

# Mixing

Dr Nizar Al-Zoubi

\* (أسهل نوع من ال Formula يكون هنا ال active + excipient  
 حلاً أو Parental ال Drops و بنية ال Dosage صلبة ال Solid  
 مثل ال Tablets أو susp. يكون فيها عدد كبير من ال Form  
 ال mixing Excipients

## Mixing

- Mixing may be defined as a unit operation that aims to treat two or more components, initially in an unmixed or partially mixed state, so that each unit (particle, molecule etc.) of the components lies as nearly as possible in contact with a unit of each of the other components.

- This may be:

- Mixing of Powdered materials (e.g. tablets, capsules, dry powder inhalers).
- Mixing of miscible liquids (e.g. solutions) or immiscible (e.g. emulsions).
- Mixing of insoluble solid and liquid (e.g. Suspensions).
- Mixing of semisolids or dispersion of particles in semisolids (e.g. pastes and ointments).

في البداية  
 تكونوا Separated

يعني لو انتزعتنا  
 ال active موادها  
 عدد من ال excipient  
 فال ideal انه  
 كل active حواله  
 عدد كامل من  
 ال excipient

يعني فيه عدد كبير من ال Excipient  
 very complete formula

قبل زيت الكبد  
 مع زيت السمك  
 Hydro-  
 Phobic interaction  
 زيت سمك  
 Chalk of each other miscible

# Mixing

## - Types of mixtures:

Ease of operation

- 1) **Positive mixtures:** Mixtures that form spontaneously (do not need energy) and irreversibly (when formed do not tend to separate).  
(e.g. gases and miscible liquids)
- 2) **Negative mixtures:** Mixtures that need energy input (work) to form and keep. Once the energy input is stopped they tend to separate.  
(e.g. Suspensions, emulsions and creams)
- 3) **Neutral mixtures:** Mixtures that do not form spontaneously (i.e they need energy input) but once formed they do not tend to separate.  
(e.g. Powder mixtures, pastes and ointments)

قابل امتزاج  
 (miscible) في كل واحد  
 في الآخر  
 → مع زيت السمك  
 Hydrophilic  
 Interaction

تحتاج إلى  
 طاقة  
 Susp  
 Shaking  
 قبل  
 العمل  
 work  
 هون

mixture of powder  
 قابل امتزاج  
 في كل واحد  
 في الآخر  
 → مع زيت السمك  
 Hydrophilic  
 Interaction

راحة مع  
 2.5  
 agent  
 حرك

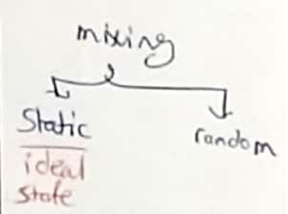
Semisolid  
 60% solid  
 Flexibility  
 Static

## The mixing Process

**Perfect mixture:** The situation in which particles of one component lay as closely as possible in contact with particles of other component.

- It is an ideal situation which is practically impossible.

**Random mixture:** A mixture where the probability of sampling a particular type of particle is the same at all positions and is proportional to the number of such particle on the total mix.

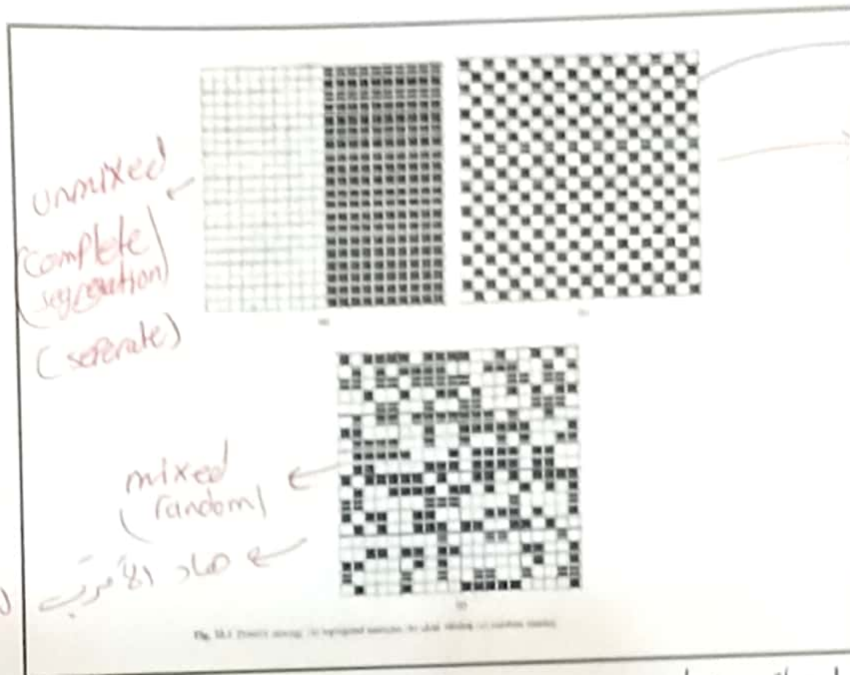


efficiency  
 of mixing  
 Color Powder

active  
 30%  
 active  
 30%

active  
 1:10  
 active  
 1:10

active  
 1:10  
 active  
 1:10



3 و 4 ابيض و اسود

mixed ordered (perfect & ideal)

unmixed  
complete  
segregation  
(separate)

mixed  
(random)

الاضافة

\* **ordered system**: Particle are arranged in iterative rule (crystalline pattern) (not random)

\* we can consider mixing as vector quantity (Spatial orientation and translational velocity of Particle)

ال P يكون الميكس  
واحد ال mixer  
كمية و اقل و اعلى  
vector quantity

### The mixing Process

- It is the weight/volume of the dosage unit that dictates how closely the mix must be examined/analyzed to ensure it contains the correct dose/concentration.
- This weight/volume is known as **the scale of scrutiny** and it is the amount of material within which the quality of mixing is important.

$x, y, z$   
المكان  
موقع  
وقت  
كمية  
دقة  
تغير من الزمان

ال كمية الى  
لا يتم تفتيش  
كمية تفتيش  
تفتيش بالكمية

\* **الكمية التي نتحقق** في ال mixer **تد** على ال Dose  
بكمية لا يتم تفتيش في الماكينة

اذا علمنا في  
اي مكان  
واعطينا نفس  
الكمية بالتد  
ال Quality  
of mixing  
مقارنة

د يوزج على الكمية الى بكمية

## The mixing Process

- For example, if the unit dose of tablets is 200 mg (containing 100 mg active drug) then 200 mg sample from the mix needs to be analyzed.
- The number of particles in scale of scrutiny depends on sample weight, particle size and particle density.

200 mg  
100 mg active  
200 mg sample

PN: ↓ PS: ↓ Variability

↓ PS: ↑ PN

inversely  
relationship  
with sample  
weight

PN: 200 mg

Scale of scrutiny is the number of particles in the sample taken for analysis. It is inversely proportional to the sample weight. SD is the standard deviation.

$$SD = \sqrt{\frac{\sum (x - \bar{x})^2}{n-1}}$$

Number of particles of a minor active constituent present in samples taken from a 1:1000 random powder mix with different numbers of particles in the scale of scrutiny

Sample number	Number of particles in scale of scrutiny		
	1000	10 000	100 000
1	1	7	108
2	0	10	91
3	1	15	116
4	2	8	105
5	0	13	84
6	1	10	93
7	1	6	113
8	2	5	92
9	0	12	104
10	1	13	90
Mean	0.9	9.9	99.6
Standard deviation	0.78	3.38	11.18
% CV	86.86	34.17	11.23
Deviation from theoretical content	±100%	±50%	±16%

Scale of scrutiny is the number of particles in the sample taken for analysis. It is inversely proportional to the sample weight. SD is the standard deviation.

100 = mixture

of particle is in milling

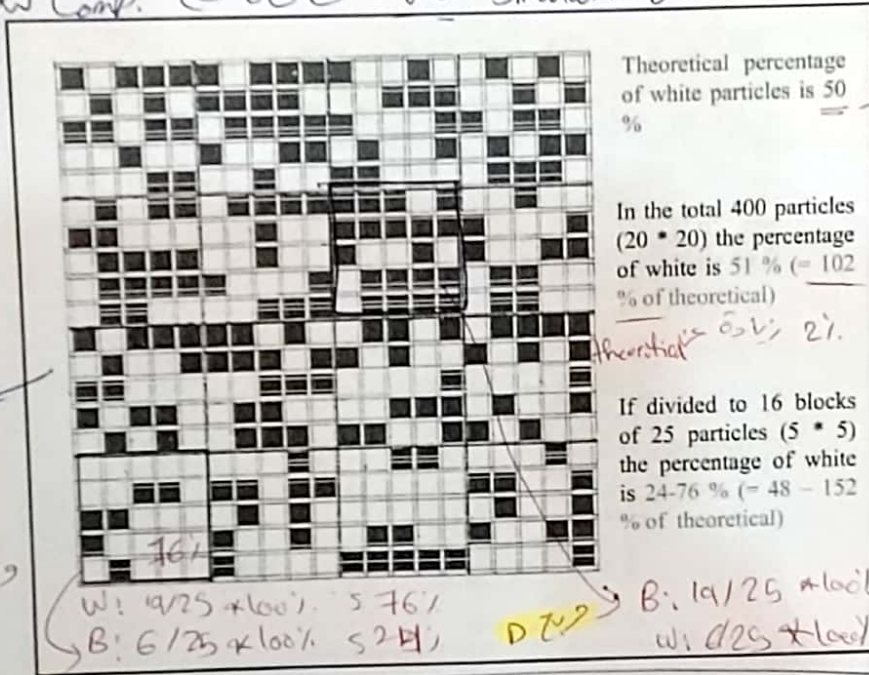
PN: 200 mg

100% deviation  
100% deviation  
100% deviation  
100% deviation  
100% deviation  
100% deviation  
100% deviation  
100% deviation  
100% deviation  
100% deviation

100% deviation

white → Active  
 Black → Inactive

Comp. في المحاكاة في حالة 50% في المحاكاة



200 Black  
 200 white  
 variability  
 200

16 Black  
 25 Black  
 25 Total  
 400 Total

مجموع A و B في الخليط

في الخليط A و B في الخليط

24% 200 = 48  
 76% 200 = 152  
 Range (48 - 152)

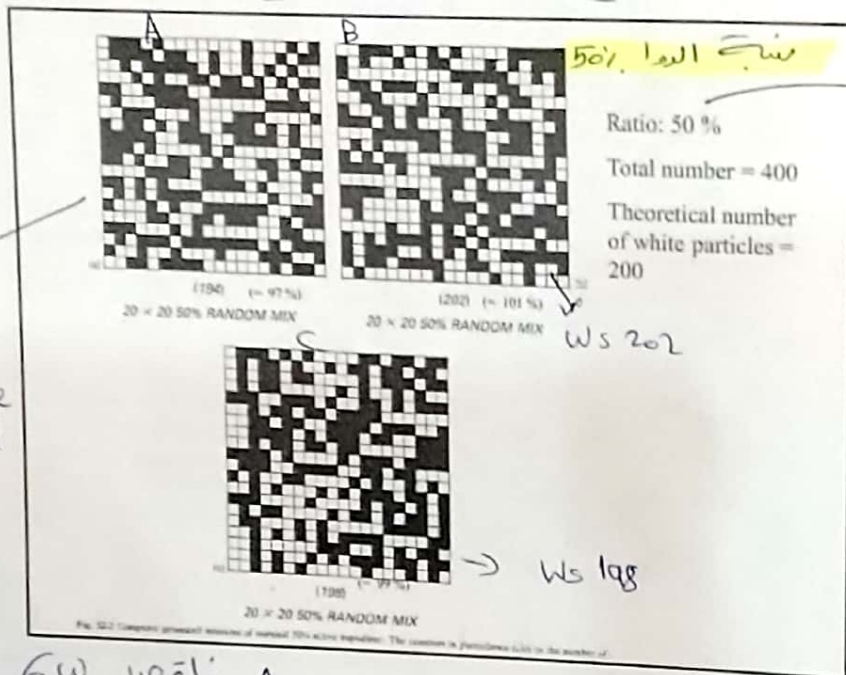
## The mixing Process

- Another factor to consider in mixing is the proportion of the active component in the dosage form/scale of scrutiny.

