6

Size Reduction

Size reduction is a process of reducing large solid unit masses (vegetable or chemical substances) into small unit masses, coarse particles or fine particles.

Normally, pharmaceutical powders are *polydisperse*, i.e., consisting particles of different sizes. Polydisperse powders create considerable difficulties in the production of dosage forms. Particles of monosize (equal size) may be ideal for pharmaceutical purposes. In practice, powders with narrow range of size distribution can obviate the problems in processing them further. Size reduction alone is not sufficient to obtain mono-size or narrow size range powder. Therefore, size reduction and size separation should be combined to obtain powders of desired size. (The fundamental aspects on powder, their characteristics and methods of evaluation are given in the book, "*Textbook of Physical Pharmaceutics*" by C.V.S. Subrahmanyam, Vallabh Prakashan, Delhi).

Size reduction process is also termed as *comminution* or *diminution* or *pulverisation.* Normally, size reduction may be achieved by two methods, namely precipitation or mechanical process.

In the *precipitation method*, the substance is dissolved in an appropriate solvent. Subsequently, it is finely precipitated by the addition of another solvent, which is miscible with the first, but in the later the substance is insoluble. This method is suitable for the production of raw materials and bulk drugs. Inorganic chemicals, such as calcium carbonate, magnesium carbonate and yellow mercuric oxide, are prepared by precipitation method.

In the *mechanical process*, the substance is subjected to mechanical forces using grinding equipment (ball mill, roller mill, colloid mill etc.). In general, dry grinding or milling is used in the production of tablets and capsules, while wet grinding is used in the preparation of suspensions, emulsions and ointments. The method of milling is applied either in the production of raw materials or as a part of the production cycle in the manufacture of dosage forms.

Size reduction of substances offers several **advantages.** These are as follows.

Content uniformity : Mixing of different ingredients can be effective, if the particle size is uniform and small. Size reduction ensures this objective. Particles of optimum size are desirable for effective mixing.

As the size of particles is small, the number of particles per unit weight (dose) is large. The larger the number of particles, the better is the mixing. Thus, better content uniformity can be obtained for a given dose. This is particularly important in formulations containing potent and low dose drugs.

Uniform flow : Smaller particle size and controlled size distribution promote the flow of the powder into dies during compression of tablets. The same principles are used in the production of capsules.

Effective extraction of drugs : Smaller particles allow rapid penetration of menstruum or solvent into the tissue or cells of vegetable and animal origin (liver and pancreas). As a result, extraction or leaching of active constituents becomes effective and complete in preparation of galenicals. The time required for extraction can be shortened. For example, pancreas is subjected to grinding action for the extraction of insulin.

Normally, fine powders are preferred for compound powders, while moderately coarse powders are used for the preparation of tinctures. Coarse powder without fines is employed in percolation process.

Effective drying : Drying of a granular mass can be rapid and effective, if the size of granules is small and uniform. Such techniques are used in the production of tablets. Similarly drying of medicinal plant parts can be quick and fast after size reduction.

Improved physical stability : In case of suspensions and emulsions, the rate of sedimentation decreases to a large extent if particle size is small.

Improved dissolution rate : Size reduction increases surface area, which facilitates intimate contact of solid particles and gastric or intestinal juices. Thus, the rate of dissolution enhances. For example, size reduction of griseofulvin led to the development of oral dosage regimen with a dose half that of the originally marketed product. In case of insufflations (preparations inhaled directly into the lungs), the drug should be usually smaller than about 5 µm. Micronized powder of aspirin is used in the preparation of tablets, microfined aspro (analgesic and anti-inflammatory agent).

Improved rate of absorption : The smaller the particle size, the faster is the absorption, because of enhanced dissolution. Chloramphenicol has been shown to absorb faster when given with particle size of 50 µm compared to particle size of 400 µm. Keeping in view of the advantages, pharmacopoeia specifies particle size as a quality control tool. For example, griseofulvin (antifungal antibiotic) should have surface area of not less than 1300 to 1700 metre square per kilogram (as per IP). If it is less, the absorption of the drug decreases. Sulphonamides attain their antibacterial activity at powder sizes of about 1 µm or below. Increased antiseptic action has been demonstrated when the particle size of calomel has been reduced.

The **disadvantages** of size reduction process are as follows.

(1) *Drug degradation* : Drug decomposition is possible due to the heat produced during milling. Thermo-labile substances are the most affected. The increased surface area also facilitates drug decomposition owing to enhanced dissolution.

Cooling support systems are provided to decrease the heat in milling equipment. Drugs containing waxy materials become soft due to heat generated during milling. Therefore the feed is chilled before milling.

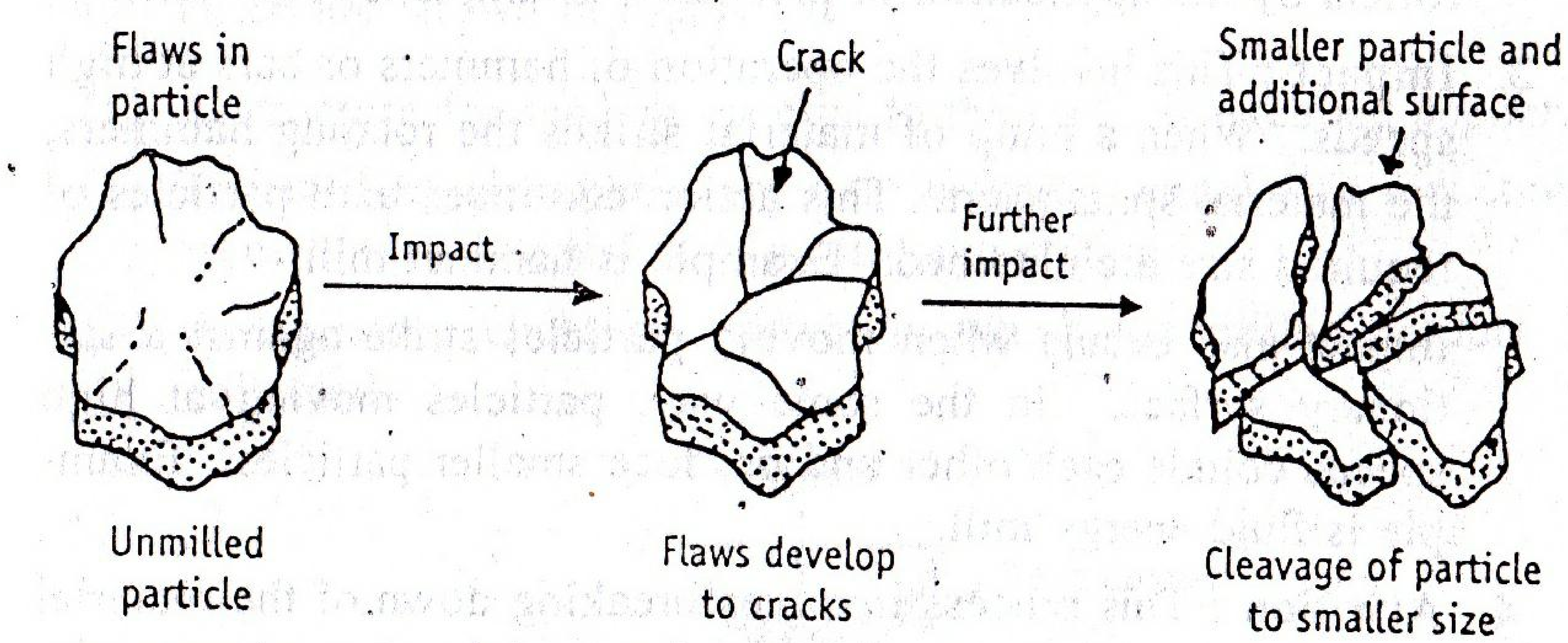
(2) *Poor mixing* : Normally, very small particles possess strong cohesive forces, hence, aggregation of particles is possible. Aggregation inhibits the effective blending of different additives. An increase in surface area may promote the adsorption of air, which may inhibit wettability of the drug during production. Therefore, optimum particle size is desirable to improve blending and to avoid poor mixing.

(3) *Contamination* : During milling and grinding, the grinding surfaces wear off (examples are ceramic or iron equipment), the particles of which are present as impurities in the powder. Such type of mills should be avoided, when drugs of high purity are required.

