SIZE REDUCTION

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Definition

- **Size reduction** is a unit operation in which the particles are reduced from large particle to smaller particles with the help of external forces.

- Coarse particles converted into fine particles.

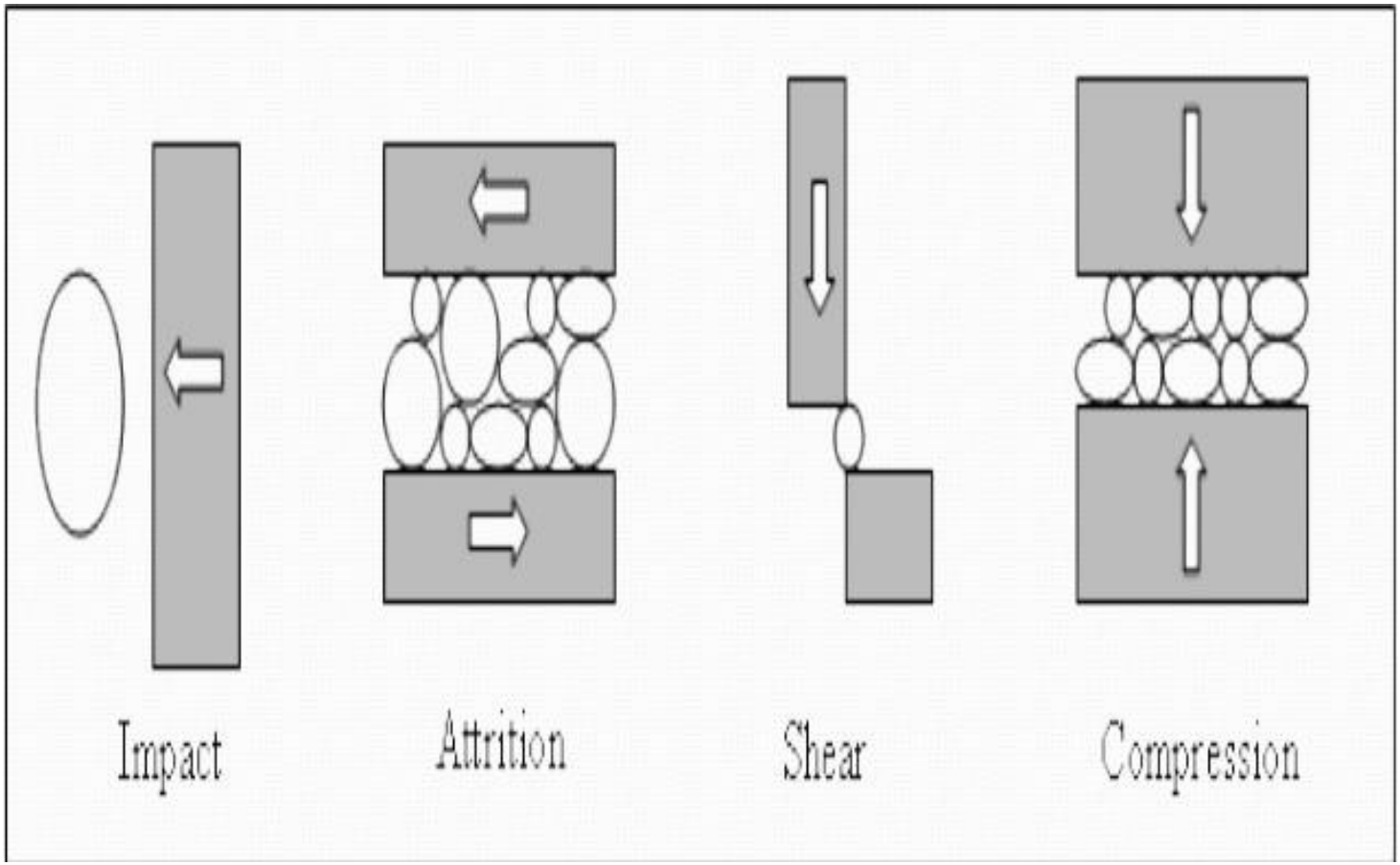
- Size reduction is also known as **comminution**, **diminution**, **grinding**, **pulverization** or **crushing**.

Mechanisms of Size Reduction

- There are **four** main mechanisms by which size reduction can be achieved.

1) **Cutting:** In this method, material is cut into small pieces by sharp penknife, scissor or cutter to reduce the size.
2) **Compression:** In this method, the material is crushed by application of pressure. **(mortar-pestle, roller mill)**
3) **Impact:** In this method, size reduction is achieved by hitting stationary material by an object moving at high speed or by striking particles on stationary surface.**(hammer mill)**
4) **Attrition:** In this method, material is kept between moving surface and pressure is applied.**(Roller mill, Colloid mill)**
5) **Impact and Attrition: (Ball mill, Fluid energy mill)**

Diagram



Objectives of Size Reduction

- To increase surface area and thus to improve rate of dissolution and rate of absorption. (increase in bioavailability)
- To improve physical stability of biphasic system.(suspension)
- To make mixing process easy and to ensure dose uniformity.
- To improve extraction efficiency of crude drug.
- To improve flow property of powder.(tablet, capsule)
- To improves appearance of ointments, creams and pastes thus to provide smooth texture.
- To improve rate of drying (↑surface area ≡↑heat transfer)

Advantages of size reduction

- **Content uniformity :** Mixing of different ingredients can be effective, if the particle size is uniform and small.
- **Uniform flow :** Smaller particle size promote the flow of powder into dies during compression of tablets.
- **Effective extraction of drugs :** Smaller particles allow rapid penetration of solvent into tissue or cells of vegetable and animal origin, as a result extraction becomes effective.
- **Effective drying :** Drying of a granular mass can be rapid and effective, if the size of granules is small and uniform.
- **Improved physical stability , Improved rate of Dissolution, Improved rate of absorption.**

Disadvantages of Size Reduction

- If size reduced for **hydrophobic materials**, then it increase the effective surface area.
- **Drug degradation** is possible due to heat produced during size reduction.
- **Aggregation of particles** is possible, as very fine particle possess strong cohesive force.
- **Contamination of powder** with metallic particle that wear off during grinding and milling.
- Finer drug particle are **more susceptible** to atmospheric degradation.(specially when they have volatile ingredients)

Laws governing Size Reduction OR Theories of Size Reduction

- The energy requirement for particle size reduction is a function of input and output of particle size, hardness, strength and other properties of solids.

