Particle Size Reduction

Dr. Isra Dmour

Credit: Prof. Nizar Al-Zoubi

Particle Size Reduction

- Other terms used to describe the operation: milling, grinding, crushing, chopping, comminution, micronizing.
- Most materials used in pharmaceuticals must be milled at some stage during the production of raw material or dosage form

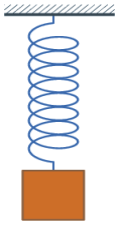
Particle Size Reduction

- ***Objectives of particle size reduction:***
  1. Facilitating drug release (dissolution rate)
  2. Exposing cells prior to extraction
  3. Reducing the bulk volume of material
  4. Facilitating drying
  5. Helping good mixing
  6. Increasing adsorption capacity
  7. Some excipients need to be in very fine powder to do well their function (lubricants, colors)

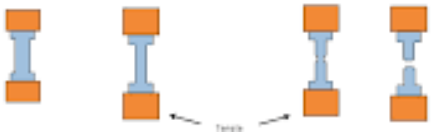
Theory of Size Reduction

Fracture mechanics

- Reduction of the particle size requires application of mechanical stress to the material.
- Materials respond to stress by **yielding**, with consequent generation of strain.
- **Hooke's law.**



- **Stress**: force
- **Strain**: deformation or elongation of a solid body due to applying a strs/force
- **Elastic**: reversible
- **Plastic**: permanent , irreversible



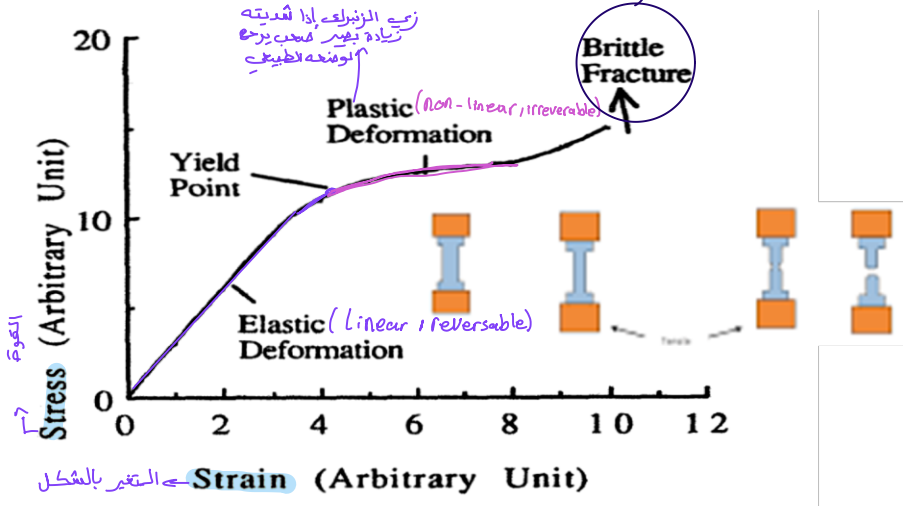


Fig. 19.1 Stress–strain diagram for a solid.

the yield point is the point on a stress-strain curve that indicates the limit of elastic behavior and the beginning of plastic behavior

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Theory of Size Reduction

Fracture mechanics

- The initial portion of the stress-strain diagram is linear and is defined by Hooke's law.
- In this portion the deformation is reversible (elastic deformation), i.e. the particle retains its shape if the stress is removed.
- After a certain point (yield point) the relation becomes nonlinear and the deformation becomes irreversible (plastic deformation).

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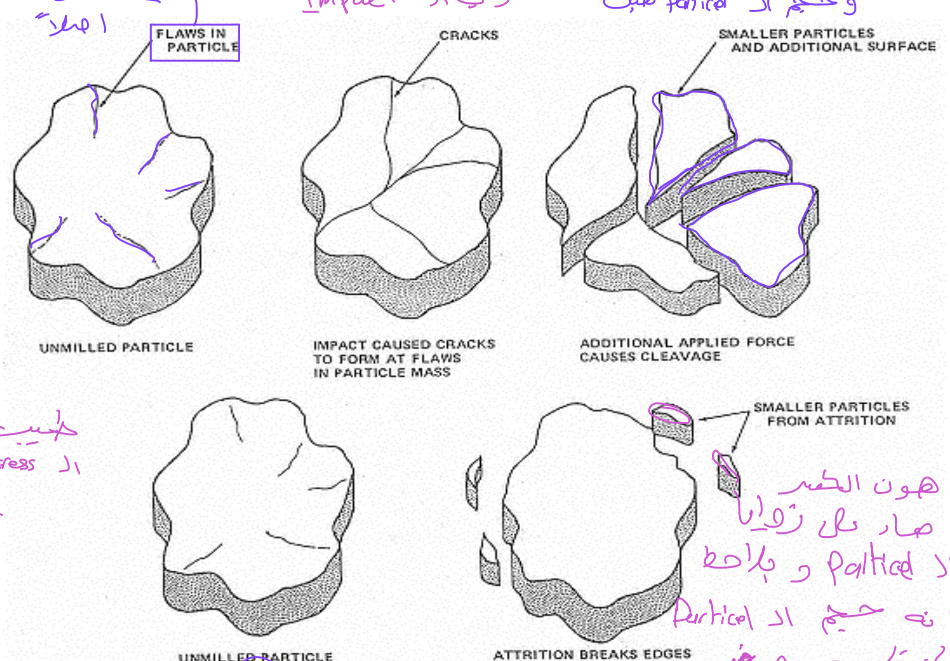
Theory of Size Reduction

