

Practical considerations in Powder mixing

عنصر C
A - B - C

أنا أبعدي C عن A
Drug mixer
المixer
المixer
السائل
الماء
B
C
بالنظر، يعطي عجيج جيد
تحقيق توزيع متساوٍ
الآن، يعطي عجيج جيد
تحقيق توزيع متساوٍ
B-C
تحقيق توزيع متساوٍ

- 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). تحقيق التوزيع المتساوٍ بالتجزئة
 - The volume of powder mixture in the mixer should be appropriate. Both overfilling and underfilling may reduce mixing efficiency. الناتج العائد للتجزئة
overfilling and underfilling
 - The mixer should produce the mixing mechanism appropriate for the formulation:
 - Potent drugs: diffusion is necessary
 - Cohesive material: shear mixingSolid : convection - shearing - particle diffusion
liquid: Bulk movement - layering - molecular diffusion
- 43

Practical considerations in Powder mixing

- In order to determine suitable mixing time, the mixing process should be checked by removing and analyzing representative samples after different mixing intervals. الآن احصل على الناتج بالتجزئة بالتجزئة
Geometric mixing time
- Static charges may be generated during mixing that result in reduction in diffusive mixing. أني أرى (1) charge
أني أرى (2) charge
أني أرى (3) charge
- This is enhanced by low humidity in atmosphere. The mixer should be suitably earthed to dissipate the static charge. الجهاز يكون مربوط بسلك يخرج من المختبر
- Vibrations may cause segregation in normal mixes and dislodging of adsorbed particles in ordered mixes. vibration
dislodging
adsorbed particles
carrier (lactose)
drug

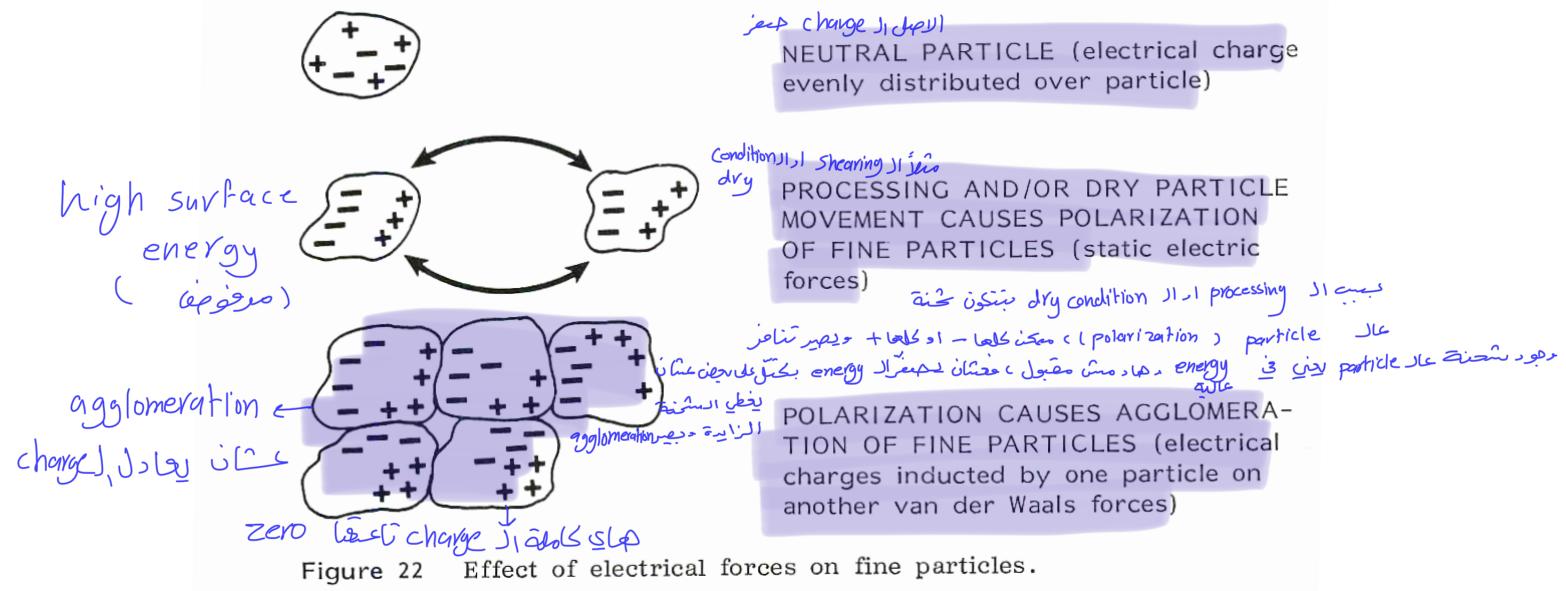


Figure 22 Effect of electrical forces on fine particles.

45

Powder mixing equipment

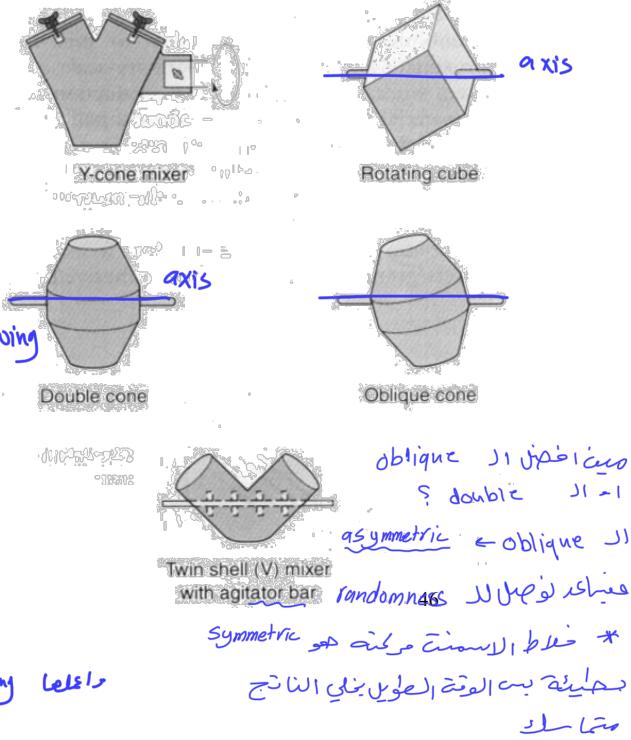
① Tumbling mixers

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.

