

Practical considerations in Powder mixing

عنصري صوت
A - B - C

• انما يعني ان Drug
يختار Drug mixer
ما يلائم هذه B, C
بالنظر، يعني حجم صيد
يتميز بـ B, C ما يلائم حجم
المسحوق mixer دبرج
بخط B, C رطوبت
لحما تخلص من الرطوبة

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). →
بالشرح من كلمة
حقاً يعني
طريقة حسابية بدون توزيع
تخفيف المكون الكبير بالنظر
بمقدار توزيع

The volume of powder mixture in the mixer should be appropriate. Both overfilling and underfilling may reduce mixing efficiency.
الاحتكاك العائد للثقل
ما يضر لا over ولا under filling

• لدرام اختار
اد mixer والزمن
المناسب رطوبة
اد mixing

The mixer should produce the mixing mechanism appropriate for the formulation:

- Potent drugs: diffusion is necessary
- Cohesive material: shear mixing

Solid : convection - shearing - particle diffusion
liquid : Bulk movement - layering - molecular diffusion

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طاحوا المواد ملزمة ببيوت اي جهاز يفكهم (Deagglomeration Delumping) من سطحهم

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.
عشان احدد اد mixing time
بخط بالماعة بالتدريج Geometric mixing
ببيلش على وقت محدد د بغير اسيب عينات

2. Static charges may be generated during mixing that result in reduction in diffusive mixing.
واحد صاحب
CAV, SD, near
الحل لا charge اني ارشد powder ب moisture رشت بسيط بدون ما تكتل

3. This is enhanced by low humidity in atmosphere. The mixer should be suitably earthed to dissipate the static charge.
الهجاز يكون مربوط ببلا لفرغ شحنات الارض
②

4. Vibrations may cause segregation in normal mixes and dislodging of adsorbed particles in ordered mixes.
vibration يعني dislodging انحرار particles تطلع من مكانها
او (carrier) lactose بتهوية بفضيل عن Drug

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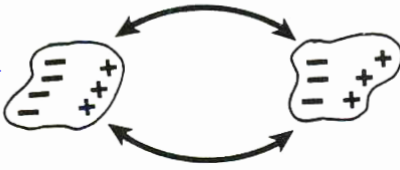
vibration ال منقلل



الاجل charge جمع

NEUTRAL PARTICLE (electrical charge evenly distributed over particle)

high surface energy (مرفوظة)

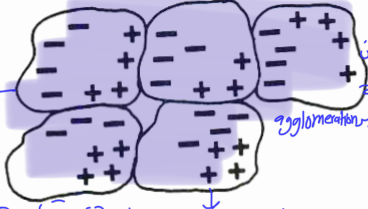


Condition dry or shearing or dry

PROCESSING AND/OR DRY PARTICLE MOVEMENT CAUSES POLARIZATION OF FINE PARTICLES (static electric forces)

بسبب ال processing او ال dry condition بتكون حنة

على particle (polarization) ممكن كلها - او كلها + ويغير تناظر energy دهاد مش مقبول ، فبتنقل لخصم ال energy بكتل على جدران



POLARIZATION CAUSES AGGLOMERATION OF FINE PARTICLES (electrical charges induced by one particle on another van der Waals forces)

agglomeration

عشان يعادل لـ charge

هناي كلمة ال charge تاخفا zero

Figure 22 Effect of electrical forces on fine particles.

بالتناوب Small particle و خلاصا Large particle بسبب static charge

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Powder mixing equipment

① Tumbling mixers

Convection: Bulk movement from left to the right / Top-bottom

- 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.

cohesive اذا راح تطلع وتنزل لونه حركتهم بسيطة او powder يكون

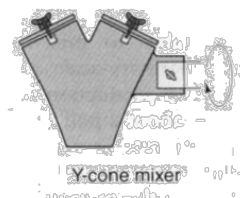
Free flowing لونها يكون spherical مثلاً بتطلع اقل واسفل

- Commonly used for mixing granules with lubricant, glidant and external disintegrant.

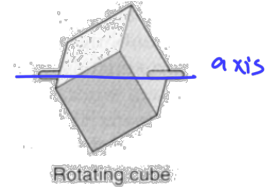
بسبب الحركه شكل الكبس ، mixing machine

① ممكن اعمل mixing بالفعالية قبل الكبس ، كل الـ حنا نكويه قبل حنا نعمل mixing بالباية قبل الـ granulation

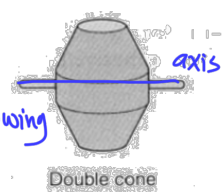
عشان اعمل mixing بالفعالية في كثير حطوان قبل الكبس من ضمنهم اني احضر granules داغلا mixing او lubricant



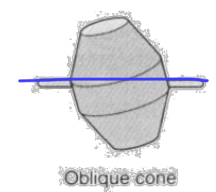
Y-cone mixer



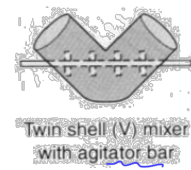
Rotating cube



Double cone



Oblique cone



Twin shell (V) mixer with agitator bar

ميت اخضر او oblique

او ال double ؟ asymmetric

عيناك لوصل ال randomness

* خلط الاسمنت مركته هو symmetric بحالته بس الوقت الطويل بني الناتج متساك

③ يكون في بار mixer ← baffles على الدالك walls نخلي
 ال powder نخلي منها ويرجع حيت تغير الحركة randomness

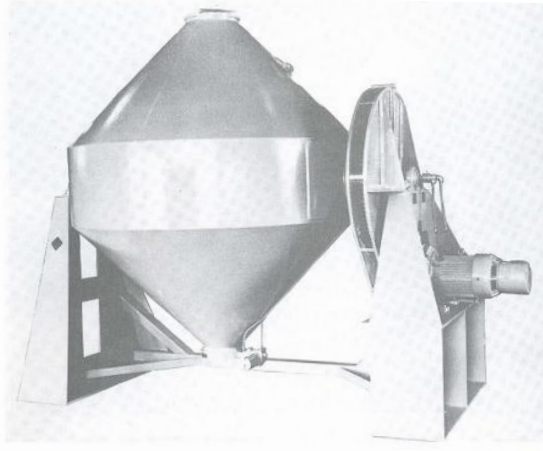


Figure 28 Double-cone blender. (Courtesy of Patterson-Kelley Company, Division of HARSco Corporation, East Stroudsburg, Pennsylvania.)