B, Product as per

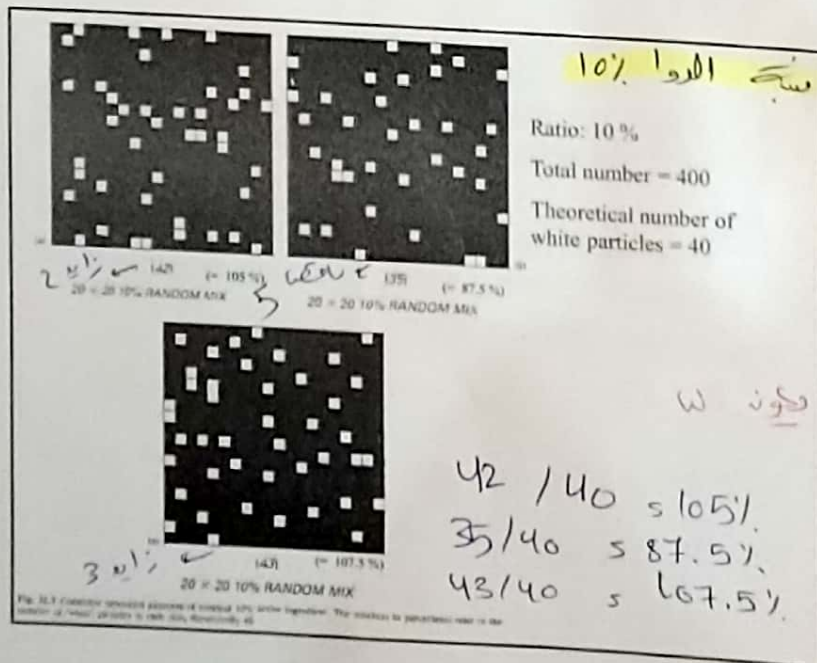
Sample weight

هون يقارن مع كمية ال active كبيرة  
ومرة كمية ال Active قليلة



نسبة active و نسبة

في نسبة من هذا المثال  
A ناقص 6 و B ناقص 2  
نسبة النوا مقارنة



على 400  
مربع 6 ال 10%  
من 400  
40%  
لازم 40 مربع

ال يكون ال active كمية كبيرة (Ratio)  
تكون ال Variability قليلة

## The mixing Process

- The variation in component percentage between different samples taken from a mixture increases:

تزداد التباين (variability)

↓ PS : ↑ CV

1. as the amount (number of particles) in scale of scrutiny decreases.
2. as the proportion of a component in mixture decreases.

↓ PS : ↑ CV

Ratio

## The mixing Process

- This indicates that:

- the lower the percentage of active ingredient in mixture, the more difficult it is to achieve an acceptably low deviation in active content.
- The more particles are present in dose (scale of scrutiny) the lower the deviation of content → The number of particles can be increased by decreasing particle size (This can be done by milling).

ليس بإحكام  
تغير سرعة  
الدوا

حجم جرعة  
أو في الجرعة  
علاقة بين  
الجرعة

كلما زاد عدد الجزيئات في الجرعة كلما تحسنت العلاقة بين الجرعة والفعالية  
مع الـ Excerpt

### Mathematical treatment of mixing process

- There will be always some variation in the composition of samples taken from random mixtures.
- The aim during formulation and processing is to minimize this variation to acceptable levels by selecting appropriate :

– scale of scrutiny

– particle size

- mixing procedure

Process  
+ machine

### Mathematical treatment of mixing process

- For random mix, if we consider that particles are all of same size, shape and density then:

$$SD = \sqrt{\frac{p(1-p)}{n}}$$

is ~~proportion~~ Proportion of  
Component in total mix

- As  $p$  increases, %CV decrease

Example:

$$n = 100\,000, p = 0.5 \Rightarrow \underline{SD} = 1.58 \times 10^{-3}, \%CV = 0.32\%$$

$n = 100\,000, p = 0.001 \Rightarrow SD = 9.99 \times 10^{-5}, \%CV = 10\%$

LP:

- The scale of scrutiny can be increased by increasing the amount of additives in the mixture but this will lead to a decrease in  $p$ .

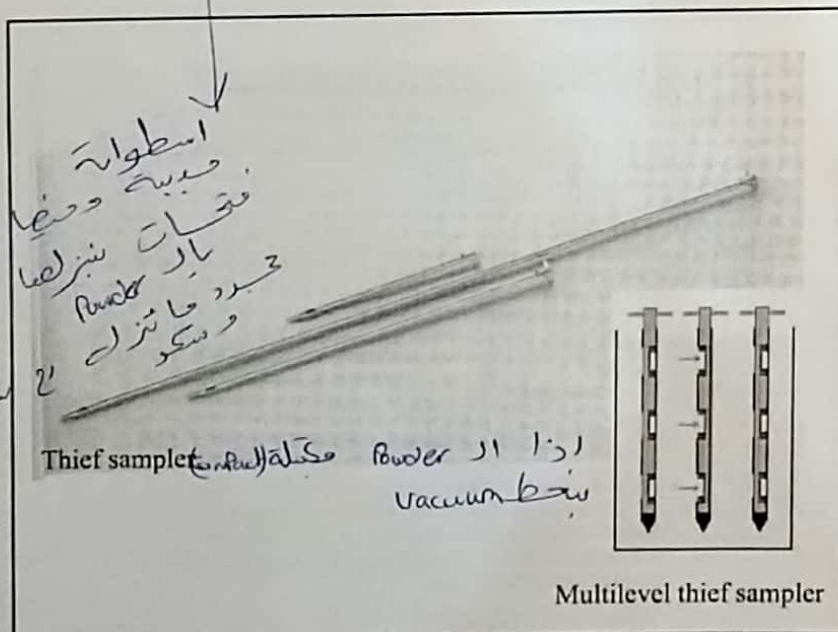
## Evaluation of degree of mixing

### Needs for monitoring of mixing:

- To follow a mixing process:
  - To indicate the degree of mixing
  - To indicate when sufficient mixing has occurred and determine the suitable mixing time
- To assess the efficiency of a mixer

### Sampling

- Scoop sampling
- Thief sampling



## Evaluation of degree of mixing

It is an indicator of quality of mixing process  
 ← Mixing Index (M) ← في حاد لسن

$$② M_s = \frac{X}{\bar{X}}$$

$$① M = \frac{S_R}{S_{ACT}}$$

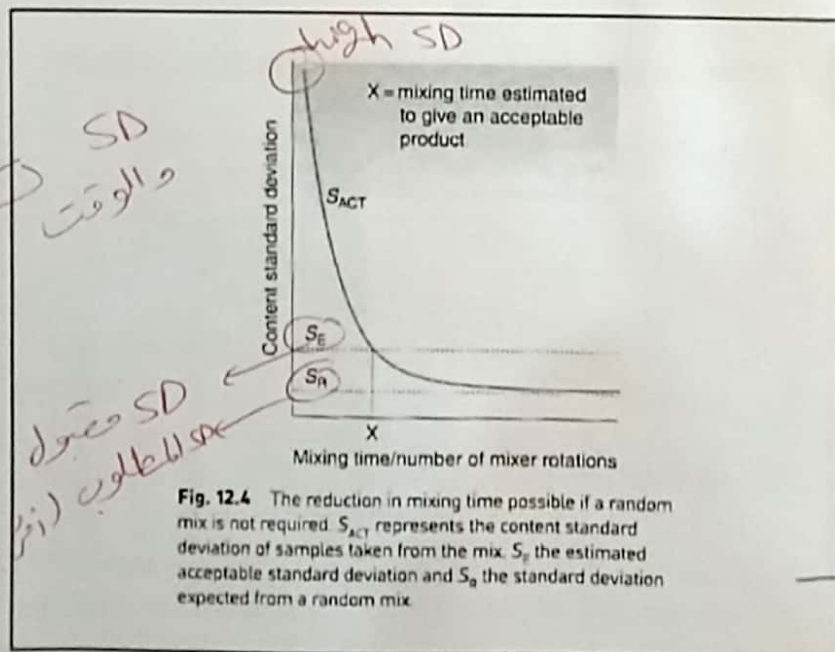
SD → SD  
 SE → acceptable SD  
 SD → SD

$S_R$ : Content standard deviation of random mixture

$S_{ACT}$ : Content standard deviation of mixture under investigation. (sample taken from the mix)

- In some cases, it is possible to achieve an acceptable variation in content before obtaining a random mix

\* The value of 1 indicates a fully mixed state while the value of 0 indicate a fully segregated state



SD والوقت  
 SD مع الزيادة

SD مقبول  
 SD المطلوب (المراد)

الطريقة الثانية بدل حاد SD هو نسبة  $X/\bar{X}$   
 Mean في Cone و شقوق تجريبية ل 10 أو 0  
 at time -

عودة  
 note 1  
 في الحاد

قسم خالص بال Powder قسم خالص بال Liq

## Mechanisms of mixing

### Powders

There are three main mechanisms for powder mixing:

- a) **Convection** (the transfer of large amount of particles from one part of the powder bed to another).

This may occur when a mixer blade or paddle moves through the mix.

This mechanism contributes mainly to macroscopic mixing of powders, but mixing does not occur within the group of particles moving together.

يكون عند حبة كبيرة

لكنوا الصبات

مضويات في الدوا (excluded)

ثم يتبع كمية

كبيرة تطلع منه

أفضل لأي

ومن ثم إلى

أفضل

عدد كمية من مكان إلى مكان

- a) **Convection** (the transfer of large amount of particles from one part of the powder bed to another).

This may occur when a mixer blade or paddle moves through the mix.

This mechanism contributes mainly to macroscopic mixing of powders, but mixing does not occur within the group of particles moving together.

يعني لا الجهاز  
ليحرك مواد فيه  
Riddle أو Blade

الجهاز يكون  
ثقافت ما يكون  
movement  
microscopic  
يكون قادرين توفوا

أي في نظام يعني  
سائنا ما وصلنا الـ mixing  
حيث ان الـ mixing  
لما يصر تراخي تام بين الـ ingredient

والمزج P  
تداخل مع بعض

عانه في عنا  
mixing

## Mechanisms of mixing

### Powders

- b) **Shear** (Layer of powder flows over another layer)

This may occur when some of the material is removed (e.g. by convective mixing) causing powder bed to collapse.

Shear صف تخرج في الـ Bulk و احنا بتطلع  
من مكان إلى أي بقدر تداخل الطبقات  
بين بعض وهي عن تطلع لأي يعني

مكانها Powder أو تزلت لأفضل بين مكانها  
Powder تاني

يكون عن طبقات

convection is more random than  
convective (تداخل أكثر)

لما يصر الـ P  
بين Surfaces 2

لكنه من قوة  
shear الـ  
milling

مكون حنا طبقتين  
excellent بينهم طبقة  
دوا تداخل الطبقات  
بعض (layering)

## Mechanisms of mixing

### Powders

#### c) Diffusion (mixing of individual particles)

This mechanism is necessary to form true random mixture.

When a powder bed is forced to move or flow it will dilate (the particles become less tightly packed and the voids between them increase). This allows particles to fall under gravity through the voids created.

بمركب عن  
P و A  
نفسها

ال P ع  
تقريباً، ادا في  
فرغ نلاحظ  
تليق نخل ونفس  
Diffusion  
ما يوصل آخر زاوية  
معلقة بال mixer

وهي عم تقرك  
بغير عنها حرية  
الحركة فتجد  
كثيرة بعضها فبكر  
Dilate  
ونفس عنها فراغات

## Mechanisms of mixing

### Liquids

#### a) Bulk transport

تقال Convection بال Powder

- The movement of a large portion of the material being mixed from one position in the system to another.