رہنہ حرکتیں بھیطہ اور powder بکھنے
F5 لادنا بخون spherical میں بٹھے اکی واسن
دھنیا میٹر (Cohesive up) میٹر
ماراج بخکم، مٹھے مٹھے
cohesive اسیں

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



جدران ازدواجی walls لولی baffle \leftarrow mixer يكون في بال ③

亂さ randomnes \uparrow - خلط صناعي ويرجع خبر تغير الوجه powder ①

亂さ randomnes

agitator bar ②

亂さ randomnes

particles تخطي بيني

regular movement حركة متسقة

رباع انه تغيرها يجدها تغير لوجه

亂さ randomnes

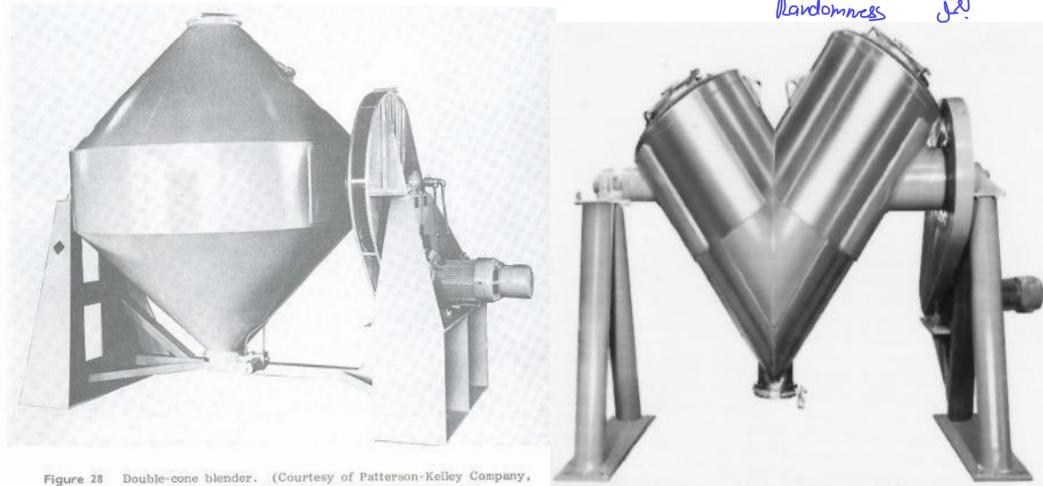


Figure 28 Double-cone blender. (Courtesy of Patterson-Kelley Company, Division of Harsco Corporation, East Stroudsburg, Pennsylvania.)

47

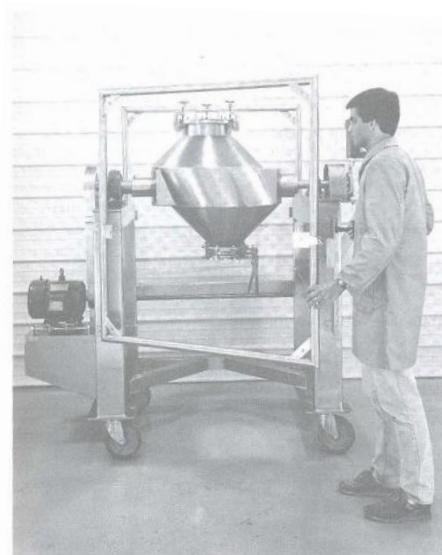


Figure 29 Slant double-cone mixer. (Courtesy Gemco, Middlesex, New Jersey.)

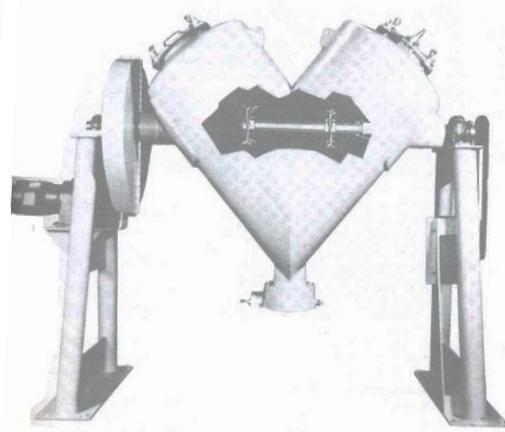


Figure 31 V-shaped blender with agitator mixing assembly. (Courtesy of Gemco, Middlesex, New Jersey.)

48

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.

آخر اساليب صين
للتخلخل الحشر وفحة
محارفها بالامانة تغير
بتتوسيع درصين في قاع
لـ دفعها بجهة
ـ كل ساقحة مانسترو
ـ الامانة بتزويق الفراخ

برعه بار
baffles

Segregation
نخل



49

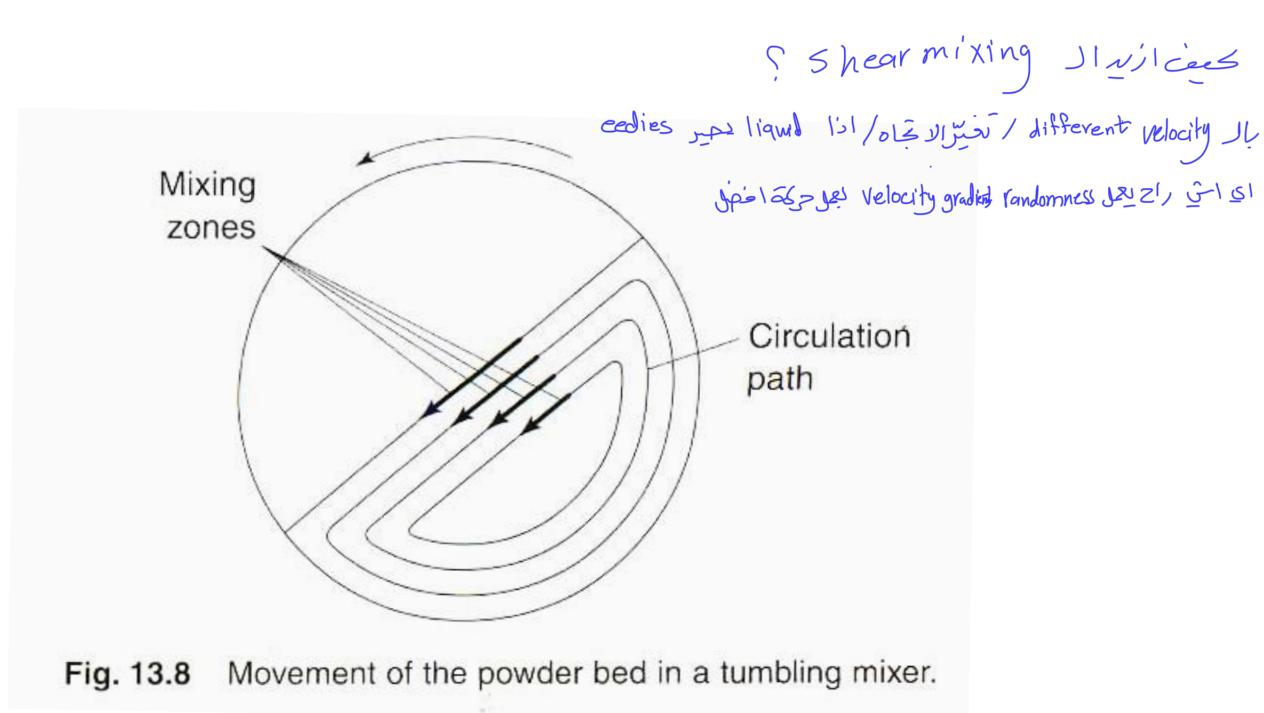
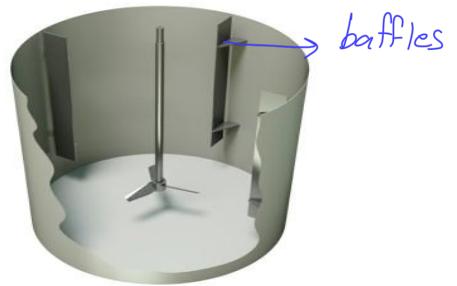


Fig. 13.8 Movement of the powder bed in a tumbling mixer.