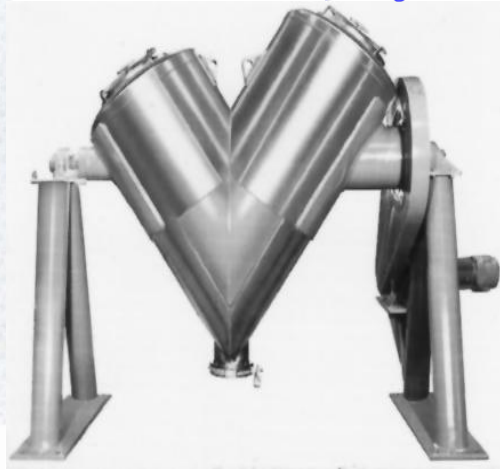


Figure 31 V-shaped blender with agitator mixing assembly. (Courtesy of Gemco, Middlesex, New Jersey.)

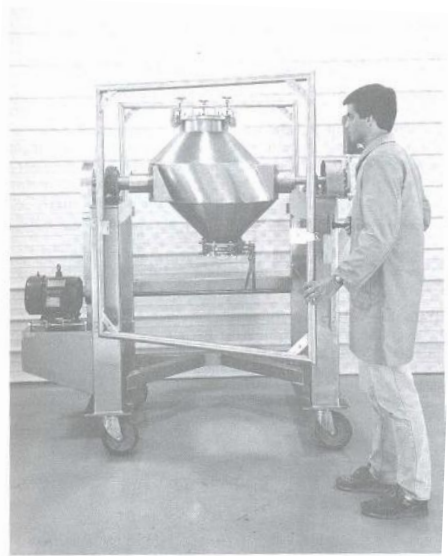
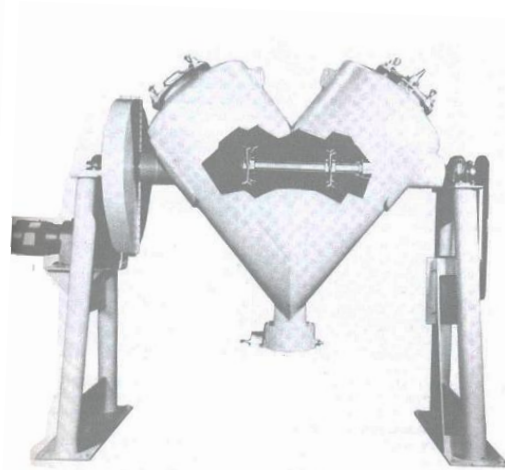


Figure 29 Slant double-cone mixer. (Courtesy Gemco, Middlesex, New Jersey.)



عشان ازيد Randomness
 ① Oblique agitation bar ②

نخلي ال particles نخلي بيها
 regular movement
 ربع انه تخيرا بجاهد تغير الحركة
 Randomness بعمل

Powder mixing equipment

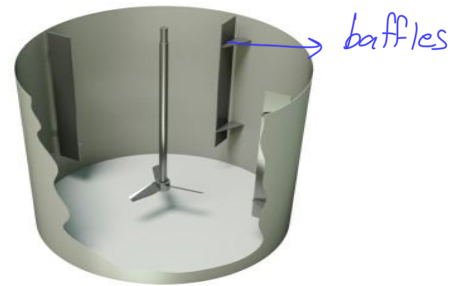
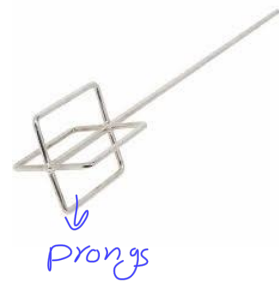
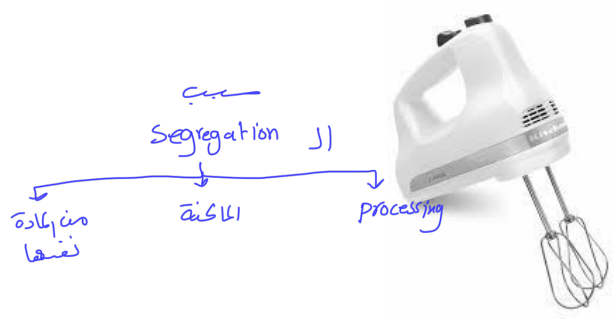
Tumbling mixers

- 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.

بسرعة بار
baffles

آخراشي بصر diffusion
لما تتحرك الحبيبات وتكون
مكتافها بالامانة يتغير particle
بنتوخ دليبر في حال particle
ربطوا مع بعض
كل ما توضع ما تسترت
بالامانة بتزيد الفراغات

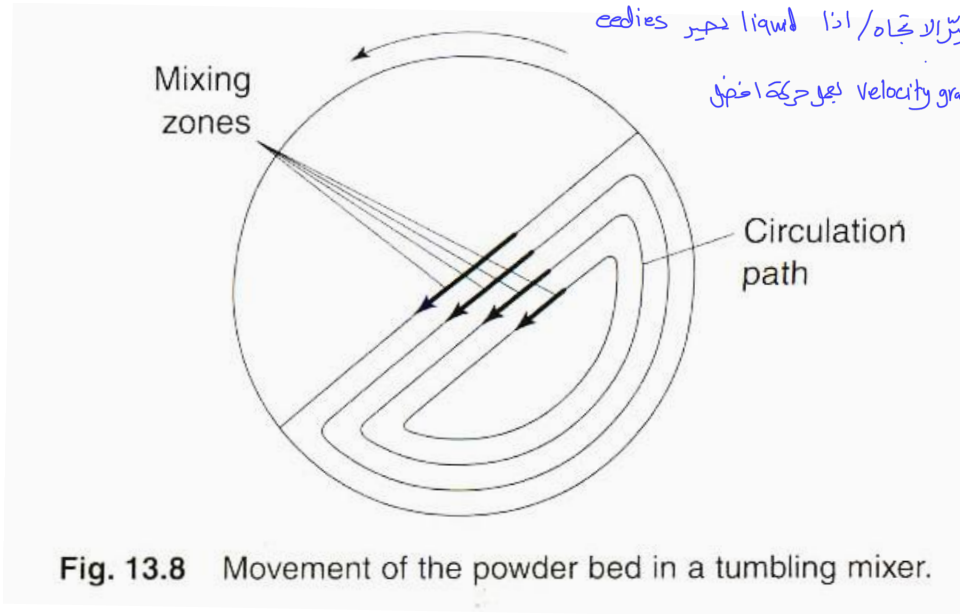
بجعل segregation



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كيف ازيد shear mixing ؟

بال different velocity / اختيار اتجاه / اذا liquid بحير edies
اي اشي راجع الى Velocity gradient randomness يجعل حركة اضمحل



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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.

ليزوم السرعة محددة عشان الحيز الاجمالي وهي يتلف انما نروح للنهنا وترجع خالصا ثمانية تترير

ما في مجال لدر convection و shearing ولا اشي

ما في توسع واد powder ما يتوخد مكانها عشان يتداخلا

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(لازوم دنته وسرعة عددان)

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

^aBlending done in double-cone blenders and times measured to obtain comparable blends.

