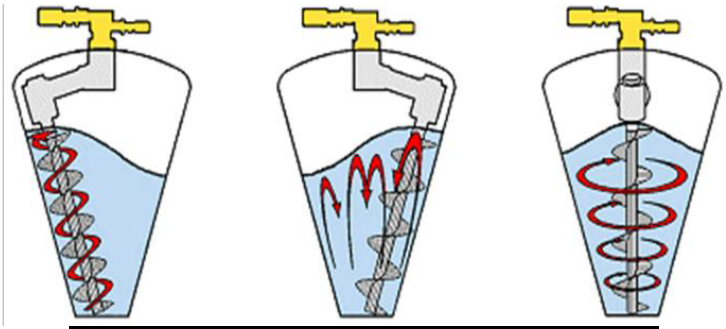
Nautamixer



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Powder mixing equipment

Fluidized bed mixers

- The fluidized bed equipment is used mainly in:
  - Drying
  - Granulation
  - Coating
- However it can be used for mixing of powders before granulation.
- Blown air fluidized and mixes the powder.
- Fluidization is very efficient mixing process.
- Diffusion of particles occur.

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Fluidized bed mixers

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Powder mixing equipment

Continuous mixers

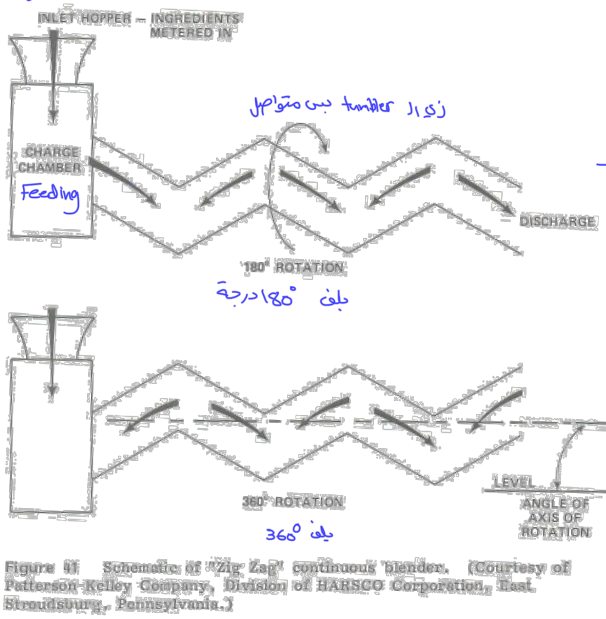

Figure 41 Schematic of "Zig Zag" continuous blender. (Courtesy of Patterson-Kelley Company, Division of HARSCO Corporation, East Stroudsburg, Pennsylvania.)

Figure 42 The "Zig Zag" continuous blender. (Courtesy of Patterson-Kelley Company, Division of HARSCO Corporation, East Stroudsburg, Pennsylvania.)

Scale-up of powder mixing

- The extent of mixing achieved at a small laboratory scale during development work may not necessarily be mirrored when the same formulation is mixed at a full production scale, even if the same mixer design is used for both.
- Often, mixing efficiency and the extent of mixing is improved on scale-up owing to increased shear forces.
- This is likely to be beneficial in most cases, although when blending lubricants care is needed to avoid overlubrication.

Scale-up of powder mixing

- The optimum mixing time and conditions should therefore be established and validated at a production scale, so that the appropriate degree of mixing is obtained without segregation, overlubrication or damage to component particles.
- Minimum and maximum mixing times that give a satisfactory product should be determined if appropriate, so that the 'robustness' of the mixing process is established.

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Types of mixers used for liquids and suspensions

Propeller (Impeller) mixers

- Three basic types of flow may be produced: radial, axial and tangential.
- Angled blades cause fluid to circulate in both an axial and a radial direction.
- The ratio of the diameter of propeller to that of the vessel is 1:10 - 1:20 and it typically rotates at speeds of 1 - 20 rps.