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.
لبرازم المزدوجة محددة سعة اعلى الايجاد وهي تبلغ اقصاها 2/3 من سعة المزدوجة
- 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. مافي مجال دوار يملي على المزدوجة
 - Very low speed will generate insufficient bed expansion and little shear mixing. مافي دوار يملي على المزدوجة

51

(لذا منتهى سرعة دوران)

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

Volume percent of blender filled with powder charge كم المليء	Approximate blend time (minutes) in production-size blenders
50	10 العقبة المعاكسة
65	14 لكل سبعة
70	18 تسبعة
75	24 ↑النسبة ↑الوقت
80 ^b	40 ^b → العقبة كبيرة جداً

^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
choke free feeding

كل ما يجيء اكبر يحتاج وقت اطول
وتحت اكبر

52

Powder mixing equipment

مختبر عين عنصر الحاوية tumblers

Tumbling mixers

التجهيز بتجهيزها

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

بوصلها على ماكينة تفريغ

- **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.

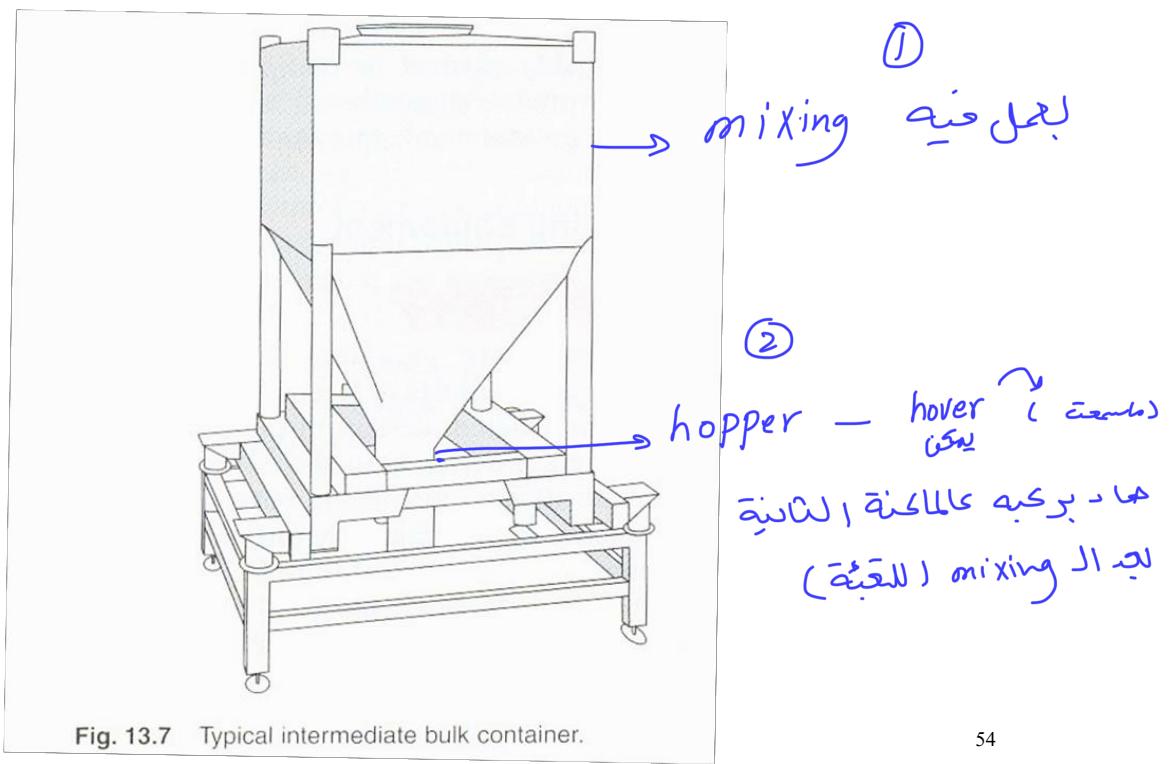
المixer هنا صنعا حركتين من بس حركة دوران / (up-down) Convection

و inversion (up-down)

53

(inversion)
up-down

كل ركي فرق كانوا بس



54

Powder mixing equipment

Shearing High speed mixer granulators

- They are used both for mixing and granulation. two in one
أولانى تجانى
 - 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
إذا كافي لما يتم البلور بسرعة الجيدة الخفيفة
 - Not normally used for blending lubricants.

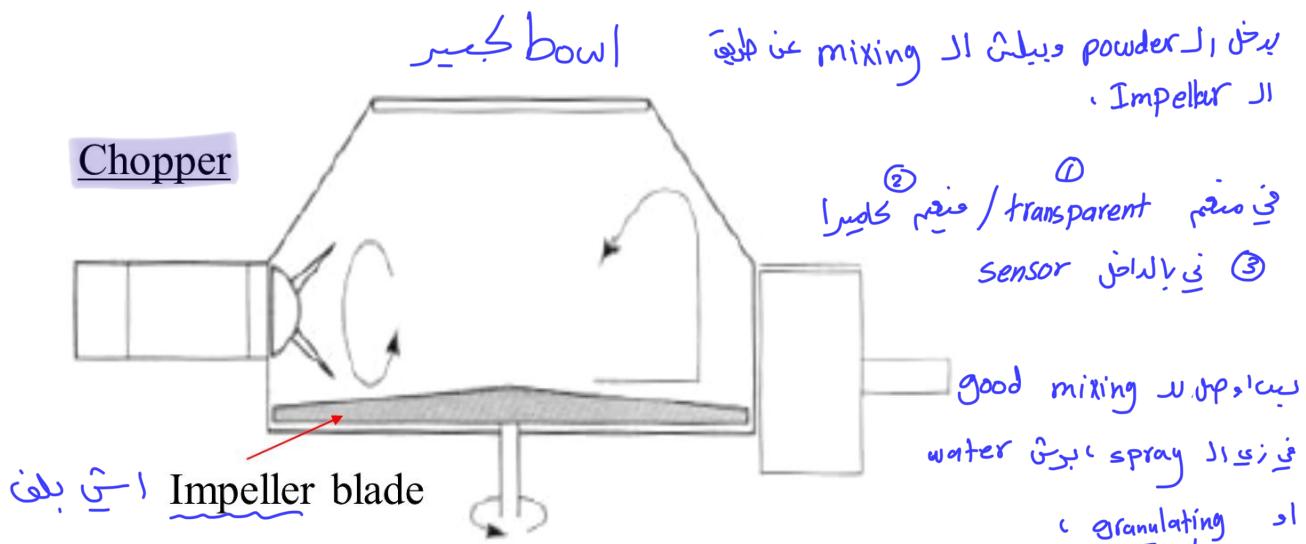


Fig. 13.9 Diagrammatic representation of a high-speed mixer-granulator.