- Various theories for energy requirement are:

1) Rittinger's theory
2) Kick's theory
3) Bond's theory

- The energy required to reduce the size of particles is inversely proportional to the size raised to the some power.

$$\frac{dE}{dD} = -c/D^{n} \qquad \ldots\ (1).$$

Where,

E= amount of energy required to produce a change

D= size of unit mass

C , n=constants

- Integration equation (1),

$$E = C \ln(d_i/d_n) \quad \ldots \quad (2)$$

(d_i/d_n) = reduction ratio.

If n=1.0 equation (2) becomes Kick's theory.

If n=1.5 equation (2) becomes Bond's theory.

If n=2.0 equation (2) becomes Rittinger's theory.

Rittinger's theory

- According to this theory energy E required for size reduction of unit mass is directly proportional to the new surface area produced.

where, $$E = K_R (S_n - S_i) \quad \ldots\ldots (3)$$

S_i = initial surface area

S_n = new specific surface area

K_R = Rittinger's constant

E = amount of energy

Applications:-

Applicable to brittle materials undergoing fine milling.

This theory ignore deformation before fracture.

Bond's theory

This theory states that energy used in crack propagation is proportional to the new crack length produced.

It also states that deforming set of particles is proportional to change in dimensions.

$$E = 2K_B \left(\frac{1}{\sqrt{Dn}} - \frac{1}{\sqrt{Di}} \right) \quad \ldots \quad (4)$$

Where

K_B = Bond's work index.

Di = initial diameter

Dn = new diameter.

- Bond’s work index is the work required to reduce unit weight from a theoretical infinite size to 80% passing from 100 µm.
- This theory is useful for rough mill sizing.
- The work index is useful for comparing efficiency of milling operations.

Kick's theory

- This theory states that the energy used in deforming a set of particles of equivalent shape is proportional to ratio of change in size.

$$E = K_k \ln \frac{d_i}{d_n} \qquad \ldots\ldots \quad (5)$$

Where

K_k = Kick's constant

D_i = diameter of particle in the initial stage

D_n = diameter of the new particles.

For compression of **large particles** kick's theory is useful.

SUMMARY

- Rittinger's theory: **(n=2.0)**

  Energy **α** new surface area formed.

- Bond's theory: **(n=1.5)**

  Energy used in crack propagation **α** crack length produced.

- Kick's theory: **(n=1.0)**

  Energy **α** ratio of change in size.

Factors affecting Size Reduction

- **Hard material**
- **Brittle material**
- **Fibrous material**
- **Sticky material**
- **Highly hygroscopic substance**
- **Thermolabile material**
- **Solids with low melting point**
- **Higher moisture content**
- **Quantity of starting material added in the mill**
- **Ratio of feed size to product size.**

SIZE REDUCTION EQUIPMENTS USED IN PHARMACEUTICAL INDUSTRIES

- All the equipments used for size reduction purpose in pharmaceutical industries are having some common parts for smooth running of equipments.
- List of basic parts/components:

a) Hooper

b) Milling chamber

c) Discharge chute or receiver

d) Sieve or screens

e) Cyclone separator/centrifugation equipments

f) Dust collectors

g) Cooling device

h) Closed system with sterile environment

Equipments used for Size Reduction

01) Hammer Mill:

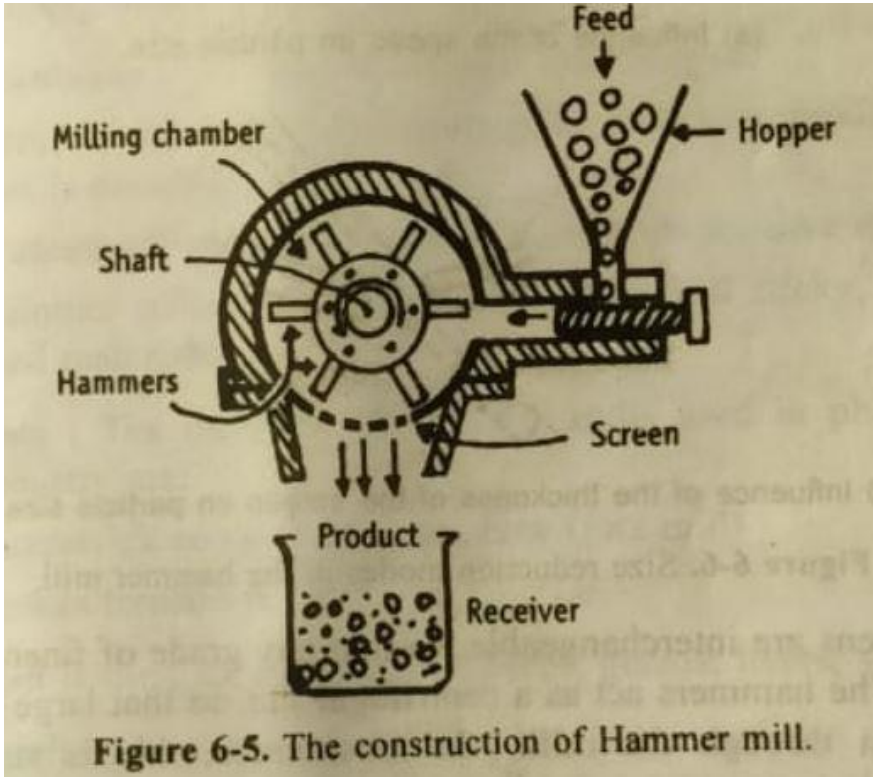


Figure 6-5. The construction of Hammer mill.

https://www.youtube.com/watch?v=oqeL2DMRYSY

- **Principle:** Hammer mill works on the principle of **impact** that is material is more or less stationary and is hit by an object moving at a high speed.
- **Construction:** Hammer mill is cylindrical drum having vertical or horizontal rotating shaft on which hammers are mounted, hammers and hammer mill both are made up of stainless steel.
- **Speed:** Hammer mill is mainly operated at 2500 rpm or 1000 to 2500 rpm for the reduction of the large size particles.
- **Working:**

  - In first step, all material to be crushed is kept in the hooper which is already attached to the rotating drum.
  - In second step, material is powdered to the desired size by maintaining the speed of rotor.
  - In the last step, material of desired size is collected under the screen.