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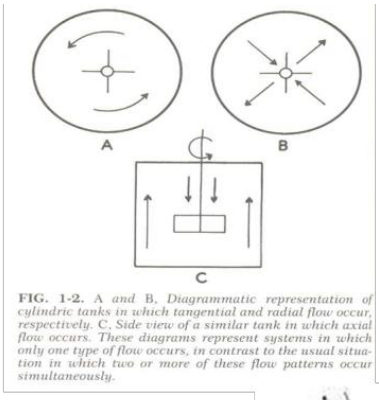
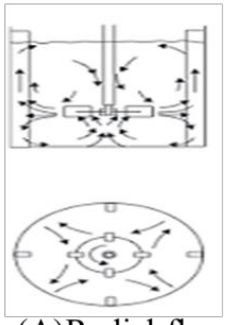
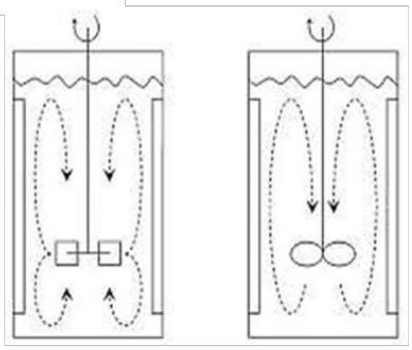


FIG. 1-2. A and B, Diagrammatic representation of cylindric tanks in which tangential and radial flow occur, respectively. C, Side view of a similar tank in which axial flow occurs. These diagrams represent systems in which only one type of flow occurs, in contrast to the usual situation in which two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



(A)Radial flow

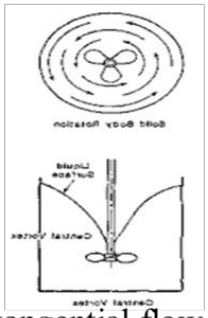
باتجاه المركز/نصف القطر



(B) axial

حركة ال liquid باتجاه ال shaft

up-down



(C)tangential flow

في نزول / انخفاض و Vortex

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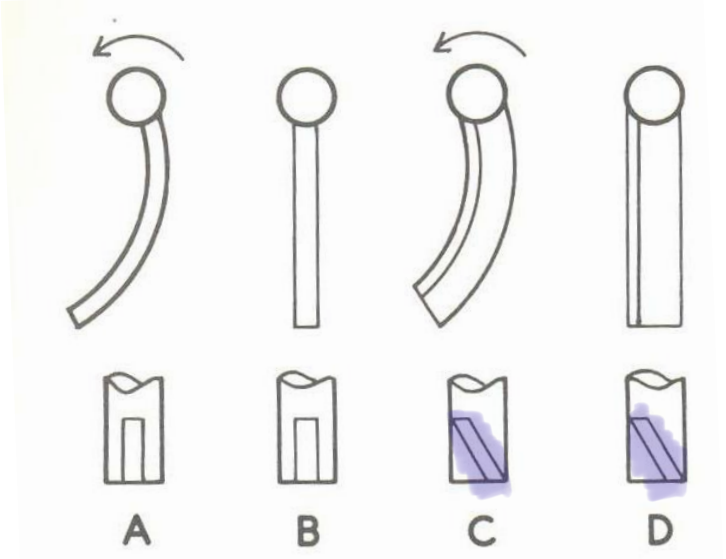

FIG. 1-3. *Impeller blade types (only one blade shown), top and side views. A and B, Radial flow design: C and D, mixed radial-axial flow design. For axial pumping, the blade must be set at an incline to the axis of the shaft.*

A+B → Radial

C+D → Radial + axial

لانه فيهم حضة / ارتفاعين

ساعدلي انه axial + radial

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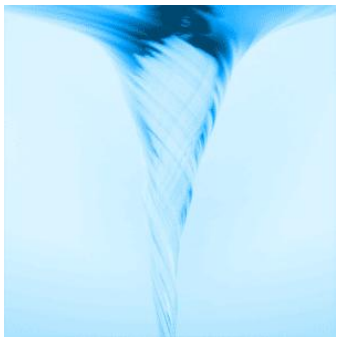
Types of mixers used for liquids and suspensions

Propeller (Impeller) mixers

- A vortex forms when the centrifugal force imparted to the liquid by the propeller blades causes it to back up around the sides of vessel and create a depression at the shaft.



Depression

- An off-center mounting of propeller and vertical baffles discourage the formation of vortex
- Propellers are more efficient when they run at high speed in liquids with low viscosity.