^bUniform blend not attainable with this fill level.

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

uniform blend ما وصلوا لا

choke Free Feeding زجاجة

كل ما تعبها الحمر بعتاج دقة اقول
دتكلة الحمر

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Powder mixing equipment

مجهزول غير عن الـ tumbler العادية

Tumbling mixers

بنها processing بتخلها

Convection
tumbling

- **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.

بوملها على ماكينة ثانية

بلف خالين

up
down

- **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.

الميزة انها حركتين من بس Convection (up-down) / حركتا rotation مكان

inversion (up-down)

(inversion)
up-down كل رلي فوق كانوا بس

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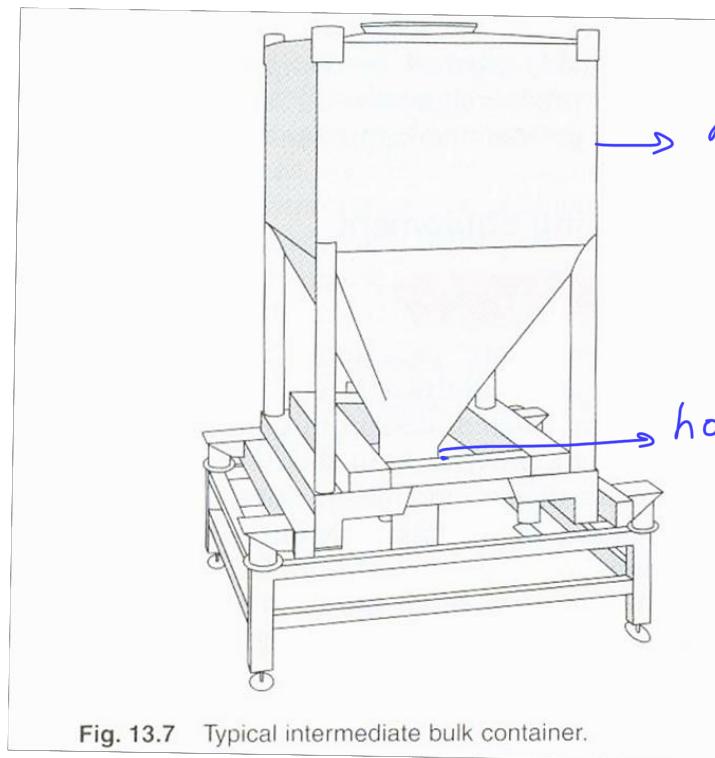


Fig. 13.7 Typical intermediate bulk container.

①

لعمل فيه mixing

②

hopper - hover (مستع) يمكن

ها - برجه على ماكينة الثانية
لعمل فيه mixing (للعبئة)

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Powder mixing equipment

زادته السرعة، صبارتي Shear mixing
segregation | High speed mixer granulators

- They are used both for mixing and granulation. *two in one*
افلاسی لجین
- 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. → إذا قابلة للتكسر

- ما سيختم high speed (سبغا) gentle speed اذا high برجه powder ري كاني ماعلة granulation

- Not normally used for blending lubricants.

احسن lubricant اور Stearate بعل Flow احسن بين مشكلة
اذا overmixing نتي ال powder يعبر hydrophobic وال solubility بقل

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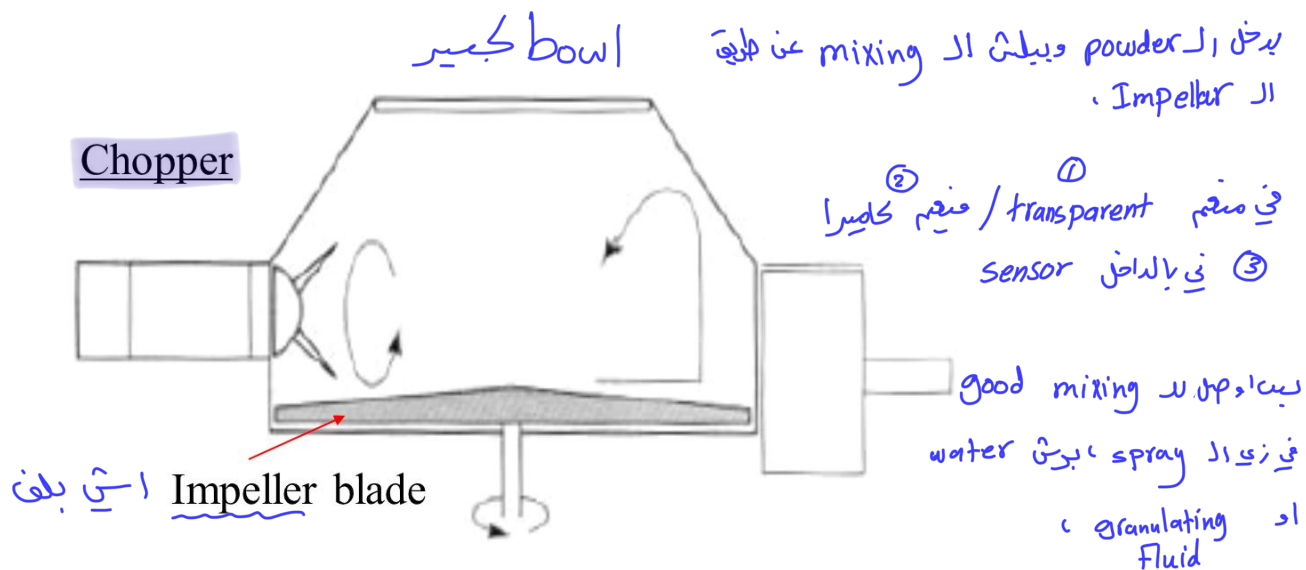


Fig. 13.9 Diagrammatic representation of a high-speed mixer-granulator.

و الجهاز يبلس يحين ويعمل wet mass
 or sensor اذا حكا انه وصل له texture
 المناسب من العجينة ⁵⁶ وشارت مقاسه ، ببلس يفتخل
 الجهاز في chopper بقمصاص Small granules
 جدين يعمل drying له granules

الخطوات

① mixing ② spraying ③ chopping ④ drying

Powder mixing equipment

الجهاز في اجزاء

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.
 (الجهاز يتحرك ويحرك المواد up-down)
 اسرع راتوي
 من Tumbling

- There are three main designs of agitator mixers:

- Ribbon mixer
- Planetary (Orbital) mixer
- Nautamixer

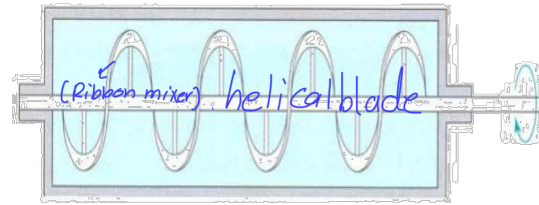


Fig. 12.10 Ribbon agitator powder mixer.