Uses : Fine to moderate grinding of powders may be obtained, depending on the speeds of the hammer. The expected particle size may vary from 10 to 400 mm. Non abrasive to moderately abrasive, brittle materials can be used as feed stock.

It is used to mill dry materials, wet filter press cakes, ointments, slurries etc. Brittle material is best fractured by impact from blunt hammers; fibrous material is best reduced in size by cutting edges.

Advantages : (1) Hammer mill is easy to setup (install), dismantle and clean up.

(2) Scale-up problems are minimal provided same type of mill is used.

(3) Various types of feed stock can be handled using screen of different sizes.

(4) Hammer mill occupies small space.

(5) It is versatile, i.e., speed and screen can be changed rapidly.

(6) As it is operated in a closed environment, dust can be reduced and explosion hazards can be prevented.

Disadvantages : (1) The screens may get clogged.

(2) Heat buildup during milling is more, therefore, product degradation is possible.

(3) Wearing of mill and screen is more with abrasive materials.

(4) Hammer mills cannot be employed to mill sticky, fibrous and hard materials.

2) Ball mill:

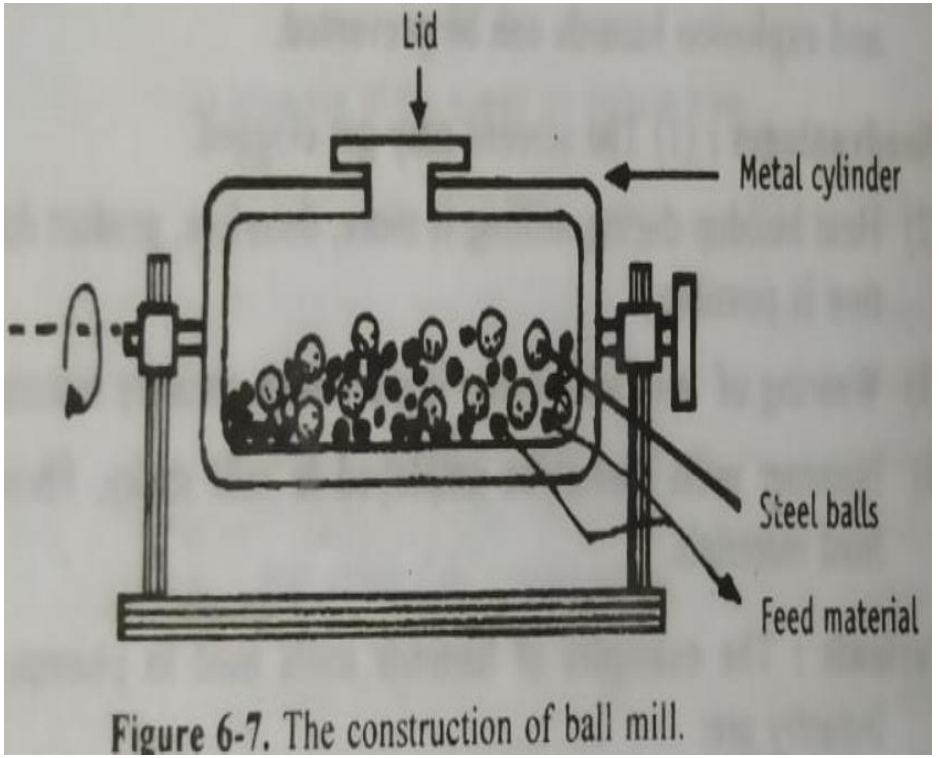
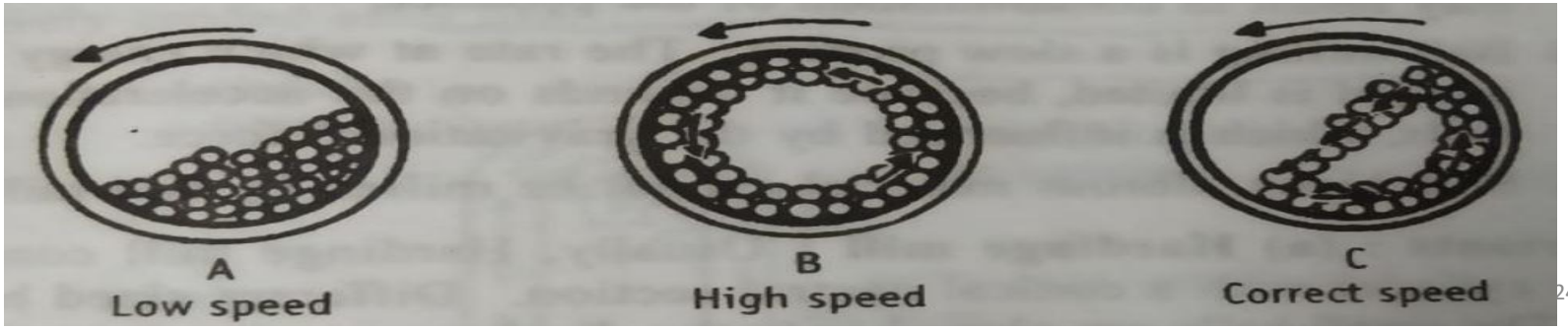


Figure 6-7. The construction of ball mill.