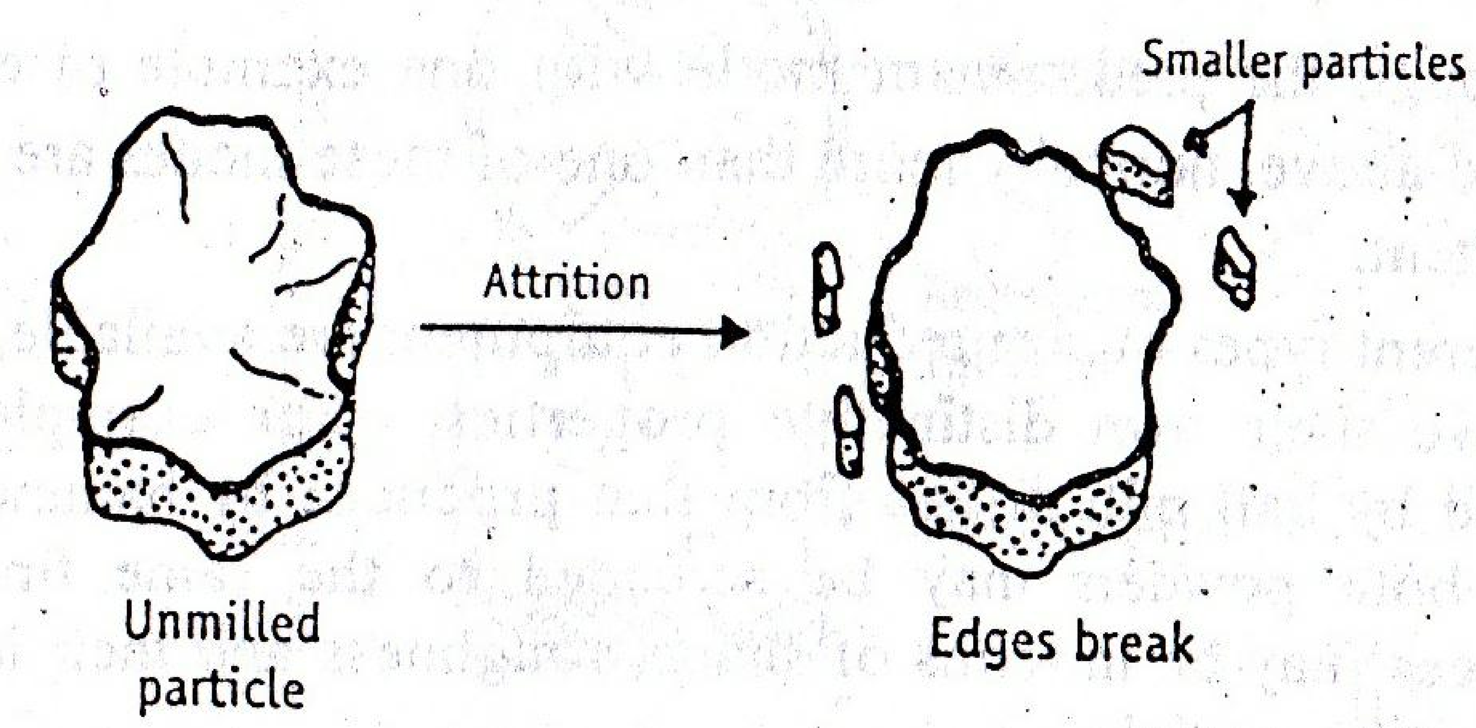
The importance of size reduction is so profound that it is used in the production of all dosage forms such as tablets, capsules, suspensions, emulsions, injections and galenicals. The principles of size reduction, construction and working of equipment are discussed in this chapter. The equipment, which are used in pharmaceutical industry, are given importance.

MECHANISMS OF SIZE REDUCTION

The mechanism of size reduction may vary with the nature of material. Therefore, each drug may require a separate treatment. However, the general mechanism may be described as follows.



(a) Mechanism of size reduction when impact type of stress is applied.



(b) Mechanism of size reduction when attrition type of stress is applied.

Figure 6-1. Mechanisms of size reduction.

Particles, be it amorphous or crystalline, will have flaws to a definite degree. These constitute weak parts in the particles. When sufficient stresses such as impact, shear and compression are applied, the weak flaws develop into cracks, which eventually lead to cleavage (Figure 6-1a). Thus, smaller particles are obtained with additional surface area.

When stress in the form of attrition is applied, the particle surfaces chip and produce small particles (Figure 6-1b).

MODES OF STRESS APPLIED IN SIZE REDUCTION

The mechanisms have demonstrated that stresses of varied nature are required to achieve size reduction. The common modes of size reduction are explained as follows.

1. **Cutting :** The material is cut by means of a sharp blade(s). Example is cutter mill.
2. **Compression :** In this mode, the material is crushed between rollers by the application of pressure. Example is roller mill.
3. **Impact :** This involves the operation of hammers or bars at high speeds. When a lump of material strikes the rotating hammers, the material splits apart. This action continues until particles of required size are obtained. Example is hammer mill.

   Impact also occurs when moving particles strike against a stationary surface. In the same way, particles moving at high speeds collide each other and produce smaller particles. Example is fluid energy mill.
4. **Attrition :** This process involves breaking down of the material by rubbing action between two surfaces, i.e., surface phenomena. Example is fluid energy mill.

Although the predominant mode with one example of equipment is discussed above, normally more than one of these modes are exhibited to some extent.

Different types of size reduction equipment are available, since materials have their own distinctive properties. For example, a powder produced by ball mill differs from that produced by hammer mill, even though both powders may be screened to the same fineness. The differences may be in terms of shape, roughness and their internal pore-structure of a particle.

CLASSIFICATION OF SIZE REDUCTION EQUIPMENT

A. Crushers, examples are edge runner mill, end runner mill.

B. Grinders: (1) Impact mill, example is hammer mill.
(2) Rolling-compression, example is roller mill.

(3) Attrition mills, example is attrition mill.
(4) Tumbling mills, example is ball mill.

C. Ultrafine grinder, example is fluid energy mill.

D. Cutting machine, example is cutter mill.

Some of them are discussed individually in the following sections.

SIZE REDUCTION—EQUIPMENT

The equipment described in this chapter are used in small-scale plants. The basic principles and working remain same even in large-scale operations. Other variants are also included in brief.

General Parts of Size Reduction Equipment

The milling or grinding equipment consists of three basic components. These are shown in Figure 6-2.

(1) A structure for feeding material to the mill. It is called *hopper*.

(2) The milling chamber is the one in which actual size reduction takes place. It consists of a rotor and a stator.

(3) A discharge chute or receiver in which the milled product is collected.

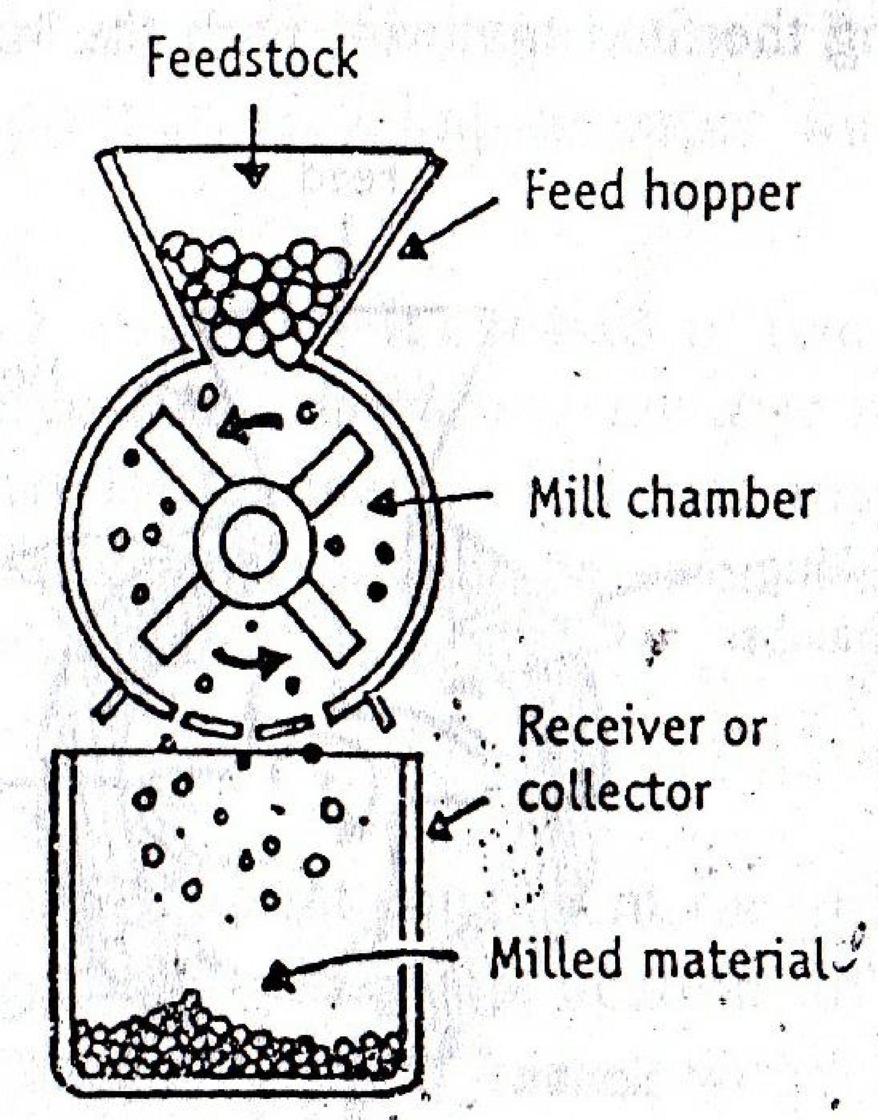


Figure 6-2. General parts of size reduction equipment. Three basic components.

Other Accessories

(1) Sieves or screens are enclosed in the milling chamber to classify the particles by size.

(2) Cyclone separator or centrifugation equipment is fitted to the mills for separation of particles by their sizes.

(3) Dust collectors are employed in order to collect the fine powder and dust that may arise during milling process.

Special Features

(1) Cooling devices are fitted to the chamber to reduce the heat produced during milling.

(2) A closed environment is desirable for milling hygroscopic substances. For this purpose, dehumidified air is necessary.

(3) Closed system with inert atmosphere (nitrogen or carbon dioxide) is desirable for milling of drugs, which are oxidisable or combustible. Similarly, material to be used in the production of parenterals should be milled under sterile environment.

Though general parts of the equipment are identical, several modifications have been incorporated in order to make the process easy to handle and to provide desired discharge.