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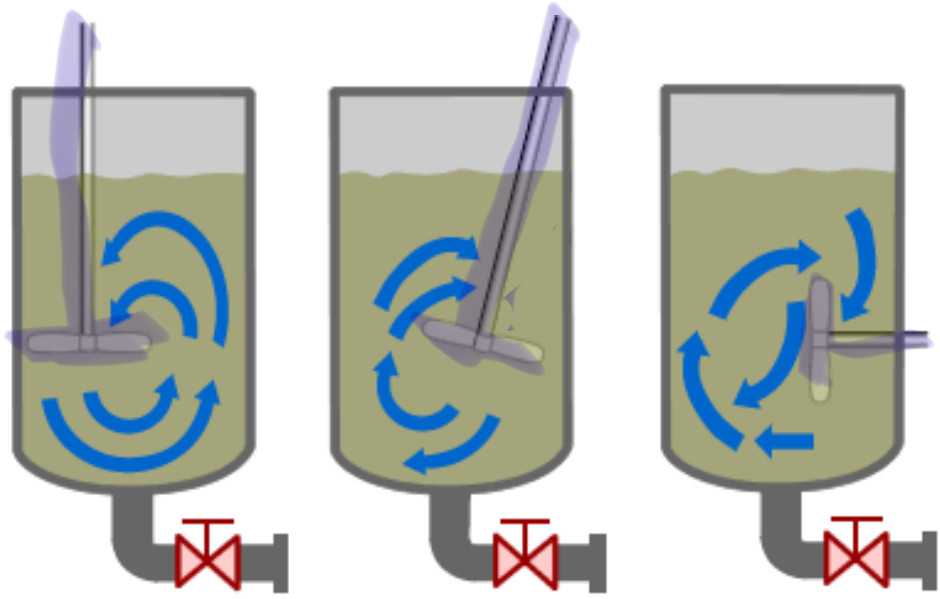

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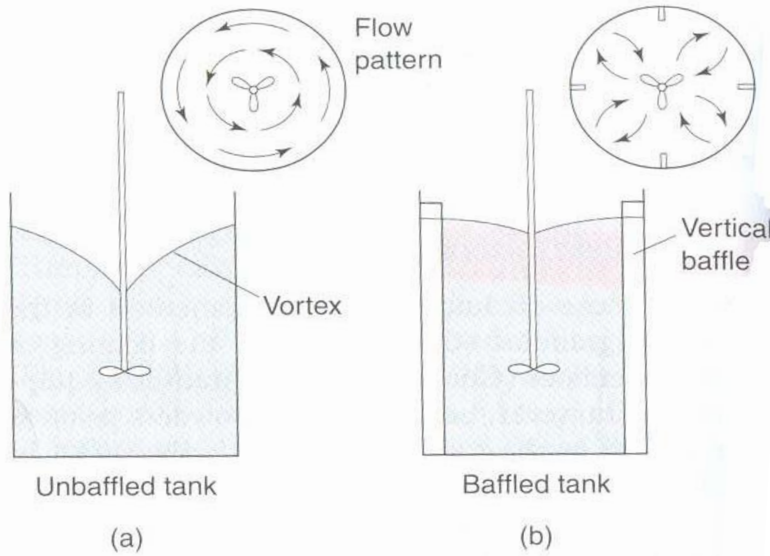


Fig. 13.13 Propeller mixer with (a) unbaffled tank and (b) baffled tank.

Types of mixers used for liquids and suspensions

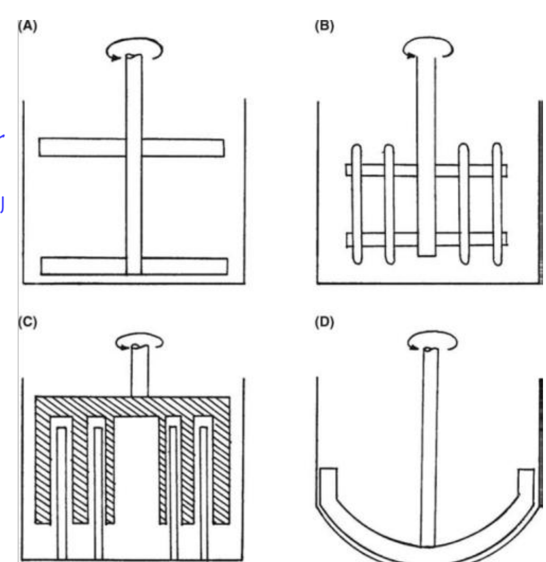
Paddle mixers

بوابة مرساة
Gate _ anchor

- The mixing element is large in relation to the vessel and rotates at low speeds (10–100 rpm).

high viscosity + low speed تناسب

ال propeller الحكس



Paddle mixers

اكبر من ال turbine, propeller

ماخذة جزء كبير من المساحة / اي shearing

شكلها زي مرساة السفينة

Types of mixers used for liquids and suspensions

Turbine mixers

- Turbine mixers may be used for more viscous liquids than those mixed by propeller.