Fracture mechanics

Crack propagation

- Size reduction begins with the opening of any small cracks that were initially present.
- Flaws (defect)
- Larger particles fracture more readily than small particles as they contain more cracks.



Influence of material properties on size reduction

Surface hardness (Mohs' scale)

- The hardness of material can be described qualitatively by its position in Mohs' scale.
  - Materials from 1-3 are described as soft
  - Materials from 8-10 are described as hard
- Hardness is related to abrasiveness.
- Hard materials may cause abrasion to the mill.

Influence of material properties on size reduction

Material structure

- **Crystalline materials** fracture along crystal cleavage planes; noncrystalline materials fracture at random.
- ***Fibrous materials*** (e.g. crude drugs) need cutting or chopping action and can not be milled effectively by compression or impact.

Influence of material properties on size reduction

Moisture content

- The presence of more than 5% water hinders comminution and often produces a sticky mass upon milling.

Stickiness

- Sticky materials may adhere to the surface of milling machine or the screen
- This is a problem of gummy and resinous materials.

Toxicity and harm

Potential of explosion (fine)

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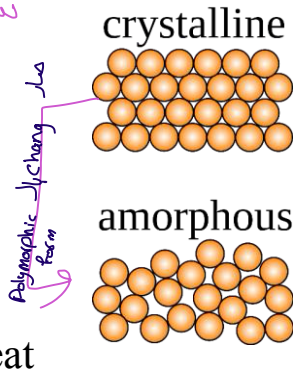
Effect of size reduction on material properties

Milling of material may lead to:

1. Change of the polymorphic form
2. Dehydration of hydrates
3. Development of amorphous structure
4. Damage of thermolabile drugs due to heat involved.
5. Development of free static charge



طاقة كهربائية ← طاقة حركية
الآله رح تستخدم 2% للطحن طب وين
ال 98% ؟؟ من 1 ← 6

Energy requirements

The most efficient mills utilize as little as 2% of the energy input to fracture particles.

- The rest of energy is lost in:
  1. elastic deformation of unfractured particles → الآله ضغطت على ال Particel بس ما وصلت ال yeild Point عشان هيك ال Particel رح ترجع لوضعها الطبيعي
  2. transport of materials within the milling chamber
  3. friction between particles
  4. friction between particles and mill → الإحتكاك بين ال Particel والآله والإحتكاك بين ال Particel نفسها رح يسبب ضياع الطاقة
  5. heat → جزء من الطاقة رح يتحول لطاقة حرارية نتيجة الإحتكاك
  6. vibration and noise → الاهتزاز والإزعاج رح يكون بسبب طاقة ضائعة (زي الخلاط)

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ترتبط بين الطاقة وبين ال surface area لل Particel

Energy requirements

ال Sn أكبر من ال Si ليش؟!
لانه ال new Particel تكون أصغر يعني ال surface area رح تكون أكبر إذا ال (Sn − Si) تكون +

Rittinger's theory

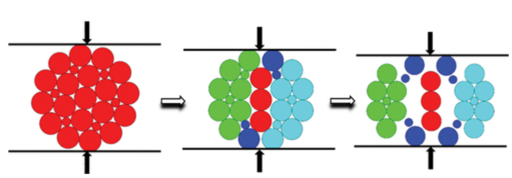
قبل الطحن

$$E = K_R(S_n - S_i)$$

S_i : the initial surface area,

S_n : new surface area → بعد الطحن

K_R = Rittinger's constant of energy per unit area → يعبر عن الطاقة المسلطة على السطح