لو كان عنا Tak وسطياً فيه 319  
ع تليق P تقرك من أي إلى آخر  
أو من آخر إلى أي أو من عين إلى  
يعني كمية كبيرة من ingredients تتحرك وتتلاقح  
كمية كبيرة من ingredients

Random movement good mixing

## Mechanisms of mixing

### Liquids

#### b) Turbulent mixing

لصق بال Shear Powder

- The haphazard movement of molecules when forced to move in turbulent manner, which means random fluctuation of the fluid speed and movement direction, so that the fluid has different instantaneous velocities at different locations at the same time.
- It can be seen as a composite of different eddies (small portions of fluid moving as a unit) of various sizes. The large ones tend to break into smaller and smaller sizes until they are no longer distinguishable.
- Turbulence is a highly effective mechanism for mixing.

المبدأ رج عشوائي  
بالشلل سرعة  
الزوايا بالمتصف  
عالية دخل فابعدنا  
تكون مختلفة رج  
تقل فاختلاف

الرجة يعطي  
Randomness  
mixture بال

وهي عم تزل في  
بسرعة دوامات  
(eddy)

وهالقي يعطي تحريك  
أكثر

Not Constant  
سرعات واتجاهات  
مختلفة  
كل كمية  
رج تفتت باجزاء  
مختلفة والدوامات  
الكيرة والصغيرة  
تتحلل وتفتت  
حتى لا يمكن  
ملاحظة mixture

molecular level reached = good mixing

## Mechanisms of mixing

### Liquids

#### c) Molecular diffusion

اللاذقة انه نوصي بالفاو

- The molecular diffusion is the primary mechanism responsible for mixing at the molecular level.
- This mechanism produces well mixed liquids if there is sufficient time.
- Considerable time is needed if this is the only mixing mechanism.

برونة ال Bulk

Turbulence  
مد ال

رج يكفي (ك)

سيتأخر لونة

طويل ولكن

مد و على

Conc. gradient حجب molecule  
مolecular level ال

الداخل بين  
ال  
layers  
مستوى ال  
molecule

(Demixing)

random mixture

## Powder segregation (demixing)

- Segregation is the opposite effect to mixing, i.e. components tend to separate out ( $S_{ACT}$  increases).
- It may cause a random mixture to change to non-random or may be responsible that a random mixture never occurs.
- Segregation is more likely to occur if powder bed is subjected to vibration and when the particles have greater flowability.

كنا نحكي سبب  
عشوائيات الحد  
قابلة SD  
العاثر ما يكونه  
random  
يجي يقل هو  
العكس

فعل اما خلل  
مخلط او  
(لا يحدث نظرياً)  
او بعد ما ينقسم  
mixing

منه التغيرات التي تسبب segregation  
او powder vibration

منه غيرة لفرقة كمان حسب او shape  
greater flowability

Segregation can be due to difference in:-

- ① Particle charge
- ② Particle density
- ③ Particle shape
- ④ Particle size & particle distribution

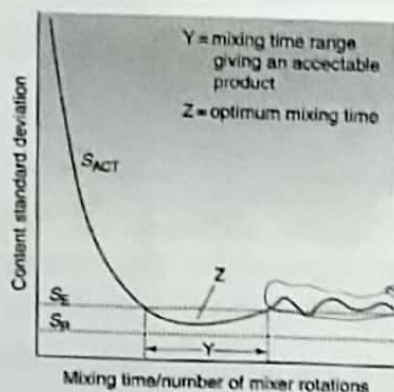


Fig. 12.5 Possible effect of extended mixing time on the content standard deviation of samples taken from a mix prone to segregation.  $S_{ACT}$  represents the content standard deviation of samples taken from the mix.  $S_E$  the estimated acceptable standard deviation and  $S_R$  the standard deviation expected from a random mix.

هذا استمر  
mixing

## Powder segregation (demixing)

Factors affecting segregation:

### 1. Particle size

#### Percolation segregation

(small particles tend to fall through voids between large particles)

#### Trajectory segregation

(large particles tend to have greater kinetic energy)

#### Elutriation segregation (dusting out)

(Air-blown small particles sediment and form a layer over coarse particles)

عكس ال Percolation و مع طلع ال Fine

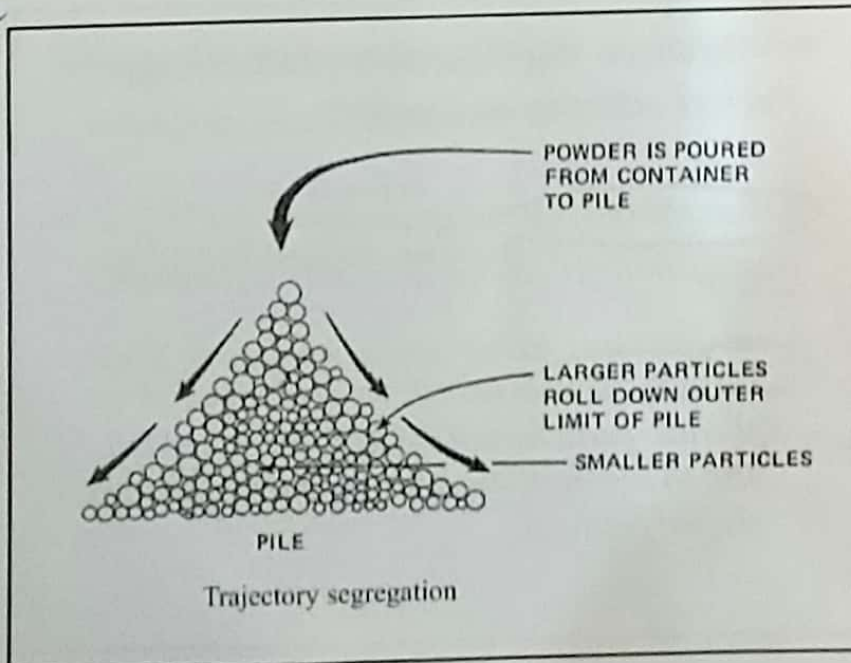
والكبرية بس كبر ال Density و هو ال Container مع ال Drum

vibration  
تنزل ال small  
لحقت مع طبقة ال large

ال Fine ال compact

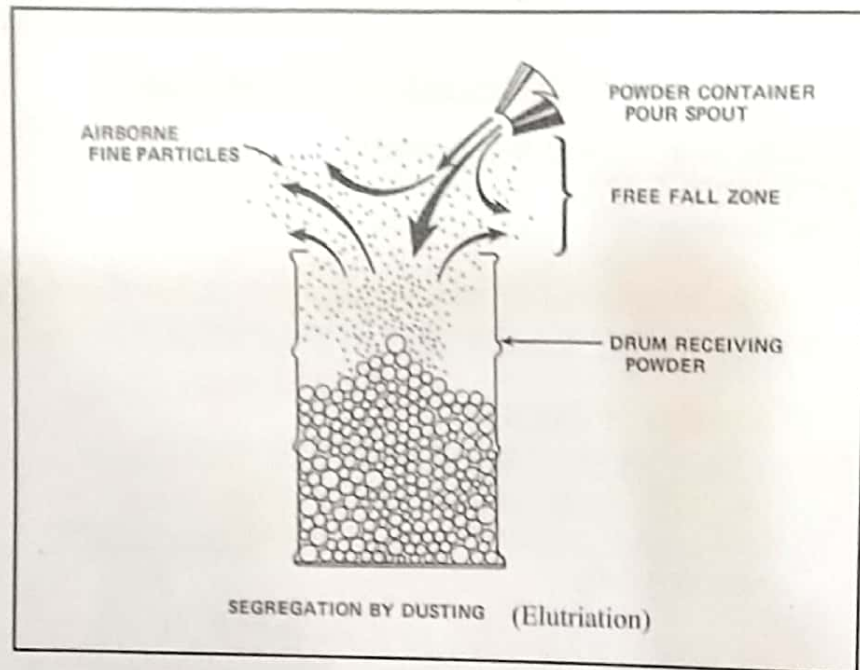
Fluidization

Dusting  
ال طبقة ال Fine



PS  
اختلاف  
بعض ال انواع  
Segregation

صوت ال  
ال ال  
Container  
large  
kinetic energy  
ال ال  
fine



## Powder segregation (demixing)

*Factors affecting segregation:*

### 2. Particle density

نشط D active  
غير نشط D inactive  
نشط لا active  
غير نشط لا inactive

Segregation occurs due to density differences.

### 3. Particle shape

Spherical particles are easier to be mixed but also to segregate than irregular or needle shaped particles.

مختلج 11  
لكن قابلية  
الخلط

### Approaches to solve the problem of segregation

- Selection of particular size fractions to achieve drug and excipients of the same particle size range.
- Milling of the components so that their size becomes small and same.
- Controlled crystallization during production of drug or excipient to give particles of particular size or shape.
- Selection of excipients which have similar density to the drug.

→ Choose narrow size range

### Approaches to solve the problem of segregation

- Granulation of powder mixture.
- Reduce the extent to which the powder mass is subjected to vibration or movement after mixing.
- Using equipments where several processes can be carried out without transferring the mix.
- Production of an ordered mix.

→ Done in all the steps

active  
powder  
wholes

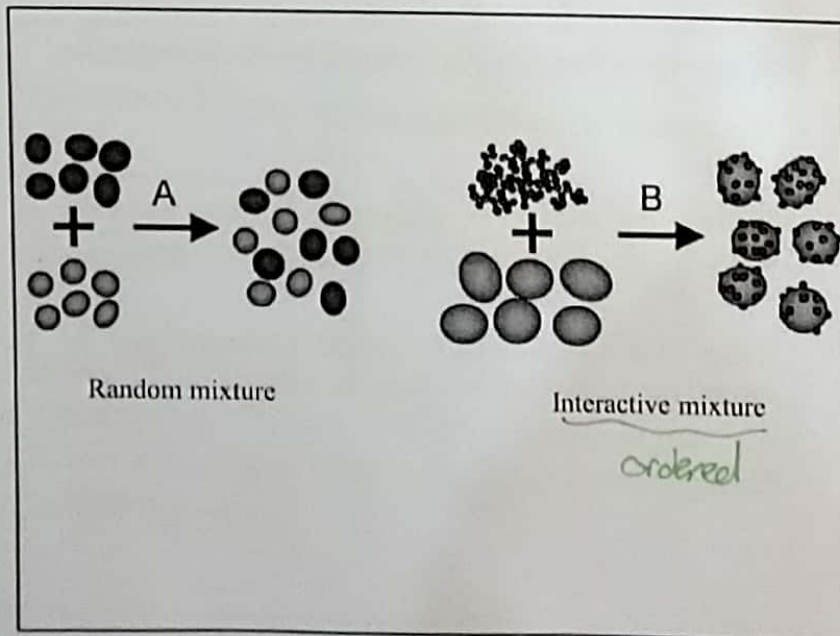
## Ordered mixing ← مرتباً

- It is termed also adhesive or interactive mixing.
- In this case, very small particles may become adsorbed onto the active sites of large particles.
- This minimizes the segregation between small (adsorbed) particles and large (carrier) particles.
- Ordered mixing is most likely to occur when the adsorbed particles are very small so that the adsorption force is higher than the gravitational force trying to separate the components.