بحرك up-down
 راتوي في مكان حثي
 بنه shearing

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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.
 (Tumbling: ليس بتسرع up-down بدون ماتخير texture)
 (Poorly Flowing: Ribbon)
 (spherical)
 اقل من ر Tumbling

Disadvantages

- Dead spots are difficult to eliminate.
- The shearing action caused by movement of the blades may be insufficient to break up drug aggregates.
 (شاور Shearing يكون قوي لما يرافة كثير حثيعة)

الافضل للجهاز يكون في استدارة من
 زوايا الزاوية (Dead spot) ما يحصل لاصار لظ
 فحجب التمثيل و يتقل Contamination

المن الماسة مش حثيعة في صافة مضبوطة
 ما بصل Very effective shearing
 منار tumbling

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– اذا الماسة lumpy مكتلة لازم افنار جهاز في صافة امينق

Powder mixing equipment

زِي حركه ا لكوكن **planetary mixers** two in one mixing granulation

حولين لفسه و حول الشمس (معوير) يتوصل بخلا لزاويا

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

Kneader = زِي العيانه

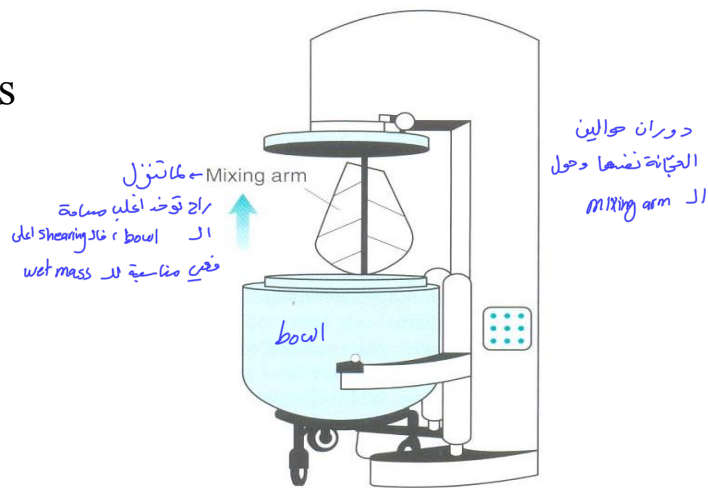


Fig. 12.11 Planetary mixer for powders and semi-solids.

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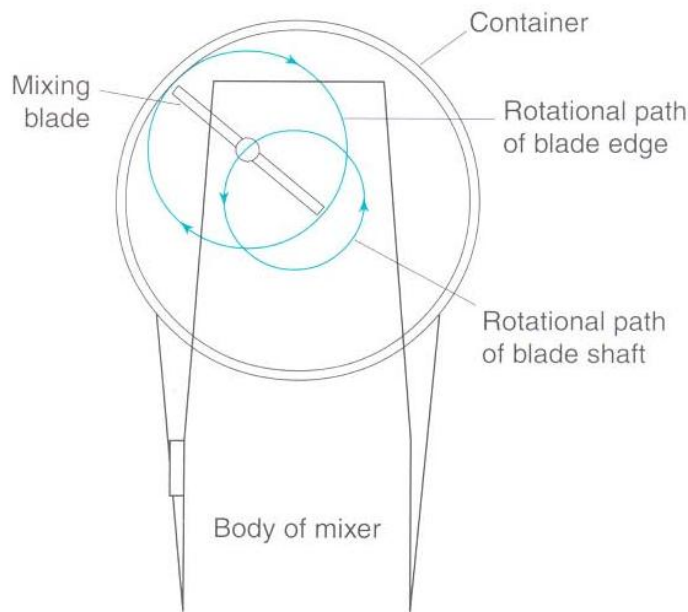


Fig. 12.12 Planetary mixer – top view, showing path of paddle.

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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

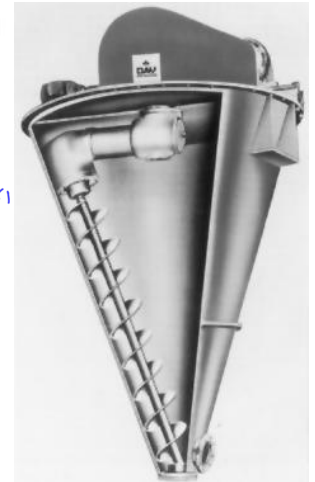
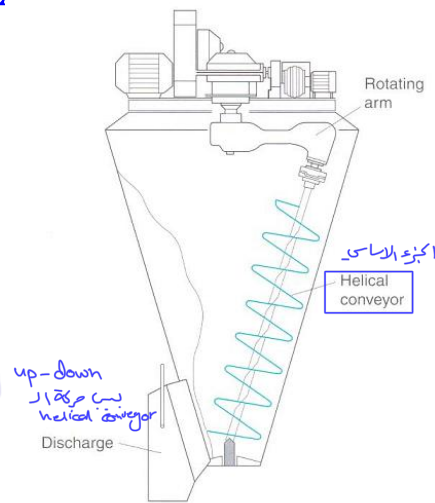


Fig. 12.13 Nautamixer (courtesy of Nautamixer Ltd).

بھرنے کی حرکت
helical
ناتامکسر

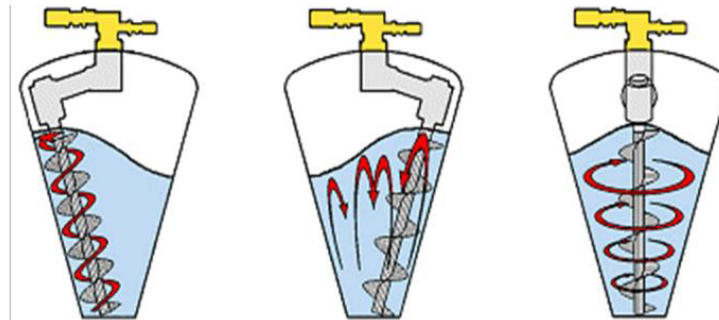
Particles
توزیع بکلا
Vessel

diffusion
Other particles
solid (particles)
liquid (molecular)
diffusion

Voides
ریخیزمناغات و

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Nautamixer



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Powder mixing equipment

liquid gas

Fluidized bed mixers

all in one مكن يوصل طايقين رغالي

- The fluidized bed equipment is used mainly in:

- Drying
- Granulation
- Coating

- However it can be used for mixing of powders before granulation.