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Energy requirements

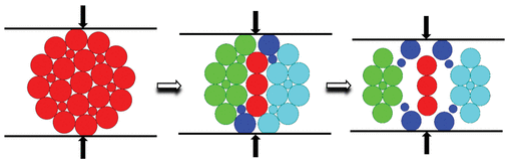
Kick's theory

$$E = K_K \log \frac{d_i}{d_n}$$

d_i : the initial particle diameter,

d_n : new particle diameter

K_K = Kick's constant of energy per unit mass



Energy requirements

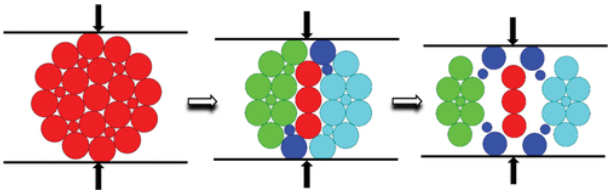
Bond's theory

$$E = 2k_B\left[\frac{1}{d_n} - \frac{1}{d_i}\right]$$

K_B : Bond's work index,

d_i : the initial particle diameter,

d_n : new particle diameter



Influence of milling on size distribution

- As milling progresses, the mean particle size decreases, and a material with initially a monomodal size distribution develops a bimodal size distribution.
- The primary component gradually decreases in weight and the secondary component increases in weight.
- Continued milling tends to eliminate the primary component to give a positively skewed (log normal) distribution with narrow size range.
- Milling rate follows first order kinetics

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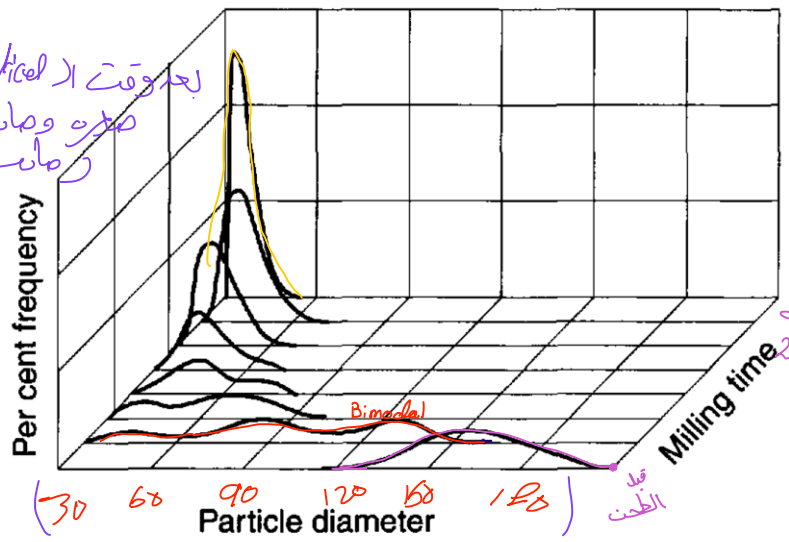

Fig. 11.2 Changes in particle size distributions with increased milling time.

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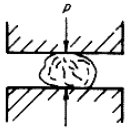
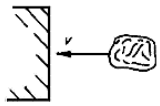
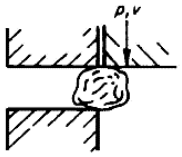
Mechanisms of size reduction

Force	Schematic diagram	Principle	Example of equipment
Compressive		Nutcracker	Crushing rolls
Impact		Hammer	Hammer mill
Attrition		File	Disc attrition mill
Cut		Scissors	Rotary knife cutter

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Mechanisms of size reduction

- There are four different mechanisms of size reduction:

a) Cutting

The material (particle) is cut by means of sharp blades or knives.

b) Compression

The particle is crushed by application of pressure.

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Mechanisms of size reduction

c) Impact

The particle is hit by an object moving at high speed, or a moving object strikes a stationary surface.

D) Attrition

This involves breaking down of the material by rubbing between two surfaces that are moving relative (**parallel**) to each other.

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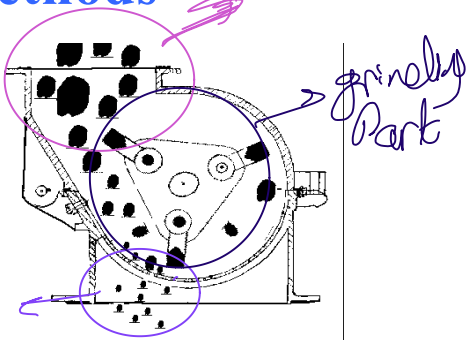
Size reduction methods

A mill consists of three basic parts:

1) Feed chute
2) Grinding part
3) Discharge chute



- The manner (way and rate) in which an operator feeds a mill affects the product.
- In most cases the grinding effect is a combination of different mechanisms.

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Size reduction methods

- There are two ways of feeding: choke feeding and free feeding.
  - In open-circuit milling, the operation is carried out so that the material is reduced to a certain size by passing it once through the mill.
  - In closed-circuit milling, the discharge from the milling is passed through a classifier and the over-size particles are returned to the grinding chamber.
  - closed-circuit milling is most valuable in reduction to fine and ultrafine size.