جاذبية  
gravity  
small ١١  
Adsorption  
large ١٢

Adhesiveness

الشد الأضعف ————— لا يكون في قابلية نقل  
Adsorption



n  
je

## Application of ordered mixing

- **Dry antibiotic formulations** (fine antibiotic powder is blended with and adsorbed onto the surface of large sucrose or sorbitol particles.
- **Dry powder inhaler formulations**
- **Direct compression formulations**
- **Formulation of potent drugs**

syrup, gelatin  
binder  
compressed

بقرين ال Tab  
بطريقين اما  
Granules  
او Powder  
مباشرة

## Segregation in ordered mixes

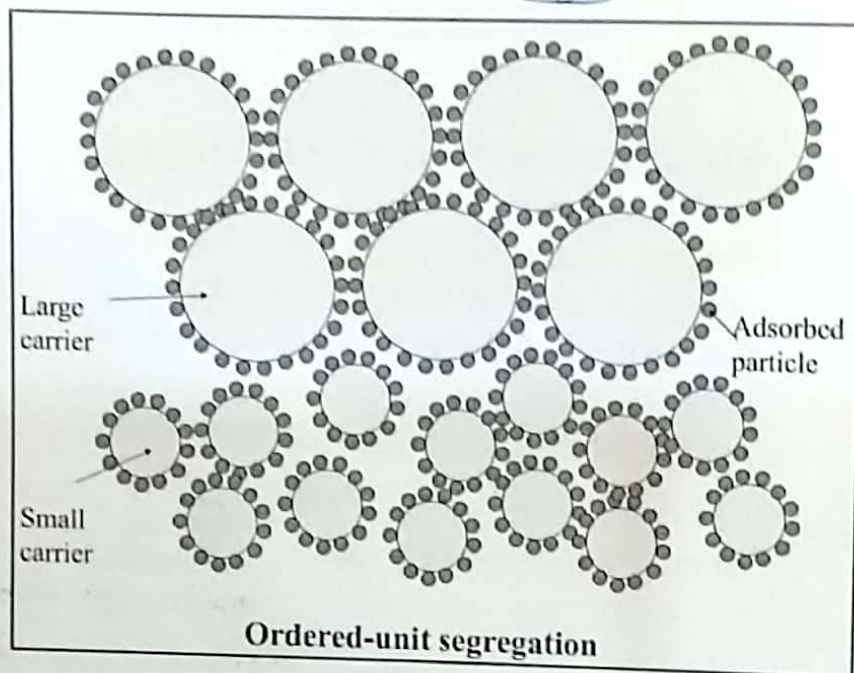
### ordered unit segregation

- **The carrier particles vary in size.**
- In this case segregation occurs within the carrier particles according to size. The small particles have higher specific surface area than the large and so higher content of adsorbed material.

Carrier او  
ما يكون دقيق  
ال size يكون  
في فيه  
small

للادوية الضعيفة  
مثل بنادول او  
Antacid  
فهي تلتصق بالسطح  
Extender او  
دواء على قدرته  
Adhesiveness

active 11 negative adsorption in small 11

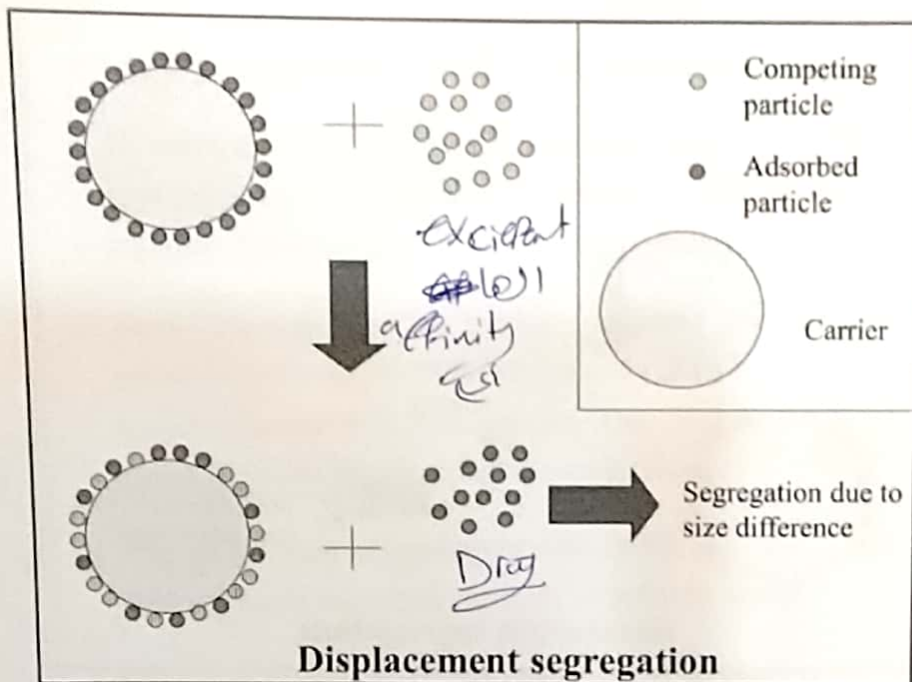


## Segregation in ordered mixes

### displacement segregation

- There is competition for the active sites on the carrier.
- This occurs when a component is added to an ordered mixture that competes with the adsorbed material for the site on the carrier and displaces it

active 11 negative  
(Competition)

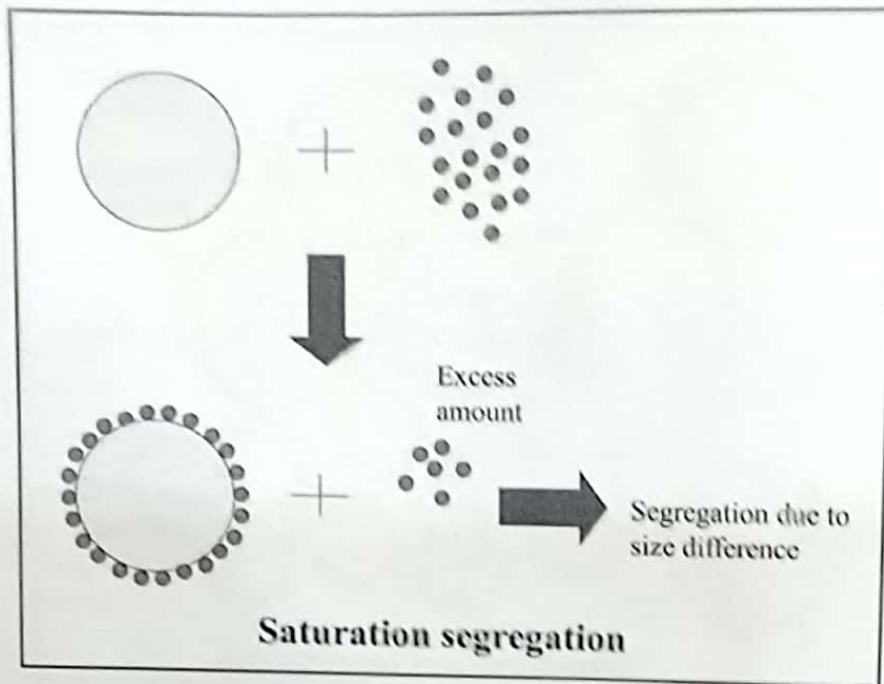


## Segregation in ordered mixes

### Saturation segregation نقص في حبات الناقل

- There are insufficient carrier particles
- If the added amount of small-sized material is higher than the capacity of the carrier particles then the excess amount will be free (not adsorbed) and it segregate due to size difference.

active layer  
في حبات الناقل  
التي carrier



### 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 overflowing 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

لو عناء كمية  
active  
خفيفة وبنسبة  
other excipients  
خفيف بأخذ الكمية

المعينة صوما  
تكاملاً متجانساً  
تألف - التان

والتجانس mixing

So  
نظام

نعم يكون وناقد ما يكافئها  
مع ال- excipients وهكذا يعني ذلك  
في أنه ينخفض ال- active

بنسبة صوب  
ال- capacity

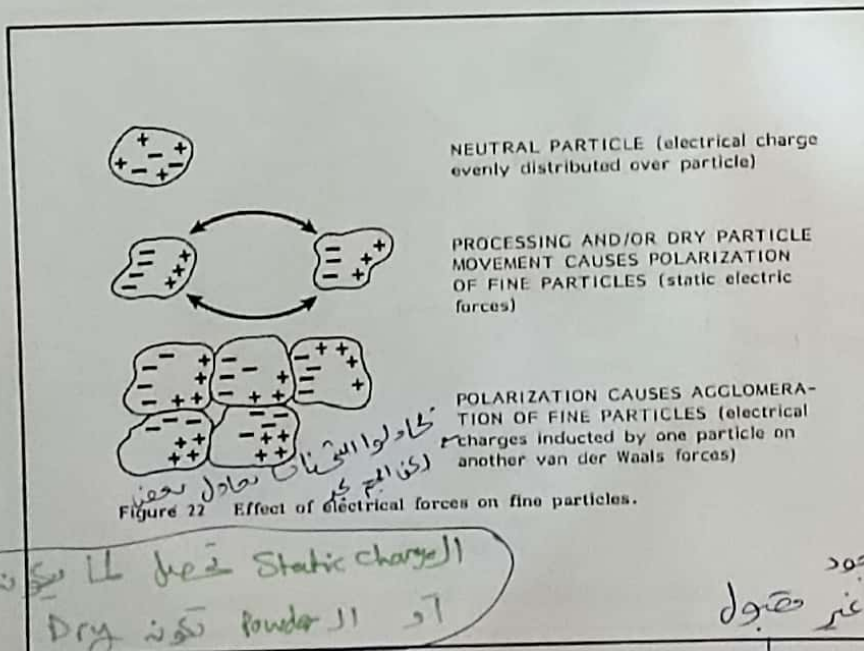
Diff  
بالنسبة  
Combination - الركل

## 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.
- Static charges may be generated during mixing that result in reduction in diffusive mixing. This is enhanced by low humidity in atmosphere. The mixer should be suitably earthed to dissipate the static charge.
- Vibrations may cause segregation in normal mixes and dislodging of adsorbed particles in ordered mixes.

humidity زيف  
static charge  
charge

segregation  
ordered



P لا حمل ان  
neutral  
millling  
generation of  
static charge  
بسبب الـ  
P  
Polymerization  
repulsion  
وكان  
نقطة P  
لات آي  
لـ E

Static charge  
Dry powder

# Powder mixing equipment

## 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.

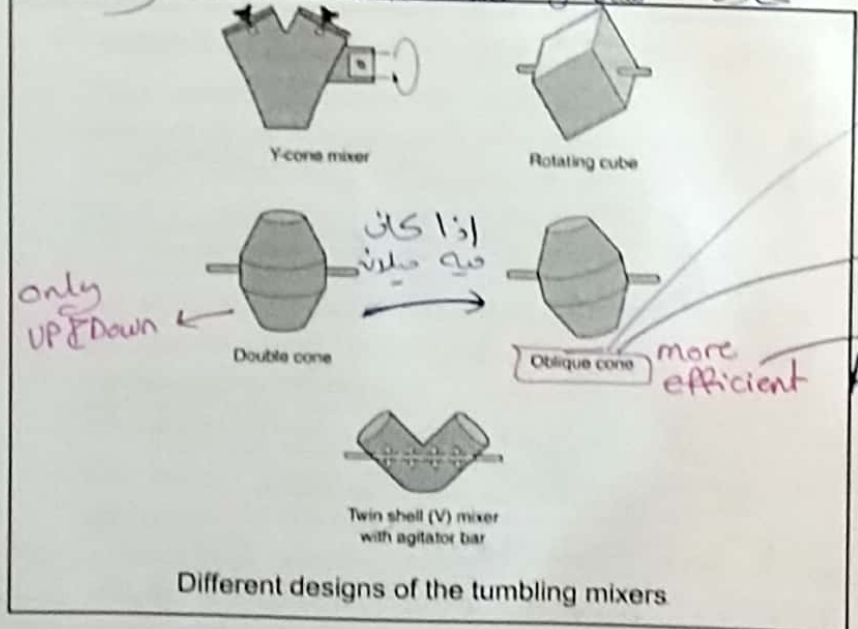
Should deagglomerated first

Simple movement  
Free flowing  
Spherical des

Granules 2 mixing

الاول :: active ...  
التالي :: ...

granulation ...  
simple mixer ...



