EXPERIMENT (1)
MIXING OF POWDERS

INTRODUCTION:

Aim of Mixing:

The main aim of powder mixing in pharmaceutical practice is to achieve dose uniformity within the solid dosage form (tablets, capsules & powders), particularly so important in case of very potent drugs like Digoxin.

Factors affecting mixing of solids:

- Parameter related to the particles : like particle size, particle shape, size distribution, particle density, Cohesive forces and Hygroscopic properties
- Mixer type and properties: Movement type of mixer, Presence of Blades The addition of baffles or rotating bars will also cause convective mixing, for example the V-mixer with agitator bar.
- Speed of mixing (Agitation Speed): Too high a rotation speed will cause the material to be held on the mixer walls by centrifugal force, and too low a speed will generate insufficient bed expansion and little shear mixing.
- Filling Volume
- Segregation tendency of individual components (based on density difference).

Mechanisms of Mixing:

1. Diffusion: It is redistribution of particles by random movement of particles relative to each other.
2. Convection: Movement of a group of adjacent particles from one place to another within the mixture.
3. Shear: It is the change in configuration of ingredients through the formation of slip planes in the mixture (Layer of powder flows over another layer) or (Sliding of particles in planes over each other).

بالبداية احنا ليش بنهتم أو ليش بنعمل mixing of powder؟؟؟

عشان نحقق شي اسمه **uniformity of dosage form**، يعني تكون الجرعة متجانسة، فمثلا انا كمصنع وصلني كمية من المادة الفعالة و كمية من المواد المضافة الها، هسا مسؤوليتي بعد خلطهم انه كل كبسولة أو حبة دوا تكون تحتوي ع نفس الكمية من الـ **active ingredient**و نفس الكمية من الـ additives،يعني في أدوية ما فيها مزح فشوية زيادة بالجرعة ممكن تدخل المريض بحالة **toxicity**مثل **Digoxin**

العوامل المؤثرة على عملية mixing of powder؟؟؟

1)Parameter related to the particles : like particle size, particle shape, size distribution, particle density, Cohesive forces and Hygroscopic properties

2)Mixer type and properties: Movement type of mixer, Presence of Blades The addition of baffles or rotating bars will also cause convective mixing, for example the V-mixer with agitator bar

3) Speed of mixing (Agitation Speed): Too high a rotation speed will cause the material to be held on the mixer walls by centrifugal force, and too low a speed will generate insufficient bed expansion and little shear mixing.

هسا سرعة الخلط لو كانت كثير عالية رح تلزق بالجهاز و ما رح يصير خلط ممتاز و لو سرعة بطيئة كمان رح ما تنخلط منيح فعشان هيك لازم تكون السرعة مدروسة

4)Filling Volume

لو في كثير powderما رح يسمح بالحركة و برضه ما رح يصير خلط كافي و منيح

5)Segregation tendency of individual components (based on density difference)

يعني حسب لهم قابلية ينفصلوا عن بعض؟؟

Mechanism of mixing

Diffusion: It is redistribution of particles by random movement of particles relative to each other

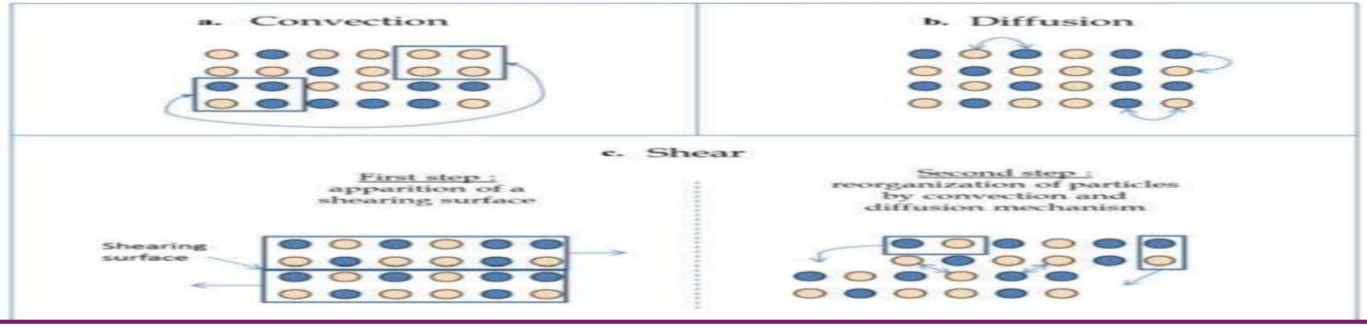
بتكون حركة الـ particle عبارة عن حركة relative to each other