بدخل هوا 16 اذ في سكة بار 20 بنخل 20 او 20

- Blown air fluidized and mixes the powder.

- Fluidization is very efficient mixing process.

دونه يوصل دغري لـ particle diffusion

- Diffusion of particles occur.

ولها مكن موجودة باي جهاز ثاني

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mixing

① بنخل powder بالقاعدة اسفل الجهاز لجدين بكسها ، ربيـ Fluidization يعني بدخلوا هوا رال powder بتغير
تطلع up-down فاعندى طبقات ، كل particle هبارت لوالها فحصلنا لـ diffusion مباشرة ، فمبصر حبال لـ mixing لـ mixing مكن
ندخل (spraying) نغسل Granulating agent ربيـ او granule ، مينه الجهاز مكن موجودة يكل الاجهزة انه في Sensor يقين نسبة الرطوبة عشان ايلت انشغاد ادمتق لـ
مكن في Carrier

Fluidized bed mixers



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Continuous Feeding
Continuous discharge

Powder mixing equipment

Continuous mixers

ستجربتها تكون الكميات كبيرة

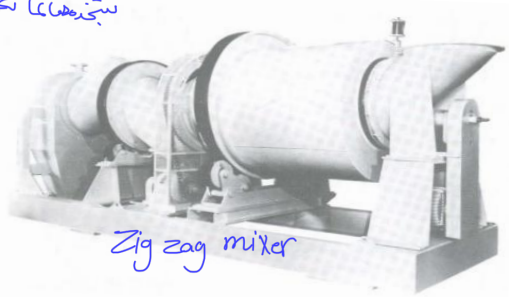
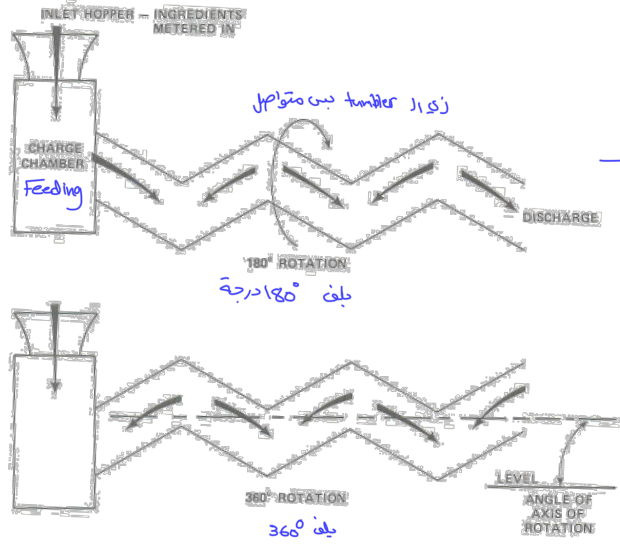


Figure 42 The "Zig Zag" continuous blender. (Courtesy of Patterson-Kelley Company, Division of HARSICO Corporation, East Stroudsburg, Pennsylvania.)

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

Scale-up of powder mixing

الى يتخذ بالادب اسمه lab scale أو pilot scale mixer

دبض الكبرار scale لمداوم production scale الى هو الماكينة الى راج تهم الى بنه بالوق

- 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. → بس اكبر الماكينة راج استخدم كميات اكبر بس لدرام ارامي اعبيها نهاده مكي -- لازم التبعة تسح بار Shearing و diffusion
- This is likely to be beneficial in most cases, although when blending lubricants care is needed to avoid overlubrication. → استرمادة بهنصفها متبل التبعة راج (tableting) احسنه نفع، hydrophobic لتجتم كميات مغيرة، لما اعده mixing اذا زدت لوقت overlubrication راج يتحول لرداء hydrophobic حتى لو كان water soluble بهن insoluble

بال Lab في parameter 3 رئيسية

- ① Formula : Inactive + active
 ② mixer : اذا بسيلة speed + time
 ③ processing : يعني ما بحت الى غلة بار Small active drug نفس الى بار large، ال active drug باراج تغير بس exponent دراسة time بالبرية والوقت يرضها

Large scale = production scale

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.

صافي حركتها
نصف الدقة
واللصق
بال Small
وال Large

- 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.

الاستاء (البراعية)
بال Small Scale لازم
اراعها بال Large
(ما يصير segregation ما تنكس)

المزيج قبل ما يصير لدم يستعمل
التسجيل معاملة موزونة بدم
لستين (بطل اعاده تسجيل كل خمس
ساعتين) ، بس الحلق الاممي يستعمل مرة
وحدة ، robustness يعني لازم method
تكون لضغط الكولي بيطبقها وتغطي لغت
النتيجة ، اي تغيير بتخرج لكان التسجيل في
وزارة الصحة ونقل معاملة جديدة ، طريقة بتسجل
نصف ال product داتا

إذا دقت عند ال acceptable minimum بطل
maximum بطل احسن mixing
درجة لهم بزيار SD

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Types of mixers used for (liquids and suspensions) كويته سائل

ببب على التبريد زبي المروحة
Propeller (Impeller) mixers
ببب ال blade ساعد ال blade ساعد ال randomness
ببب ال diffusion

- 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.

عدد الجولات ما يفرق

- 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.

لستين ال
Impeller
لل
Vessel
كامل

propeller vessel

لنظم هاي البنية تراهي محبة ال Liquid عشان ما يصير vortex زبي السافرة ديطع من ال vessel

blades في turbine ، مختلف عن ال propeller انه قاعدة وعلي blades
Impeller Impeller

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في helical

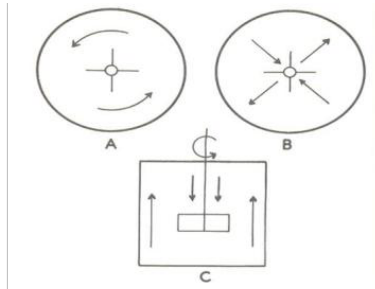
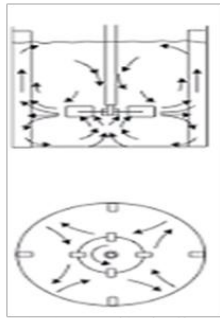
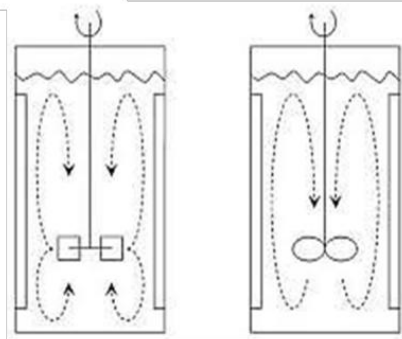