mixer granulator

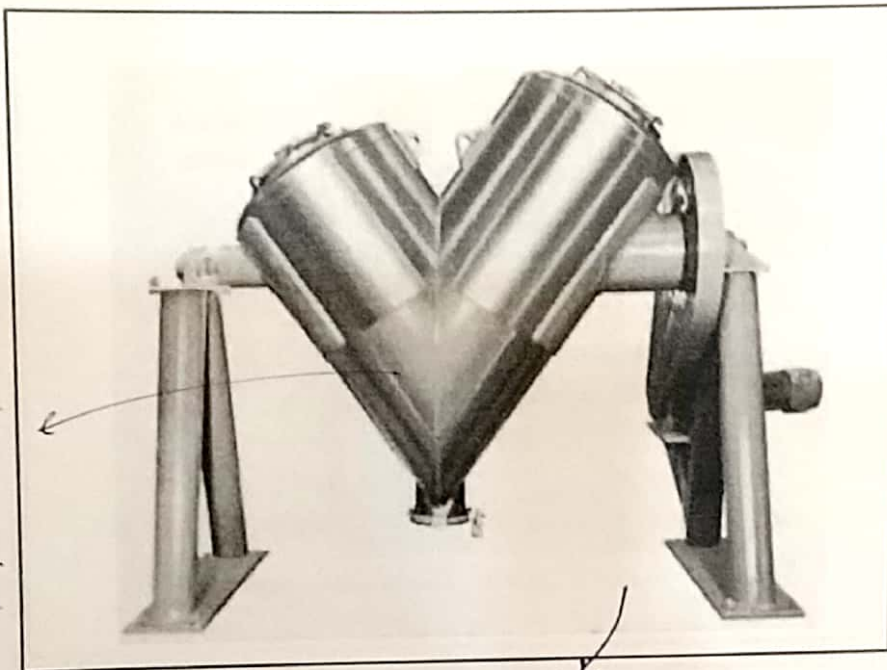
Called oblique or Slant

more efficient

due to high randomization

Different designs of the tumbling mixers

شتوی موزن  
 accessories  
 mixing  
 more effectively  
 agitator  
 velocity  
 orientation



randomization

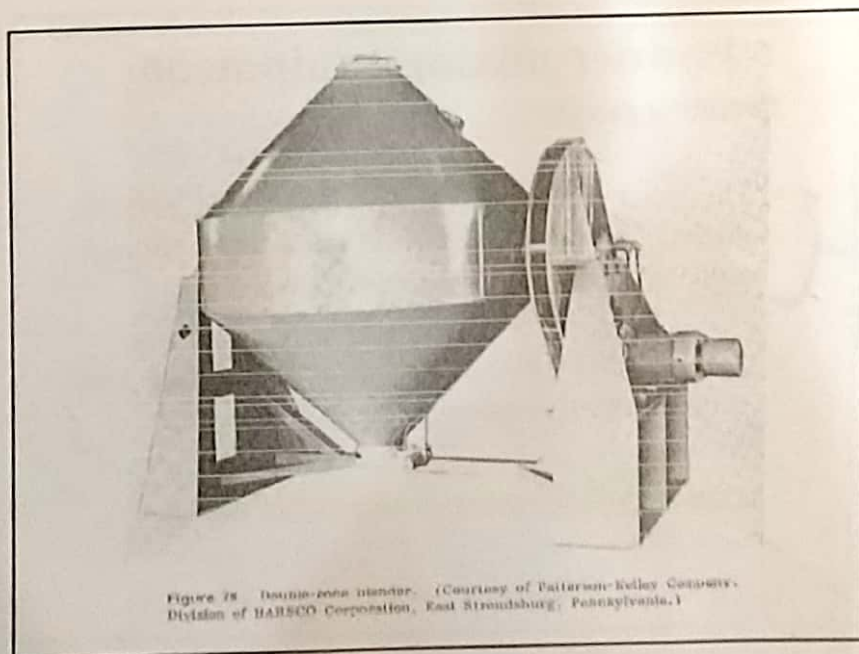


Figure 28 Double-zone blender. (Courtesy of Patterson-Kelley Company, Division of HARSco Corporation, East Stroudsburg, Pennsylvania.)

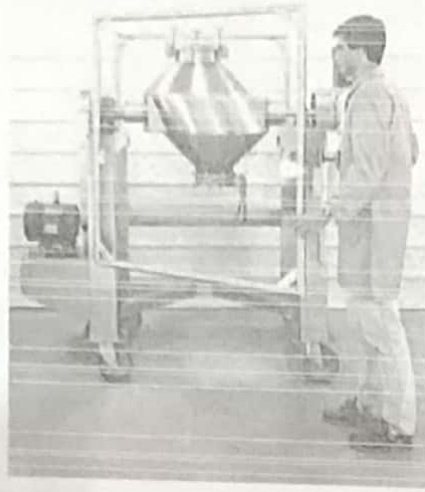


Figure 29 Slant double-cone mixer. (Courtesy Genco, Middlesex, New Jersey.)

## 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.

Shear  
Bulk movement

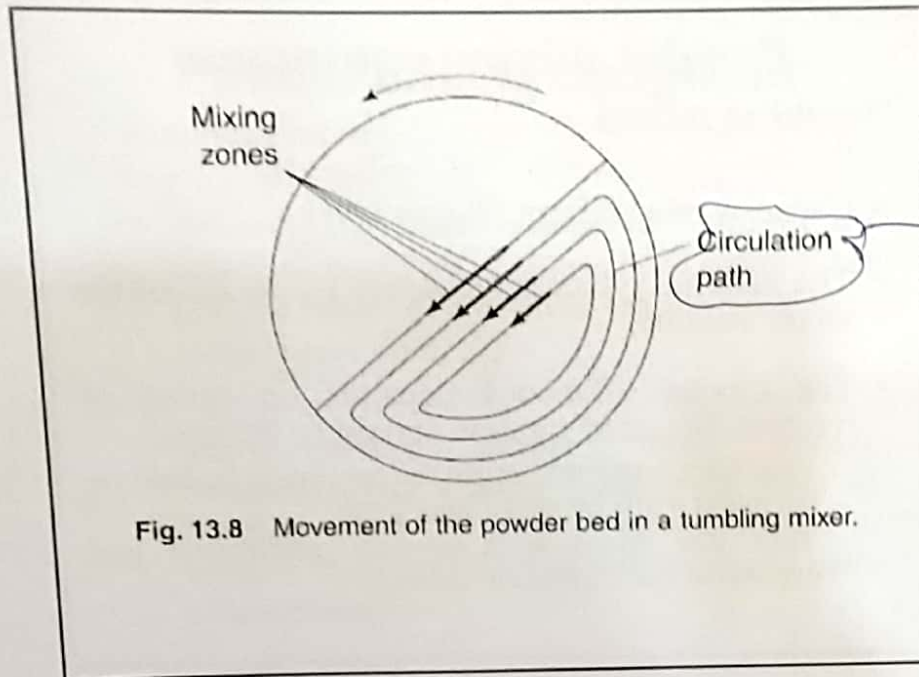
هنا انشطار  
لا نظار  
Diff  
تحتاج للمزج  
Shear لا

عندما  
segregation

Diff

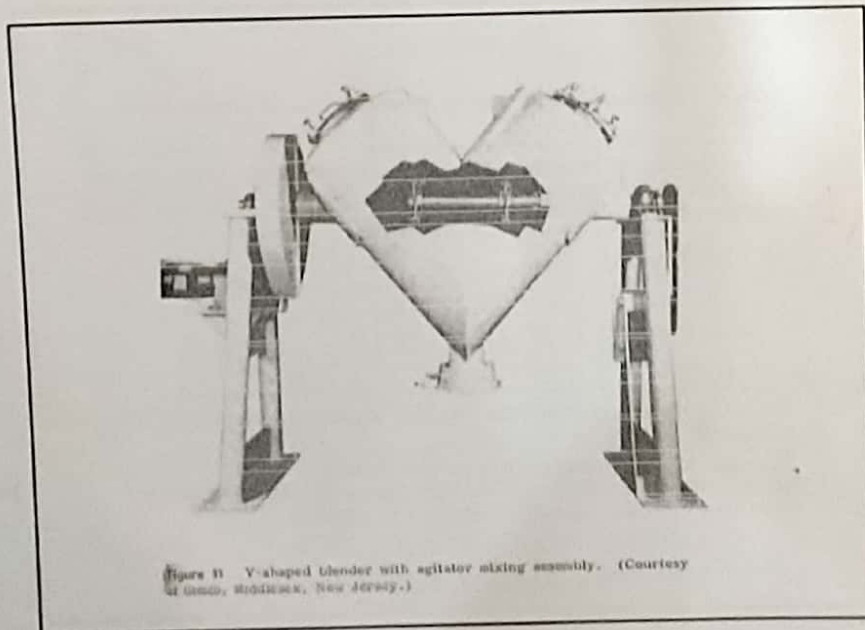
به خنبل  
فهم مع  
تغير سرعة  
Orientation  
الهم  
فشار  
Randomization

Slow movement  $\rightarrow$  not good mixing  
high speed (centrifugation)  $\rightarrow$  not good mixing



Optimum  
mixing

as a result  
Randomization



## 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.

Table 9 Effect of Powder Fill on Blending Time of Double-Cone Blenders<sup>a</sup>

Volume percent of blender filled with <u>powder charge</u> <sup>Powder Peak</sup>	Approximate blend time (minutes) in <u>production-size blenders</u>
50	10
65	14
70	18
75	24
80 <sup>b</sup>	40 <sup>b</sup>

<sup>a</sup>Blending done in double-cone blenders and times measured to obtain comparable blends.

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.

## Powder mixing equipment

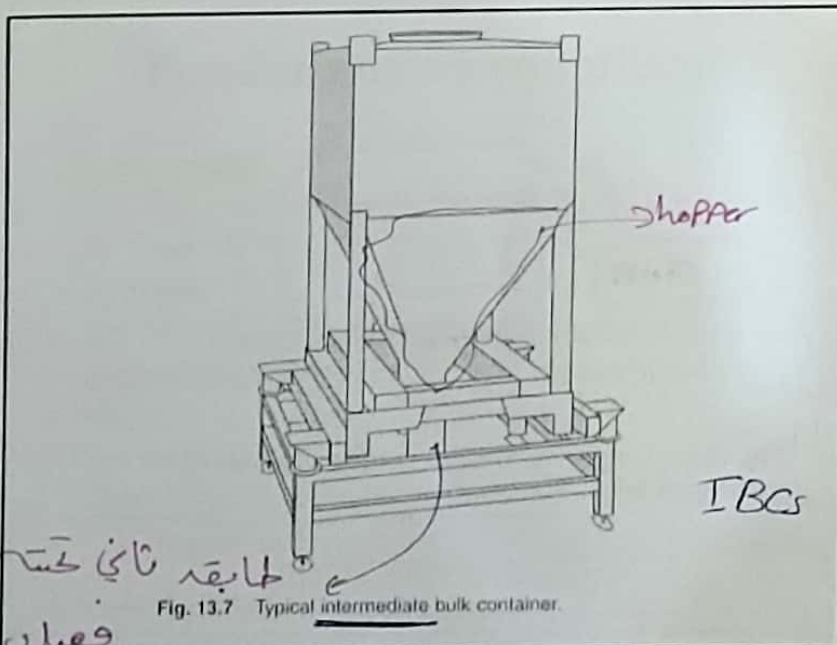
### Tumbling mixers

- 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.

Powder tab  
 machine  
 hopper  
 mixer  
 Tableting machine

(K) هي اعلى  
 جارية

(K) هو في  
 rotation  
 Randomization  
 axis



Tableting machine  
 mixing on time  
 Tab

## Powder mixing equipment

### High speed mixer granulators (high shear mixer granulator)

- 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.