الخطاب

① mixing ② spraying ③ chopping ④ drying

العازل Small granules \rightarrow chopper

المناسع من العجينة ⁵⁶ وصارت متسائلة ، ببلئن يشتعل

بعد ين بعمل granules II drying

Powder mixing equipment

الجهاز في الجملة

Agitator mixers

الجهاز يدور
Tumbling (ceo)

- These types of mixers depend on the motion of a blade or paddle through the product, and hence the main mixing mechanism is convection. (جهاز يتحرك داخل المكونات)
- There are three main designs of agitator mixers:
 - Ribbon mixer
 - Planetary (Orbital) mixer
 - Nautamixer

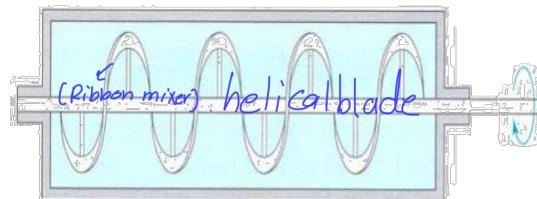


Fig. 12.10 Ribbon agitator powder mixer.

57

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 texture)
- Segregation is less likely to occur than in tumbling mixer (Geric Poorly Flowing: Ribbon spherical and)

Disadvantages

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

البعض من الجهاز يكون في اسفله من

مروانات الزاد (Dead spot) ماء ماء، لعنة، لعنة

فجعي التهابي دينار

- جهاز الماء من هندة في ماء ماء ماء

ماء ماء ماء ماء ماء

Very very effective shearing

tumbling jar

- اذ اعادة هندة لزام افنا جهاز في ماء ماء ماء

58

29

Powder mixing equipment

Kneader = العجناء

الصاعق الكوكبي
السائل رغبته وحمل
الكتل (محور)
بتوصيله لزطيا

planetary mixers

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

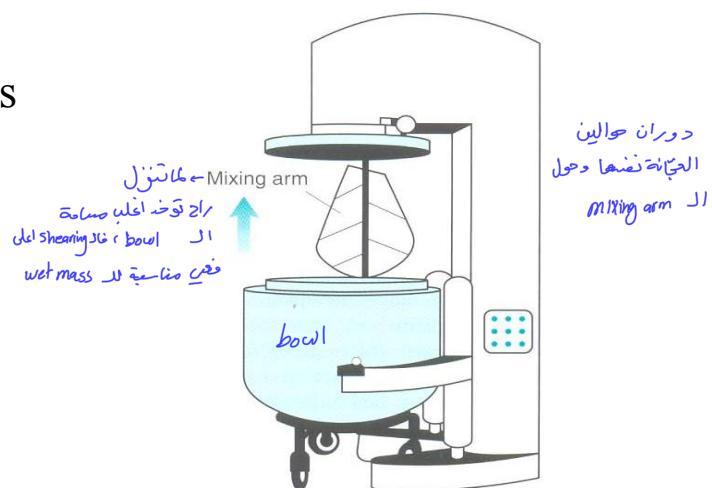


Fig. 12.11 Planetary mixer for powders and semi-solids.

59

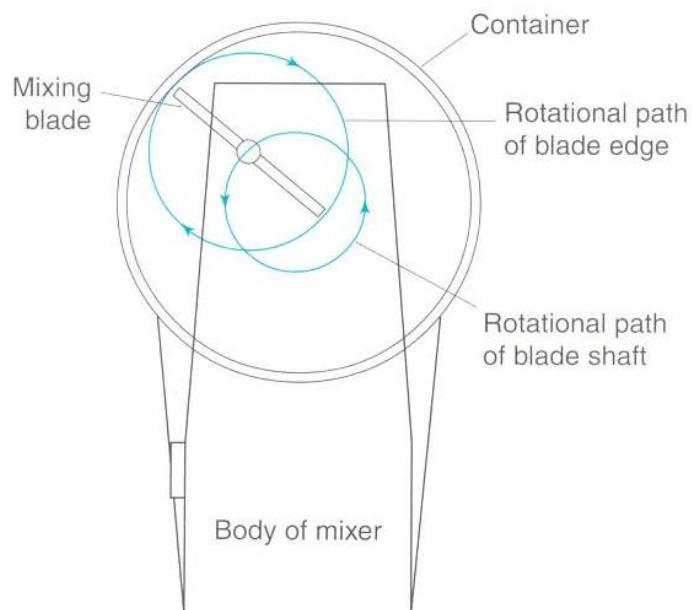


Fig. 12.12 Planetary mixer – top view, showing path of paddle.

60

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. ⑦
 - This mixer combines convective, ³ shear and diffusion mixing a3

مکان حینہ
helical سینہر
والا

vessel)، (150 μ g/cm² particles)، (150 μ g/cm² بصر

يغير مزاعات و voids other particles \downarrow diffusion

Solid (particles) diffusion liquid (molecular diffusion)

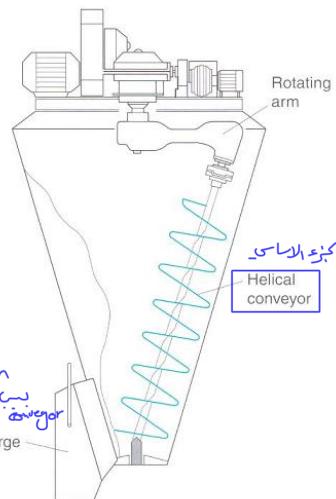
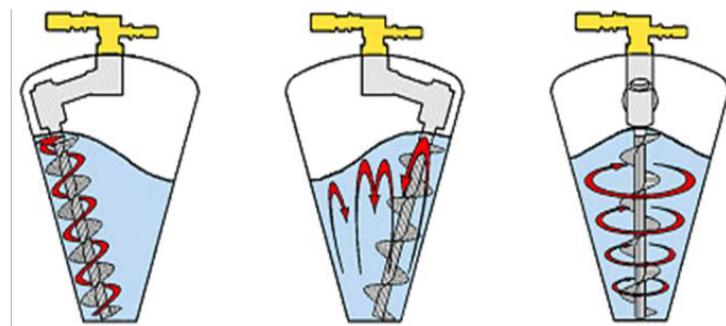


Fig. 12.13 Nautamixer (courtesy of Nautamixer Ltd).