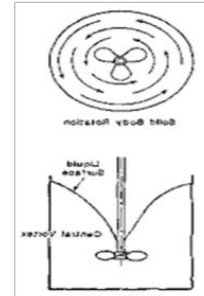
FIG. 1-2. A and B, Diagrammatic representation of cylindric tanks in which tangential and radial flow occur, respectively. C, Side view of a similar tank in which axial flow occurs. These diagrams represent systems in which only one type of flow occurs, in contrast to the usual situation in which two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



(A) Radial flow
سأ تجاه المركز لضف القطر

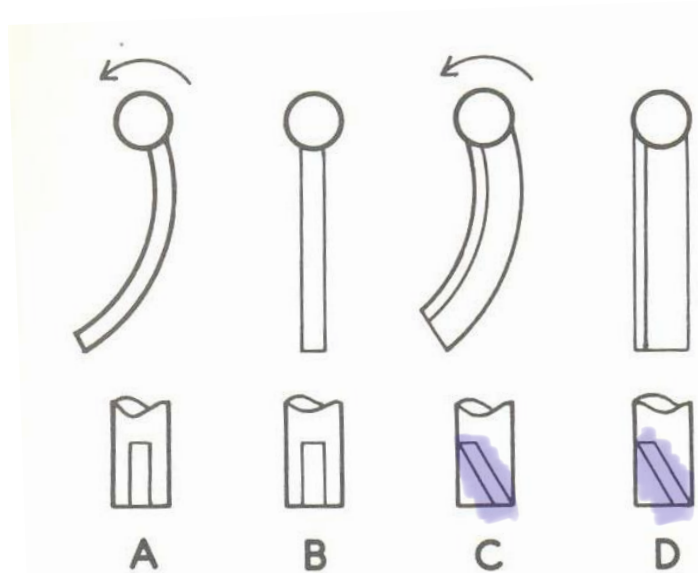


(B) axial
حركة لى liquid باتجاه shaft
up-down



(C) tangential flow
في نبرول / ارتفاع
في السطح

69



A+B → radial

C+D → Radial + axial
لا تة فنيهم حصّة / ارتفاعين
ساعة في انة radial + axial

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.

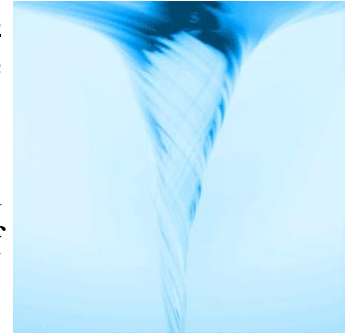
70

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.

→ صاعقة التحريك بهر توجه لورا بهر
centrifugal force ، بهر نزدن تحت و ارتفاع علا طرف
↓



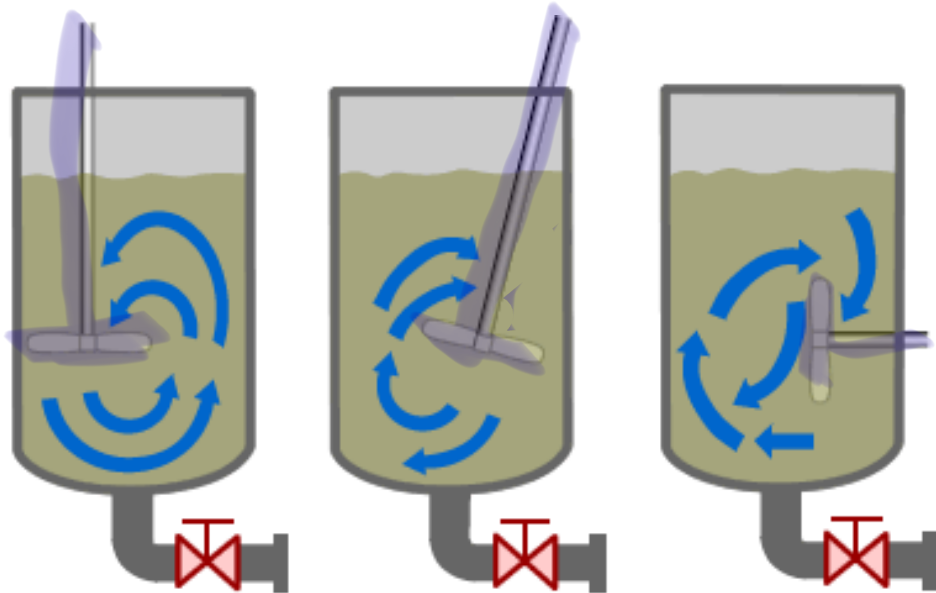
Depression جزعوتف و نزول

- An off-center mounting of propeller and vertical baffles discourage the formation of vortex.
 حواجز داخل (chamber) بهر از لایه سطح میا دایره فتنه
 بطلو برا
- Propellers are more efficient when they run at high speed in liquids with low viscosity.

← هاد، لایه
Propeller Pumping
ما تون بالنها

↓
Vortex Speed عالية عن ما بهر
ا هاد، لایه اذا ال
Viscosity

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Pumping، لایه

بهر التحريك (propeller) من

بالنها، ما لازم تون یکان ال Pumping

72

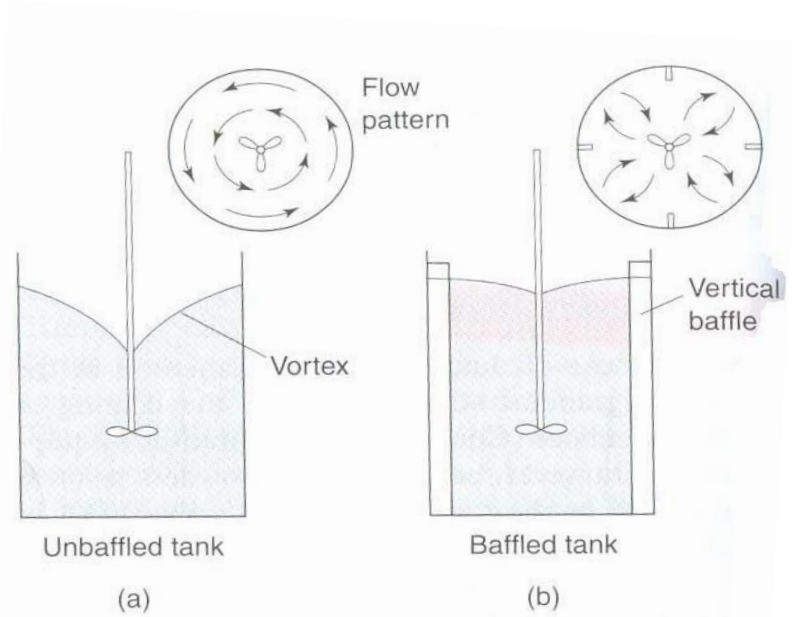


Fig. 13.13 Propeller mixer with (a) un baffled tank and (b) baffled tank.