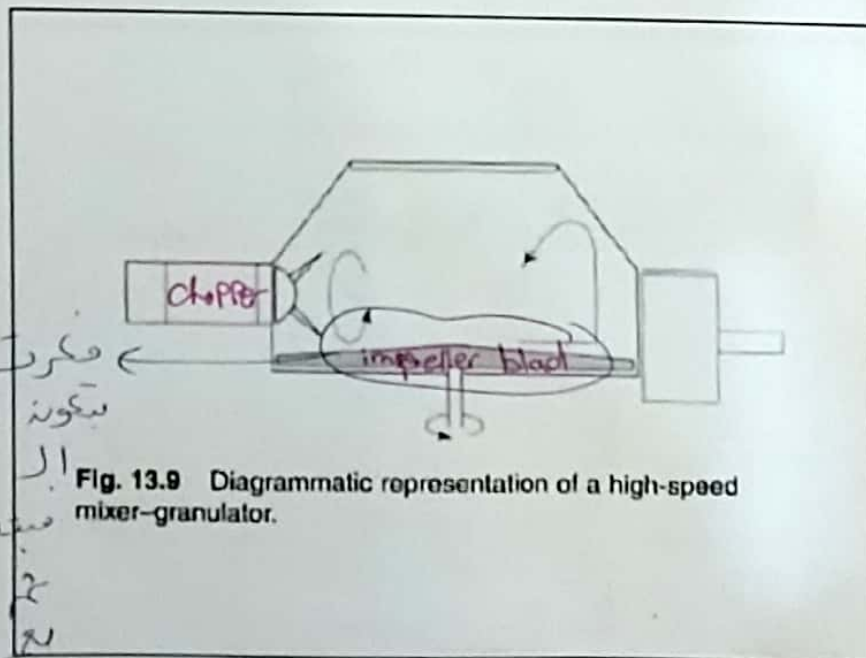


Fig. 13.9 Diagrammatic representation of a high-speed mixer-granulator.

High speed wet mass granulator  
لحمية و  
لحمية و  
لحمية و  
granules

إذا بلشت نوجد  
Binders

فكرتها زي المروحة  
بتكون القاعدة ونخل  
ال Powder عليها

مبتحرك لزمن معين  
(mixing)

ننخل 11 chopper  
نقطع فيه

granules

مرلنا (granulation)

## Powder mixing equipment

### Agitator mixers

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

## 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.

لكن Tumblers  
تساعد في  
segregation

الزوايا لا يمكن الوصول لها  
فلا يتم خلطها  
الجهاز  
مغسول

shear غير كافٍ للتفكيك Deaggregation

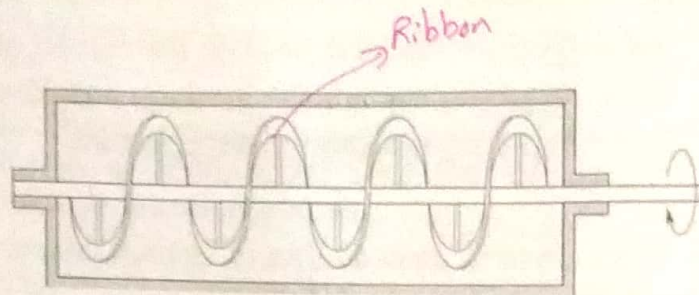


Fig. 12.10 Ribbon agitator powder mixer.

بعض الحركات  
Shear و Convection  
لكن هو - حركته

## Powder mixing equipment

### 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)

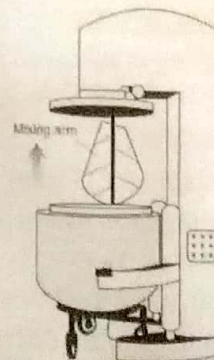
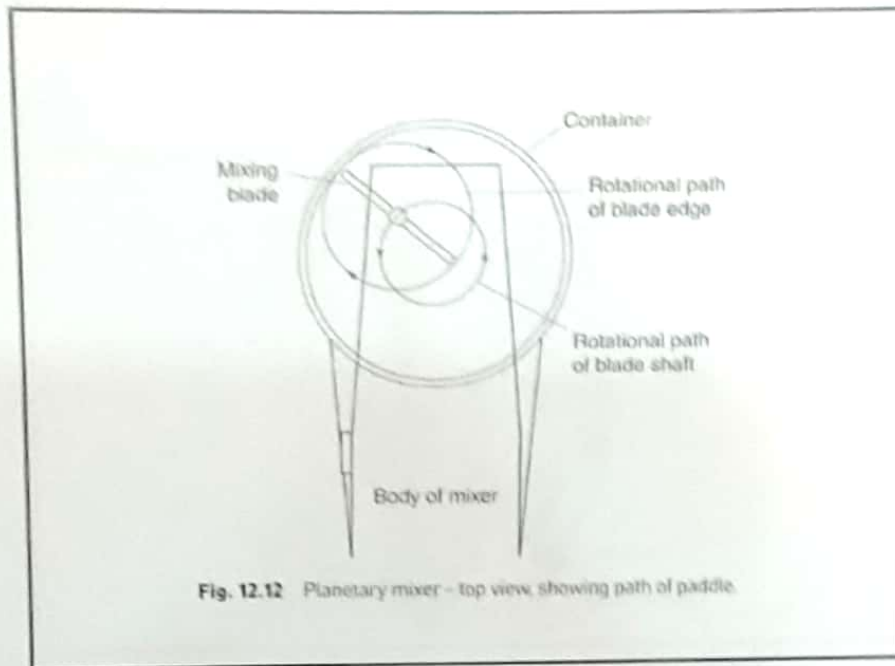


Fig. 12.11 Planetary mixer for powders and semi-solids.

بعض الحركات  
وتنقل الحركات  
الماكنة



Convection then cascading then shearing then diff

## 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

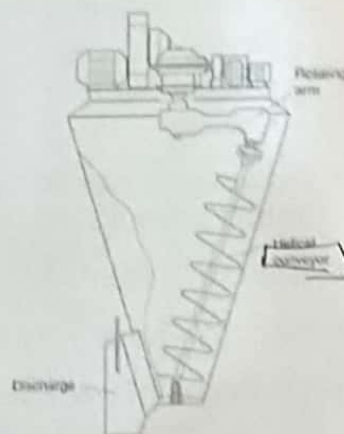
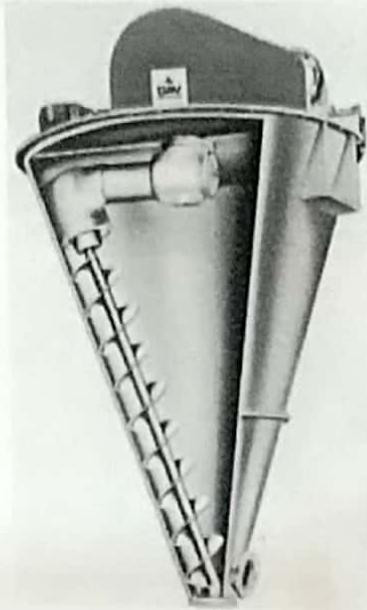


Fig. 12.13 Nautamixer (courtesy of Nautamixer Ltd).

Convey  
↓

Nautamixer



## Powder mixing equipment

### Fluidized bed mixers *All in one*

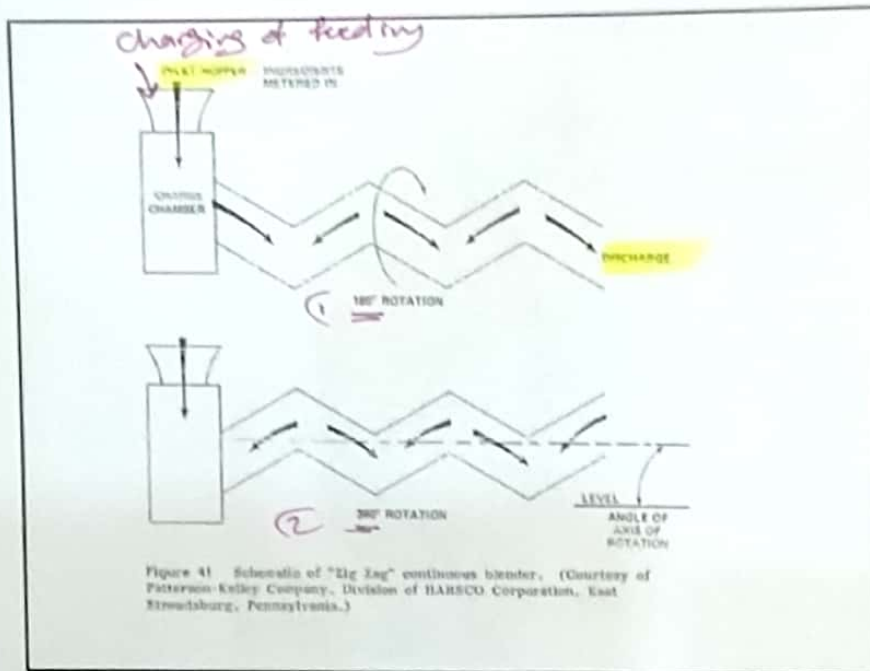
- The fluidized bed equipment is used mainly in:
  - Drying
  - Granulation
  - Coating
- However it can be used for mixing of powders before granulation.
- Blown air fluidized and mixes the powder.
- Fluidization is very efficient mixing process.
- Diffusion of particles occur.