61

Nautamixer



62

Powder mixing equipment

liquid gas

Fluidized bed mixers

all in one

مکتبہ یونیورسٹی طالبین رعایتی ملکہ

- 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
دifrیو دیffوو
 - Diffusion of particles occur.

63

writing

١) سبطار powder بالقاعة اصل لجهاز بعدين يكينا ، بغير Fluidization لعن بخلو دوا رال powder يتميز تطلع updown غامضه بقيات كل particle خواصها عواملها عواملها (mixing ميغرة) فيه حال good mixing (جيد) good mixing معنی نخل (granulating agent) spray (spraying) و يمكن ان granule ، صناعة لجهاز ميغرة يخل لجهاز انه في Sensor لقياس نسبة الرطوبة عنان ايلش انتش اد اعفه لتنقى

Fluidized bed mixers



Powder mixing equipment

Continuous mixers

Continuous mixers

ستَرِّي هَمَّا تَكُونُ الْكَمَيَاتُ كَبِيرَةً

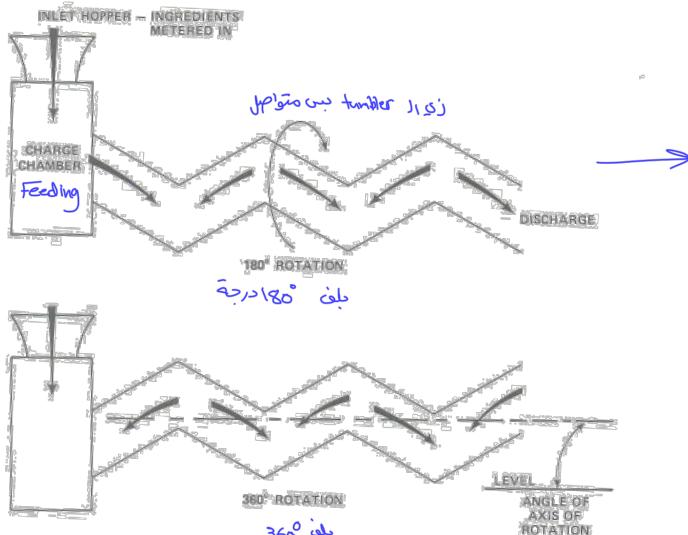


Figure 41. Schematic of "Zig Zag" continuous blender. (Courtesy of Patterson-Kelley Company, Division of Harsco Corporation, East Stroudsburg, Pennsylvania.)



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

65

الى ينتحه بالدب اساه
mixer

Scale-up of powder mixing

ويمثل اكبر اداره scale في اداره scale production scale

بال یاری 3 parameter فی Lab

نقطها التي يار بعدها على ملأ
Small Scale 66
بعض اذا بعزمي كل اتنى مثلاً بـ 10

الخطاب المفهومي Condition ؟

ام اکب عینی و احصی Small مابینت ال علامة بار

لقد ادى الـ large drug active drug الى بار انتفاخ

Potent drug

islands Feeding all cis geometric mixing in pairs Inactive + active : Formula

speed + time \rightarrow is 1 : mixer

Dynamic

processing

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.
- 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.

الاسناد في برايم
بار Small scale
اراعي بار Large scale
(م) بار Segregate

التحليل معاشرة طريقة توصيل
لستين بعد إعادة تجفيف بودرة
ستين ، بـ الماء المائي بتخفيض من
دجاجة ، يعني لذذ ، و ،
 تكون لذذ ، لذذ ، بطبقها ، تطهير
النستين ، اي تغيير بترجع لذذ التسخين في
وزارة الصحة وتحل معاشرة جذذ ، ملقطة بتغطية
نستار ، لذذ ،

اذا وفقت عند ال
acceptable minimum بخطير
mixing بجملتك احسن maximum
SD برجيم برجيم

67

Types of mixers used for liquids and suspensions (Flow) كورسية

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.

Impeller
Vessel
كامل

لذذ ، لذذ ، تراكي ، تجفيف ، لذذ ، ملقطة ، لذذ ،

blades في propeller مختلف عن turbine ، في قاعدة دعاين Impeller

68

helical في -

34

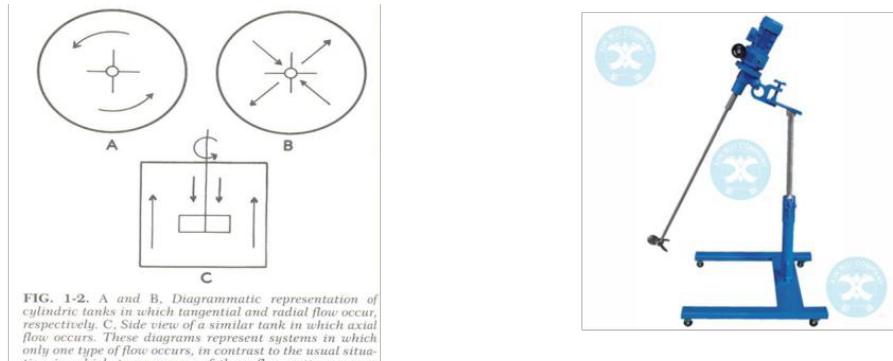
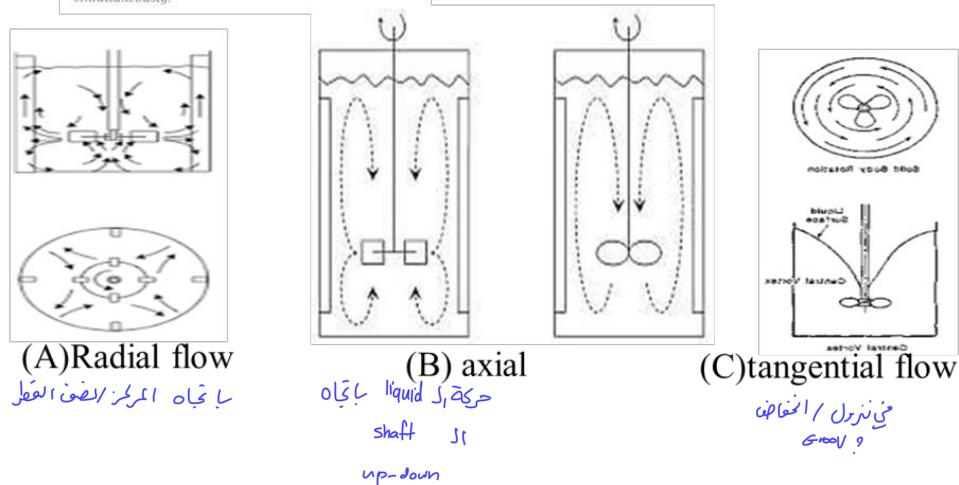