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Types of mixers used for liquids and suspensions

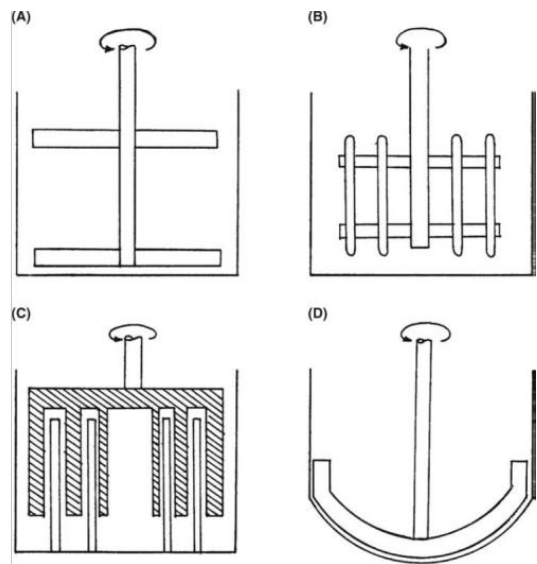
Paddle mixers مرآة بوابة Gate - anchor

- The mixing element is large in relation to the vessel and rotates at low speeds (10–100 rpm). high viscosity + low speed
Propeller الجرس

Paddle mixers

أكبر من turbine, propeller

مادة جزء كبير من الطاقة التي shearling



تكاليف مرآة المرآة

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

المكان حيث
من شحار عالي

- They can produce stable emulsions. high viscosity
بـو high shear

75

high viscosity

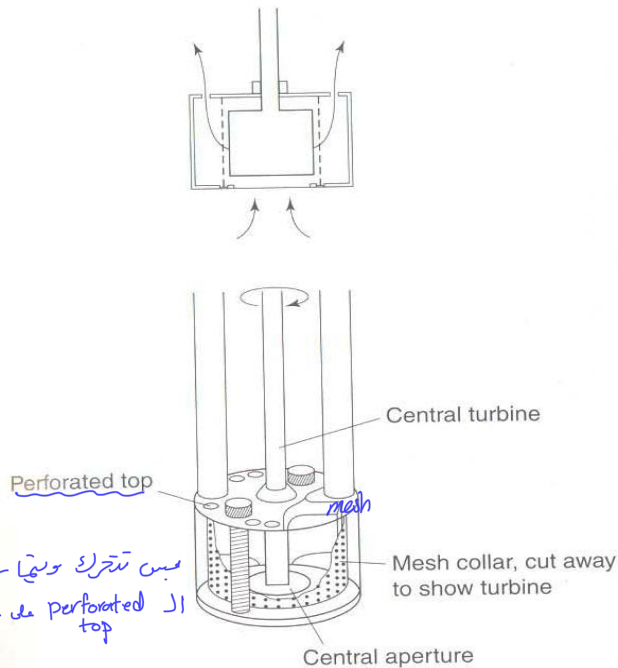
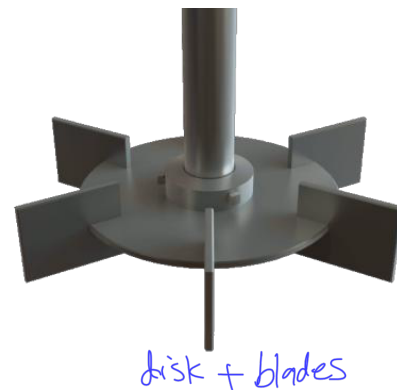


Fig. 13.14 Turbine mixer.

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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. $N_2 - CO_2$
- The liquid must be of low viscosity, **non-foaming**, unreactive with the gas employed and reasonably nonvolatile. →

إذا المارة تتأكل سبتم CO_2/N_2

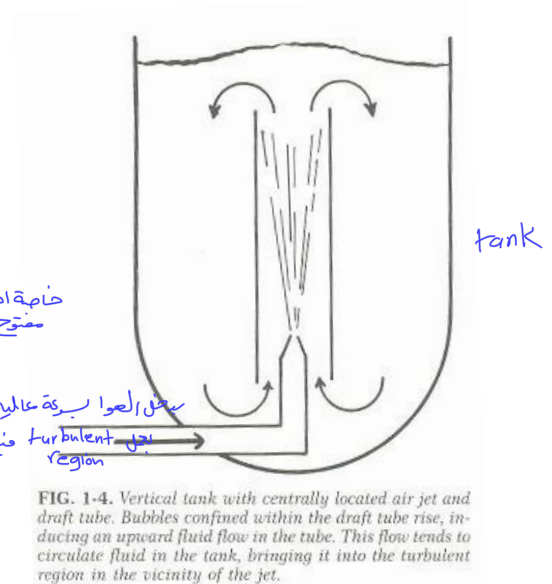


FIG. 1-4. Vertical tank with centrally located air jet and draft tube. Bubbles confined within the draft tube rise, inducing an upward fluid flow in the tube. This flow tends to circulate fluid in the tank, bringing it into the turbulent region in the vicinity of the jet.

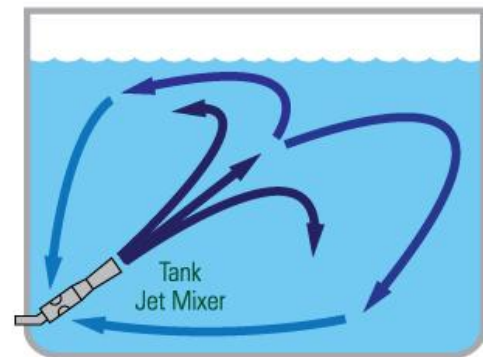
77

Types of mixers used for liquids and suspensions

Fluid jet mixers

بدخل الـ Liquid / by pumping

- 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. *برول ما داخل هوا به خط مای / برخل ر ل liquid تا عی به خط*



عالي، رطوبتي، diffusion و turbulent region

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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.