ROTARY CUTTER MILL

Principle : In the cutter mill, size reduction involves successive cutting or shearing the feed material with the help of sharp knives.

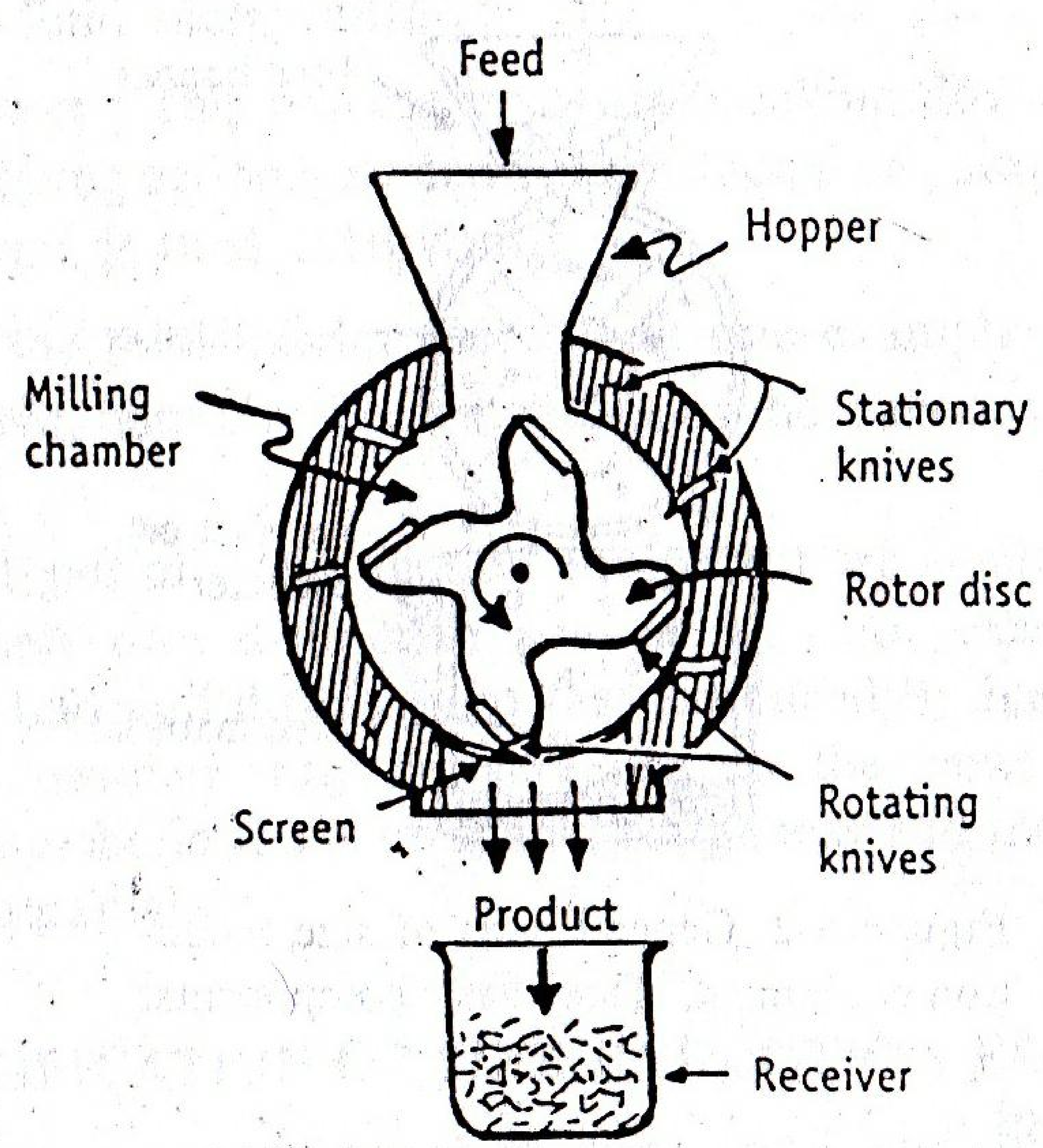


Figure 6-3. The construction of cutter mill.

Construction : The construction of a cutter mill is shown in Figure 6-3. The milling chamber consists of two types of knives, namely 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 hopper is placed above it. The bottom of casing holds a screen that controls the size of the material. Discharge chute is attached at the bottom of the mill.

Working : The rotor disc is allowed to rotate at speeds from 200 to 900 revolutions per minute. The feed material is loaded into the hopper, 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. The knives lift the coarser particles up while rotating and promote further size reduction. The product is collected into a receiver.

The particle size and shape are determined by the rotor size, gap between the rotating and stationary knives and opening of the sieve.

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.

Variants : *Double-runner disc mill*—It consists of two-vertical discs, each rotating in opposite directions. *Single runner disc mill*—only one disc may rotate and the other is stationary. The disc may be provided with cutting faces, teeth or knives. Clearance between the discs may be adjusted to obtain the desirable particle size.

MORTAR AND PESTLE

This is the classical and the simplest equipment for grinding. In this method, the material is crushed by the application of attrition and pressure. The apothecaries used an array of metal, wooden and ceramic mortars and pestles for the production of pills. In this equipment, both mortar and pestle are rotating, whereas a scraper is static. Heavy pestles provide the force of compression, which is an efficient process for wet grinding. This equipment cannot be provided with a sieve for continuous removal of fines.

ROLLER MILL

Principle : The material is crushed (compressed) by the application of stress, though attrition also influences. Stress is applied by rotating heavy wheels, mullers or rollers.

Construction : The construction of a roller mill is shown in Figure 6-4. Roller mill consists of two cylindrical rollers made of stone or metal, which are mounted horizontally. Rollers can have a diameter ranging from a few millimetres up to a metre. Rollers are capable of rotating on their longitudinal axes. Generally, one of the rollers is driven directly using a motor, while the second one runs freely. The gap between the rollers can be controlled to obtain the desired particle size.

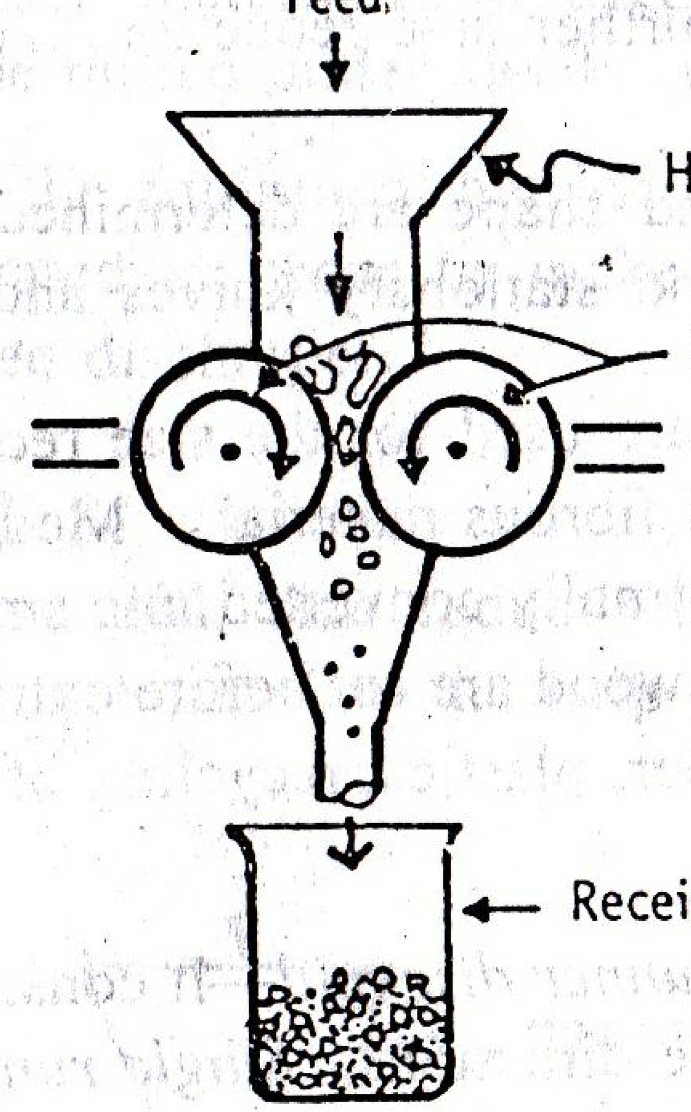


Figure 6-4. The construction of roller mill.

Working : The rollers are allowed to rotate. The material is fed from the hopper into the gap between the two rollers. The material is crushed while passing through the rollers under high pressure. The clearance (gap) between the rollers can be adjusted to control the degree of 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.

Variants : Multiple smooth rollers or corrugated, ribbed, or saw-toothed rollers can provide cutting action also.

HAMMER MILL

Principle : The hammer mill operates on the principle of impact between rapidly moving hammers mounted on a rotor and the powder material.

Construction : The construction of a hammer mill is shown in Figure 6-5. The hammer mill can be either the horizontal or the vertical shaft type. Hammers are usually made of hardened steel, stainless steel with impact surface made of an extremely abrasive resistant material such as haystellite and carbaloy. Stainless steel hammers are sufficient for pharmaceutical purposes.