FIG. 1-2. A and B, Diagrammatic representation of cylindrical tanks in which tangential and radial flow occur, respectively. C, Side view of a similar tank in which axial flow occurs. These diagrams represent systems in which only one type of flow occurs, in contrast to the usual situation in which two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



69

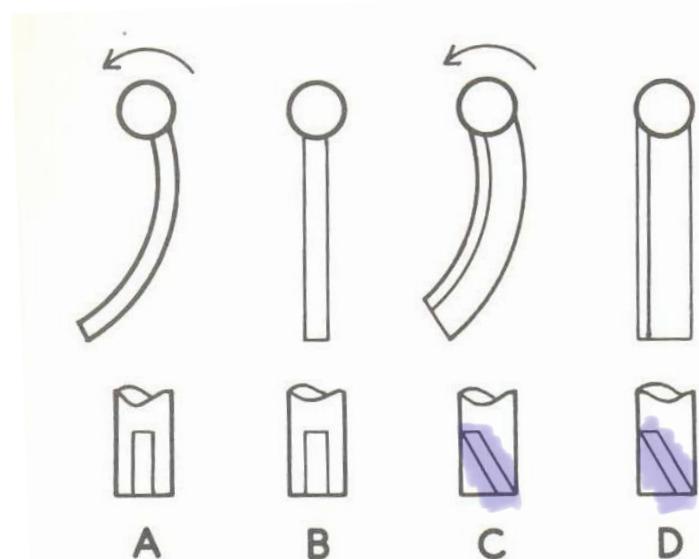


FIG. 1-3. Impeller blade types (only one blade shown), top and side views. A and B, Radial flow design; C and D, mixed radial-axial flow design. For axial pumping, the blade must be set at an incline to the axis of the shaft.

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.
- 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.

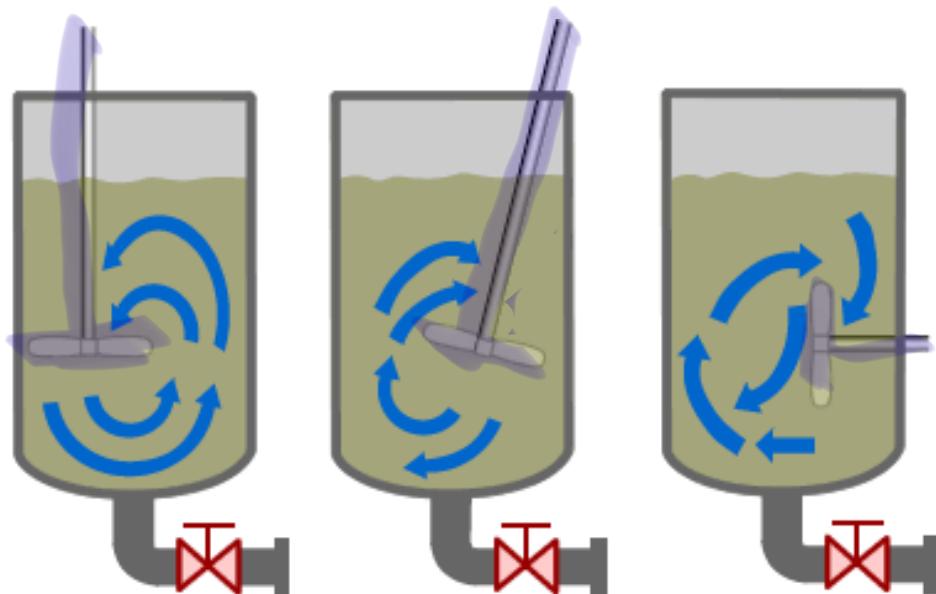
لایبلک هنریک بھر ترچ لے را بی
centrifugal, بھر نزول ہے ارتفاع علاوہ اف
↓



جیموٹھ ڈیپریشن

71

Vortex speed میسر سرعت میں میسر
low viscosity میسر



upi, is pumping

72

upi (propeller) لے لے لے

Pumping میں اس کوں یعنی اس کوں اس کوں

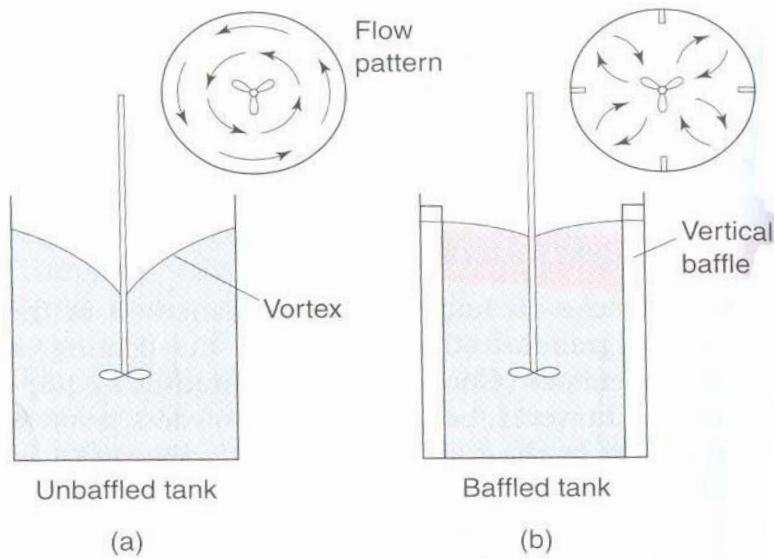


Fig. 13.13 Propeller mixer with (a) unbaffled tank and (b) baffled tank.

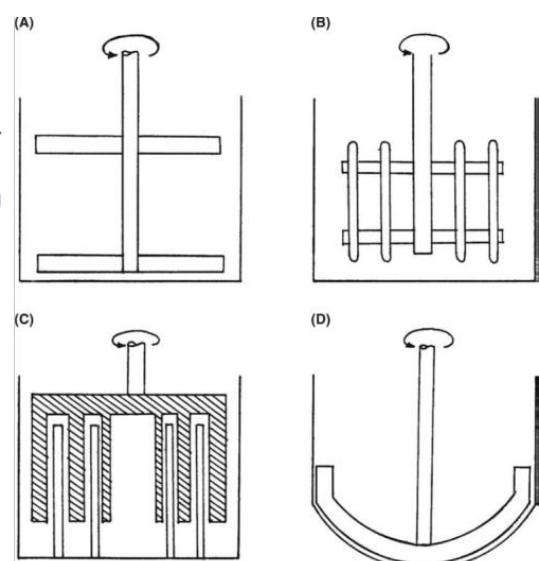
73

Types of mixers used for liquids and suspensions

Paddle mixers جبل مخلط Gate - anchor

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

high viscosity
+ low speed
small propeller



mixer, shear, shear, shear

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. *high viscosity*
high shear