- **Principle:** Ball mill works on the principle of **impact** and **attrition**.
- **Construction:** Ball mill is basically a hollow metallic and cylindrical vessel or drum like structure which is set for the rotation. 30 to 50% volume of drum is filled by the required size of balls. Inner surface of hollow cylindrical vessel of the ball mill is made abrasion free by coating with an abrasion-resistant material such as manganese steel, porcelain or rubber.
- **Working:**

  - In first step, material to be crushed is introduced along with stainless steel balls in the ball mill.
  - In second step, drum will rotate at the desired speed to crush the material.
  - In the third and last step, crushed material is sieved and desired sized fine particles are collected for formulation development.

Uses : Fine grinding with a particle size of 100 to 5 mm or less can be obtained, particularly for hard and abrasive materials. Stainless steel balls are preferred in the production of ophthalmic and parenteral products, as there is a less chance of contamination due to wear. Ball mill at low speeds is used for milling dyes, pigments and insecticides.

Advantages : Ball mill offers several advantages and is widely used. These are:

(1) It can produce very fine powder.

(2) It is used for batch operation. It can be made continuous operation by including a chamber next to the cylinder. These are separated using a sieve.

(3) Ball mill is suitable for both wet and dry grinding processes.

(4) Toxic substances can be ground, as the cylinder is a closed system.

(5) Since the mill is a closed system, sterility can be achieved.

(6) Milling operation can be accomplished in an inert atmosphere, if oxygen sensitive substances are to be milled.

(7) Balls can be of various shapes and sizes. Rods or bars may be used instead of balls. Rod mill is particularly useful for milling of sticky materials.

(9) In ball mill, installation, operation and labour costs are low.

Disadvantages : Some of the disadvantages are:

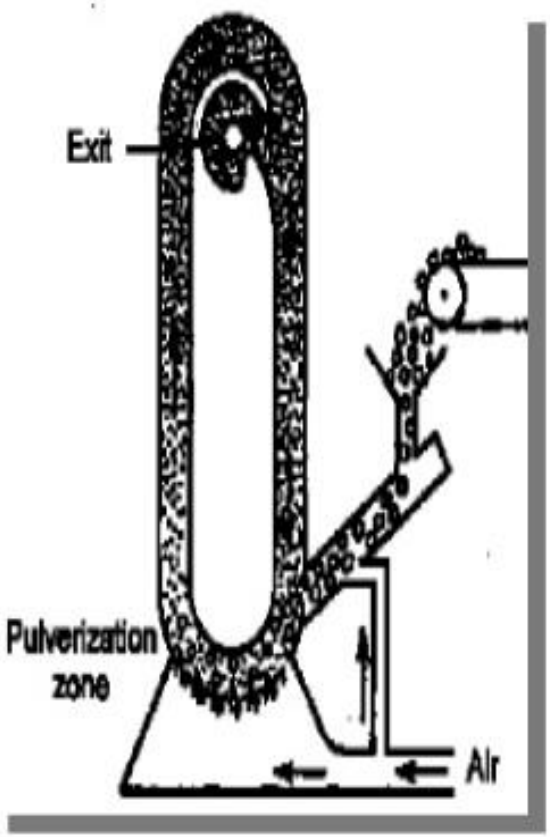
(1) The ball mill is a very noisy machine.

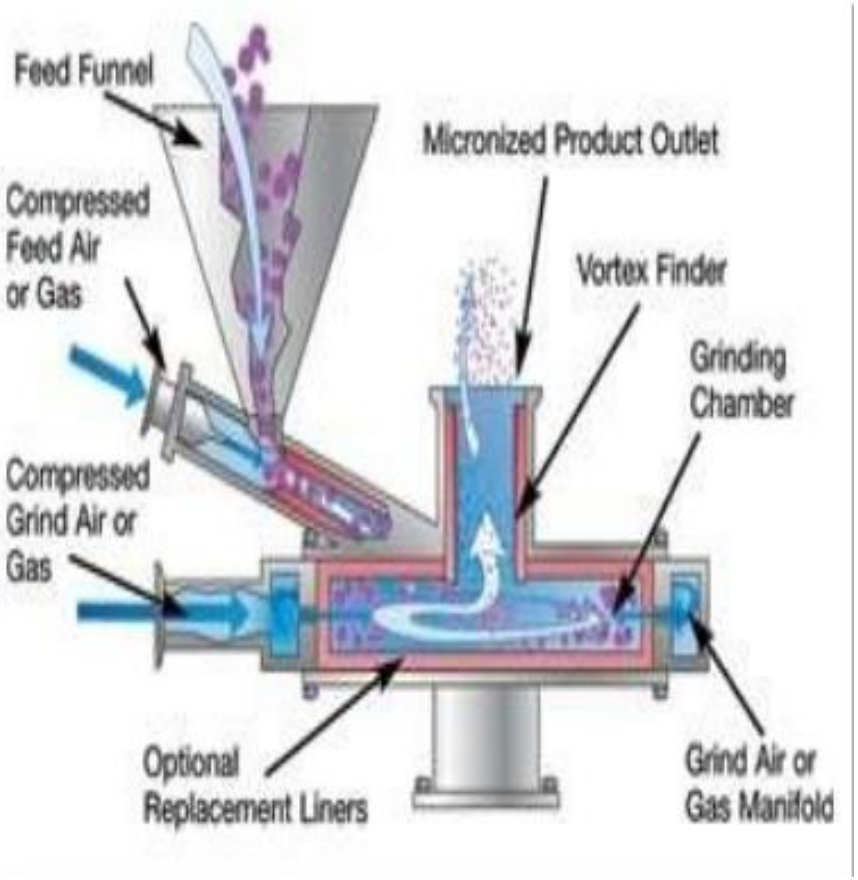
(2) Wear occurs from the balls as well as from the casing, which may result in contamination of the product.

(3) Ball milling is a slow process. The rate at which energy can be applied is limited, because it depends on the acceleration of the balls, which is influenced by the gravitational force.

(4) Soft, tacky, fibrous material cannot be milled by ball mill.