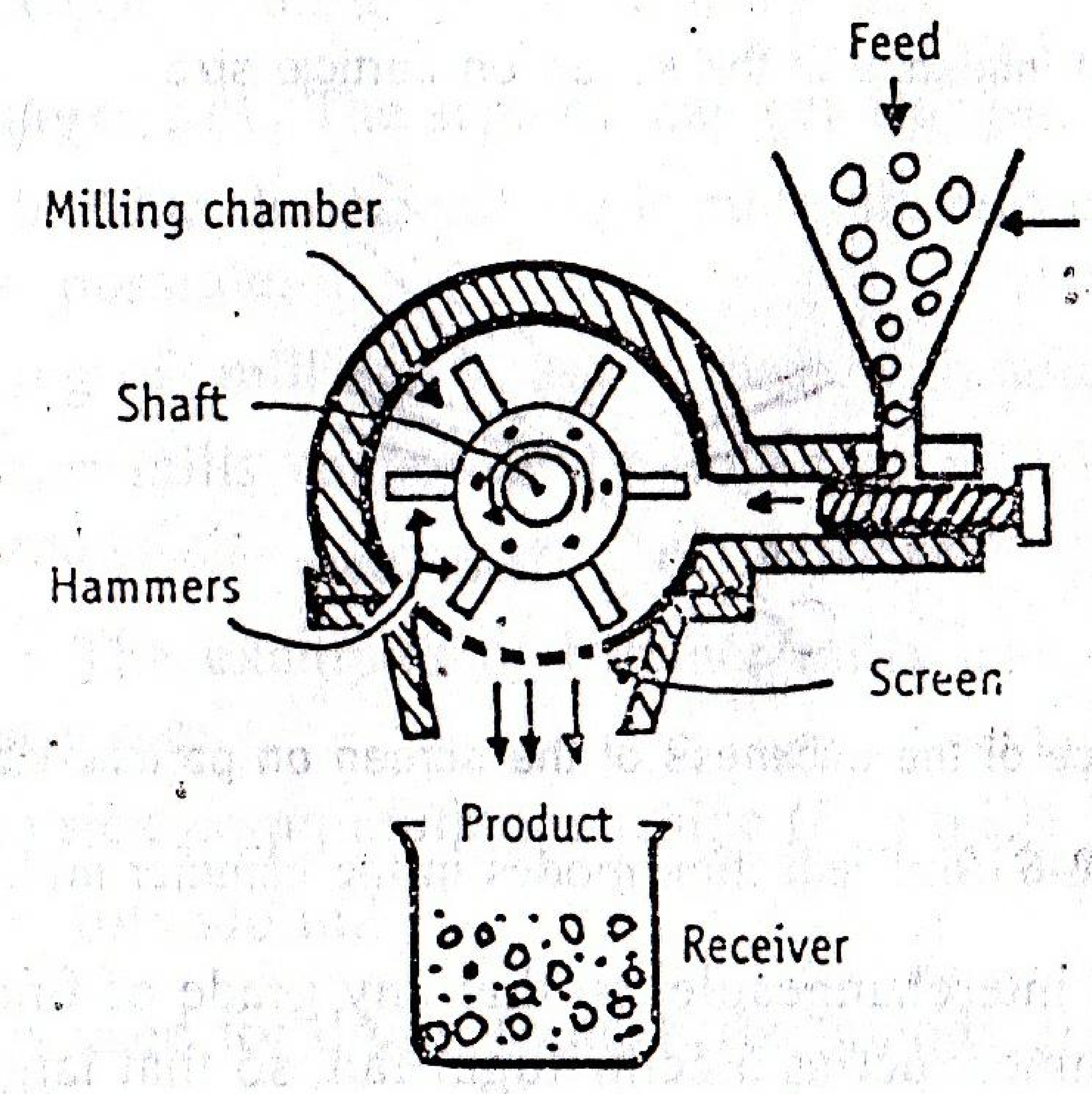
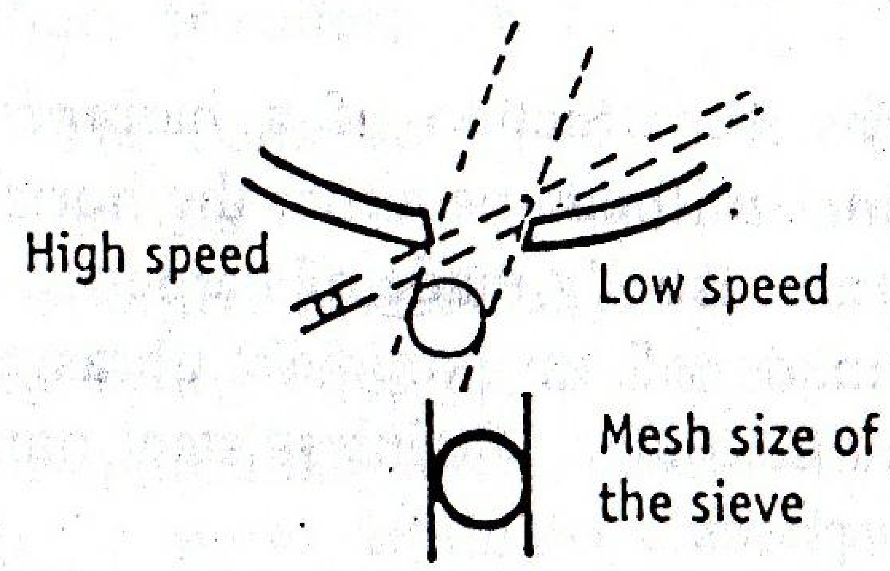


Figure 6-5. The construction of Hammer mill.

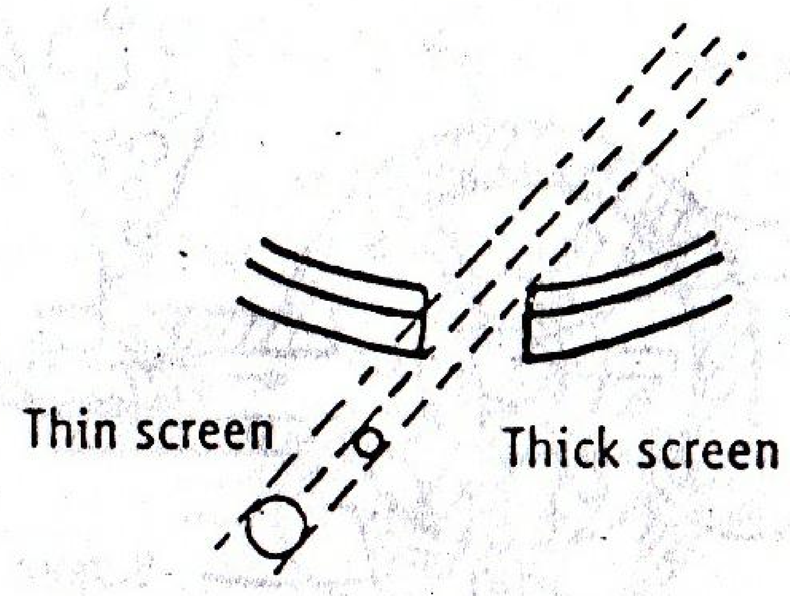
Hammers may take several shapes. Two basic shapes are the stirrup and the bar. Bar-shaped hammers are used extensively in tablet granulation. The hammer blades can be with flat edges or sharp edges or both on each side. Hammers may be either rigid or swing-type. Free swinging type has an advantage that there will be increasing clearance between hammers and screen, if excessive build occurs in the mill.

This unit is enclosed with a chamber containing a grid or removable screen through which the material must pass. These screens are not of woven type. Screens are prepared using metal sheet of varying thickness with perforated holes or slots.

Working : The hammers are allowed to be in continuous motion (8000 to 15000 revolutions per minute). The feed material is placed into the hopper, which flows vertically down and then **horizontally**, while hammers are in continuous motion. These rotating **hammers beat** the material to yield smaller particles. Then, these pass through the screen. Due to the tangential exit, the size of the product is considerably smaller than the aperture of the screen as seen in Figure 6-6a.



(a) Influence of the speed on particle size.



(b) Influence of the thickness of the screen on particle size.

Figure 6-6. Size reduction modes in the hammer mill.

The screens are interchangeable, so that any grade of fineness can be achieved. The hammers act as a centrifugal fan, so that large amount of air is drawn through the mill. In most cases, this is sufficient to counteract the heat generated during milling.

The fineness of the product can be regulated by altering:

- rotor speed,
- feed rate,
- clearance between hammers and grinding plates,
- number and type of hammers,
- size of the discharge opening (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.

Variants : The examples of hammer mills used in pharmaceutical industry are:

(a) Fitzpatrick comminuting machine (Fitz mill)

(b) Stokes tornado mill

Fitz mill is used for drugs, roots, herbs, glands, livers, soaps etc.

Micropulveriser : Micropulveriser has been used for sugar, chemicals, pharmaceuticals and cosmetics. The construction is almost same as shown in Figure 6-5. The liner of the mill housing is made of multiple serrations, which promote the breakage of particles thrown against the wall by the rotating hammers. An air injection feeder can be used to project the feed directly in front of the hammer tips, which are fitted with tungsten carbide inserts. This arrangement increases mill efficiency.

Hammer crusher and *vertical impact pulveriser* work on the principle of impact for size reduction.

BALL MILL OR PEBBLE MILL

These are also known as *tumbling mills*.

Principle : The ball mill works on the principle of impact between the rapidly moving balls and the powder material, both enclosed in a hollow cylinder. At low speeds, the balls roll over each other and attrition (rubbing action) will be the predominant mode of action. Thus, in the ball mill, impact or attrition or both are responsible for the size reduction.