75

high viscosity

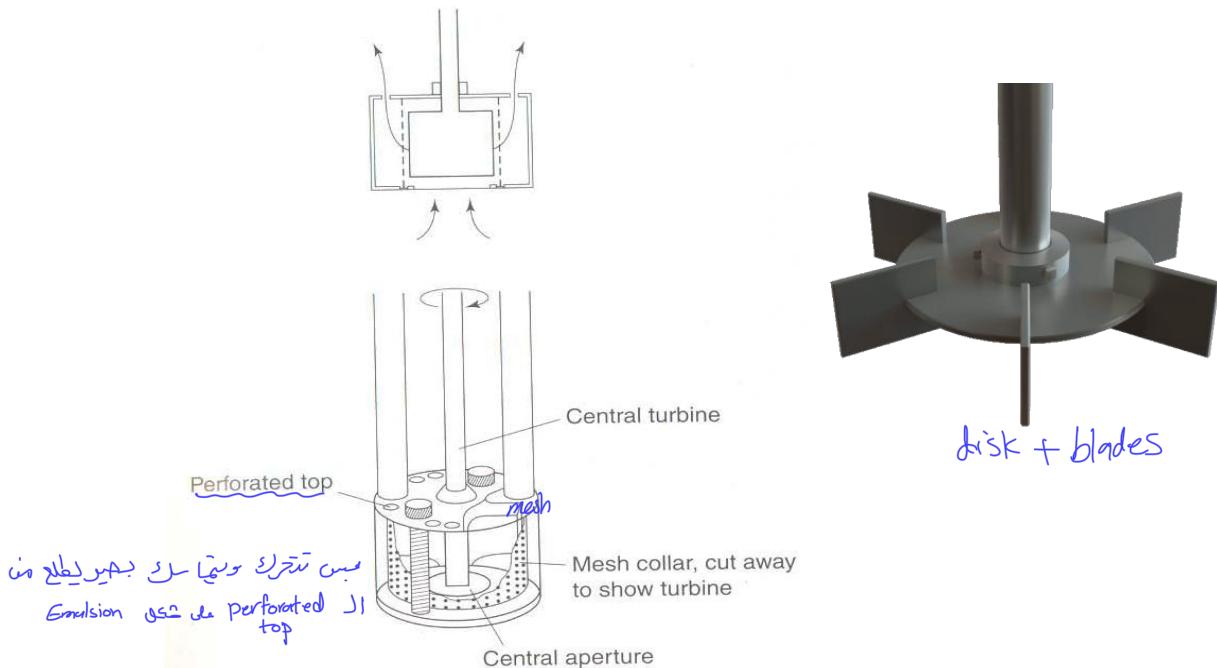


Fig. 13.14 Turbine mixer.

76

Types of mixers used for liquids and suspensions

Air jet mixers *high speed with pressurized air*

- 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.

bulb bubbling
Foaming اول
فيسبل ببل دبل
Contamination امارة

CO_2/N_2 لجأة تجارة

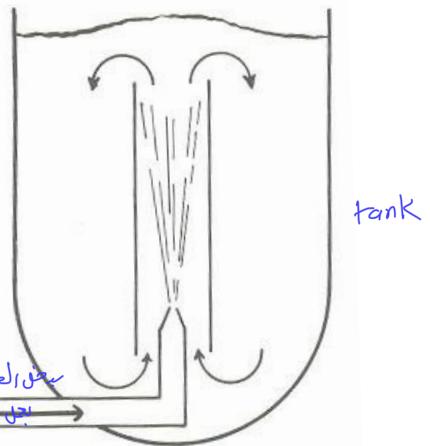


FIG. 1-4. Vertical tank with centrally located air jet and draft tube. Bubbles confined within the draft tube rise, inducing an upward fluid flow in the tube. This flow tends to circulate fluid in the tank, bringing it into the turbulent region in the vicinity of the jet.

77

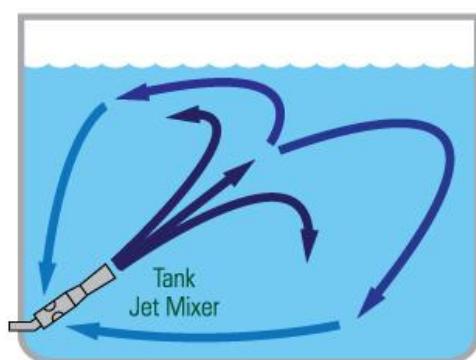
Types of mixers used for liquids and suspensions

Fluid jet mixers

by pumping / Liquid

- 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.

برل مادنی دوا بخط مان / بخط دوا تا مان
diffusion, turbulent region



78

Types of mixers used for liquids and suspensions

Inline mixers (Continuous mixing)

↑ powder
↓ liquid

- 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.

discharge بارج دار \rightarrow chock عقب ساده سازی \rightarrow Feeding دارم ترکیب کار

79

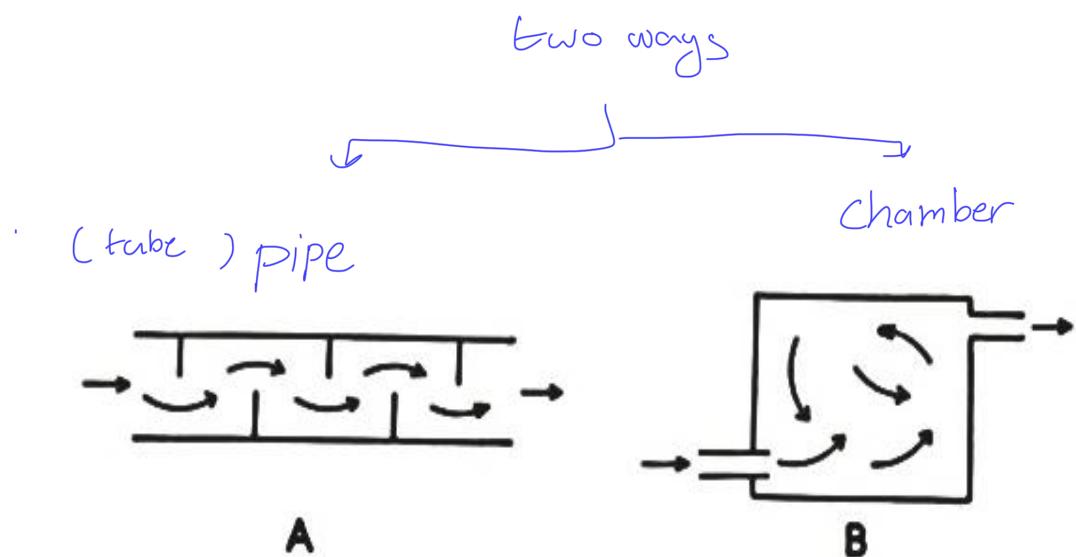


FIG. 1-5. Continuous fluids mixing devices. A, Baffled pipe mixer; B, mixing chamber with flow induced recirculation.

