

بلقمة ميللايد 45 لآخر الك بين تركت سلايد 61  
درجته لاول سلايد

# Granulation

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1

## Granulation

Granulation is the process in which the primary powder particles are made to adhere to form larger, multiparticulate entities called granules.

ما يكون granule منها نوع من Adh و Coh بعض التعلق به Adh به طريقه او نسبية اضافة binder

Granules are either used in their own right as a dosage form or as an intermediate product in the production of tablets or capsules.

يكونا ايسر dosage form  
او استعماله في GP ولا tablets



2

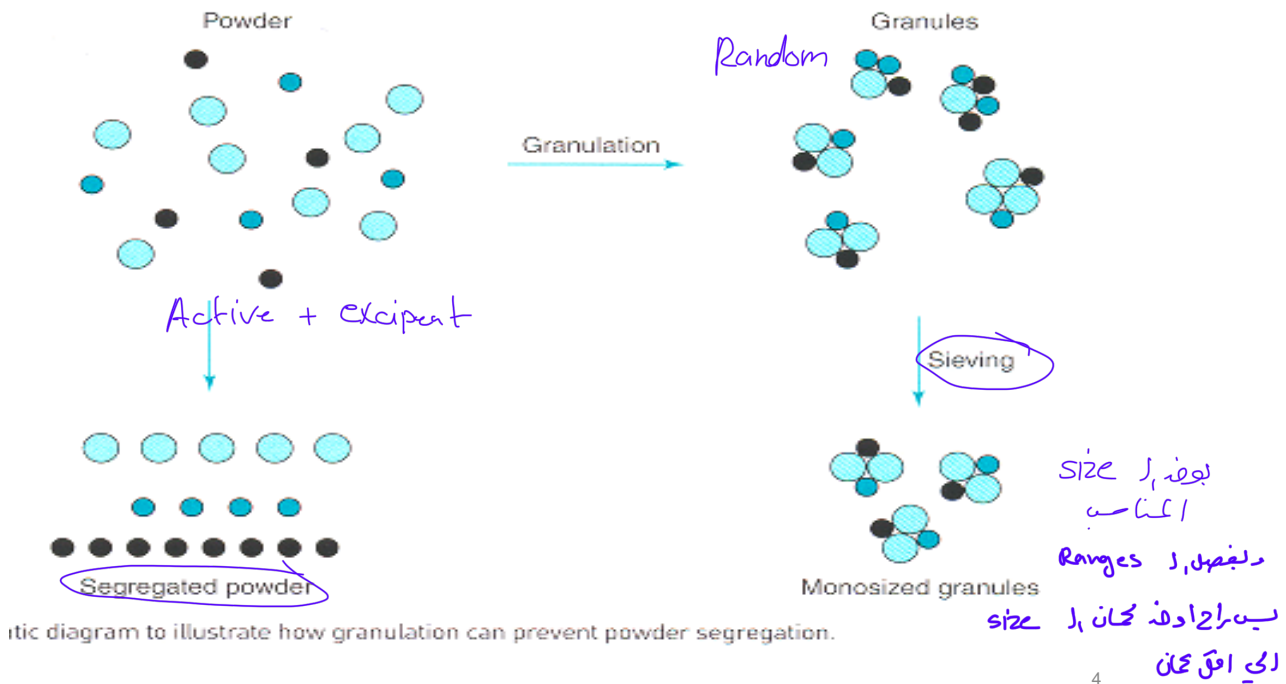
# Granulation

## Reasons for granulation

The main aims of granulation are:

1. To prevent segregation and thereby improve homogeneity. حلل segregation
2. Improve the flowability of mix to ensure complete and uniform filling of tablet dies, capsules etc. This lead to less weight and dose variations. تجارب بار حبات دسختن در tablet / لازم ابعادها بهارویه تا یکون في حوا
  - Granules produced from cohesive materials will be larger and more isodiametric Diameter نسبت در isodiametric
3. Improve the compactability of powder. Isodiametric + كبره
  - Some materials have bad flow and compression properties so that they can not be formed by direct compression and therefore need granulation. بند + powder : granules (binding solid)

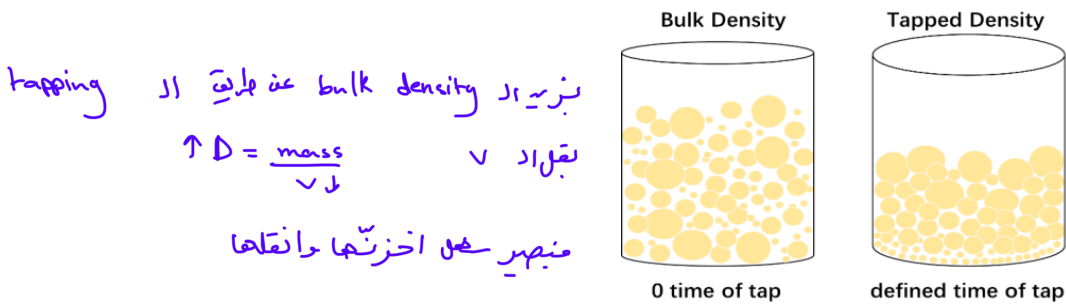
طريقة ثانية ترتبط فيها powder بدون binder ← binder powder، ان، powder، تكون coh  
Direct Compression : طريقة بخرایة بسله فقط mixing + compression اما اذا الما صوب يتكس بعله لخرایة (granulation) زي حليه الاطبال عنان صيد غاليه  
\* من در در process ورم lubricant  
طريقة اول tableting التحلية  
3  
granulation (wet - dry) : زمن المدة - اكثر steps - مواد اكثر - اقل - اغلب الادوية



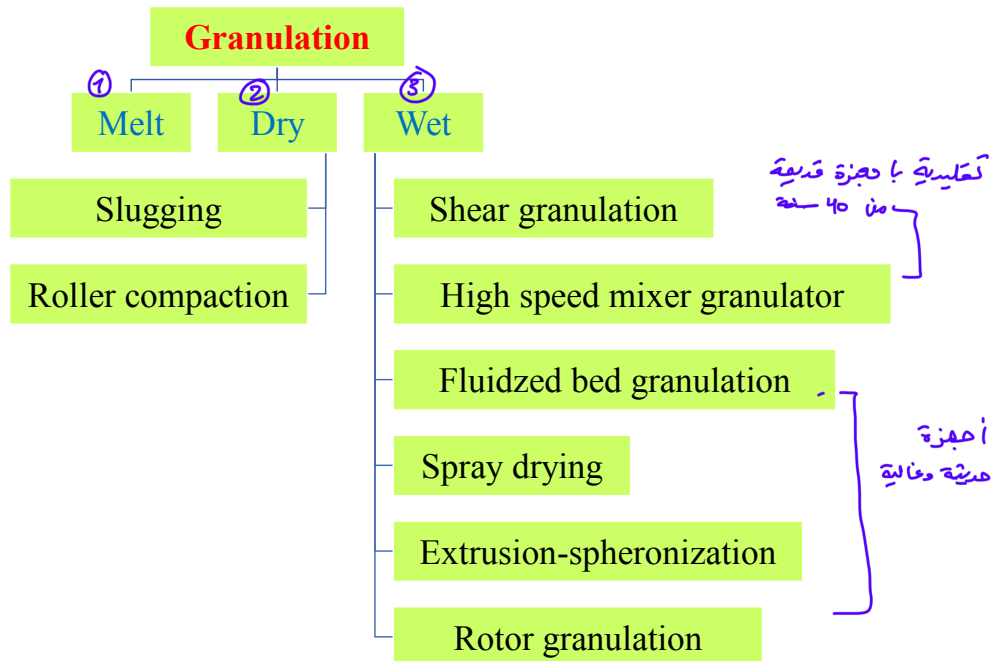
# Granulation

## Reasons for granulation

4. Eliminate problems due to dust (e.g. toxic materials). operator  $\rightarrow$  drug  $\rightarrow$  loss of material
5. To reduce the problem of caking of hygroscopic materials. contamination explosion / static charge
6. Increase bulk density of the powder mixture making them more convenient for storage or shipment. fine S.A.  $\rightarrow$  Adsorption



5



6

# Granulation methods

Dry granulation no liquid (water) → لا في تسخين (dry (ing)

- Other term used to describe the process is compression granulation.
- It converts the powders into granules by application of pressure without the intermediate use of liquid.
- This method is used mainly with heat and moisture sensitive materials like aspirin and many vitamins.
- There are two main processes of dry granulation: Slugging & Roller compaction

7

## Dry granulation methods

### Slugging

Procedure:

- Powders (drug and additives like diluent, binder and disintegrant) are mixed and compressed on high capacity tableting machine.

- The compacted masses (slugs) are subsequently comminuted and screened into smaller granules.