3) Fluid energy mill:





- **Principle:** Fluid energy mill also works on the principle of **impact** and **attrition**. In this mill force for the size reduction of coarse particles is provided by high velocity air.
- **Construction:** This mill is made up of hollow loop like structure. Diameter of this pipe is 20 to 200 mm and height is approximately about 2 meter. Mill is mainly made up of stainless steel or of ceramic.
- **Working:**

  - In first step, powder is introduced through the inlet.
  - In second step, compressed air is introduced through the series of grinding nozzles with high pressure. As this high pressure air comes in contact with particles, turbulence is created and a result forces are applied and it lead to size reduction of material.
  - In third step, small particles are removed by cyclone separator and coarse particles undergoes for re-circulation until desired size of particles achieved.

Uses : Fluid energy mill is used to reduce the particle size of most of the drugs such as antibiotics and vitamins. When strict quality control is desirable for the purpose of better absorption (bioavailability), this mill is the preferred one. Ultrafine grinding can be achieved. Moderately hard materials can be processed for size reduction.

Advantages : (1) It has no moving parts, hence, heat is not produced during milling. Therefore, heat-labile substances can be milled. Examples are sulphonamides, vitamins and antibiotics. Due to the expansion of gases under pressure cooling effect is produced during milling.

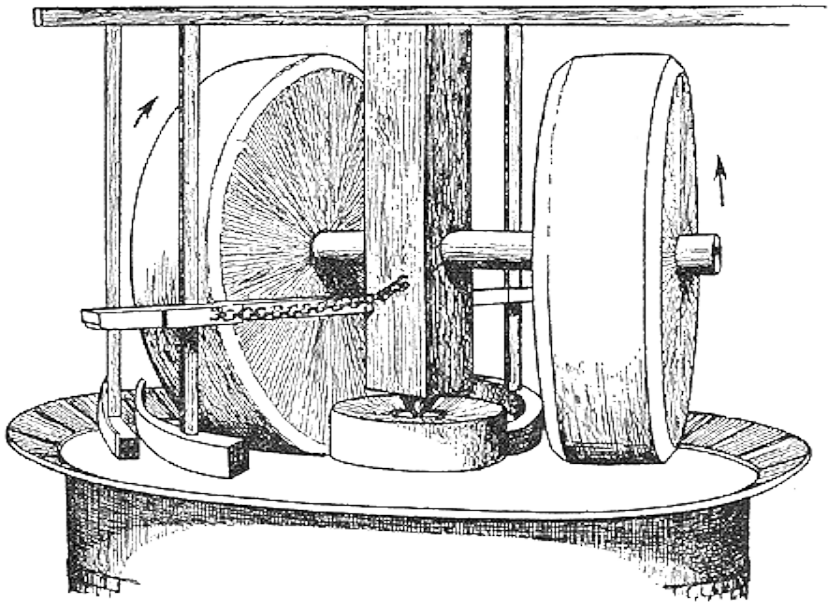
(2) It is a rapid and an efficient method for reducing powders to 30 mm or less.

(3) Since there is no wear of the mill, contamination is not possible.

Disadvantages : (1) Fluid energy mill is not suitable for milling of soft, tacky and fibrous materials.

(2) The equipment is expensive, because it needs additional accessories particularly fluid energy source and dust collection equipment.

4) Edge runner mill:



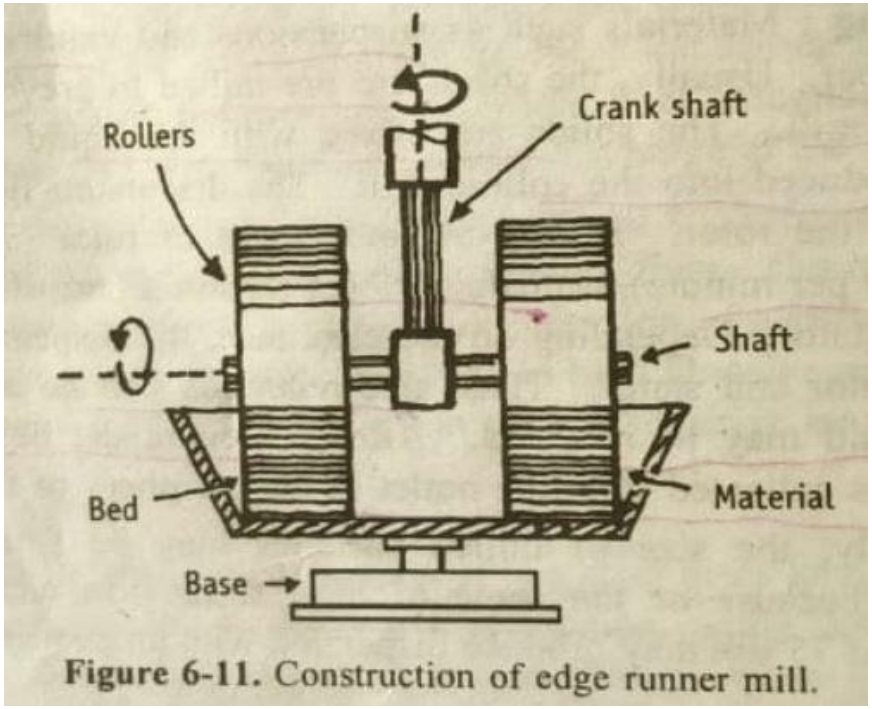


Figure 6-11. Construction of edge runner mill.

- **Principle:** The basic principle behind edge runner mill is **compression** and **shear.**
- **Construction :** Edge runner mill is made up of two heavy rollers and a bed made up of stones and granite. One shaft is present at the center. Rollers are mounted on the horizontal shaft for moving around the bed. One electric motor is fitted at the base of mill for the rotation of rollers.
- **Working:**

  - In first step, material is to be crushed kept on the bed.
  - In the second step, rollers evolves on its central axis and at the same time they also moves on their horizontal axis for providing compression as well as shear force on the material.
  - In third step, after a definite time crushed material is sieved and collected.

Uses : Edge runner mill is used for grinding tough materials to fine powder. It is still used for plant-based products, while more sophisticated mills are used for chemicals and drugs.

Advantages : Edge runner mill does not require attention during operation.

Disadvantages : (1) Edge runner mill occupies more space than other commonly used mills.

(2) Contamination of the product with roller material is possible.

(3) The milling process is time consuming.

(4) It is not used for sticky materials.