Construction : The construction of a ball mill is shown in Figure 6-7. Ball mill consists of a hollow cylinder, which is mounted on a metallic frame in such a way that it can be rotated on its longitudinal axis. The length of the cylinder is slightly greater than its diameter. The cylinder is made of a metal and is usually lined with chrome. In pharmaceutical industry, sometimes the cylinder is lined with rubber or porcelain.

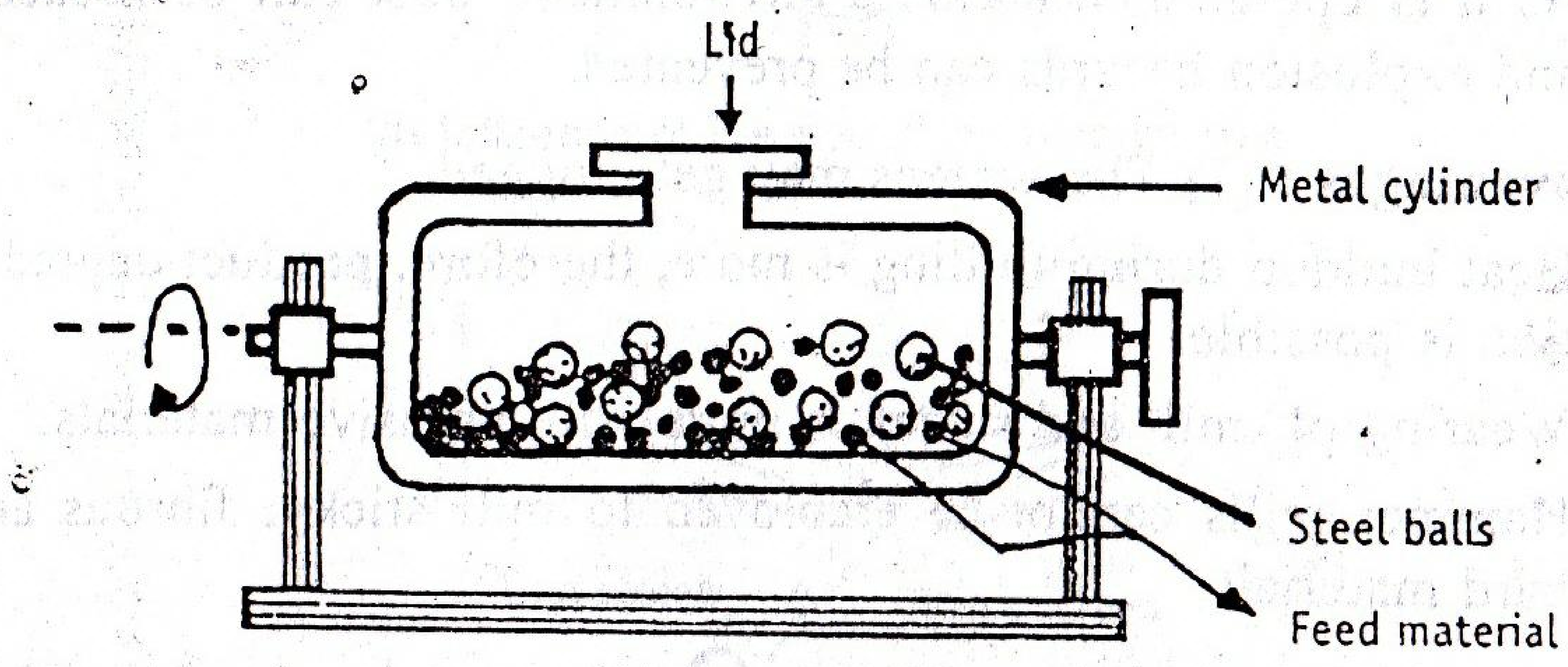


Figure 6-7. The construction of ball mill.

The cylinder contains balls that occupy 30 to 50 % of the mill volume. The weight of the balls is kept constant. The ball size depends on the size of the feed and the diameter of the mill. Balls are made of steel, iron or stoneware. These act as the grinding medium.

Working : The drug to be ground is put into the cylinder of the mill in such a quantity that it is filled to about 60% of the volume (material to void ratio). A fixed number of balls are introduced and the cylinder is closed. The mill is allowed to rotate on its longitudinal axis.

The speed of rotation is very important. At low speeds, the balls roll over each other and attrition will be a predominant mode of stress (Figure 6-8A). The use of small balls (or glass pebbles) is recommended so that the surface is the greatest. This mode of attrition is used for wet grinding. It may be useful to add surface active agents to prevent agglomeration.

At correct speed, the centrifugal force just occurs, as a result the balls are picked up by the mill wall and carried nearly to the top, where they break contact with the wall and fall to the bottom to be picked up (Figure 6-8C). In this manner, impact stress will also be induced and the size reduction is made effective.

At still higher speeds, the balls are thrown out to the wall by centrifugal force. Hence, grinding will not occur. The compression by the balls against the wall will not be sufficient for effective comminution of the substance. (Figure 6-8B)

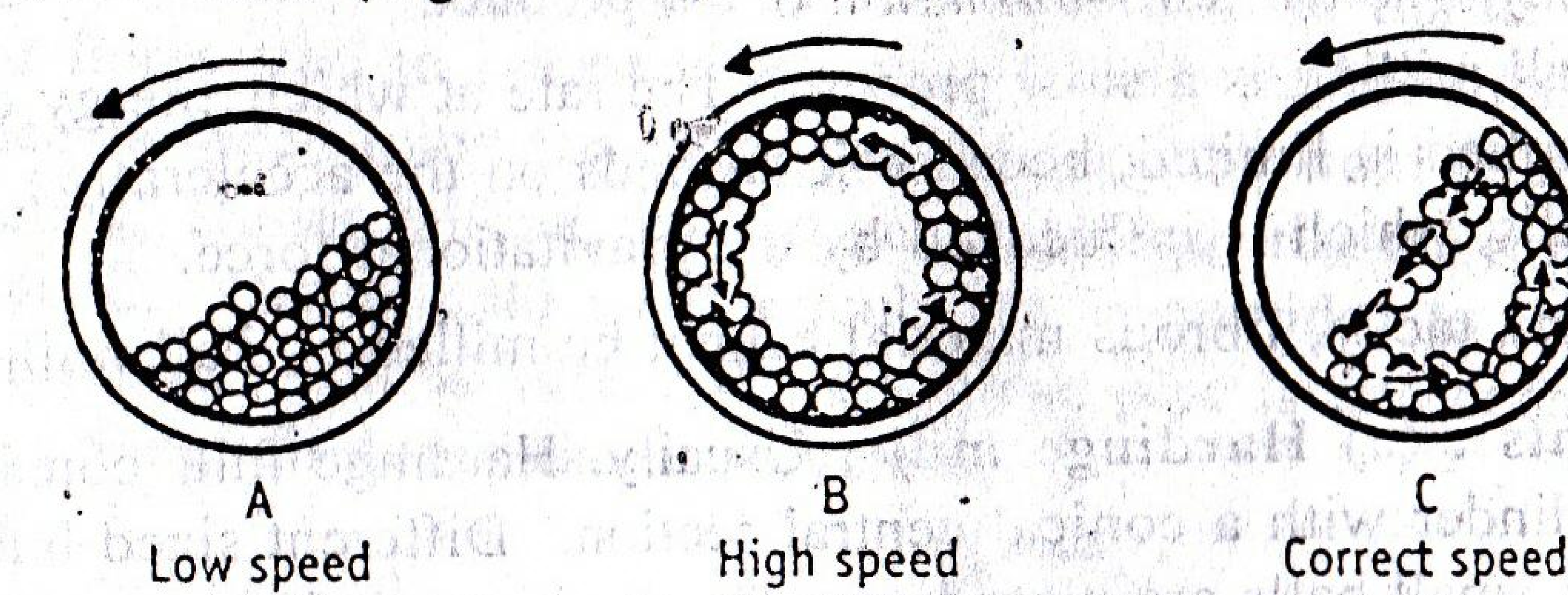


Figure 6-8. The modes of rolling of balls in the ball mill operations.

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.

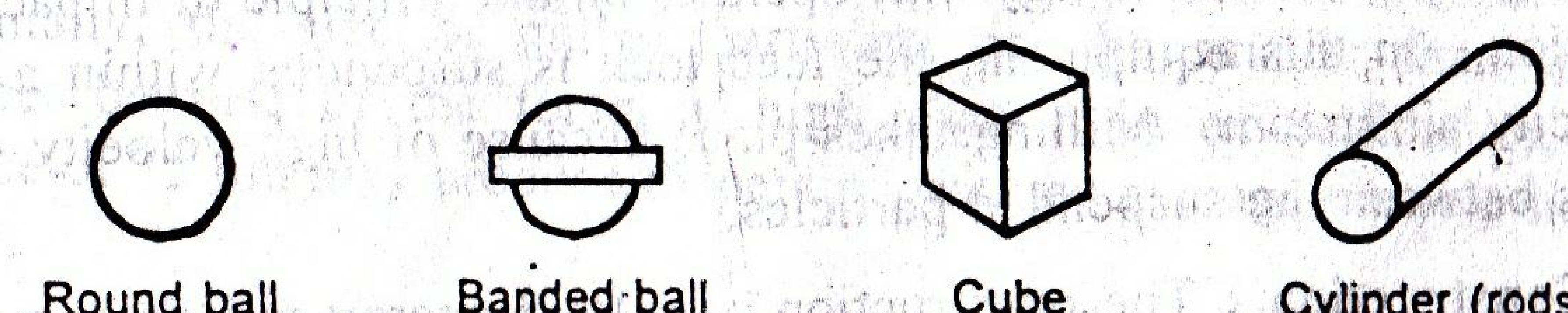
(4) Toxic substances can be ground, as the cylinder is a closed system.