8

Direct Compression

granules إلى بطلع يكون hard. لها انكسرة بمرحلة اولية قبل compression



بعلام Seiving دختاراد (العناب size)

بلا تكة، slugs (القطع الكبيرة)  
fine milling بطين granules من powder

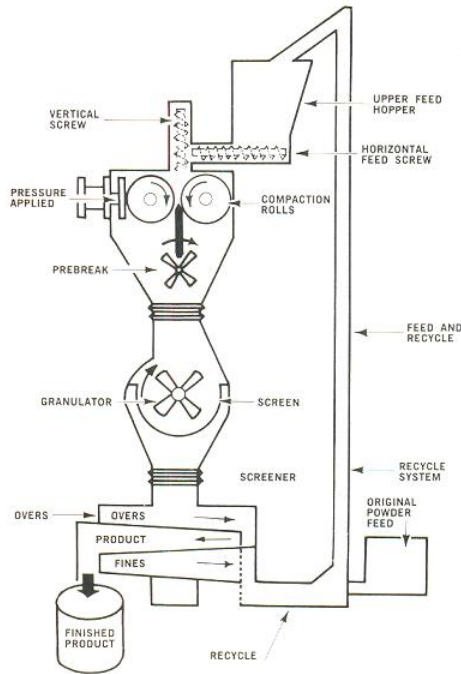
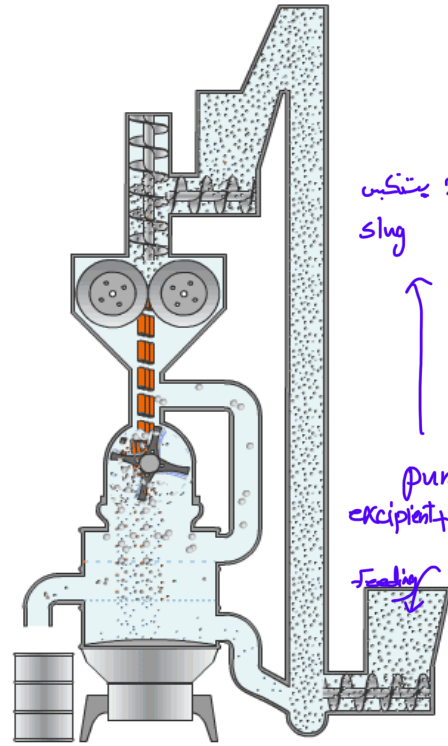
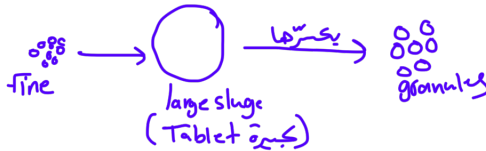


FIG. 11-13. Schematic diagram of a Chilsonator roller compactor in a granulation production system. (Courtesy of the Fitzpatrick Company, Elmhurst, IL.)



تبروح 1 slug 2 بتكيب  
لقطع كبيرة اسما slug

pumping  
excipient drug  
Feeding  
good mixing  
pellets

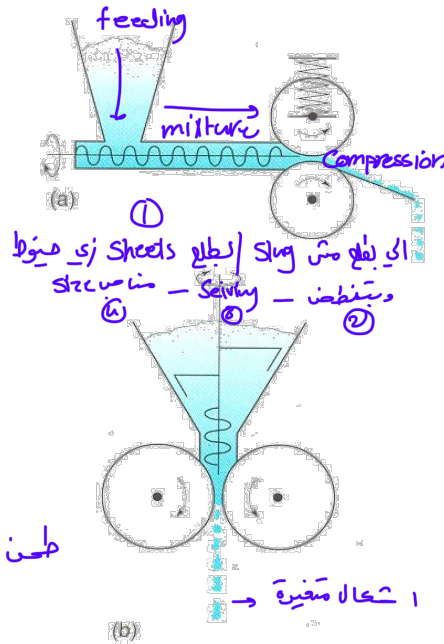


## Dry granulation methods

### Roller compaction

- On large scale, dry granulation can be performed on a specially designed machine called **roller compactor**.

- The powder is squeezed between two rollers to produce a sheet of material which is then comminuted and screened to small granules.



2 Rollers  
vertical - horizontal

Fig. 29.12 Roller compaction: (a) Alexanderwerk and (b) Protec types.

10

slugging

① Slug (large tablet) highly compressed → Comminution

② Roller Sheet → Comminution

screen



11

## Dry granulation methods

### Advantages of the roller compaction process:

1. The process is economical. → (pumping (feeding) → sheet → slugs → Communi → screening) كله  
لبنفسه لا يمكنه
2. There are relatively low investment costs compared with alternative granulation processes using multiple, and more expensive equipment. <sup>من الشراء بالباية رخيص</sup> الماكينة بتعمل كلها من
3. It can cope with a wide range of materials, particle size, bulk density and flowability (But not all materials)
4. The process is easily scaled up. <sup>الأجهزة الحديثة متجاكيز Premiers / القديرة بسيطة مثلاً Scaling up time + speed</sup>
5. The product has uniform properties with respect to its mechanical strength. <sup>لها اصنع من املا patch للمزجائين او mechanical strength يخن القابلية للكسر / بتتحسن اد Stress</sup>
6. Additionally, the more gentle 'squeeze' of roller compactors leaves the resulting granules capable of further compaction into tablets without the work-hardening problems encountered with slugging.

12

بها time + force اكثر  
ال granules الى من ال slugging بتكون hard فمجب احلها لاجي الجسها لانها انكبت بالباية ل tablet

تكيل ال granules الى حاي من ر Rollers اصل  
Squeeze

# Dry granulation methods

## Advantages of dry granulation:

- Utilizes less equipment and space than wet granulation.

صافي تجين ولا drying

- Eliminates the need for binder solution and drying process.

ما في binder بي لازم  
تكون اصله cohesive

13

Wet - لما احضر tablet الى صرافعات صمارة مخفها ليجاي الطريقة  
ولمبي احضرا حتى لازم اكون حريص بتحصينه زي potent  
لازم اكون حريص بكل الخطوات متزوج دار wet  
منها اصله Mixing و wet mass

## Granulation methods

بار solid  
دخلت liquid خلال التمنج  
لازم صداد liquid اسفله بالآتر  
بل drying

### Wet granulation

في liquid زي water

مجانر mechanical الى شغل في مغوطة ، حسب الضغط ما يزوج عال wet granulation  
تزوج عال direct compress لانها ما بتعمل

- This is the main method for preparation of pharmaceutical granulation and the granules prepared are of good quality.

### Disadvantages

- High cost
- Long operation procedure
- The use of binding liquid and heat creates problem for heat and moisture sensitive drugs. Sometimes alcohol is used in binding liquid instead of water if the drug is sensitive to moisture.

لازم potent  
لانه فيها خطوات كثير بتضمن انه ما يعنجل / كل خطوة فيها تحريك  
uniformity  
good quality  
mechanical strength  
wet  
ار اجن

14 Granulation Liquid  
- اذا دوا water sensitive و potent هو اخل  
خط استي ثاني بديل water زي ethanol - بروبانول - dichloroethane - ايتون بحمية قليلة - chloroform  
organic solvent  
حصل ميزنهم انما drying بغير حرارة منخفضة 30-35

ار drying لا water ما بوجهد 100 ، 5-6 مرات

residual ست لازم ليعزل

إذا عطينا وادمن حمول، organic solvents نيجل (residual) test بقى c gas chroma to. -- عشان انما عدا اذا بتجبر انما solvents لازم evaporable

## Granulation methods

### Procedure

1. The ingredients to be granulated are mixed to achieve good homogeneity.
2. In addition to the active drug, the mixture may contain a diluent, disintegrant, binder. ← safe ← diluent, disintegrant, binder. : to bind particles → granules  
(bulking agent) بزره و mass عشان تنكس الحبة حتى لو ضمت قوة الكبس  
disintegration عشان يفرق خط صاف
3. The binder (adhesive) is either mixed with powders or dissolved in the granulation liquid.

binder لازم في يكون في حصة ادا ارضانه لا powder ؟ لازم يكون cohesive



15

## Granulation methods

4. Granulation liquid is prepared (Volatile solvents are used such as water, ethanol and isopropanol, so that they can be removed by drying).
5. The granulation liquid is added to the powder mixture and mixing continues until uniform dispersion (wet mass) is obtained. This process is termed **wet massing**. → another mixing ⇒ potent
6. The wet mass is screened to obtain the desired coarse particle size and the particles are then tray -dried. Alternatively fluid-bed drying is applied.
7. Size reduction of granules may be done using a hammer mill.

الخطوات 16

① mixing محطينا بمزيج ② صيف granulation liquid ③ تلبس على التجين kneading ④ wet mass ⑤ Screen بطين wet granules حجمها عزمنا ب  
⑥ drying ← tray dry (تج) ← oven تجرها بجمية ⑦ milling ⑧ size اختلاف لازم لمي تجر  
Fluid bed غاي

# Granulation mechanisms

## Particle bonding mechanisms

There are five primary bonding mechanisms between particles:

1) Adhesion and cohesion forces in the immobile liquid films between individual primary powder particles.

- An immobile layer (thin film) around particles will increase the diameter and decrease interparticulate distance, therefore it increases van der Waals forces.