*powder 11 jin  
choke one  
feeding  
compressed air*

*space  
بکری  
بکری*

Charging (or feeding) Powder bed 1) 2) 3) 4) 5) 6) 7) 8) 9) 10) 11) 12) 13) 14) 15) 16) 17) 18) 19) 20) 21) 22) 23) 24) 25) 26) 27) 28) 29) 30) 31) 32) 33) 34) 35) 36) 37) 38) 39) 40) 41) 42) 43) 44) 45) 46) 47) 48) 49) 50) 51) 52) 53) 54) 55) 56) 57) 58) 59) 60) 61) 62) 63) 64) 65) 66) 67) 68) 69) 70) 71) 72) 73) 74) 75) 76) 77) 78) 79) 80) 81) 82) 83) 84) 85) 86) 87) 88) 89) 90) 91) 92) 93) 94) 95) 96) 97) 98) 99) 100) 101) 102) 103) 104) 105) 106) 107) 108) 109) 110) 111) 112) 113) 114) 115) 116) 117) 118) 119) 120) 121) 122) 123) 124) 125) 126) 127) 128) 129) 130) 131) 132) 133) 134) 135) 136) 137) 138) 139) 140) 141) 142) 143) 144) 145) 146) 147) 148) 149) 150) 151) 152) 153) 154) 155) 156) 157) 158) 159) 160) 161) 162) 163) 164) 165) 166) 167) 168) 169) 170) 171) 172) 173) 174) 175) 176) 177) 178) 179) 180) 181) 182) 183) 184) 185) 186) 187) 188) 189) 190) 191) 192) 193) 194) 195) 196) 197) 198) 199) 200) 201) 202) 203) 204) 205) 206) 207) 208) 209) 210) 211) 212) 213) 214) 215) 216) 217) 218) 219) 220) 221) 222) 223) 224) 225) 226) 227) 228) 229) 230) 231) 232) 233) 234) 235) 236) 237) 238) 239) 240) 241) 242) 243) 244) 245) 246) 247) 248) 249) 250) 251) 252) 253) 254) 255) 256) 257) 258) 259) 260) 261) 262) 263) 264) 265) 266) 267) 268) 269) 270) 271) 272) 273) 274) 275) 276) 277) 278) 279) 280) 281) 282) 283) 284) 285) 286) 287) 288) 289) 290) 291) 292) 293) 294) 295) 296) 297) 298) 299) 300) 301) 302) 303) 304) 305) 306) 307) 308) 309) 310) 311) 312) 313) 314) 315) 316) 317) 318) 319) 320) 321) 322) 323) 324) 325) 326) 327) 328) 329) 330) 331) 332) 333) 334) 335) 336) 337) 338) 339) 340) 341) 342) 343) 344) 345) 346) 347) 348) 349) 350) 351) 352) 353) 354) 355) 356) 357) 358) 359) 360) 361) 362) 363) 364) 365) 366) 367) 368) 369) 370) 371) 372) 373) 374) 375) 376) 377) 378) 379) 380) 381) 382) 383) 384) 385) 386) 387) 388) 389) 390) 391) 392) 393) 394) 395) 396) 397) 398) 399) 400) 401) 402) 403) 404) 405) 406) 407) 408) 409) 410) 411) 412) 413) 414) 415) 416) 417) 418) 419) 420) 421) 422) 423) 424) 425) 426) 427) 428) 429) 430) 431) 432) 433) 434) 435) 436) 437) 438) 439) 440) 441) 442) 443) 444) 445) 446) 447) 448) 449) 450) 451) 452) 453) 454) 455) 456) 457) 458) 459) 460) 461) 462) 463) 464) 465) 466) 467) 468) 469) 470) 471) 472) 473) 474) 475) 476) 477) 478) 479) 480) 481) 482) 483) 484) 485) 486) 487) 488) 489) 490) 491) 492) 493) 494) 495) 496) 497) 498) 499) 500) 501) 502) 503) 504) 505) 506) 507) 508) 509) 510) 511) 512) 513) 514) 515) 516) 517) 518) 519) 520) 521) 522) 523) 524) 525) 526) 527) 528) 529) 530) 531) 532) 533) 534) 535) 536) 537) 538) 539) 540) 541) 542) 543) 544) 545) 546) 547) 548) 549) 550) 551) 552) 553) 554) 555) 556) 557) 558) 559) 560) 561) 562) 563) 564) 565) 566) 567) 568) 569) 570) 571) 572) 573) 574) 575) 576) 577) 578) 579) 580) 581) 582) 583) 584) 585) 586) 587) 588) 589) 590) 591) 592) 593) 594) 595) 596) 597) 598) 599) 600) 601) 602) 603) 604) 605) 606) 607) 608) 609) 610) 611) 612) 613) 614) 615) 616) 617) 618) 619) 620) 621) 622) 623) 624) 625) 626) 627) 628) 629) 630) 631) 632) 633) 634) 635) 636) 637) 638) 639) 640) 641) 642) 643) 644) 645) 646) 647) 648) 649) 650) 651) 652) 653) 654) 655) 656) 657) 658) 659) 660) 661) 662) 663) 664) 665) 666) 667) 668) 669) 670) 671) 672) 673) 674) 675) 676) 677) 678) 679) 680) 681) 682) 683) 684) 685) 686) 687) 688) 689) 690) 691) 692) 693) 694) 695) 696) 697) 698) 699) 700) 701) 702) 703) 704) 705) 706) 707) 708) 709) 710) 711) 712) 713) 714) 715) 716) 717) 718) 719) 720) 721) 722) 723) 724) 725) 726) 727) 728) 729) 730) 731) 732) 733) 734) 735) 736) 737) 738) 739) 740) 741) 742) 743) 744) 745) 746) 747) 748) 749) 750) 751) 752) 753) 754) 755) 756) 757) 758) 759) 760) 761) 762) 763) 764) 765) 766) 767) 768) 769) 770) 771) 772) 773) 774) 775) 776) 777) 778) 779) 780) 781) 782) 783) 784) 785) 786) 787) 788) 789) 790) 791) 792) 793) 794) 795) 796) 797) 798) 799) 800) 801) 802) 803) 804) 805) 806) 807) 808) 809) 810) 811) 812) 813) 814) 815) 816) 817) 818) 819) 820) 821) 822) 823) 824) 825) 826) 827) 828) 829) 830) 831) 832) 833) 834) 835) 836) 837) 838) 839

Figure 92. The "Big Zag" continuous blower. (Courtesy of Torrington Rotary Company, Division of HARSCO Corporation, East Stroudsburg, Pennsylvania.)



ما يلي في  
①

lubricant Tableting machine flow freely  
يجب قبل الكبس اذنا انخل لا lubricant او mixing  
لغاية تجزئة الطبقات layers و P is hydrophobic

### 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.

مثلاً تجربة المختبر  
تستعمل في جهاز  
خفيف فحسباً تلك  
5min مختبرات  
على سرعة 100  
صا الى خلية  
المواد - وفقاً لذلك  
مربطاً بها ب 10  
و رصاصه او  
cubic mixer  
الكبير فحسباً  
السرعة نصف  
از Speed  
يتم mix  
من mirror

Bulk  
من

layers  
يعني عال الى لا  
ستأخذ

عالباً او mixing  
افضل الى نخل  
Scaling up  
البب ان  
لغاية على  
Shearing force  
الكل

اضافة لا lubricant آخر

## 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.

نتائج انفا  
بشكل  
result

Attrition

امكانية تغيير ال method  
الاختصاص والجر و كذا مثل  
Phenomenon

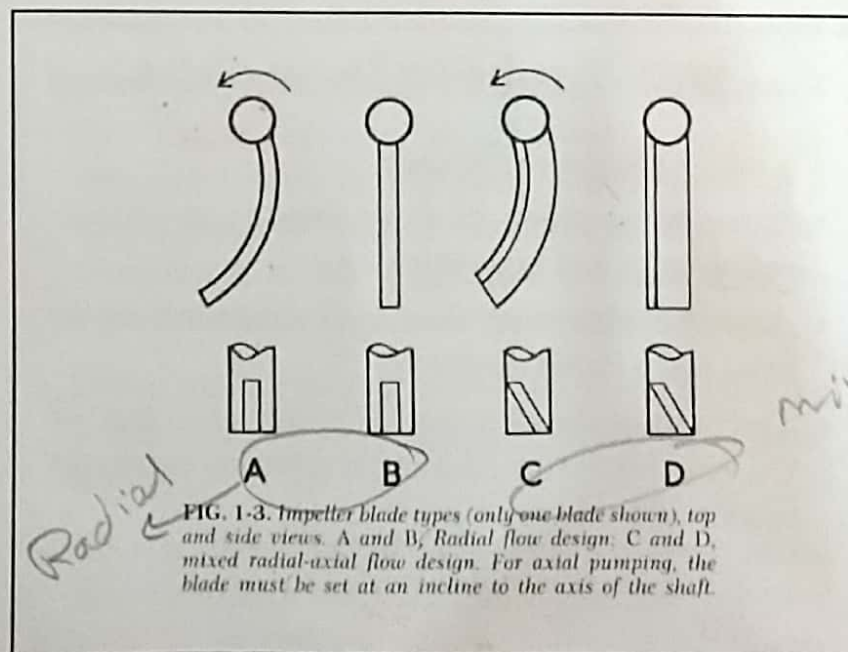
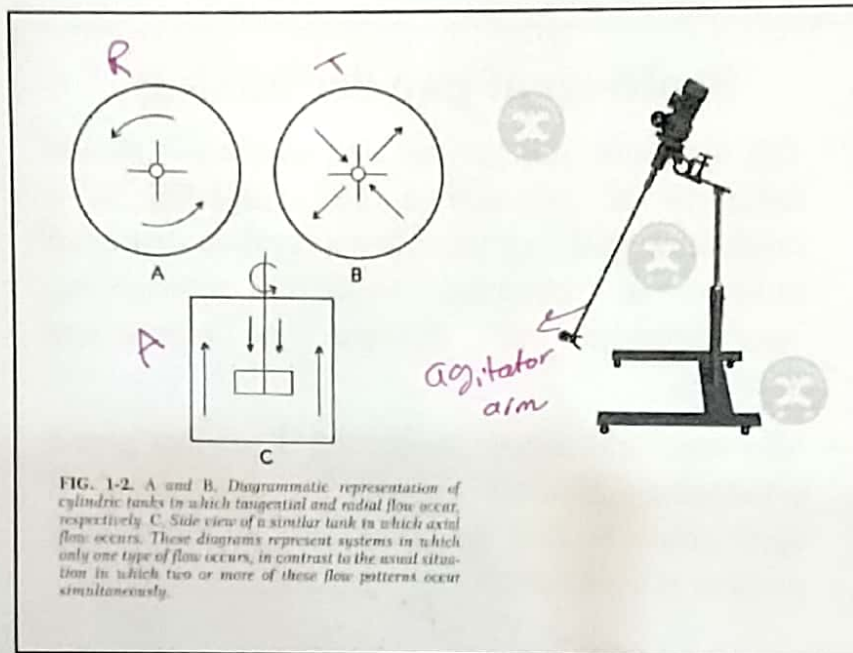
## Types of mixers used for liquids and suspensions

### 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.

اتجاه تدفق  
ال Blade  
الزاوية

Propeller نسبة ال  
المزج في Tank



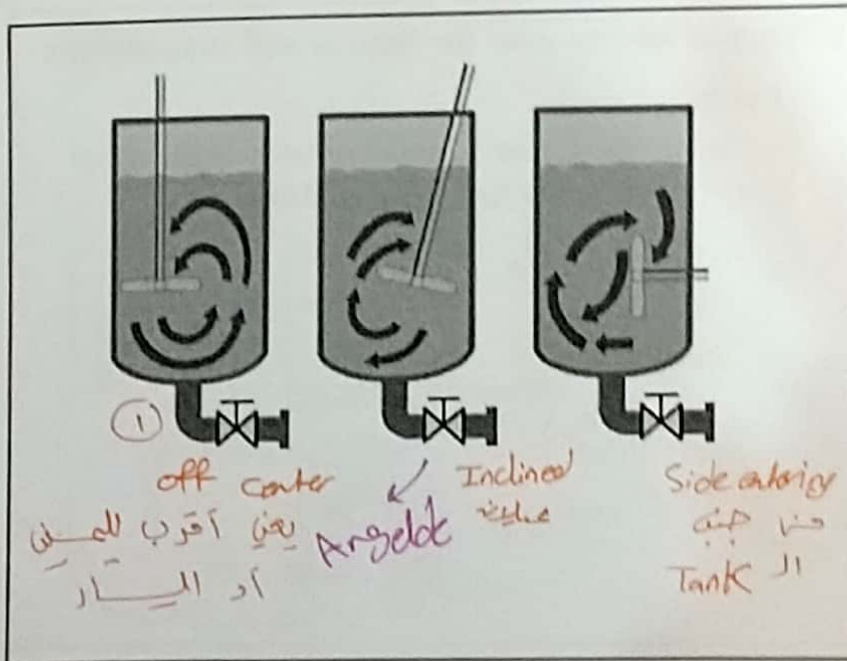
## Types of mixers used for liquids and suspensions

### Propeller (Impeller) mixers

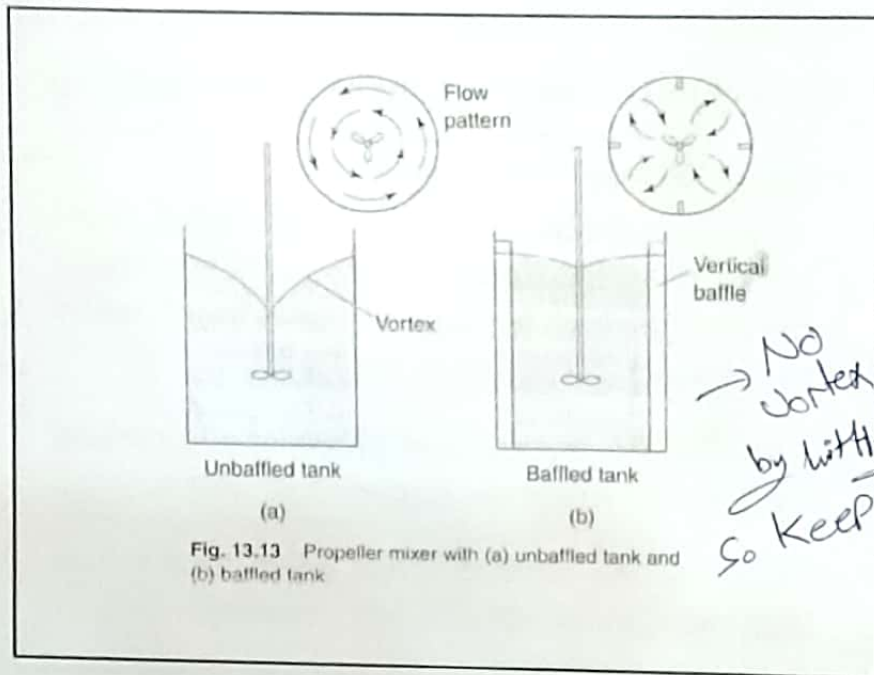
- A vortex forms when the centrifugal force imparted to the liquid by the propeller blades causes it to back up around the sides of vessel and create a depression at the shaft.
- An off-center mounting of propeller and vertical baffles discourage the formation of vortex.
- Propellers are more efficient when they run at high speed in liquids with low viscosity.