(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.



Commonly used balls

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.

Variants : (a) Hardinge mill : Usually, Hardinge mill consists of hollow cylinder with a conical central section. Different sized balls are used. The small balls are placed near the discharge end, where they can perform the finest grinding. The largest balls remain in the cylindrical feed-end with gradual decrease in size of balls. As the charge rotates, differential centrifugal force causes the finer particles to move towards the discharge end. In this equipment, removal of discharge can be done from the side covers. So the mill operates simultaneously for size reduction as well as classification.

(b) Continuous ball mills : In the simple type of ball mill, it is not possible to remove fines without emptying the mill. Sieving of powder should be done separately. In continuously operating ball mills, a series of chambers are separated by sieves of successively finer mesh size. The equipment is positioned under a small slope so that the powder can pass to the next chamber.

(c) Vibrating ball mills : In vibrating ball mills, the metallic cylinder is supported on a spring base and subjected to forced vibrations induced by electromagnetic means. These have several advantages: (1) Mill is free from rotating parts, (2) It is easy to integrate the mills by classifiers and other ancillary system, (3) Vibrating mill grinds at rates often as high as 20 to 30 times that of the conventional mills, (4) Grinding efficiency is also high.

FLUID ENERGY MILL OR JET MILL OR MICRONIZERS OR ULTRAFINE GRINDERS

Principle : Fluid energy mill operates on the principle of impact and attrition. In this equipment, the feedstock is suspended within a high velocity air stream. Milling takes place because of high velocity collisions between the suspended particles.

Construction : The construction of a fluid energy mill is shown in Figure 6-9. Fluid energy mill consists of an elliptical pipe, which has a height of about 2 metres and diameter may be ranging from 20 to 200 millimetres. The mill surface may be made of either soft stainless steel or tough ceramics. Usually, mills are constructed such that the contact surfaces are merely linings, which can be removed or replaced, if excessively eroded after use.

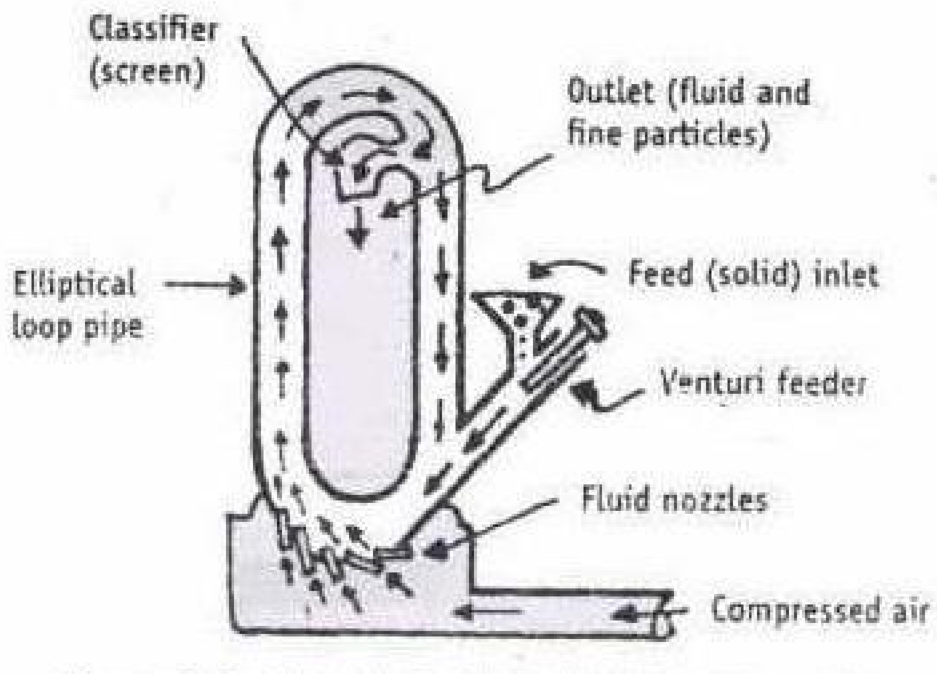


Figure 6-9. The construction of fluid energy mill.

Grinding nozzles (usually two to six) may be placed tangential and~~/or opposed to the initial flow path of a powder~~. Normally, compressed air is used at 600 kilopascals to 1.0 megapascals. Inert gases can be used to minimize or eliminate the oxidation of susceptible compounds.

Venturi feeder is provided in the path of the airflow. An outlet with a classifier (cyclone separator or bag filter) is fitted to allow the escape of air.

Working : Powder is introduced through the inlet of venturi. The air entering through the grinding nozzles transport the powder in the elliptical or circular track of the mill. In the turbulent stream of air, the suspended particles collide with each other and break. Thus, impact and attrition forces operate in size reduction. The resultant small particles (by entrapment of air) are carried to outlet and removed by cyclone or filters.

The coarser particles undergo re-circulation in the chamber on account of its own weight. These re-circulated particles collide again with new in-coming feed stock particles. The powder remains in the mill, until its size is reduced sufficiently. Later it leaves via the sieve. Hence, fluid energy mill produces particles with narrow size distribution.

Some times the particles, which are entrapped by the drag of gas, leave the mill and carried out to a cyclone separator or bag collector for size separation.

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.

Variants : *Centrifugal-impact pulverizer*—In centrifugal impact pulverizers, a rotor is spinned to induce high centrifugal force on the feed particles. The particles move towards the impactors, which are set at the periphery of the rotor. On striking these impactors, the material is further hurled against the outer casing where final reduction is achieved. The material is removed from the conical discharge at the bottom.

Particle size reduction in the range of 10 to 325 meshes can be obtained with this type of mill with minimum fines. Centrifugal impact pulverizers have been used for the size reduction of a variety of materials ranging from soft organic molecules to hard abrasive materials. It is also well suited for the size reduction of heat sensitive materials.

COLLOID MILL

Principle : Colloid mill consists of two steel discs having very small clearance between them. One disc is rotating, while the other one is stationary. When the material is passed through these discs, they get sheared. Thus, coarse particles are broken down into small particles due to shear.

Construction : The construction of a colloid mill is shown in Figure 6-10. The colloid mill consists of high-speed rotor and stator with conical milling surface. The milling surfaces may be smooth surfaced or rough surfaced. Rough surfaced mills are used for fibrous material because fibres tend to interlock and clog smooth surfaced mills. The clearance between rotor and stator can be adjusted from 0.05 to 0.75 millimetres. During milling, the heat generated may rise the temperature up to 40°C. Hence, cold water circulation is provided to reduce the temperature as much as 20°C. The discharge pipe is also connected to hopper, so that discharge can be recycled.

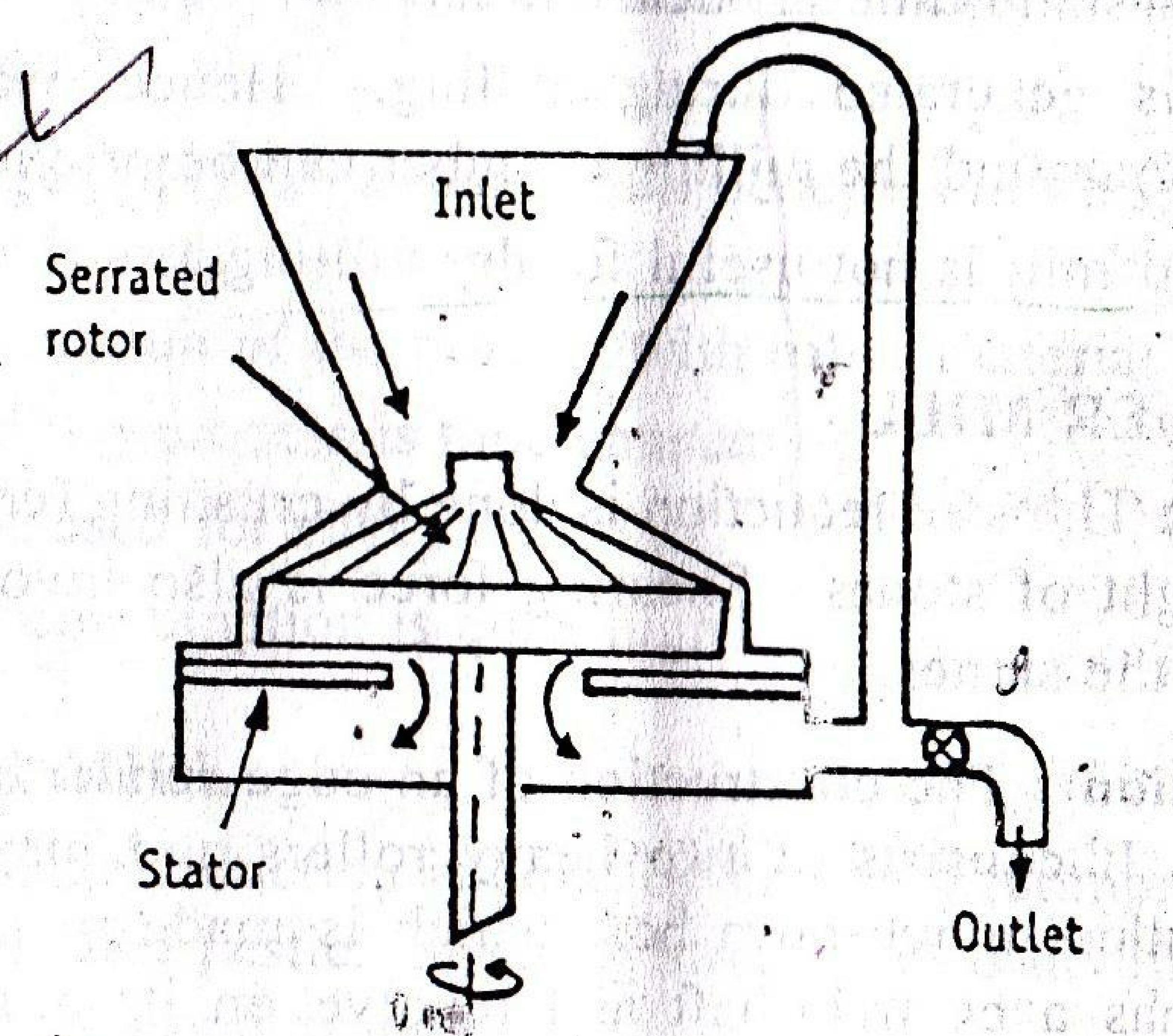


Figure 6-10. Construction of colloid mill.