2) Interfacial forces in (mobile liquid films) within the granule.

- During wet granulation, sufficient liquid is added to produce a mobile film.
- There are different states of liquid distribution between particles according to moisture content:

- Pendular
- Funicular
- Capillary
- Droplet (Suspension)

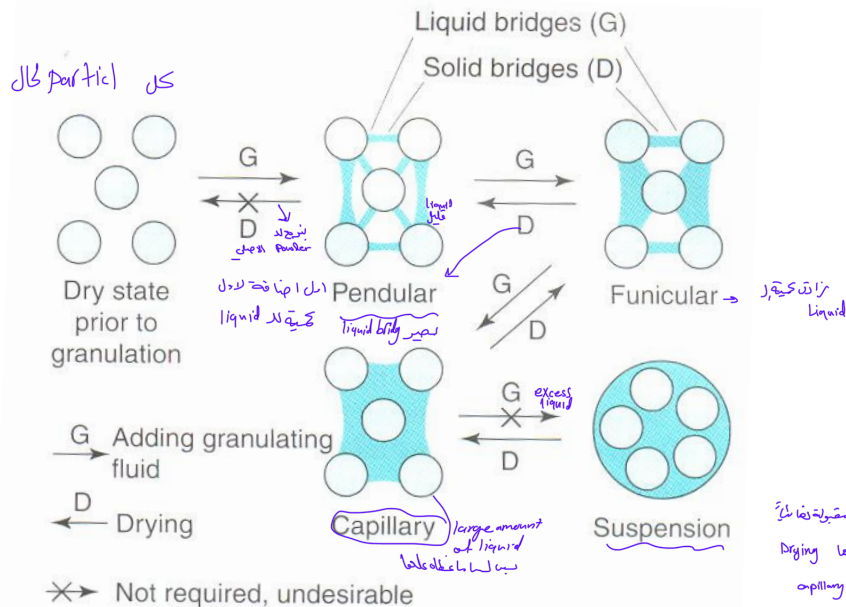


Fig. 29.2 Water distribution between particles of a granule during formation and drying.

G: adding granulating liquid

D: Drying

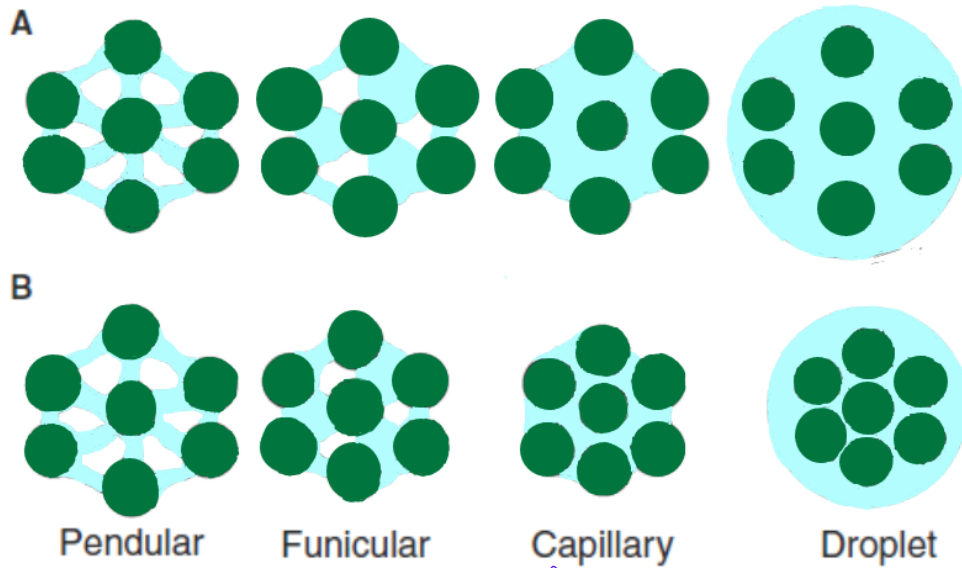


Fig. 2 Liquid-bridging state of agglomerates undergoing (A) binding liquid addition and (B) densification

mass  
Volume

ظلمت را لا عن ارنيد  
D

19

و الفرق بين A و B : A Space بـ A كبر / B Volume اقل عن طريق انحراف liquid bridging بصيرلهم  
solidification يعني ان liquid bridging صافحوي  
د صاف اقل من solid bridging

## Particle bonding mechanisms

3) The formation of solid bridges after solvent **evaporation(drying)**.  
These can be formed by:

- Partial melting
- Hardening binders
- Crystallization of dissolved substances

- بيليت ال bridging بمرحوب solidification

- ال binder زي اللصق او سكرور همدل sticky  
عتله كحق بيطه صاف water

4) Attractive forces between solid particles

- Electrostatic forces
- Van der Waal forces

- لما يتغزاي بتغير لعل hardening - binding

دمن مواد dissolved يعني لما صغر سيرب ويرج عنه المي

5) Mechanical interlocking

بصير crystallization او اي binder يعني solid bridging



تسايف ال particles دفاي اي  
energy ال بياض بيقرب من بعض ادا  
كانت arrangement دتسايف  
ماف Charge ولا Force

- partial melting  
20: صاف دالو ككلا بيجن مواد بصيرلها  
drying partial melting  
دبدا طولها واطولها حرارة لغزيت ترجع solidification



# Pharmaceutical granulation equipment

الأجهزة

## Wet granulators

### 1) Shear granulators two surfaces with narrow gap

- This is a **traditional method** of granulation
- It often uses a **planetary mixer** for wet massing of the powders.   
 (1) زي الحواشي بتكون حاليها زي العجينة
- Mixing of powders is either done in a separate mixers or in the same planetary mixer.   
 (2) باقي نوع من mixer معين اجيبهم عاد
- The liquid is added as the paddles of mixer agitates the powder.
- The moist mass is then transferred to a granulator (such as **oscillating granulator**)   
 (2) زي السنبول

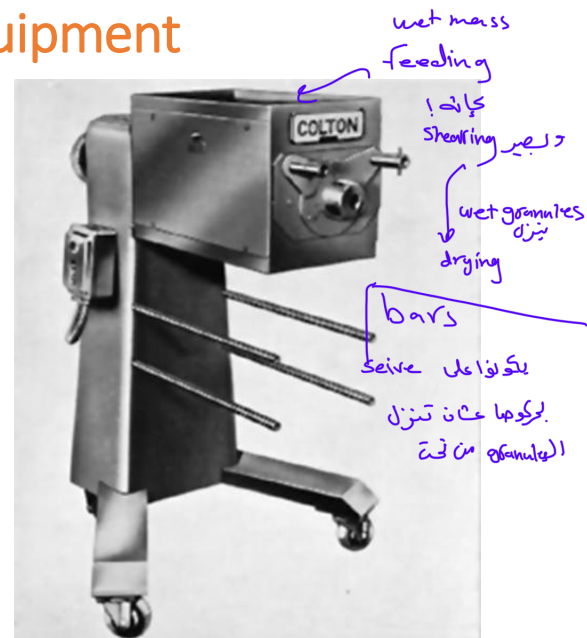
Oscillator بوجاز wet mass ويردح عاز

21

# Pharmaceutical granulation equipment

- The rotor bars of this granulator oscillate and force the moist mass through the sieve screen.
- The mass should be sufficiently moist to form discrete granules:   
 (3) صحتل
- If excess liquid → strings of material will be formed   
 (4) بنسك عجينة هتكون بدل granules
- If too dry → the mass will be sieved to powders and not granules   
 (5) بعل طحن رينزل powder بدل granules
- The granules can then be collected on trays and transferred to a drying oven or dried using fluidized-bed drier.

v. wet

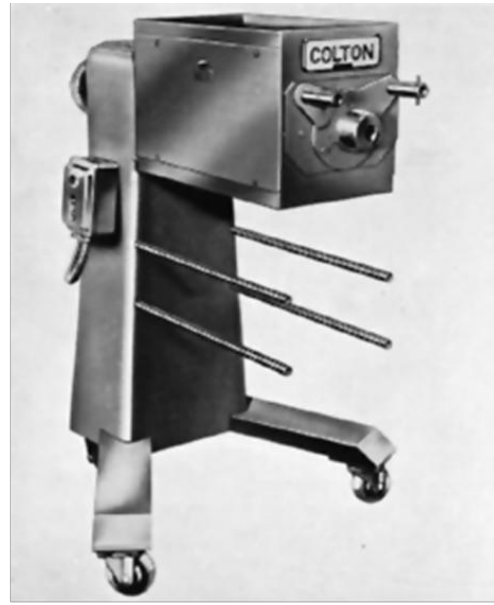


Oscillating granulator

22



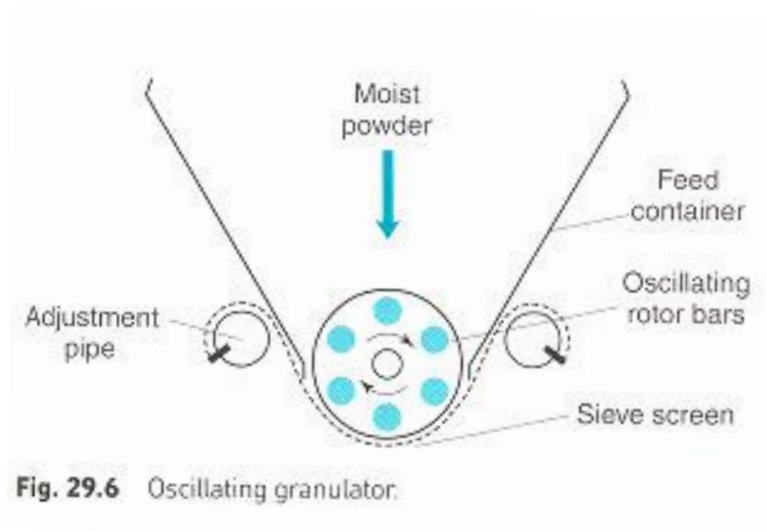
*planetary mixer*



*oscillating granulator*

23

If excess liquid → strings of material will be formed  
 If too dry → the mass will be sieved to powders and not granules