- The impeller has four flat blades surrounded by perforated inner and outer diffuser ring.

- The rotating impeller draws the liquid into the mixer head and forces the liquids through the perforations

- They can produce stable emulsions.

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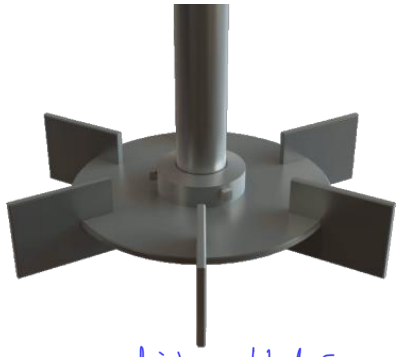

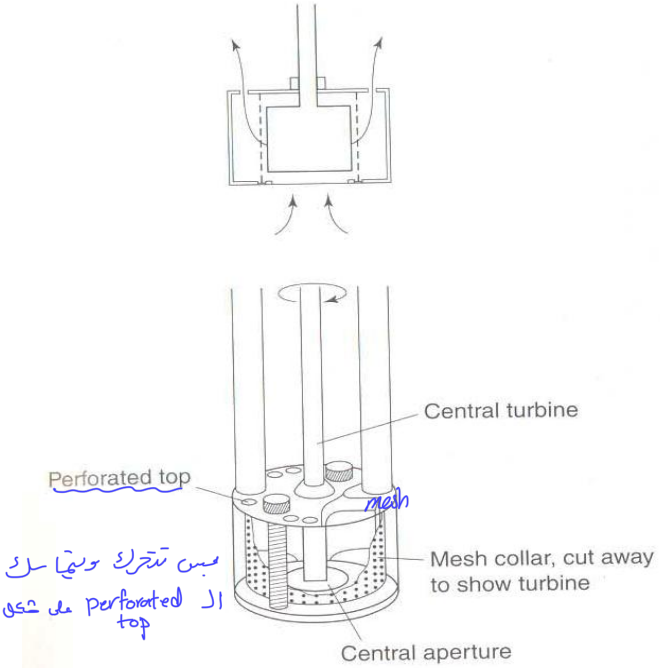

Fig. 13.14 Turbine mixer.

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Types of mixers used for liquids and suspensions

Air jet mixers

- These mixers utilize jets of air or some other gases.
- The liquid must be of low viscosity, non-foaming, unreactive with the gas employed and reasonably nonvolatile.

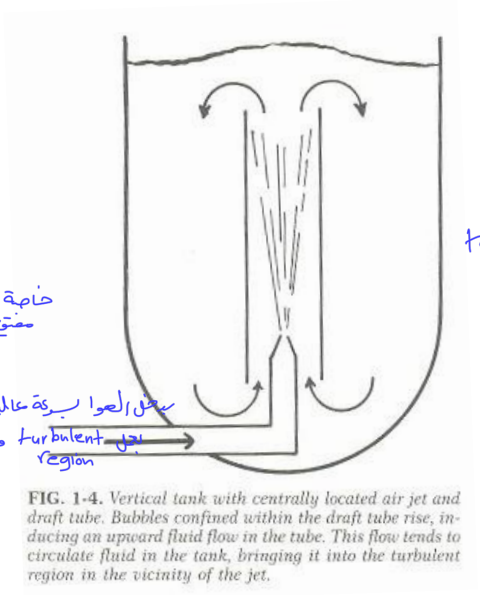

FIG. 1-4. *Vertical tank with centrally located air jet and draft tube. Bubbles confined within the draft tube rise, inducing an upward fluid flow in the tube. This flow tends to circulate fluid in the tank, bringing it into the turbulent region in the vicinity of the jet.*

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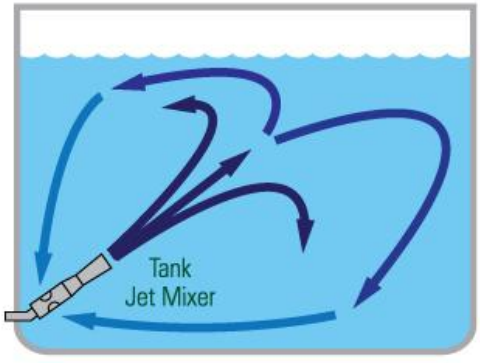
Types of mixers used for liquids and suspensions

Fluid jet mixers

- When liquids are to be pumped into a tank for mixing, the power required for pumping is often used to accomplish the mixing.
- The fluids are pumped through a nozzle arranged to permit good circulation of the material through the tank.
- It is also possible to pump the liquid from the tank through the jet into the tank.