Convection: Movement of a group of adjacent particles from one place to another within the mixture

حركة الـ particle على شكل blocks

Shear: It is the change in configuration of ingredients through the formation of slip planes in the mixture (Layer of powder flows over another layer) or (Sliding of particles in planes over each other).

بتكون الـ powder مقسمة الطبقات على شكل Sliding و بعدين عن طريق
هي الحركة بتسحل الطبقات فوق و بتتبدل



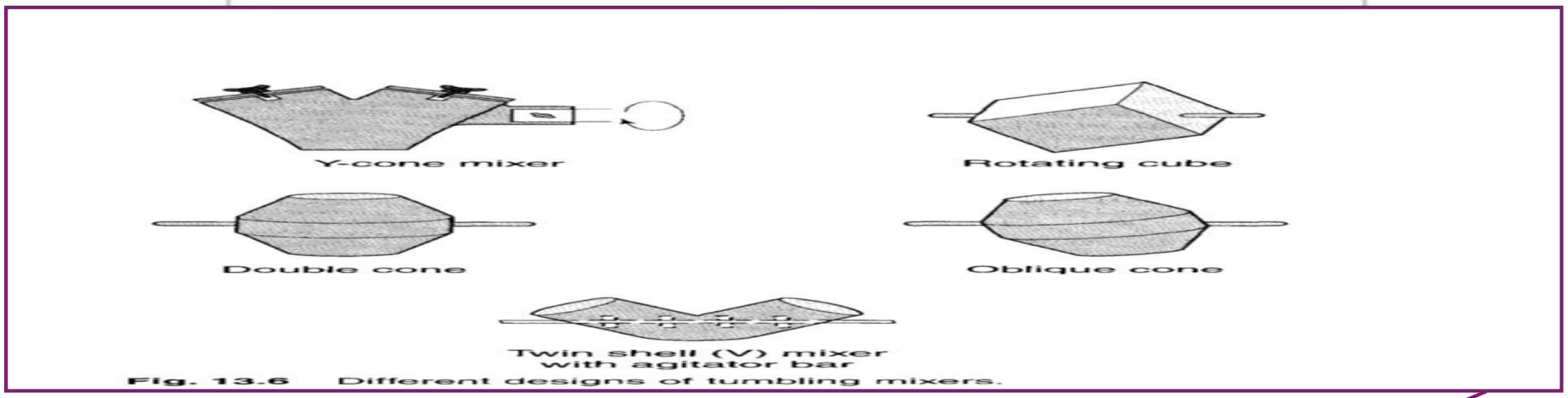


Fig. 13.6 Different designs of tumbling mixers.

Tumbling mixers are rotating vessels of variable shapes. The container is designed in a way to avoid symmetry (symmetry gives poor mixing) ?!

7

homogeneous mixtures عشان يعطونا **Asymmetrical** كلهم

In this Experiment Cube mixer or V-mixer will be used:-

- **Cube mixer**:
  - motor drive mixer
  - The housing in the Cube Mixer is manufactured from glass.
  - Equipped with Baffles but not Blades
  - Tumbling movement, in which ingredients are tilted by the rising side of the drum until they exceed their normal angle of repose, hence they will fall over their selves.
  - Cube mixer provides the three mechanisms of mixing, but in different ratios ... shear is the predominant.
  - Cube mixer is problematic due to the presence of corners, why?