24



### Disadvantages of tray drying:

- The drying time is long *لازمن في transfer لازم تطلع الي طبقات من السطح جدين ٧-٨*
- Dissolved material may migrate to the upper surface of the bed on the tray *مذاب material قد يهاجر الى السطح من طبقاته غير متساوية mixing non uniform*
- Granules may aggregate due to bridge formation at the points of contact of granules *قد يتجمع الحبيبات في نقاط التماس بسبب تكون جسر بين الحبيبات aggregation*

فوق drug  
تحت excipient  
(collating agent)

- To deaggregate the granules and remix them a **sieving** stage is necessary after drying

دائماً بعد drying ← sieving لانه size تحير

25

### Advantages of the traditional method (shear granulation) *فديحة*

1. The process is not very sensitive to changes in the characteristics of the granule ingredients *بتجربوا اي formulation التي راج احضرتي تقليدي متساوية consistency متساوية*
2. The end-point can often be determined by inspection *متساوية end point: by inspection اصل المادة والتأكد انضامك من اوقف ال granulation*

منزلة متساوية  
speed و time

### Disadvantages of traditional granulation

1. Too long duration
2. The need for several pieces of equipment (mixer — dryer — — — )
3. High material loss because of the transfer stages

صافي تفريخ ١٠٥٪ بعض waste بالهجر

26

# Pharmaceutical granulation equipment

## 2) High-speed mixer/granulators (High shear granulators)

- This machine have a three-bladed main impeller, which revolves in the horizontal plane, and a three-bladed auxillary chopper which either revolves in the vertical or horizontal plane.
- The unmixed dry powders are placed in the bowl and mixed by the rotating impeller for a few minutes.
- The granulating liquid is then added via a port in the lid of the granulator while the impeller is turning.
- The chopper is usually switched on when the wet mass is formed to break up the wet mass to produce a bed of granular material.

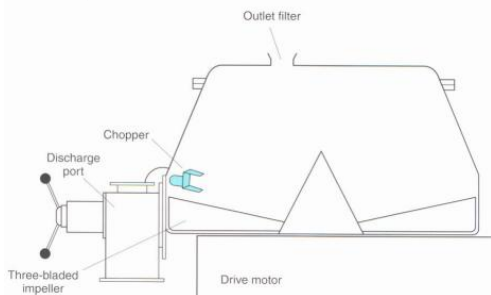
① mixing dry powder → ② spraying (granulating fluid) ③ chopper after wet mass forming ④ drying

27

الـ impeller بالـ سفـل  
Bottom-driven



الـ chopper بالـ سفـل

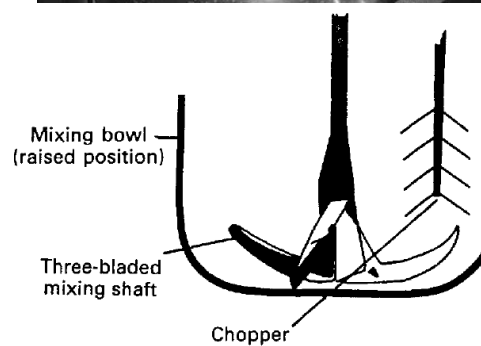


بالـ اعلى  
Top-driven



الـ impeller

الـ rotating bar / impeller



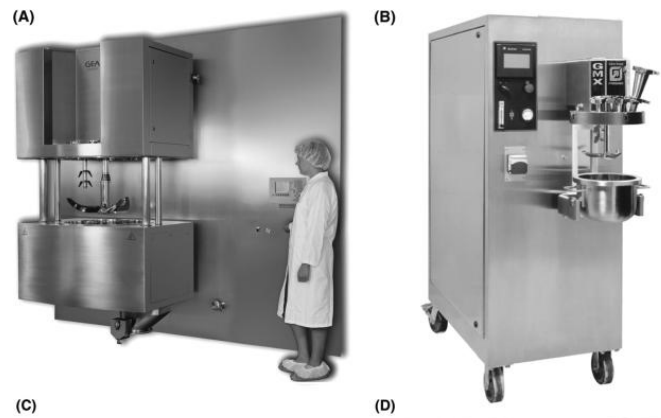
الـ powder اعلى  
الـ mixing اذا  
الـ wet mass  
الـ chopper  
الـ tray  
الـ fluid bed

عملية الـ wetting سريعة يتسبب ebbet الماء ، ظاهرة التلج ، أو حتى حنيريا يتسبب عليه يا يكبر ( اذا تركت ) وmanu وجر كثير دبطل مقبول



Bottom-driven high shear granulators

29



Top-driven high shear granulators



30

## Snow Ball

### High-speed mixer/granulators

- Once a satisfactory granules has been produced, the granular product is discharged, passing through a wire mesh that breaks up any large aggregates, into the bowl of a fluidized-bed drier.
- Granulation proceeds rapidly and controlling with care is necessary as granules can proceed very rapidly to unusable, overmassed system.
- The process is sensitive to variations in raw material. → sensitive لد Size Volume
- Advantage: Mixing, wet massing and granulation are done in few minutes. ديفضا مكان

② loss of materials بسبب ال transfer  
① مافى مشكلة، لوقت (طويل) دار

31

بفض الحجان mixing + granulation

## Pharmaceutical granulation equipment

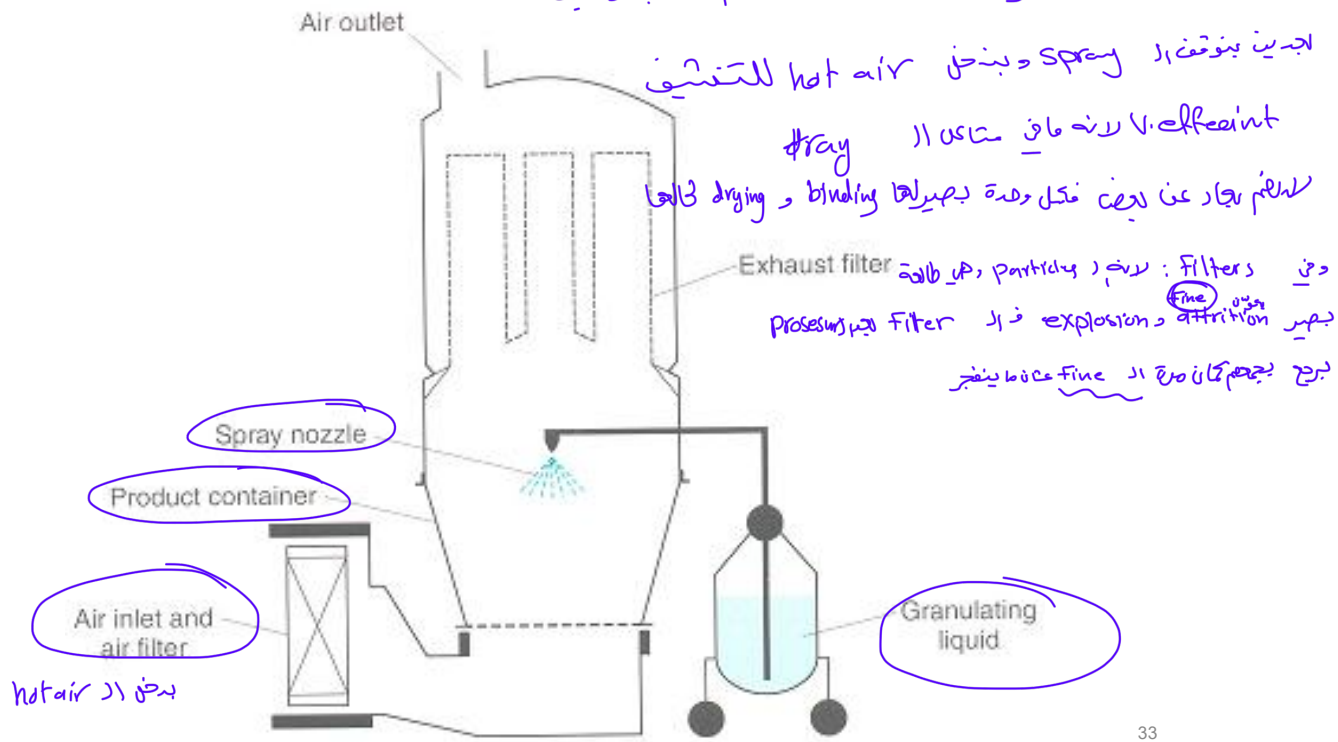
### 3) Fluidized-bed granulators

- Fluid-bed granulators are similar in design and operation to fluid bed dryers, but in addition fluid is sprayed from a nozzle on to the bed of powder. عالى بس efficient
- Heated and filtered air is blown through the bed of unmixed powders to fluidize the particles and mix the powder.
- Exhaust filters allow the prevent the escape of <sup>fine</sup> powders.
- Granulating fluid is pumped over the bed of powder which cause particles to adhere and form granules.
- After formation of granules, the spraying is stopped and the fluidizing hot air continues to dry them. mixing + granulation + dry