سرعة عالية  
بسبب القوة  
المرتكزة  
Back up around  
the side of vessel  
Depression

نسالة LL  
يكون لا  
low viscosity  
High speed  
عنا ناقتورة زي  
الدوامه ويطرقت  
بطلع نبرا  
حتى نفتح  
حالتها



Uses: To prevent Vortexing



## Types of mixers used for liquids and suspensions

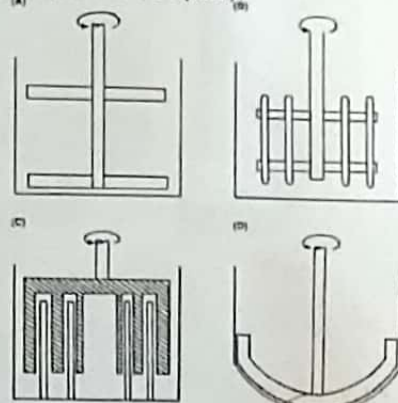
### Paddle mixers

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

تاسا بجان فوئيد  
(Tank باغصه كي ال Paddle)  
شيش

### Paddle mixers

اشكال ال Paddle



Tank

stirring device

بينهم فافه (gap) اللى فيه clearance  
فيس gap لسا  
شكون shearings

## Types of mixers used for liquids and suspensions

### Turbine mixers

emulsion

- 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.

مع صر 1:2  
Diffusor ring  
من خلال  
Perforation  
فيمكن  
شعير 2 شعيرة  
بأن تكون  
1:1 Shear  
emulsion

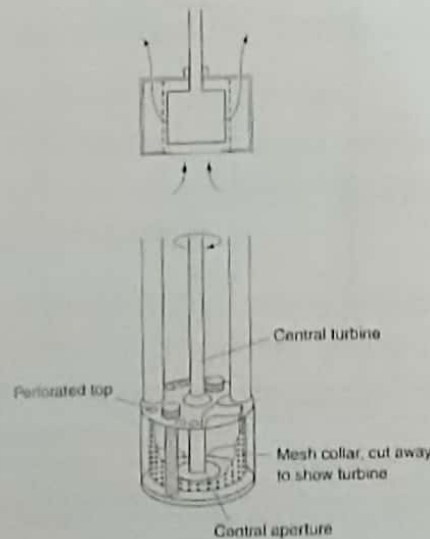


Fig. 13.14 Turbine mixer.

## 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, nonfoaming, unreactive with the gas employed and reasonably nonvolatile.

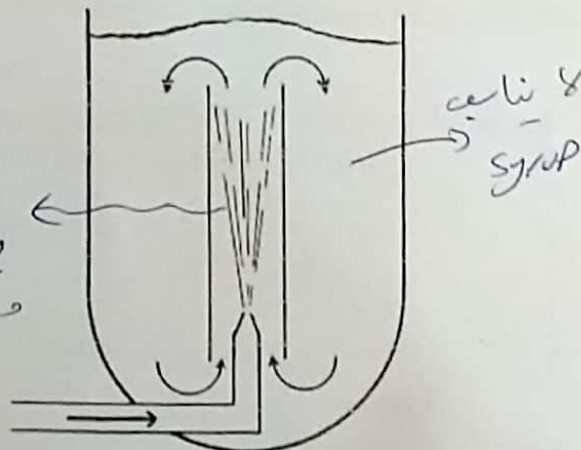
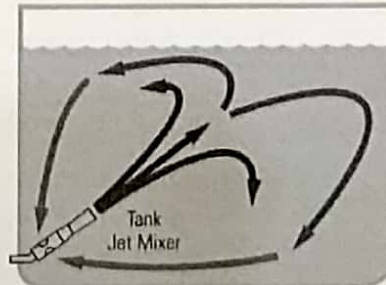


FIG. 1-4. Vertical tank with centrally located air jet and draft tube. Bubbles confined within the draft tube rise, inducing an upward fluid flow in the tube. This flow tends to circulate fluid in the tank, bringing it into the turbulent region in the vicinity of the jet.

## 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.



نحوه کار و نحوه  
عملکرد فشار بالا

So good mixing

## 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.

via Pipe (tube) or tank

continuous feeding & continuous discharge

to give randomization

نرخ ورود



Ointment, Paste

## Mixing of semisolids

- Semisolids, unlike liquids and powders, do not flow easily.

agitator stirring

levure, etc

- The suitable mixers must have rotating elements with narrow clearances between them selves and the mixing vessel to avoid dead spots

## Types of mixers for semisolids

- 1) Planetary mixers → ملا ينزل ال arm يماخذ مكانه منيح
- 2) Sigma blade mixer → شفرة
- 3) Vessels (tanks) with counter-rotating mixing bars → حركة معاكسة

- 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.

في البداية 2 نقطة  
تخلو mixing

Paste أو Ointment  
بإستعمال فامد  
من الأحصنة  
التلوي

لكن لازم نتجنب

فقد الجسيمات

بواسطة فامد

Ointment

مزيل جسيمات يكون حبيباته دقيقة  
فتمنع عن حبيبات Roller mill  
فتمنع

أسفل  
أسفل  
Planet

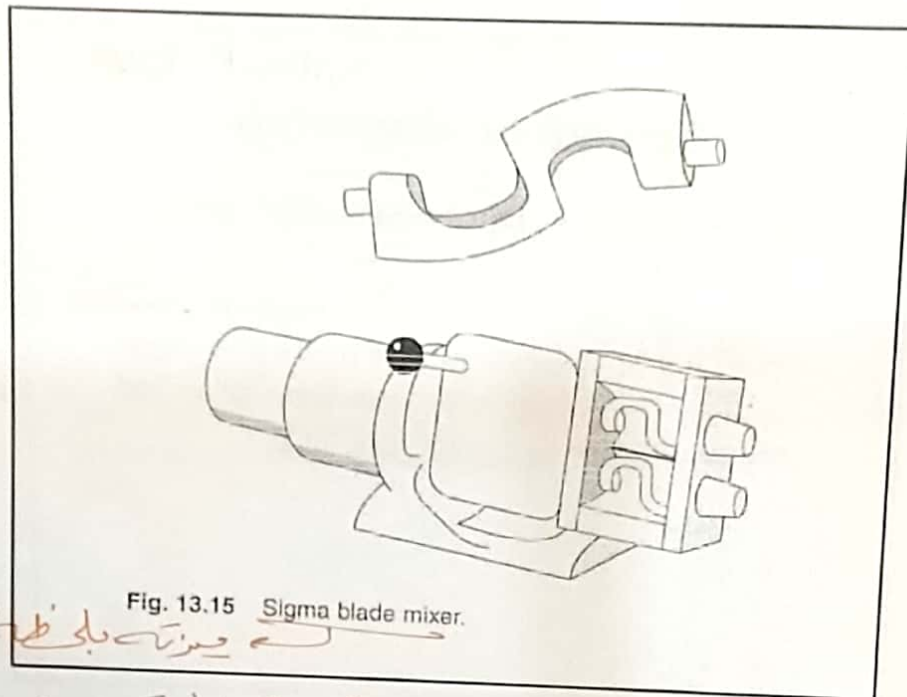


Fig. 13.15 Sigma blade mixer.

میکسنگ بلڈز  
 مے ہکونوا قریب مے بعض فعالی  
 Particle - Grittiness  
 Semi Solid Particulate

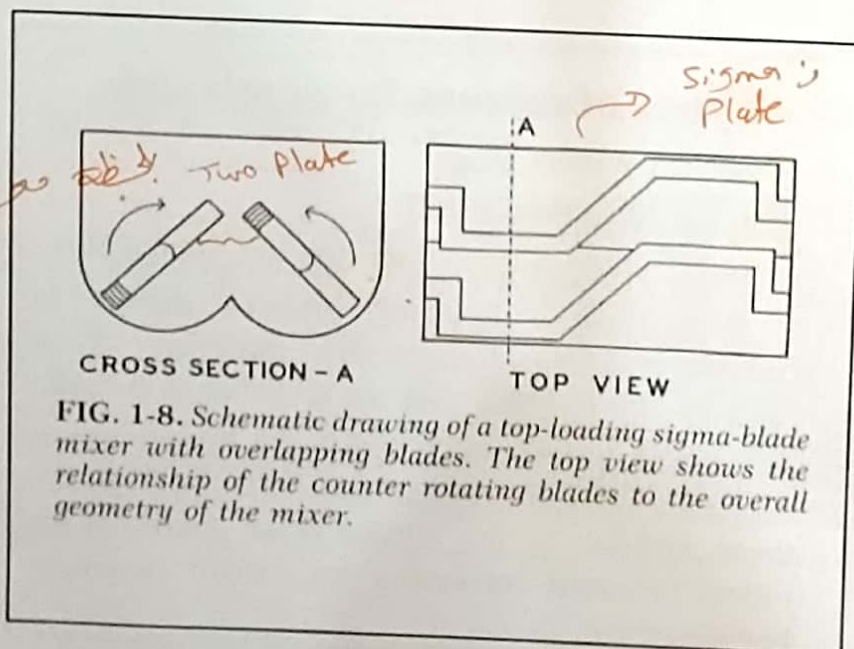
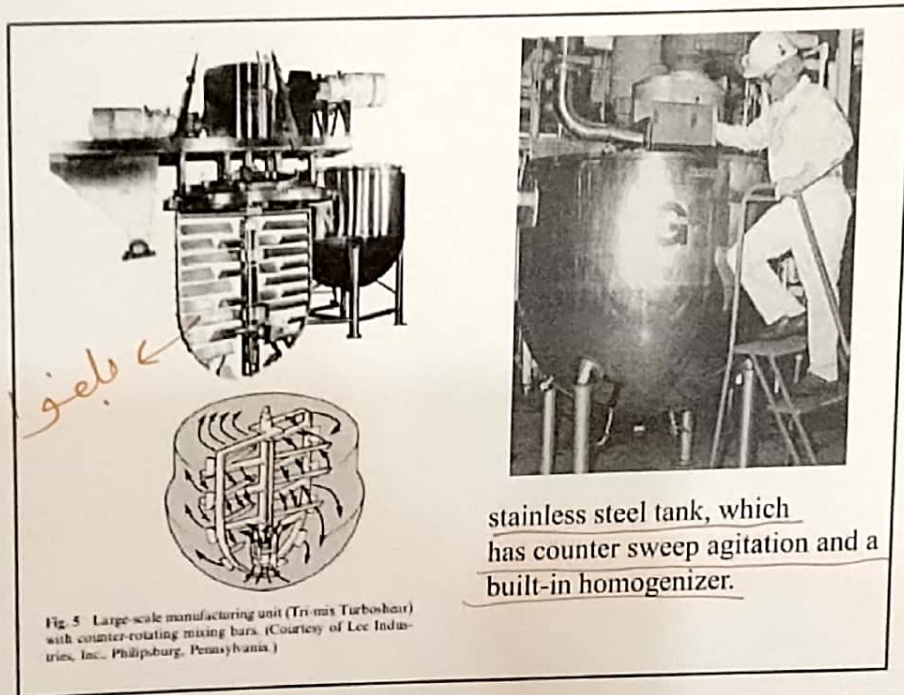


FIG. 1-8. Schematic drawing of a top-loading sigma-blade mixer with overlapping blades. The top view shows the relationship of the counter rotating blades to the overall geometry of the mixer.

بلوف عكر بجان



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

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

بلاطة صينية بجر Ch حبة فلبس  
Shear عاكس