نحو (الفرق بين) داد Chamber و Pipe

او Baffle في pipe بدل الحركة موحدة ، راح تختلا (liquid) فيه ، وترجع عبئ تردد (randomness) دار

دار بطلع انتها لا يمehr (liquid holding up) / good mixing دار فتحة صل مارطاخ (chamber) دار

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.)

81

Mixing of semisolids

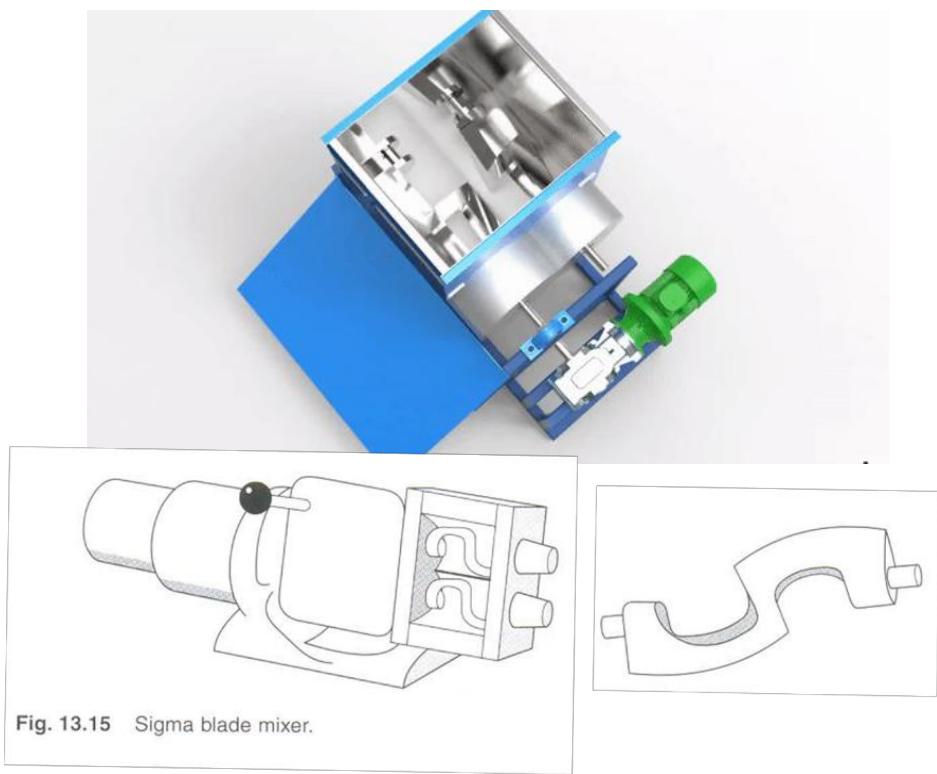
- Semisolids, unlike liquids and powders, do not flow easily.
- The suitable mixers must have rotating elements with narrow clearances between them selves and the mixing vessel to avoid dead spots

82

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.

83



84

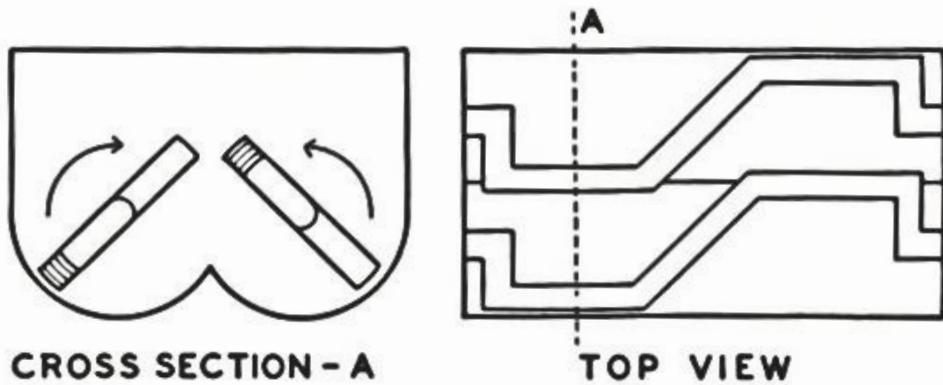


FIG. 1-8. Schematic drawing of a top-loading sigma-blade mixer with overlapping blades. The top view shows the relationship of the counter rotating blades to the overall geometry of the mixer.

85

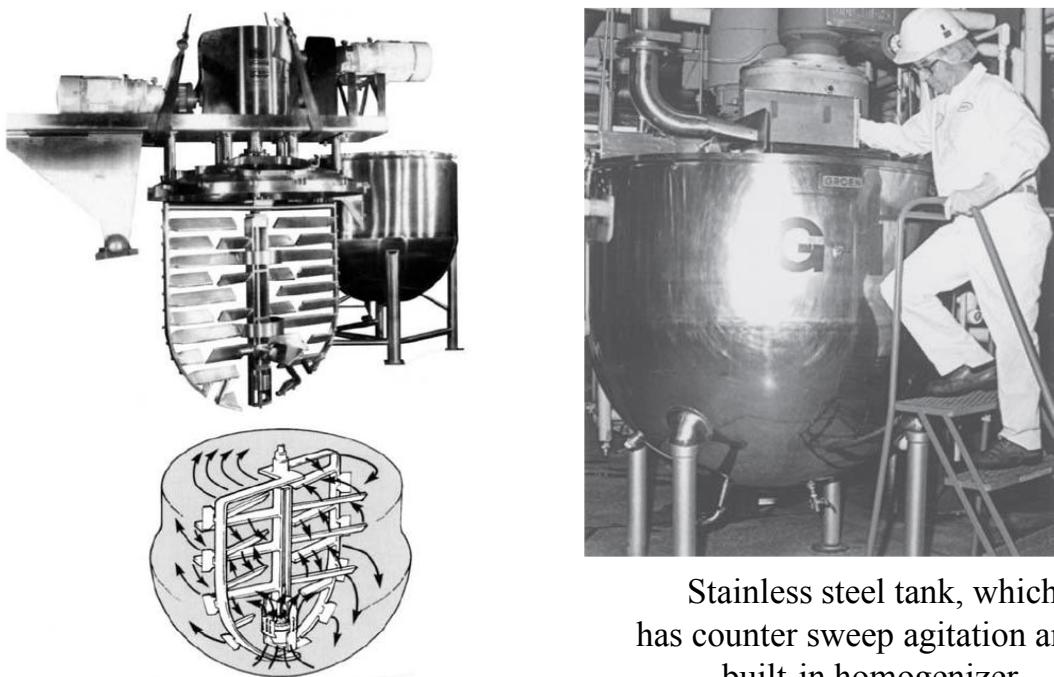


Fig. 5 Large-scale manufacturing unit (Tri-mix Turboshear) with counter-rotating mixing bars. (Courtesy of Lee Industries, Inc., Philipsburg, Pennsylvania.)

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

86