32

في window و sensor عشان اعرف انه دبت للدرجة المطلوبة  
↓  
لجوف الحرارة

يُنحط الـ powder من لاسف ويستقره كيف ربيات يعني fluidization يعني كى particle حرة الحركة في fluid dynamic و جين spraying دار particle ترتبط و جين.



33



34

# Fluidized-bed granulators

## Advantages

1. The performance of many steps (mixing, granulation and drying) in one equipment. *All in one*
2. The Process can be automated once the conditions affecting the granulation have been optimized. *Speed time*

*صنّري ال granulator بي فيه حفاتر*  
*هاد في كتر steps / بيثبت ال parameters (condition)*

## Disadvantages

- A. Expensive instrument
- B. Optimization needs extensive work



*لازم اربط كل (condition) عن  
 احوال للمادة ال صح*

35

## Apparatus, process and product variables influencing fluidized-bed granulation

Apparatus parameters <i>المكانة</i>	Process parameters	Product parameters <i>الم ا حتى formula</i>
Air distribution place <i>المكانة لمادة للتنقية والازداد والافلية في الفلتر ماضنة ماسة</i>	Bed load <i>كم راح ادخل material</i>	Type of binder <i>polymer — Polymers — Synthetic</i>
Shape of granulator body <i>(سطح كاسية ولا بتتغير من ادا في مكشوف)</i>	Fluidizing air flow rate <i>Volume of air غاز - نقل - دمية</i>	Quantity of binder
Nozzle height	Fluidizing air temperature <i>عن ذل mixing بال fluidization</i>	Binder solvent <i>اد ا مضاف organic فا ناعارة كم</i>
Positive or (negative) pressure operation <i>Volume suction filtration buckner الزفة + فخط الخاز atmospher ما نزلو عالارة بيجز على حرارة اقل</i>	Fluidizing air humidity <i>كم T و humidity</i>	Concentration of granulating solution <i>لجتمعي طريقة التبعين</i>
Atomization • Nozzle type • Spray angle • Spraying regime • Liquid flow rate <i>الكمية الي بيصلها spray ظل زمن مينة</i>	Atomizing air flow rate • Atomizing air pressure • Droplet size <i>intermittent : spray Continuous v/min لاد binder</i>	Temperature of granulating solution Starting materials • Fluidization • Powder hydrophobicity <i>انتجاد attrition binding agent فالب water مراح يكد في موية بال gram phobic + phillie</i>

36



سرعت در هانتسندل ری

البوتن / موهن / انهم

## Pharmaceutical granulation equipment

### 4) Spray driers →

به ضربه → spray (التي تحصل بينه وبين) Flyer → powder

• This differs from other methods of granulation in that granules are formed from a solution or a suspension rather than initially dry powder particles.

→ ما يدخل powder

• The components (drug, diluent) are suspended in a liquid that may contain a dissolved binder.

thick في الحليب

• The solid percentage should be relatively high.

• The suspension is pumped / as a drops under continuous agitation in a stream of hot air.

slurry dispersion solution

تبصاف

• The liquid evaporates leaving the solid in form of free-flowing hollow spherical granules with uniform size.

❖ Used mainly for the preparation of direct compression diluents. →

ال diluent الذي يراعى استخدامه لما قبل

37

drying سريع و efficient / طريقة تحضير حبيبات اللفاف اقل ما اطع عليه في بهرله dispersion غير متطابق الكبير

السبب انه حفر بجدار الطارية السخنة Sphere amorphous فان solubility عالية وغالب

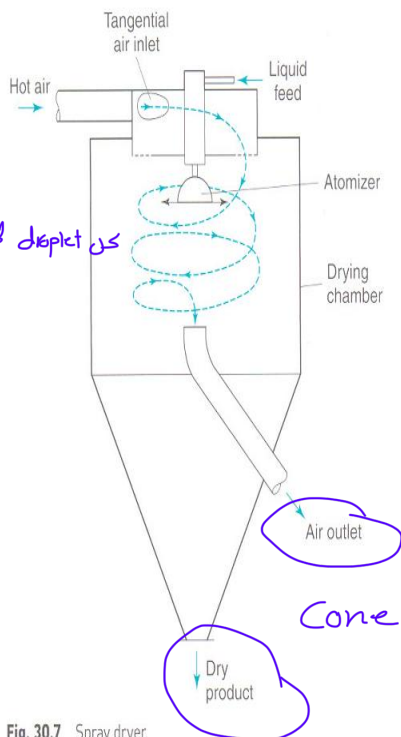
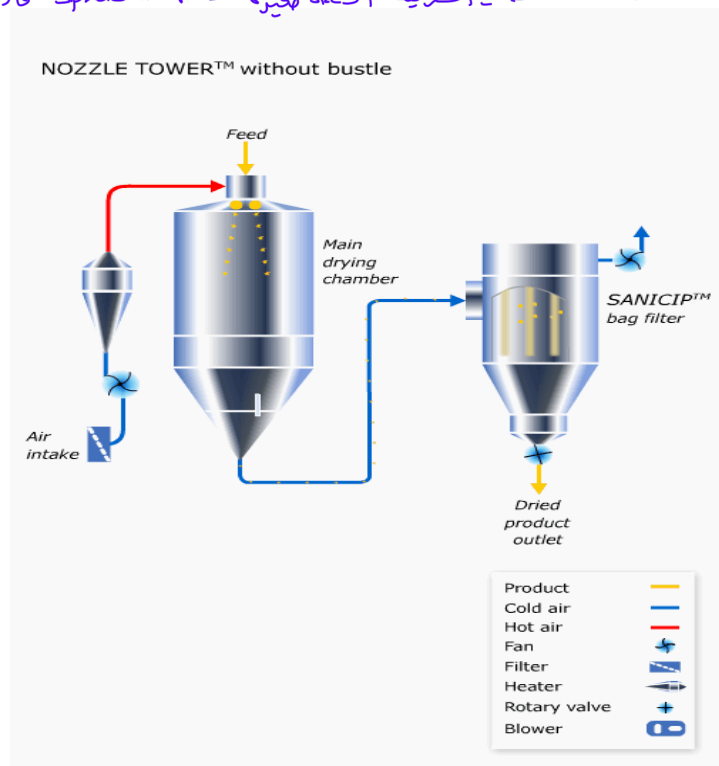
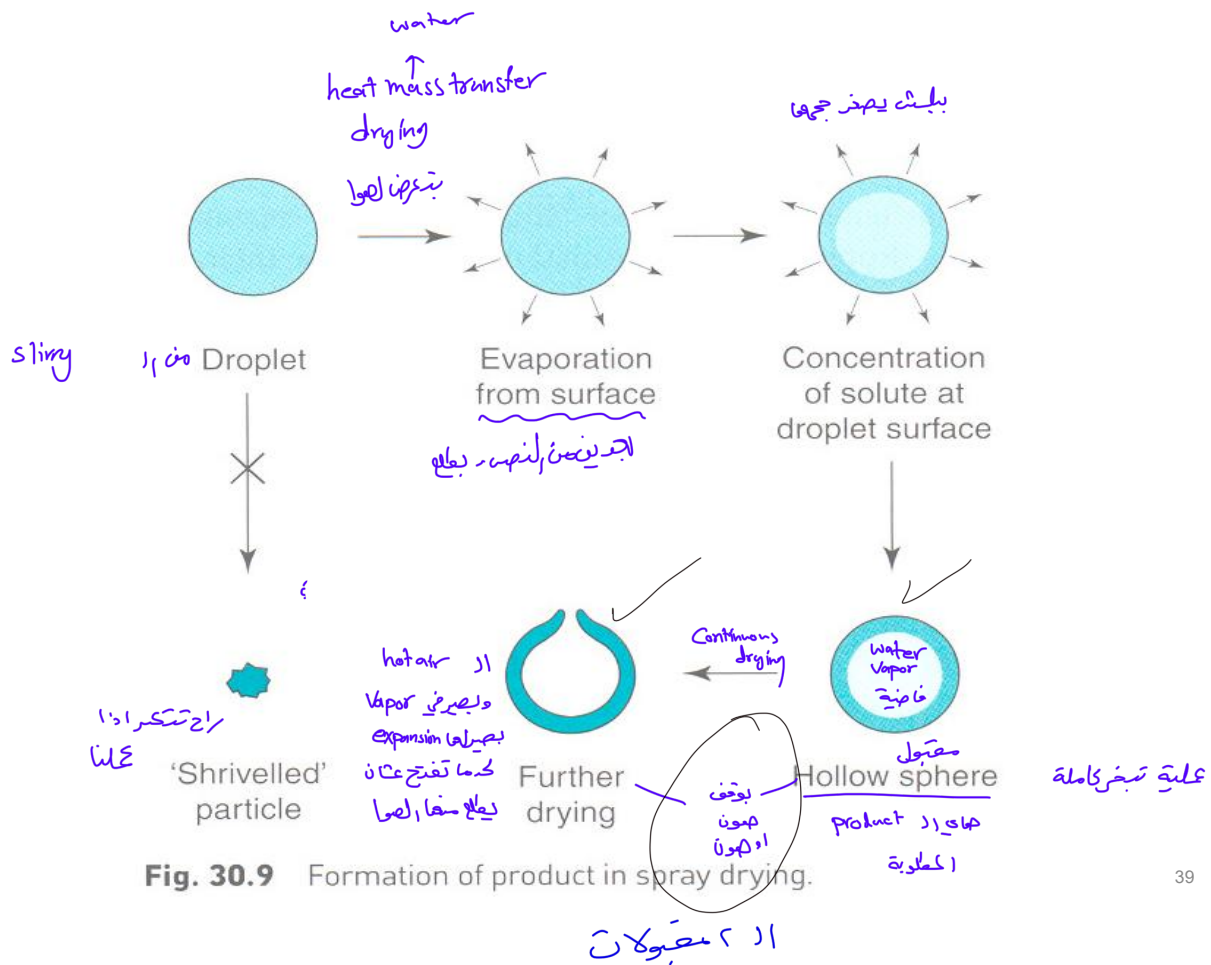