Working : Materials such as suspensions and emulsions are placed in the hopper. Usually, the solids are pre-milled to prevent the damage of colloid mill. The solids are mixed with the liquid vehicle before being introduced into the colloid mill. The dispersion flows down and adheres to the rotor. During the movement of rotor (3000 to 20000 revolutions per minute), 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 milled liquid may be recycled. After achieving the desired size, the discharge is collected from the outlet in the periphery of the housing.

Normally, the size of milled particles may be smaller than the clearance, because of the force of high shear. In emulsification, a clearance of 75 µm may produce dispersion with an average particle size of 3 µm.

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.

EDGE RUNNER MILL

Principle : The size reduction is done by crushing (compression) due to heavy weight of stones. Shearing force is also involved during the movement of the stones.

Construction : The construction of an edge runner mill is shown in Figure 6-11. It consists of two heavy rollers and may weigh several tons. The rollers move on a bed, which is made of stone or granite. Each roller has a central shaft and revolve on its axis. Further, the rollers are mounted on a horizontal shaft and move around the bed.

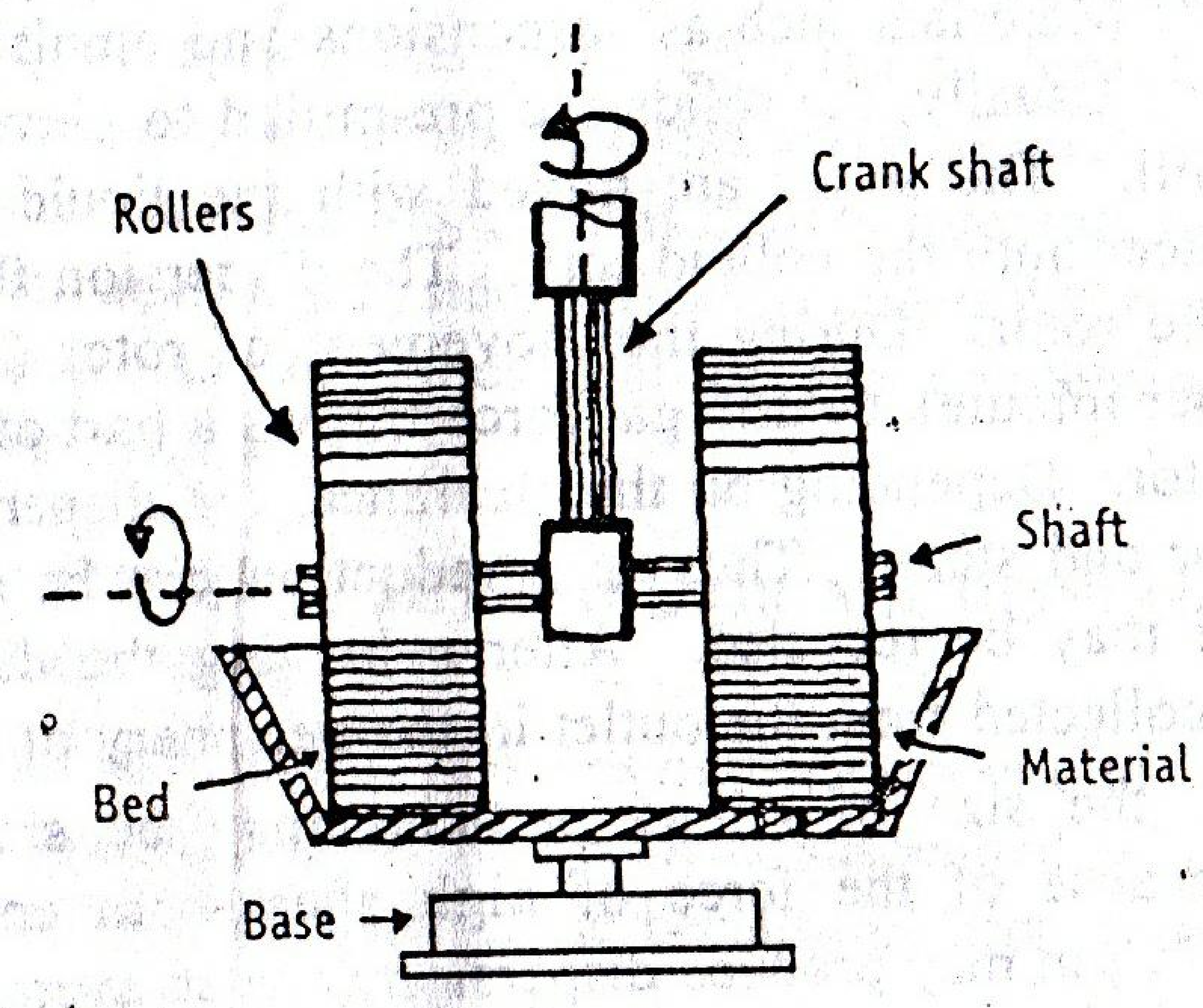


Figure 6-11. Construction of edge runner mill.

Working : The material to be ground is placed on the bed. With the help of a scrapper, it is kept in the path of the stone wheel. The stones revolve on its axis, and at the same time travel round the shallow stone bed. The outer part of the wheel has to travel a greater distance than the inner, so that size reduction is achieved by shearing as well as crushing. The material is ground for a definite period. The powder is collected and passed through a sieve to get powder of the required size. It is a batch process.

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.

END RUNNER MILL

Principle : Size reduction is done by crushing (compression) due to heavy weight of steel pestle. Shearing stress is also involved during the movement of mortar and pestle.

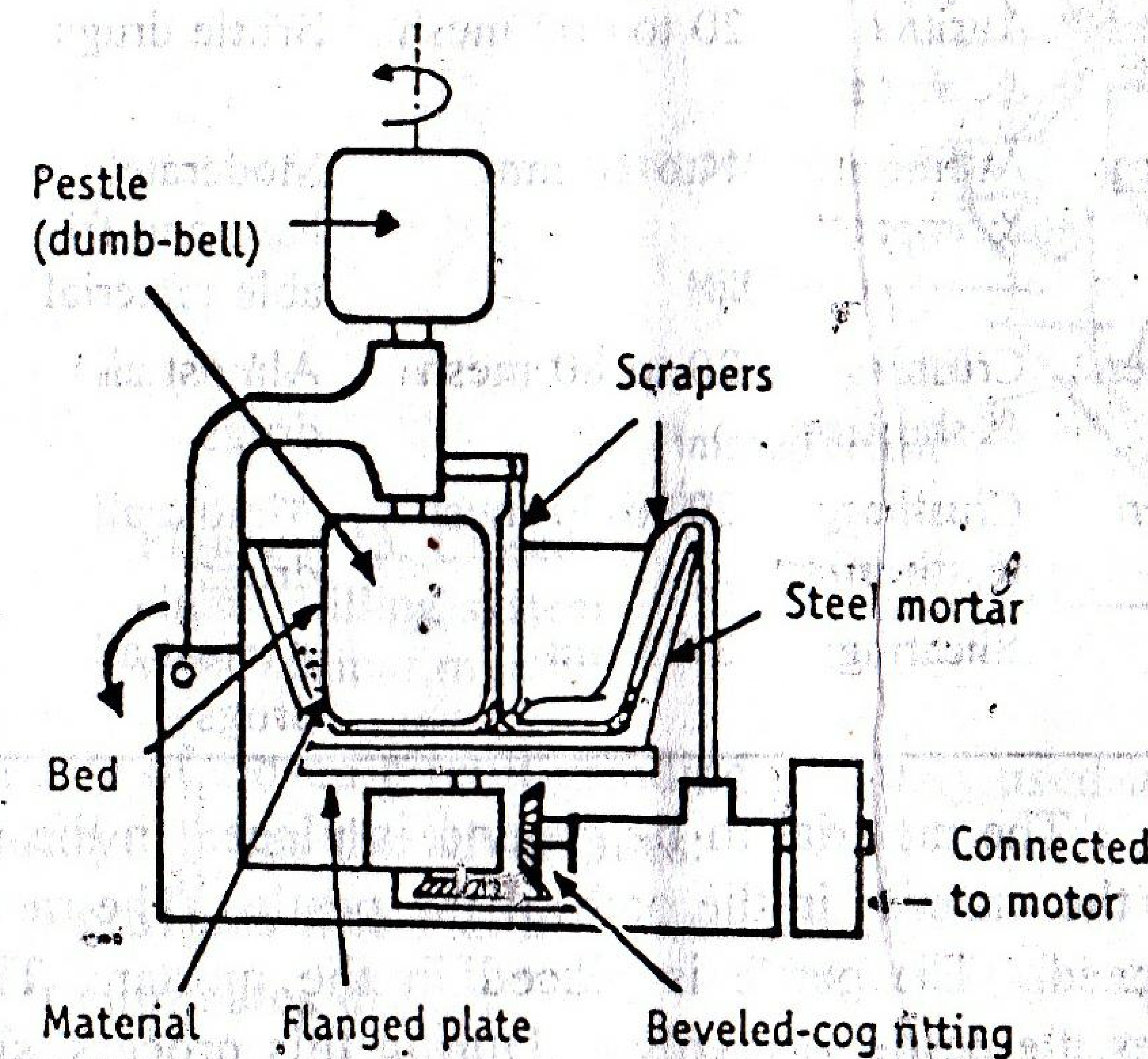


Figure 6-12. Construction of end runner mill.