(5) Energy consumption is quite high.

5) End runner mill:

- **Principle:** End runner mill is nothing but the automatic mechanical form of mortar and pestle. This mill is as same as the principle of edge runner mill like **compression** and **shear.**
- **Construction:** End runner mill is consists of a mortar and pestle which are made up of steel or porcelain and fixed on a flanged plate. Pestle situated at the end runner mill is very heavy and placed vertically at the corner of the mortar.
- **Working:**
  - In the first step, material to be crushed is placed in the mortar.
  - In the second step, rotation of pestle is started with the help of motor. Scraper is used for guiding the movement of material between mortar and pestle.
  - In the final step, crushed material is sieved and collected.

Uses : End runner mill is suitable for fine grinding. Now a days, this mill is replaced by more efficient and sophisticated milling equipment.

Disadvantage : End runner mill is not suitable for drugs, which are in unbroken or slightly broken conditions.

General Characteristics of Various Types of Mills

Sl. no.	Name of the mill	Action	Product size	Uses	Not used for
1.	Cutter mill	Cutting	20 to 80 mesh	Fibrous, crude (animal and vegetable drug)	Friable material
2.	Roller mill	Compress-ion	20 to 200 mesh	Soft material	Abrasive material
3.	Hammer mill	Impact	4 to 325 mesh	All most all drugs	Abrasive material
4.	Ball mill	Attrition & impact	20 to 200 mesh	Brittle drugs	Soft mate-rial
5.	Fluid energy mill	Attrition & impact	1 to 30 mm	Moderately hard and fri-able material	Soft and sticky material
5.	Edge runner mill	Crushing & shearing	20 to 80 mesh	Almost all drugs	Sticky material
6.	End runner mill	Crushing & shearing	20 to 80 mesh	Almost all drugs	Sticky material
7.	Colloid mill	Shearing	3-75 μm	Almost all drugs	Dry milling

6) Colloid mill:

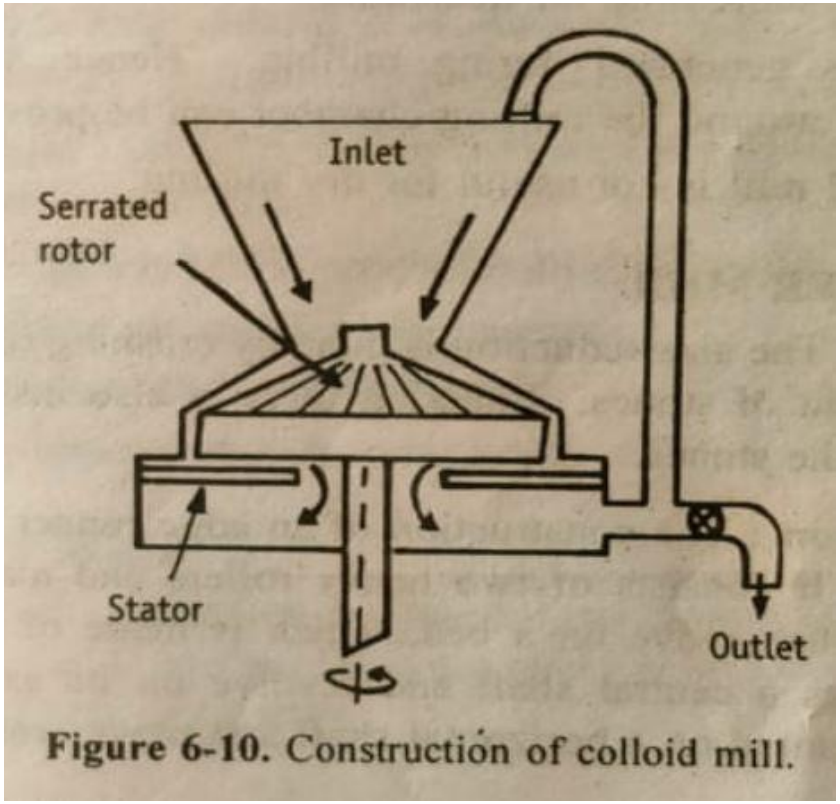


Figure 6-10. Construction of colloid mill.

- **Principle:** Colloid mill works on the principle of **shear.**
- **Construction:** The colloid mill consists of two steel discs , one is high speed rotor and stator with conical milling surface. The clearance between rotor and stator can be adjusted from 0.05 to 0.75mm. Cold water circulation is provided to reduce the temperature.
- **Working:**
  - The solids are mixed with the liquid vehicle before being introduced in the colloid mill.
  - The dispersion flows down and adheres to the rotor.
  - During the movement of rotor (3000 to 20000 rpm), centrifugal force throws a part of the dispersion on to the stator.
  - Depending on the clearance, the dispersion is sheared between rotor and stator, thus size reduction can be achieved.
  - The capacities of colloid mills range from 2 to 3 L/min for small mills to 440 L/min for the larger mills.

Uses : Colloid mill is used for preparing colloidal dispersions, suspensions, emulsions and ointments. It is not used for dry milling. Particle size as small as 3 μm can be obtained. Fibrous material can be milled using rough surfaced rotor and stator.

Advantage : Colloid mill can be sterilised. So it can be used in the production of sterile products.

Disadvantages : (1) Colloid mill tends to incorporate air into the finished product. Therefore, the product should be allowed to rest for some time for deaeration.

(2) Heat is generated during milling. Hence, water circulation facility around the milling chamber can be provided.

(3) Colloid mill is not useful for dry milling.