Fig. 30.7 Spray dryer.

• جمع ال product



ممكن يكون fine cyclon بضم بار حقه لآخر اسي



39

## Spray driers

### Advantages

- Short drying time <sup>مكن Kgs / 10 min</sup>
- Minimal exposure of the product to heat → little deterioration of heat-sensitive materials. <sup>حليق الاطعام في برودتين وسرعة تنكسر بالارة، مع ذلك عادة يتخذ من لانهما كثر سرعة العملية خلال لقائي بتسريع وتغير droplet او sphere</sup>
- The characteristic particles have large surface area and so rapid dissolution. <sup>amorphous ← Spherical</sup>
- The powder has a uniform and controllable particle size.
- The product formed has excellent flow and compaction properties.
- Labor costs are low. <sup>full automated فافي عاتة</sup>

### Disadvantages

- It is costly process and the machine is expensive.
- The overall thermal efficiency is low.

40

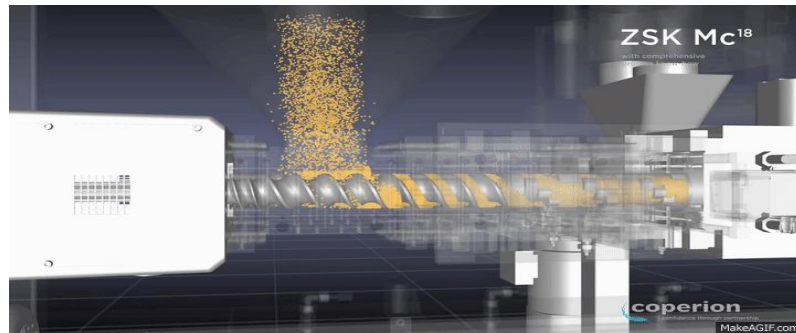
↑ thermal eff ↓ thermal eff  
↑ الجوارز ↓ الجوارز  
\* اد 1 Droplet كالهوااد thermal eff عالية (محول الهواء الساخن واد 1 drying)  
\* overall ؟ لحي الجوارز رت يكو مكان ال heat نفعها يجرع عن ال walls غير عنر Source of heat نجا كجر ريقو هوا الجير (الهوا اي يبرقنا صا 1111 اف (عادة) عنر احاطة كالهوا  
كثير لكمية قليلة منهاد كله صانج وسحب للكهرباء / wall كالهوا لانه في condensation كالهوا صانفت ونزلت لرقعة كالهوا well



# Pharmaceutical granulation equipment

## 5) Extruders/Spheronizers

- Extrusion/spheronization is a multistep process used to make uniformly sized spherical particles.
- It is used mainly to produce multiparticulates for controlled drug release applications.

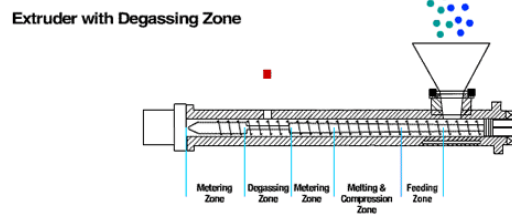
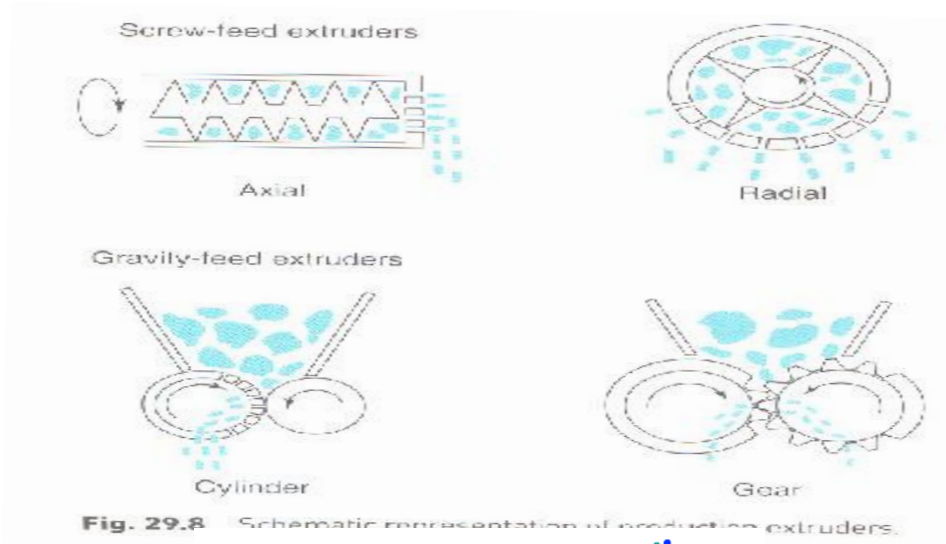


41

## Extruders/Spheronizers

- The main steps of the process are:
  - 1. Dry mixing of ingredients**
  - 2. Wet massing**
    - More amount of liquid is used than other methods.
    - Uniform dispersion of liquid is necessary
  - 3. Extrusion**
    - The wet mass is forced through dies to form rod-shaped particles of uniform diameter.

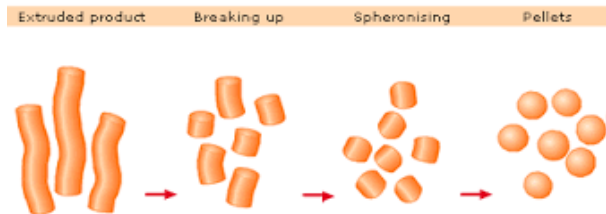
42



43

#### 4. Spheronization

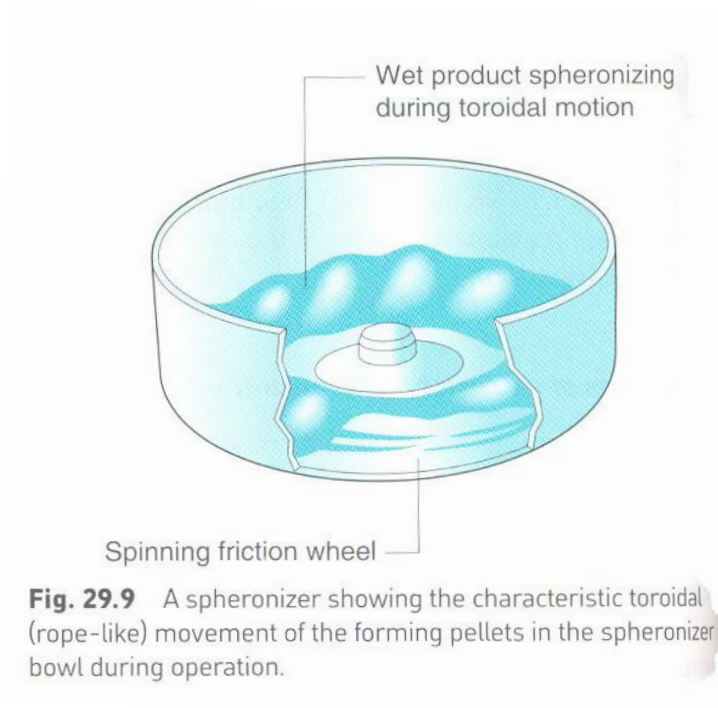
- To round off the rods into spherical particles
- This is done in a simple apparatus with fixed side walls and rapidly rotating bottom plate with grooved surface.
- The rounding is done by particle-particle and particle-surface frictions.