لرغم نتاجه ما يغير chock Feeding
دلا بطور بار discharge

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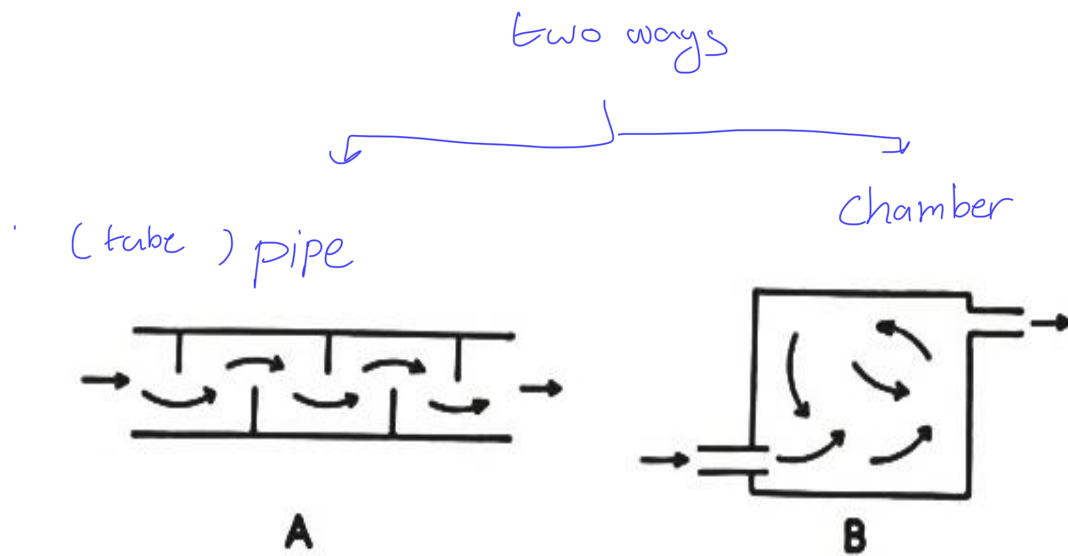


FIG. 1-5. Continuous fluids mixing devices. A, Baffled pipe mixer; B, mixing chamber with flow induced recirculation.

توالفوق بين اد Pipe واد Chamber ؟

80
اد pipe فيه Baffle يعمل الحركة موجهة ، راح تنبسط ال liquid فيه وترجع منتزعة ال randomness
baffles

اما اد chamber في recirculation راح يطلع المادة ال ما يغير mixing / في holding up يعني ال liquid بهل فترة قبل ما يطلع

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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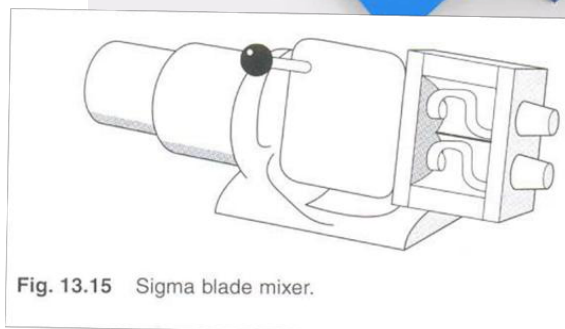
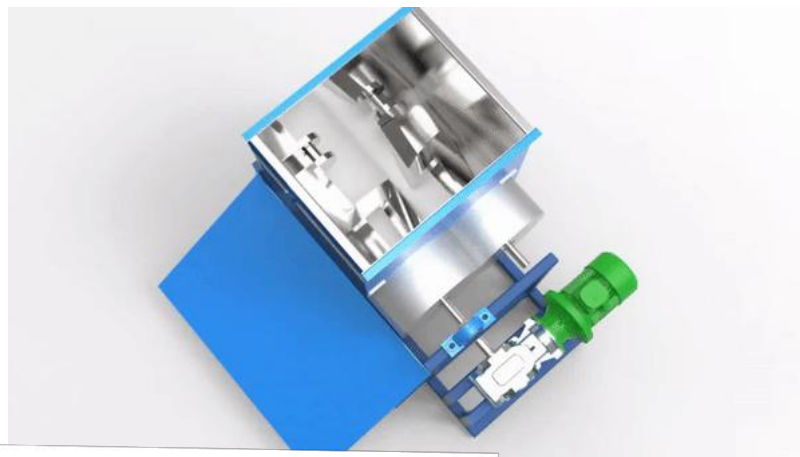
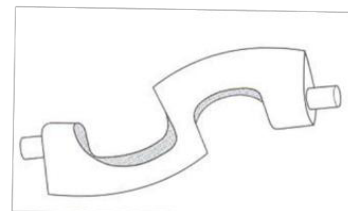


Fig. 13.15 Sigma blade mixer.



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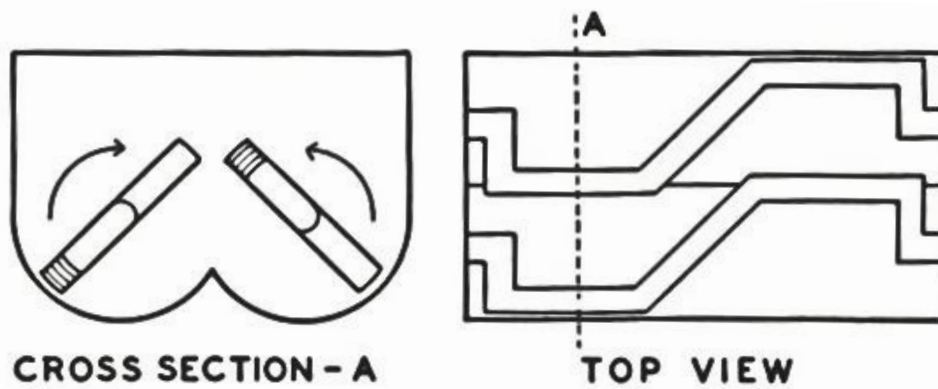


FIG. 1-8. Schematic drawing of a top-loading sigma-blade mixer with overlapping blades. The top view shows the relationship of the counter rotating blades to the overall geometry of the mixer.

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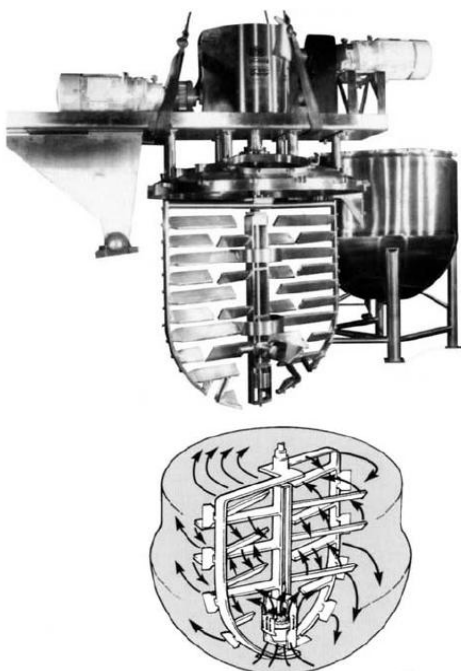


Fig. 5 Large-scale manufacturing unit (Tri-mix Turboshear) with counter-rotating mixing bars. (Courtesy of Lee Industries, Inc., Philipsburg, Pennsylvania.)



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

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