7) Roller mill

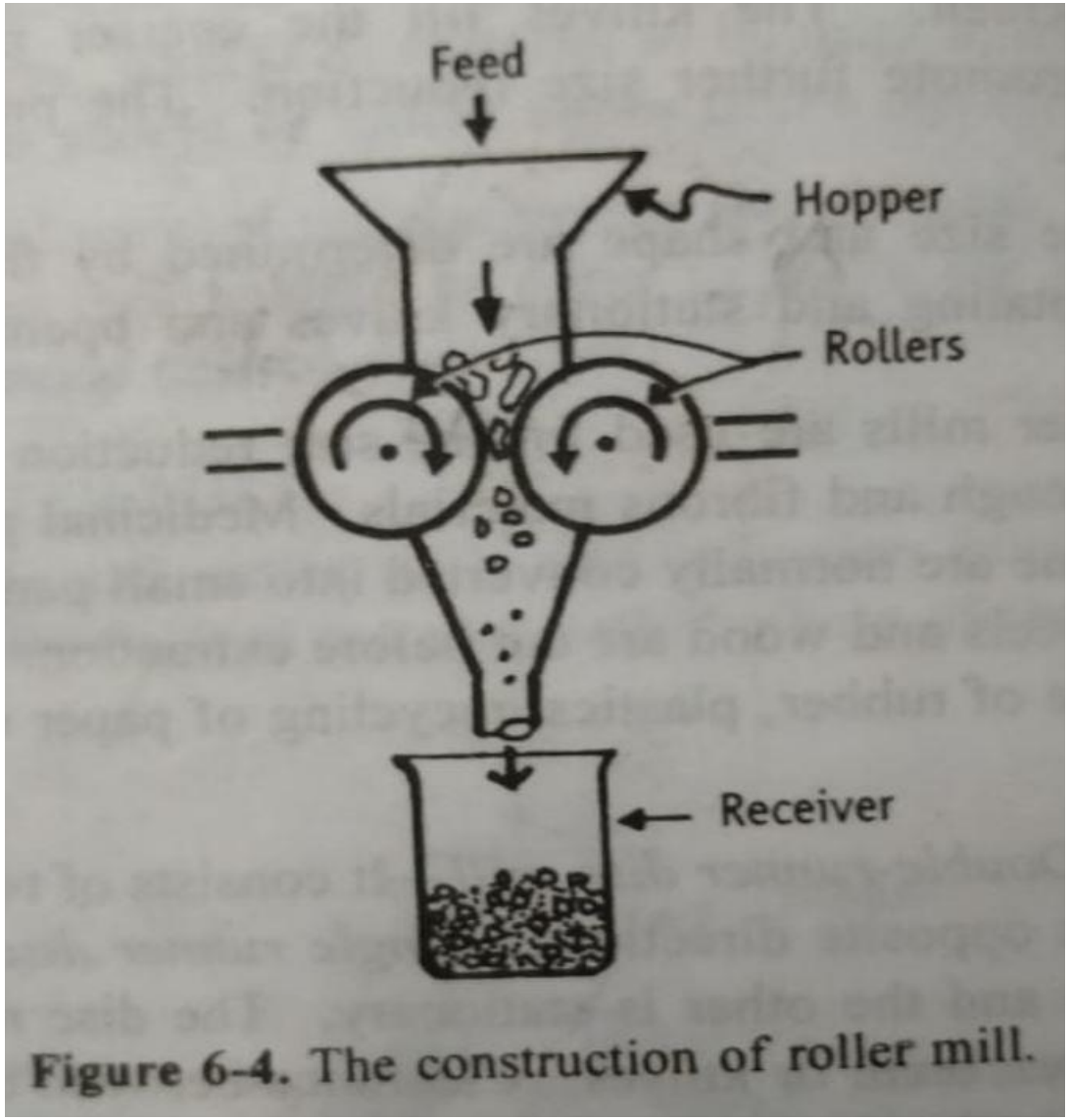


Figure 6-4. The construction of roller mill.

- **Principle:** The material is crushed by the application of **stress**, though **attrition** also influences.
- **Construction:** Roller mill consists of two cylindrical rollers made up of stone or metal, which are mounted horizontally. Rollers can have a diameter ranging from a few mm up to a meter. Rollers are capable of rotating on their longitudinal axes. One of the rollers is driven directly using a motor, while the second one runs freely. The gap between rollers can be controlled to obtain the desired particle size.
- **Working:**

  - The rollers are allowed to rotate.
  - The material is fed from the hooper into the gap between the two rollers.
  - The material is crushed while passing through the rollers under high pressure.
  - The clearance gap can be adjusted to control for desired size reduction.
  - The product is collected into a receiver.

Uses : Roller mill is used for crushing and cracking of seeds before extraction of fixed oils. It is also used to crush soft tissue to help in the penetration of solvent during extraction process.