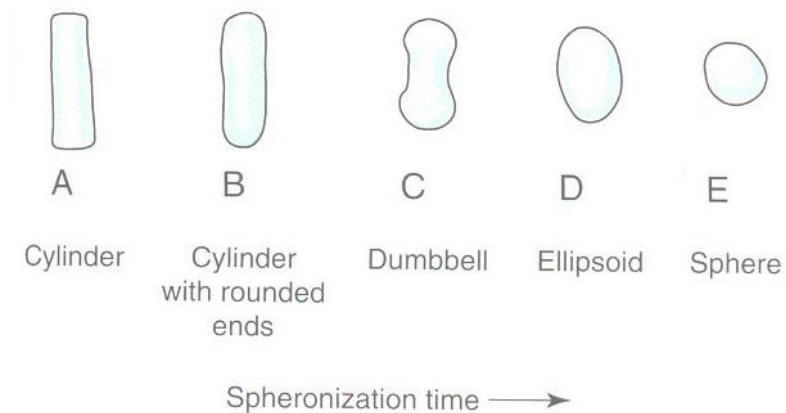
**5. Drying:** Either fluidized-bed or tray drying.

**6. Screening:** To obtain suitable narrow particle size

44



45



**Fig. 29.10** Representation of a mechanism of spheronization. The diagram shows a transition from cylindrical particles (a) into cylindrical particles with rounded edges (b), then dumbbells (c), to ellipsoids (d) and finally spheres (e).

46

## Pharmaceutical granulation equipment

### 6) Rotor granulation

- This process allows the direct manufacture of spheres from dry powder.
- In the Freund granulator, the powder mix is added to the bowl and wetted with granulation liquid from a spray.
- The baseplate rotates at high speed and centrifugal force keeps the moist mass at the edges of the rotor.
- The velocity difference between the rotor and the static walls, combined with the upward flow of air around rotor plate, causes the mass to move in a toroidal motion, resulting in the formation of discrete spherical pellets.

47

## Pharmaceutical granulation equipment

### 6) Rotor granulation

- These spheres are dried by the heated inlet air from the air chamber, which acts also as a positive pressure seal during granulation.
- Using this technique, it is possible to continue the process and coat the pellets by subsequently spraying coating solution on the rotating dried pellets.
- In addition, layered pellets can be formed by using uncoated pellets as nuclei in a second granulation with a powder mix of a second ingredient.

48

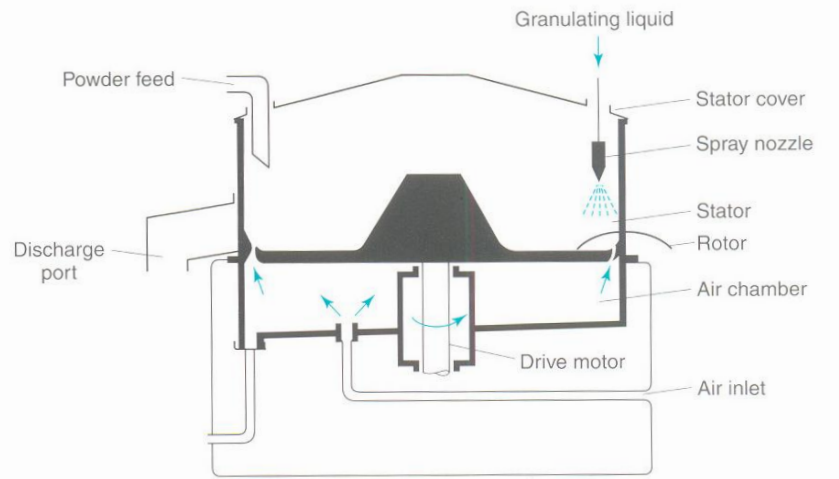


Fig. 29.11 Rotorgranulator.

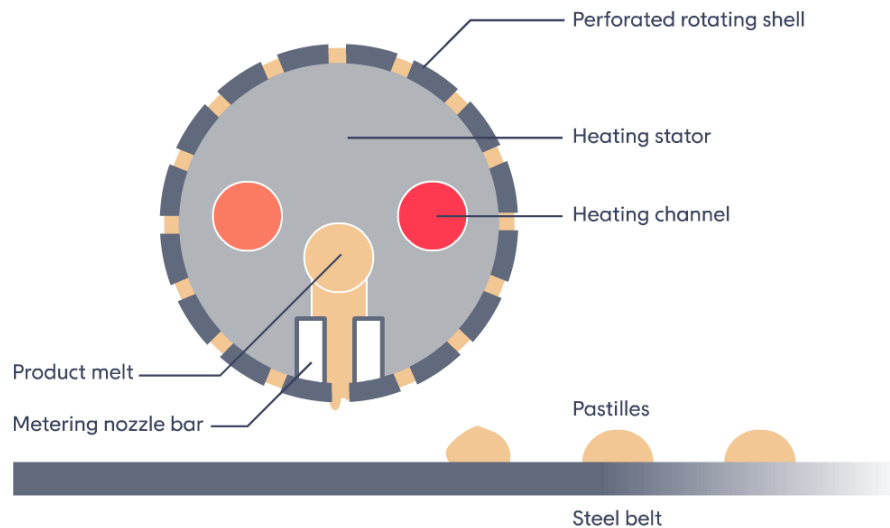
49

## Melt granulation

- Melt granulation and melt pelletization processes that have gathered increasing interest in the pharmaceutical industry.
- Unlike the conventional use of aqueous or organic solutions of binders, a molten liquid which remains as a constituent of the formulation is utilized as a binder.
- However, the basic principles in melt granulation processes are relatively similar to those of wet granulation processes with solvents except that the interpretation of the melt agglomeration processes is not complicated by an evaporation of the molten binding liquid.

50

# Melt granulation and melt pelletization



51

## Melt granulation

### Hot melt binders

- Hydrophilic:
  - Polyethylene glycols (PEGs): Grades between 2000 - 6000
- Hydrophobic (water insoluble)
  - Carnauba wax
  - Hydrogenated castor oil
  - Hydrogenated cotton-seed oil
  - Stearic acid
  - Fatty acids derivatives (glyceryl behanate, glyceryl monostaearate, glyceryl trilaurate, glyceryl tripalmitate, glyceryl tristearate, hexadecyl palmitate)

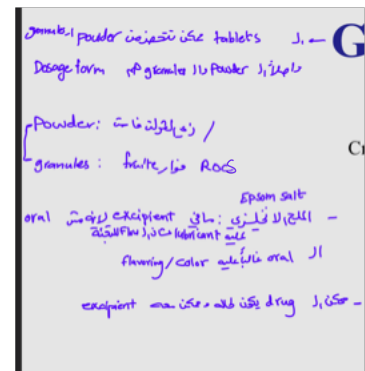
52

# Melt granulation

## Hot melt processes

- The following methods (machines) have been adapted for melt granulation:
  1. Shear granulation
  2. High speed mixer granulators
  3. Spray drying
  4. Spray congealing is similar to spray drying. However a molten sample is sprayed and subjected to cold air for congealing.
  5. Fluidized bed granulation
  6. Extrusion/spheronization

## Powders and granules



- The term 'powder' when used to describe a dosage form describes a formulation in which a drug powder has been mixed with other powdered excipients to produce the final product.
- The function of the added excipients depends upon the intended use of the product (ex. Colors, flavors, sweetening agents may be added to powders for oral use).
- Granules which are used as a dosage form consist of powder particles that have been aggregated to form a large particle, which is usually 2 – 4 mm in diameter.