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Types of mixers used for liquids and suspensions

Inline mixers (Continuous mixing)

- In this case, mobile, miscible components are fed through an inline mixer designed to create turbulence in a flowing fluid stream.
- It can be accomplished essentially in two ways: in a tube (pipe) through which the fluids flow,or in a chamber in which a considerable amount of hold up and recirculation occur.
- Controlling the feeding rate of raw materials is necessary to ensure uniform mixtures.

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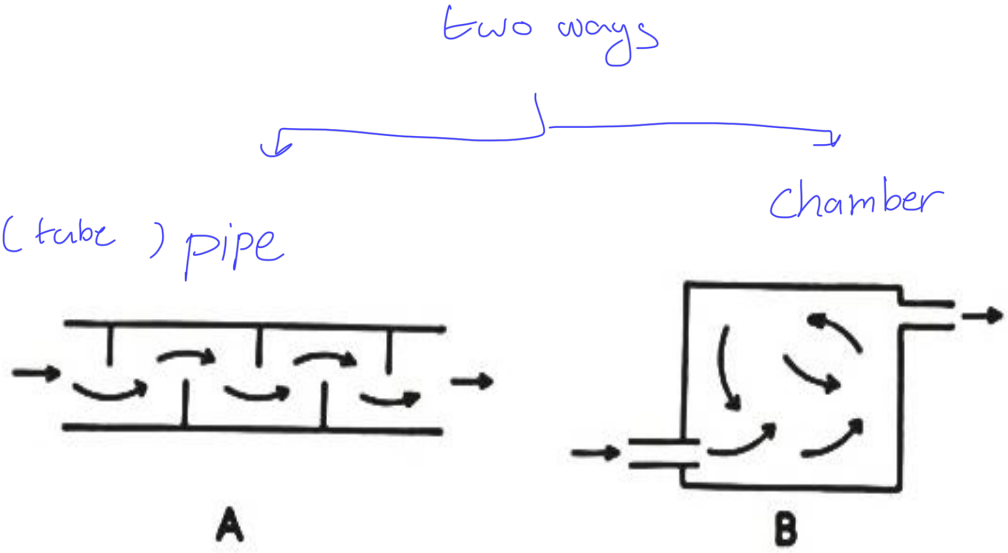

FIG. 1-5. *Continuous fluids mixing devices. A, Baffled pipe mixer; B, mixing chamber with flow induced recirculation.*

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Types of mixers used for liquids and suspensions

•On an industrial scale, solutions are prepared in large mixing vessels with ports for mechanical stirrers.

•When heat is desired, thermostatically controlled mixing tanks may be used.

FIGURE 13.1 Large-scale pharmaceutical mixing vessels. (Courtesy of Schering Laboratories.)

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Mixing of semisolids

- Semisolids, unlike liquids and powders, do not flow easily.
- The suitable mixers must have rotating elements with narrow clearances between them selves and the mixing vessel to avoid dead spots

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Types of mixers for semisolids

1) Planetary mixers

2) Sigma blade mixer

3) Vessels (tanks) with counter-rotating mixing bars

- It is very difficult using primary mixers to completely disperse powder particles in a semisolid base so that they are invisible to the eye.
- The mix is usually subjected to the further action of a roller mill or colloid mill, so as to 'rub out' these particles by the intense shear generated by rollers or cones set with a very small clearance between them.