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Cutting methods

- Cutter mill
  - Principle of operation: It consists of a feed, a series of knives attached to a rotor which act against a series of knives attached to the mill casing, and a screen fitted in the base which control the particle size.
  - **Uses**:
    - Coarse degree of size reduction of dried granulations
    - Grinding of crude drugs such as roots and barks before extraction

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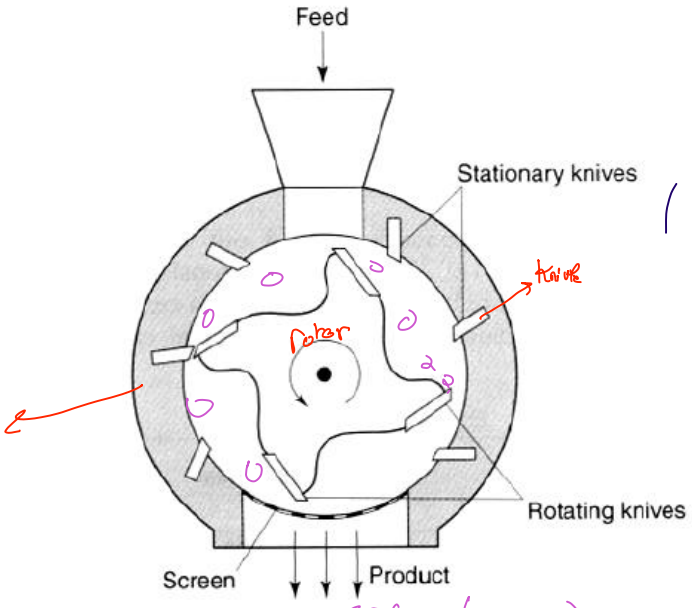

Fig. 11.6 Cutter mill.

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Compression methods

- Size reduction by compression can be carried out on a small scale by pestle and mortar.
- End runner and edge runner mills are mechanized forms of mortar and pestle-type compression.

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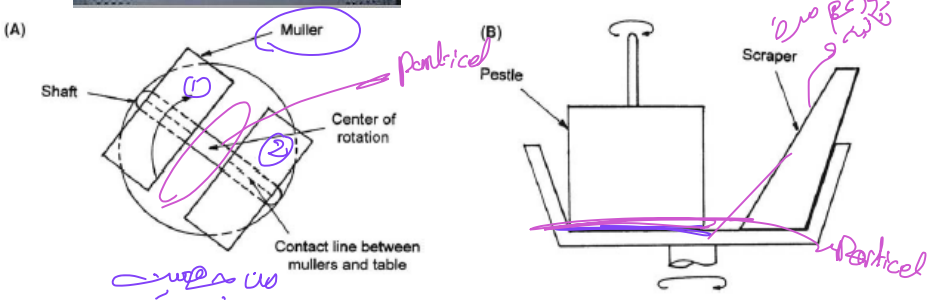

FIGURE 12.3 (A) Edge runner mill and (B) end runner mill.

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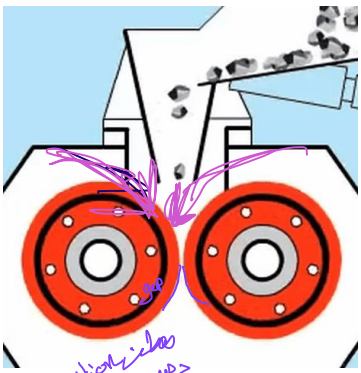
Compression methods

Roller mills

- Roller mills use two cylindrical rolls, mounted horizontally, and rotating about their longitudinal axis
- One of the rolls is driven directly while the second is rotated by friction as material is drawn through the gap between the rolls.
- Compression and attrition



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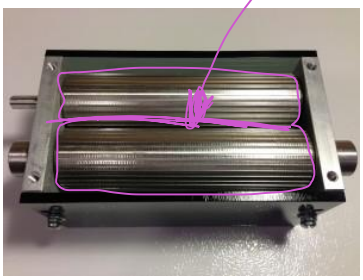

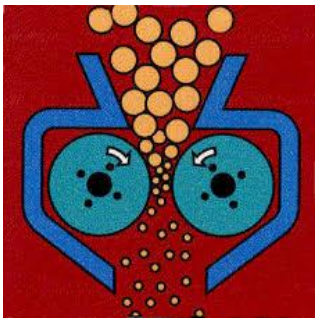

Roller mill (compression method)

Compression methods

Roller mills

- The *gap* between the rolls can be adjusted to control the degree of size reduction.
- Roller mills are used for crushing such as cracking seeds prior to extraction.
- This form should not be confused with the type used for milling ointments and pastes where both rolls are driven but at different speeds, so that size reduction occurs by attrition.