في فرق بين granules و aggregated و agglomerate



size بال

shape و texture

aggregation و ارتباط

محدد و محدد

صاغة مكثبة

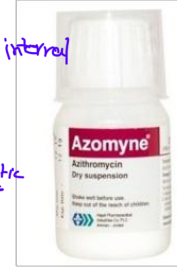
منفرد و منفرد

agglomerate (not spherical)

# Powders and granules

- Powders and granulated dosage forms are traditionally dispensed as:

- Bulk powders or granules for internal use → bulk  
 (عربة صمغ كل الجرعات) <sup>زيتي دشولت فاص Sachet</sup>
- Divided powders or granules (i. e. single preparation) for internal use → divided → internal
- Dusting powders for external use. <sup>Baniciin</sup> <sup>antibiotic</sup> <sup>بنزوت مابجوج</sup>
- Insufflations for administration to ear , nose or throat
- Antibiotic syrups to be reconstituted before use <sup>بفتح قبل الاستخدام</sup>
- Powders for reconstitution into injections <sup>الابراني صمغ</sup>
- Dry powder inhalers. <sup>sterile (minimum number of excipient)</sup> <sup>hypnotized powder</sup> <sup>excipient</sup> <sup>sterile</sup> <sup>عن</sup>  
 - حرضناه بار ordered mixing (مخزرة Sheets) <sup>لوتكها بتدقي صمغ</sup> (drug + Carrier (lactose)) <sup>omny</sup> <sup>اد صارة قايض بي</sup>



55

# Powders and granules

## Advantages of powders and granules as a dosage form

- Solid preparations are more chemically stable than liquid ones. <sup>microbial growth</sup> <sup>liquid</sup> <sup>powder</sup> <sup>ما في بي</sup> <sup>سجل</sup> <sup>hydrolysis</sup> <sup>reaction</sup> <sup>دسط صحرك بسج</sup>
- Powders and granules are a convenient form in which to dispense drugs with a large dose (ex. Mg trisilicate oral powder dose is 1 – 5 g). <sup>مافان كبركة دقي</sup> <sup>Mg silicate</sup> <sup>بفتح</sup> <sup>لا</sup> <sup>قبل الصيرة لا</sup> <sup>Dose - الجرعات ما بيحي بسجوة</sup> <sup>د صج بيومن</sup>
- Orally administered powders and granules of soluble medicament have a faster dissolution rate than tablets and capsules. <sup>disintegration</sup> <sup>اصغر من</sup>

ال dissolution أسرع لانه ما في خطوة ال disintegration  
 اصغر من

56



# Powders and granules

## Disadvantages of powders and granules

1. They are less convenient to carry than a small container of capsules and tablets (except laminated sachets). غالباً يكتفى بـ glass و ختمال / في sachet
2. The masking of unpleasant taste may be a problem. اصحابه، اكتسبوا دال tablet
3. They are not suitable for administration of potent drugs with a low dose. ار من و العوار، لا يوفون، ليرة لوزاد و اقله عادي لا يخفف بغير potent drug بفرم Dose صعدة
4. They are not suitable for the administration of drugs which are inactivated in, or cause damage, to the stomach. الادوية التي يتعمل Stomach irritation و ادوية ال Stomach تفرجها بيسه و acids و proteases اي digestive enzyme هاي Contraindicated

57

هناك العديد من الـ جبه فكرين

هاي در powder

## Powders and granules

### Dispensed preparations:

#### Bulk powders

- The mixed ingredients are packed into a suitable container, such as wide-mouthed glass jar. لوشت بكيين بلا ستك
- The constituents are usually relatively non-toxic medicaments with a large dose. يكن بطيعة و mouth تانفاديع من عاية الزوان



Cultrinal

#### Divided powders

- Divided powders are similar formulations to bulk powders but individual doses are separately wrapped. لوشت بكيين بلا ستك
- Modern packaging materials of foil and plastic laminates have replaced paper wrapping. نخطا + large Dose non-toxic



58

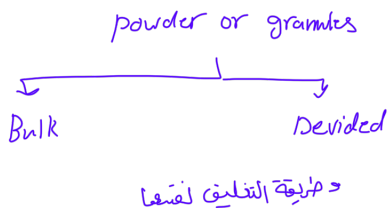
# Powders and granules

## Bulk granules

- Demixing  
diff. shape  
size  
charge  
size
- Segregation & degranulation
- Segregation, If present in bulk powders, can be prevented by granulation.
  - Bulk granules contain similar medicaments to powders (I.e. those with low-toxicity, high dose drugs).

## Divided granules

- These are granulated products in which amount sufficient for one dose is individually wrapped.
- Effervescent granules can be presented in this manner



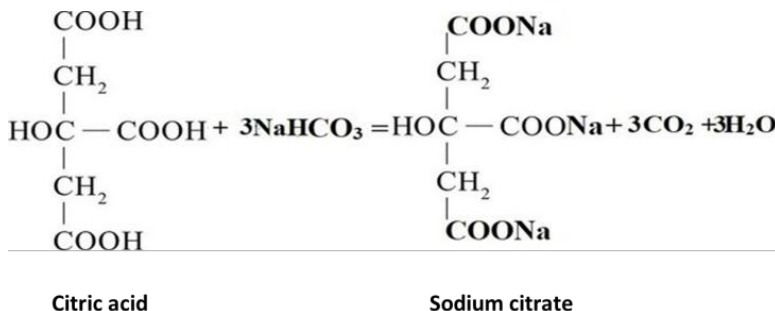
59

## Effervescent granules

- Effervescent pharmaceutical preparations generally contain acid substances and a source of CO<sub>2</sub> (carbonates or bicarbonates salts of sodium, potassium and calcium).



- Traditional acid materials are the citric and tartaric acid. However, ascorbic acid, fumaric acid and acetylsalicylic acid may be used.



60

acid ما يطلقه لانها مرتبطة بـ Carbolant  
base (Carbonate - bicarbonate) يطلقه CO<sub>2</sub> باد

✓ ✓  
✓ ✓

نرحبكم في سلايد 62

# Preparation of effervescent granules

## Wet Granulation Methods

- The acid and carbonate parts of the effervescent formulation can be granulated either separately or as a mixture with water (crystal water of citric acid, liquid water, or water vapor), ethanol (possibly diluted with water), isopropanol, or other solvents.

## Dry Granulation

- Granulation by slugging or roller compaction is suitable for active ingredients that cannot be wet granulated.

61

# Powders and granules

## Dusting powders

- Dusting powders contain ingredients used for therapeutic, prophylactic, or lubricant purposes and are intended for external use.
- Only sterile dusting powders should be applied to open wounds. =sterile
- Dusting powders for lubricant purposes or superficial skin conditions need not be sterile but they should be free from pathogenic organisms.
- Containers: glass, plastic or metal containers with a perforated lid.
- The powder must flow well from such a container, so that they can be dusted over the affected area.
- The active ingredients must therefore be diluted with materials having reasonably good flow properties, e.g. purified talc or maize starch.



62

## Powders and granules

### Insufflations <sup>bulb مع sacet</sup>

- Insufflations are medicated powders which are blown into regions such as the ear, nose and throat using an insufflator.
- The use of traditional insufflations had declined <sup>no more use</sup> because:
  - They are not very acceptable
  - Dose non-uniformity (if the drug has systemic activity)
- Some <sup>CNS</sup> potent drugs are now presented in this way because they are rapidly absorbed when administered a fine powder via the nose.



<sup>nose - brain pathway</sup>  
لـ CNS / زي الاذن

63

## Powders and granules

<sup>حكة حرقان</sup>  
ordered mixing  
دوران

### Dry powder inhalers

- The use of dry-powder systems for pulmonary drug delivery is now extensive.
- This dosage form has developed into one of the most effective methods of delivering active ingredients to the lung for the treatment of asthma and chronic obstructive pulmonary disease.

<sup>COPD</sup>

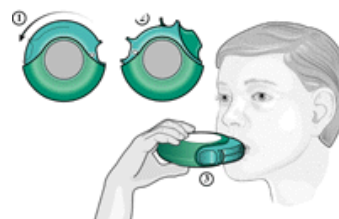


Figure 1: Diskus

64

# Powders and granules

## Oral antibiotic syrups

- For patients who have difficulty in taking capsules and tablets, e.g. **young children**, a liquid preparation of a drug offers a suitable **alternative**.  
Pediatric or Geriatric
- However many drugs, e.g. antibiotics, are physically or chemically unstable when formulated as a solution or suspension.
- The method used to overcome this instability problem is to manufacture the dry ingredients of the intended liquid preparation in a suitable container in the form of a powder or granules.
- When pharmacist dispenses the product, a given quantity of water is added to reconstitute.
- Shelf life of reconstituted syrup is 1-2 weeks.



65

reconstitution بطلع من مسحوق powder واحد واحد  
و يخلط بالماء على دقة (2-8)

ليس 'عجزه' powder ؟

unstable ①

thermostability : sus ②

المحافظة على solution & مجهزة بدون مواد حافظة  
preservative لمنع و مستقر زيار unstable

# Powders and granules

## Powders for injection parenteral : ① oral ② sterile

- Injections of medicaments that are unstable in solution must be made immediately prior to use and are presented as sterile powders in ampoules.
- Sufficient diluent, e.g. sterile water for injection, is added from a second ampoule to produce the required drug concentration.



66

preservative → excipient ؟ water for injection يمكن ييجي مع

(0.9 saline) hemolysis ← Isotonic ← NaCl (salt) ①

pain ← buffer ②

7.4 pH

## Preparation of effervescent granules

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- The acid and carbonate parts of the effervescent formulation can be granulated either separately or as a mixture with water (crystal water of citric acid, liquid water, or water vapor), ethanol (possibly diluted with water), isopropanol, or other solvents.

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