8) Rotary Cutter Mill

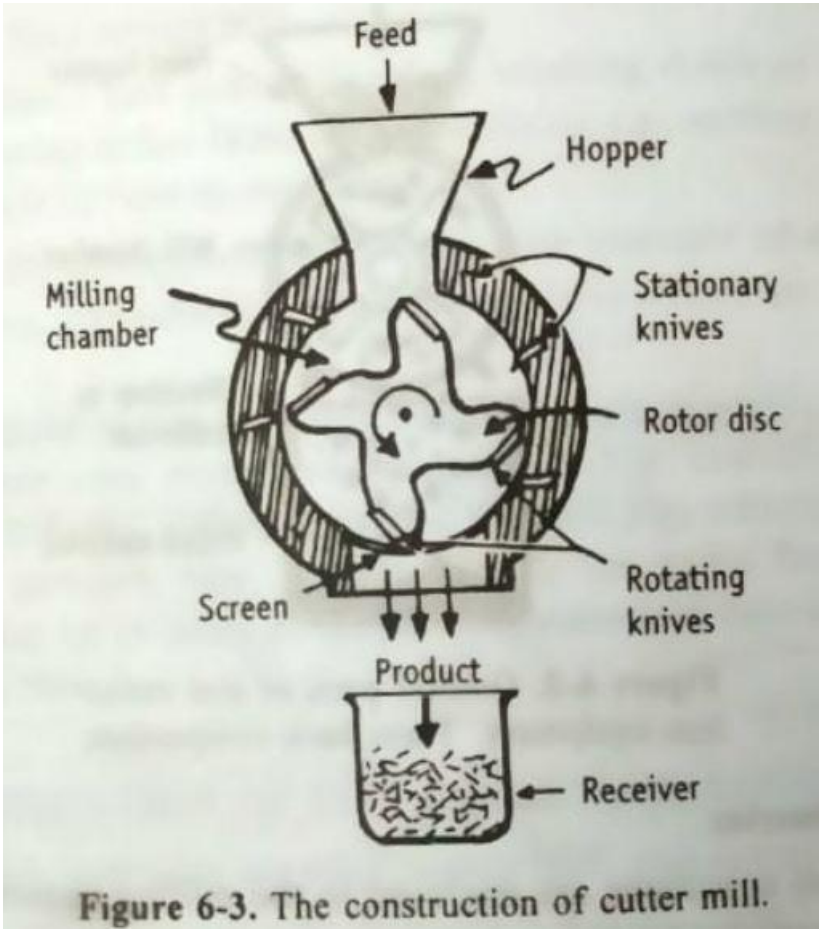


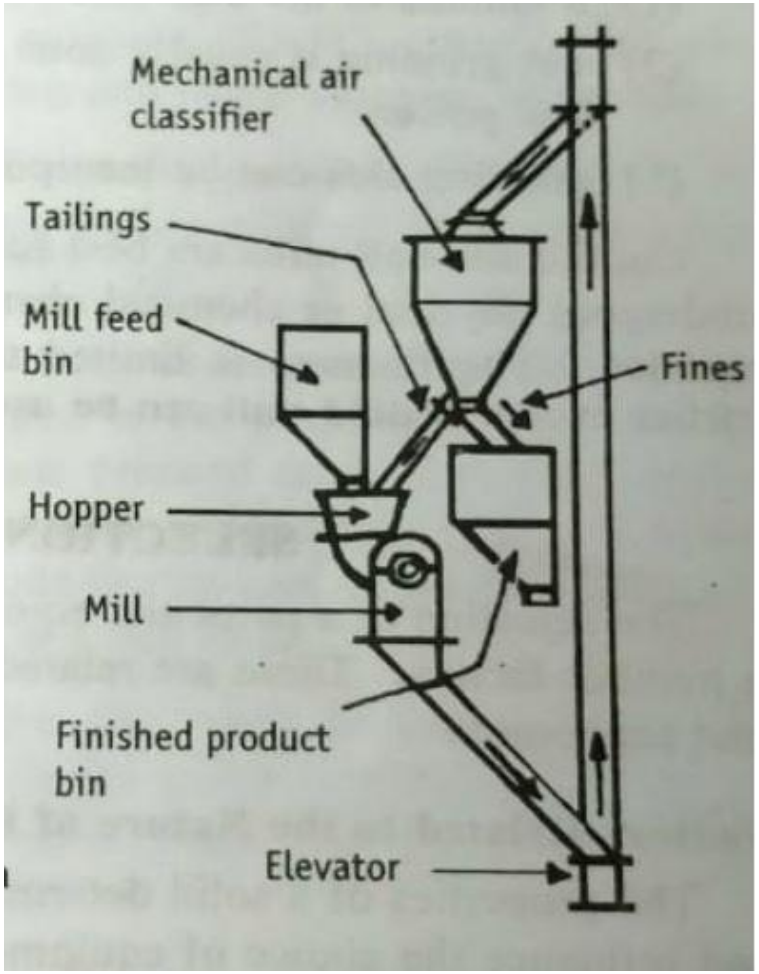
Figure 6-3. The construction of cutter mill.

- **Principle:** In the cutter mill, size reduction involves successive **cutting** or **shearing** the feed material with the help of sharp knives.
- **Construction:** The milling chamber consists of two types of knives, rotating knives and stationary knives. A horizontally mounted rotor disc consists of 2 to 12 knives spaced uniformly. The casing also has several stationary knives. The hooper is placed above it. The bottom of casing holds a screen that controls the size of the material.
- **Working:**

  - The rotor disc is allowed to rotate at speeds from 200 to 900 rpm.
  - The feed material is loaded into the hooper, which flows down by the force of gravity.
  - During the rotation of disc, the material comes very close between the stationary and rotating knives, thereby the material is cut into small pieces.
  - Smaller particles pass through the screen, coarse particles remains up for further size reduction.
  - The product is collected into a receiver.

Uses : Cutter mills are used for the size reduction (finer than 80 to 100 mesh) of tough and fibrous materials. Medicinal plants, plant parts and animal tissue are normally converted into small parts. Soft materials such as roots, peels and wood are cut before extraction. It is also used in the manufacture of rubber, plastics, recycling of paper waste and plastic materials.

9) Open Circuit and Closed Circuit mill



- **An open-circuit mill** is one in which milling operation is carried out in one attempt , i.e., by passing the feed material through the mill to obtain the desired size.
- **A closed-circuit mill** is one in which the discharge from the milling process is passed through a size separation device or classifier, and the oversize particles are returned to the grinding chamber for further size reduction.

The principle of closed circuit grinding is widely used in the pharmaceutical industry. It has the advantages…

a) It provides fine and ultra-fine sizes.

b) It eliminates dust.

c) It eliminates overheating.

d) It produces a product that is free from oversize or undersize.

10) MORTAR AND PESTLE

- This is classic and simplest method.
- In this method, the material is crushed by the application of attrition and pressure.
- It could be made up of metal, wooden or ceramic.
- This equipment cannot be provided with a sieve for continuous removal of fines.

Mills used for Size Reduction

- Cutter mill, Ball mill, Hammer mill, Fluid energy mill, Edge runner mill, End runner mill, Triple roller mill, Colloid mill.

Mill	Size of particles obtained	Materials Handled	Materials can not be handled
Cutter Mill	20-80 #	Fresh vegetable drugs, fibrous materials like, roots and stems, animal tissues, etc.	Friable
Hammer Mill	20-200 #	Soft and wet	Abrasive and hard
Ball Mill	20-200 #	Brittle	Soft and wet
Fluid energy Mill	1-30 mm	Hard and friable	Soft and sticky
Roller Mill	20-200 #	Soft	Abrasive
Colloid Mill	3-75 µm	Almost all	Dry grinding not possible
Edge Runner and End runner Mill	20-80 #	Almost all. Specially spherical shape material like, seeds	Sticky

Thank you…