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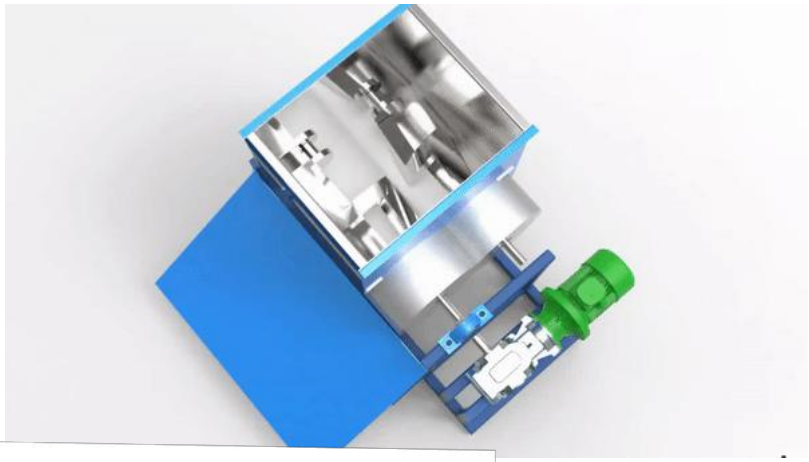

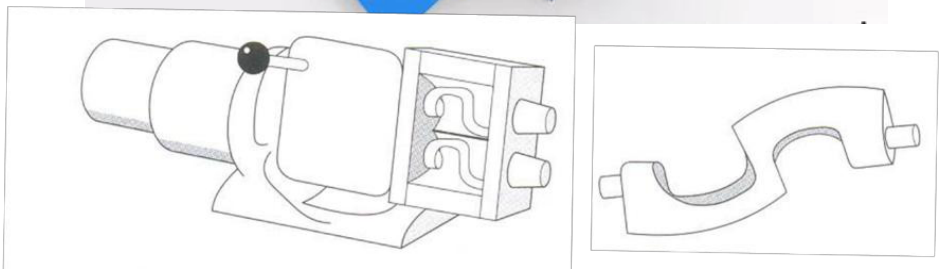

Fig. 13.15 Sigma blade mixer.

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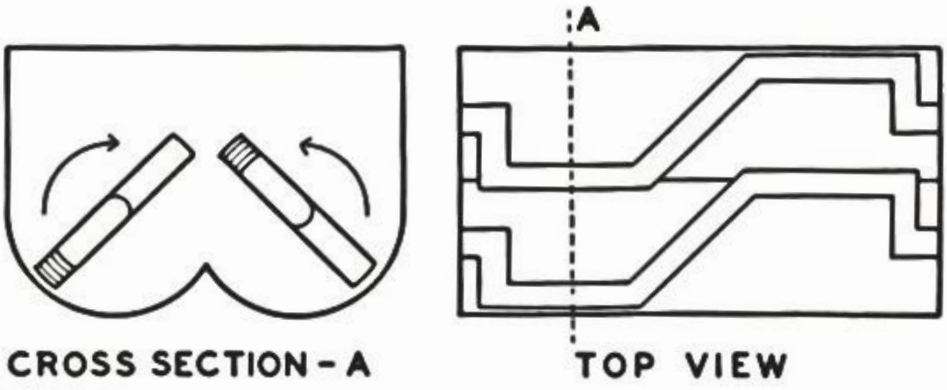

FIG. 1-8. *Schematic drawing of a top-loading sigma-blade mixer with overlapping blades. The top view shows the relationship of the counter rotating blades to the overall geometry of the mixer.*

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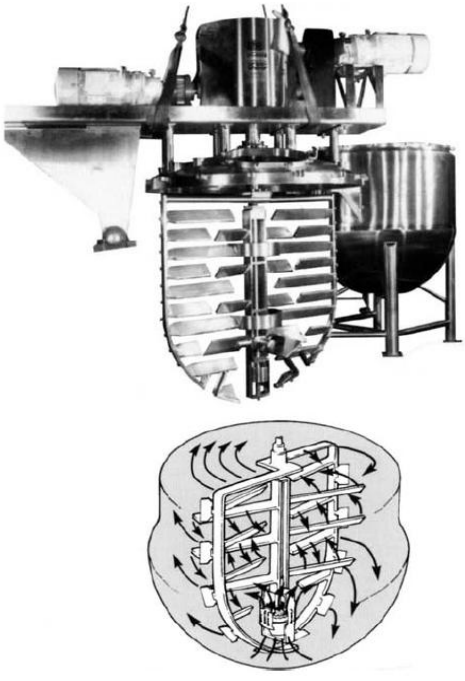

Fig. 5 Large-scale manufacturing unit (Tri-mix Turboshear) with counter-rotating mixing bars. (Courtesy of Lee Industries, Inc., Philipsburg, Pennsylvania.)

Stainless steel tank, which has counter sweep agitation and a built-in homogenizer.

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