- **V- mixer:**
  - motor drive mixer
  - The housing in the V- Mixer is manufactured from stainless steal
  - The function is based on a special 3D blending effect in the pant-leg region, which is generated through a combination of: dividing, cascading and an intermeshing mixing mechanism.
  - During blending, materials tumble periodically towards the apex and the legs, while they move along the horizontal rotation at the same time.

OBJECTIVE:

1. To study the efficiency of "Revolvo-Cube Mixer or V- Mixer" in preparation of 5% wlw mixture of Sodium Salicylate in Lactose (Particle Size < 1mm), when operated at 25 rpm.
2. To study the Effect of time on the homogeneity of 5% wlw mixture of Sodium Salicylate in Lactose (Particle Size < 1mm) prepared using Revolvo-Cube Mixer V- Mixer operated at 25 rpm.
3. To estimate the "Optimal Mixing Time" for 5% wlw mixture of Sodium Salicylate inLactose (Particle Size < 1mm) prepared using Revolvo-Cube Mixer or V- Mixer operated at25 rpm.

Cube mixer

الـ housingتاعه مصنوع من الزجاج و نوع معدته هي baffles مش ال blades،نوع الحركة فيه هي tumbling movementيعني الـ cubeبطلع لفوق بسحب الـ powderلتحت لحد ما توصل ارتفاع معين، وعشان نوع الحركة هي رح نلاحظ انه اكثر نوع من الـ mechanism of movmwntمسؤول هو الـ Shearأكبر نسبة و ال diffusion and convectionاقل نسبة حركة بتبين بالجهاز

Blades:

هي عيدان تسمح بحركة الـ powderبطريقة أفضل

المشكلة بالجهاز هي الزوايا اللي فيه ممكن يتجمع فيها الـ powderفعشان لا يتجمع و نخسر جزء منهم لازم نضيف الكمية الأكبر أول ثم الكمية القليلة

The main objective in our experiment today

To estimate the “Optimal Mixing Time” for 5% wlw mixture of Sodium Salicylate in Lactose (Particle Size < 1mm) prepared using Revolvo-Cube Mixer or V- Mixer operated at 25 rpm.

بدنا نشوف تأثير الوقت على الـ **homogenicity**

* بتجربة اليوم بدنا نحضر 500 gm من 5% w/w Na-Salicylate in lactose

5 gm ⟶ 100 gm

X ⟶ 500 gm

⇒ X = 25 gm Salicylate

ونكمل باقي وزنة الـ 500 gm بـ lactose

500 − 25 = 475 gm lactose

Procedure steps

sieve lactose then sieve Na salicylate then weight 25 gm Na-Salicylate and 475 gm of lactose

Place the powders in the mixing chamber

Take 5 samples (200 mg = 0.200 gm each) at 5, 10, 20 & 30 minutes, (such that 5 sample at each time)

200 mg sample dissolved in up to 100 ml distilled water

UV spectrophotometer

Absorbance

By using calibration curve

Concentration in mg% w/v was calculated (x is conc. Of Na Salicylate in 100 ml)

Calculate conc. in mg% w/w

* ملاحظات مهمة :.

① بنعمل Sieving أول للمواد قبل التوزين لسببين :.

① عشانه نكسر ال Aggregation حيث أن ال lactose هو عبارة عن Sticky Powder.

② لو وزّنا قبل ال Sieving ممكن Particle تعلقه فوقه وهيك رح تقل الوزنة وتكون غير دقيقة.

③ ال Blank المستخدم هو :- Lactose in distilled water (Dw)

④ تم استخدام Na-Salicylate in Dw لتحضير Calibration curve

λ is used in UV spectrophotometer

is = 254 nm

Calibration Curve equation ⟹ $y = 0.0193x + 0.0071$

mixing time	sample No.	Abs	Conc mg% w/v	Conc mg%. w/w	mean	Standard deviatio	variance	Coefficient of variance
5 min	1	0.233	11.70	5				

① Conc. mg% (w/v)

$$\underset{\text{Abs}}{\underline{y}} = 0.0193x + 0.0071 \rightarrow \frac{(0.233 - 0.0071)}{0.0193} = x \rightarrow \bar{x} = 11.70 \text{ mg\% w/v}$$

② Conc. mg%. (w/w)

Conc. mg%. (w/v) / Amount of sample in the final volume $= (11.70 / 200 \text{ mg}) \times 100 = \frac{5}{5}$

So Conc. mg%. w/w = ~~5.85~~ 5 mg% w/w

← لكن هون نتبه بنقسم ع الوزنة اللي بـ 100ml !!

مثلاً ← 500 mg in 200 ml & calculate Conc mg%. w/w

if you know conc. w/v = 10.90 mg% w/v

الحل ∴

500 gm → 200 ml
X → 100 ml

→ X = 250 mg

هي الوزنة اللي بنعتبرها نذوبها ب 100 ml

$$\text{Conc. mg\%. (w/w)} = \frac{\text{Conc. mg\%. (w/v)}}{250} * 100$$

$$= \frac{10.90}{250} * 100 = 4.36\ \%\ w/w$$

③ mean ~~± Tolerance~~ + ④ SD] حسبهم الدكتورة عن إكسل ال Function المستخدمة كدكتور بعينيو العملي

⑤ Variance = (standard deviation)^2 = $(SD)^2$

⑥ Coefficient of Variance (C.V) = $\frac{SD}{mean} * 100\%$

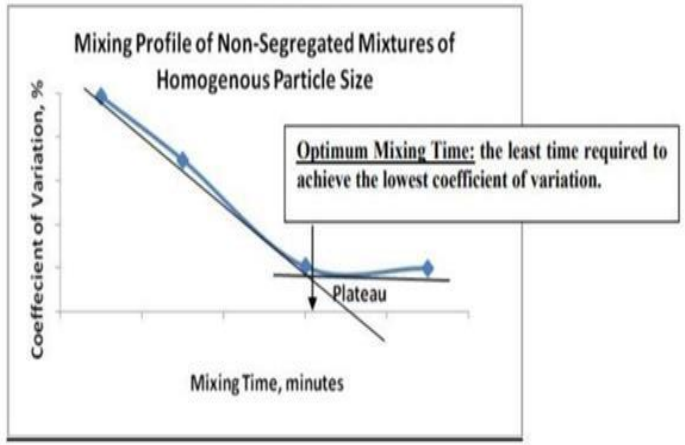
---

① ↑ C.V : ↓ homogenicity

② Dilution Factor = $\frac{\text{Final volume}}{\text{Intial volume}}$

Examples on Mixing Profiles:

Case 1:



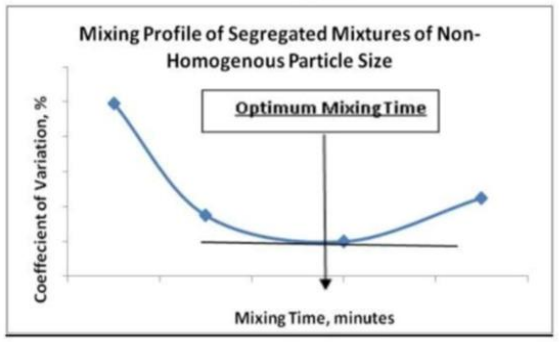
هون كلما زاد الـ **mixing time** كلما قل الـ **coeffecient of variation**، يعني عيناتي بتصير قراءتها قريبة لبعض عبين لنوصل **optimum mixing time** وهون بثبت الـ **C.V.** فشو ما عملنا **Mixing** ما رح يتغير و هاي تسمى **paltu**

المماسين بيعطوا **optimum mixing time**

Optimum mixing time :

هو أقل وقت بنقدر نحصل أقل **C. V.** أو لنحضر **homogeneous mixture**

Case 2:



هون ما بضل **platu** ولكن برجع يزيد الـ **C. V.** حيث برجع يفصل