Construction : The construction of an end runner mill is shown in Figure 6-12. It is considered as a mechanical mortar and pestle. It consists of a steel mortar, which is fixed to a flanged plate. Underneath the flanged plate, a bevelled cog fitting is attached to a horizontal shaft bearing a pulley. Hence, the plate with mortar can be rotated at a high speed.

The pestle is dumb-bell shaped so that balancing and efficient grinding by its weight can be achieved. The bottom of pestle is flat rather than round. The pestle carries an arm, which is hinged. By this arrangement, the pestle can be raised from the mortar to facilitate emptying and cleaning. The narrow central portion of the pestle is longer than the band of the arm around it. Hence, pestle can rise and fall over the material in the mortar.

TABLE 6-1

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	Compression	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 material
5.	Fluid energy mill	Attrition & impact	1 to 30 mm	Moderately hard and friable 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

Working : The material to be ground is placed in the mortar. The scraper puts the material in the path of the pestle. The mortar revolves at a high speed. The pestle is placed in the mortar. The revolving mortar causes the pestle to revolve. During this process, size reduction is achieved by shearing as well as crushing. The material is collected and passed through a sieve to get the powder of desired size.

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.

In summary, several size reduction equipment are described. Some general characteristics of various types of mills are given in Table 6-1.

OPEN CIRCUIT AND CLOSED CIRCUIT MILL

The size reduction process may be achieved in open circuit or closed circuit conditions.

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..

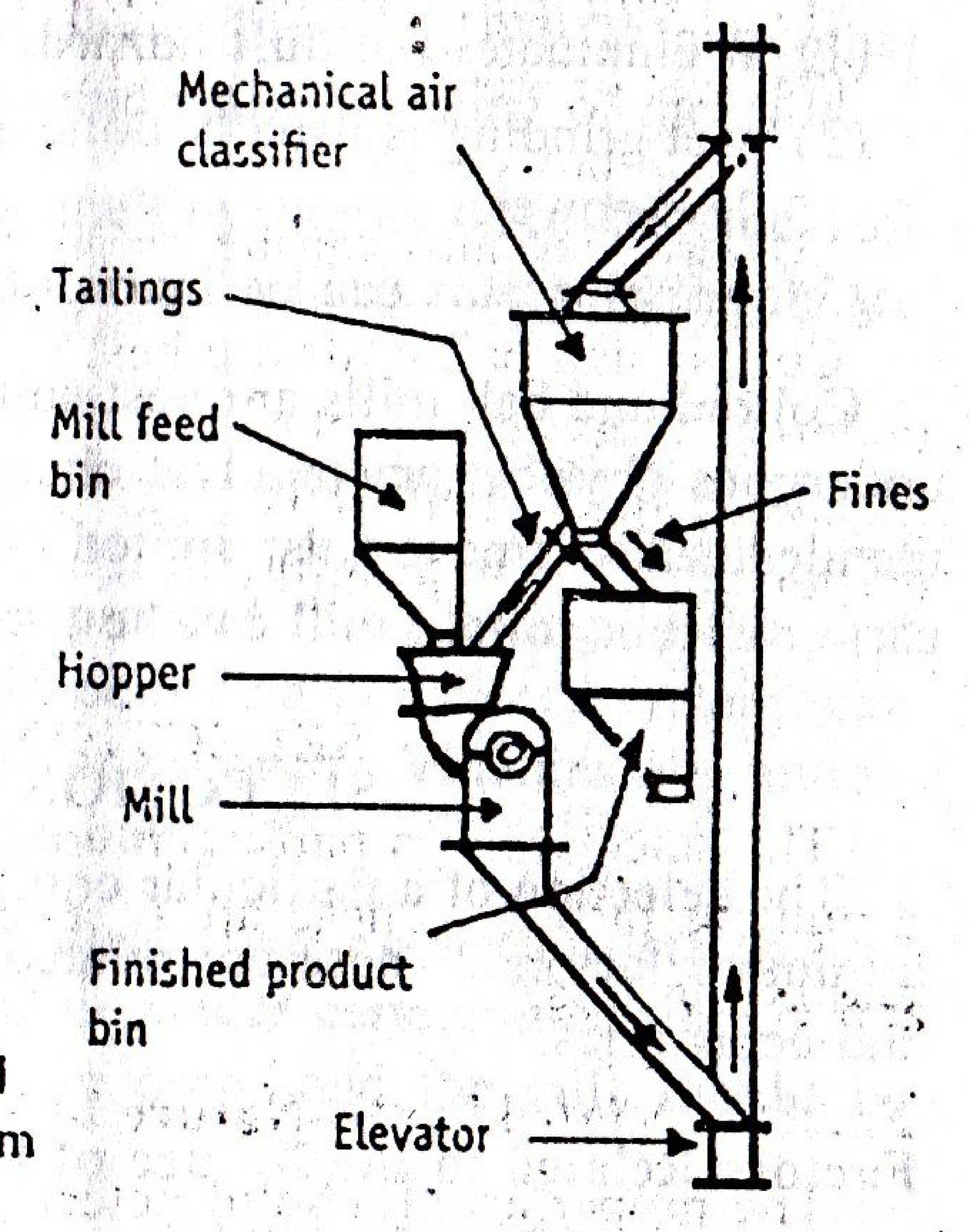


Figure 6-13. Closed circuit milling system with hammer mill.

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.

A closed circuit with an air classifier is shown in Figure 6-13. In this type, size reduction is combined with size classification. The working of hammer mill is illustrated in Figure 6-13. The coarse material returning to the mill by a classifier is known as *circulating load.*

Dry and Wet Grinding

The use of a product and subsequent steps mainly decide the type of equipment used. In the preparation of colloidal dispersions, suspensions, emulsions and ointments, wet grinding offers advantages. In the production of suspensions and emulsions, wet grinding has become an integral part of the processing. For example, mill can be used as mixing equipment. Triple roller mill, colloid mill are used for such a purpose.

In practice, it is found that finer size can be achieved by wet grinding than by dry grinding. Wet grinding is used in the production of flocculated suspensions. In wet grinding, surfactants are added to attain particle size of 0.5 μm. The advantages of wet grinding are that:

(1) it eliminates the dust hazards,
(2) wet grinding is usually done at low speed, therefore, it consumes less power,
(3) grinding aids can be incorporated.

Colloid and ball mills are best suited for wet grinding. If the product undergoes physical or chemical changes in water, dry milling is recommended. The fineness is limited to 100 μm. All the mills reported earlier except colloid mill can be used for dry grinding.

SELECTION OF A MILL

The selection of a particular equipment for size reduction depends on a number factors. These are related to the feed, milled product, safety, and economics.

Factors Related to the Nature of Raw Materials

The properties of a solid determine its ability to resist size reduction and influence the choice of equipment used for milling. Some physical properties of the feed are as follows.

Hard materials : Iodine and pumice are hard and abrasive. In general, hard materials are most difficult to comminute. For iodine, hammer mill or fluid energy mill is used. Size reduction process of such materials can lead to abrasive wear of milling parts, which then cause contamination.

Fibrous materials : Glycyrrhiza, rauwolfia, ginger etc., are fibrous in nature and cannot be crushed by pressure or impact. Fibrous materials are tough in nature. They must be teared by a cutter. Nux vomica and ipecacuanha are processed in two stages to get fine powders.

Friable materials : Sucrose and dried filter-cake are friable and tend to fracture along well-defined planes. Brittle substances can be easily converted to smaller particles. Such materials are milled by the mechanisms such as attrition, impact or pressure. For example, sugar is milled using hammer and fluid energy mills.

Elastic materials : Synthetic gums, waxes and resins become soft and plastic during milling. These low-melting substances should be chilled before milling. Such materials are milled using hammer, colloid or fluid energy mill.

Hygroscopic materials : Substances such as potassium carbonate absorb moisture rapidly. This wet mass sticks and clogs the mill. They are prepared in a closed system such as porcelain ball mill.

Solvated materials : Sodium sulphate ($Na_2SO_4.10H_2O$) and other hydrates liberate water during milling and cause clogging of the mill.

Melting point : Solids with low melting points often become soft and melt owing to the heat generated during milling. Such materials are chilled before milling.

Thermolability : Certain substances undergo degradation reactions such as hydrolysis and oxidation due to the presence of moisture and atmospheric oxygen. Such reactions proceed faster owing to the heat produced during milling. They should be milled in a closed system with an inert atmosphere of carbon dioxide or nitrogen. Vitamins and antibiotics are milled using fluid energy and ball mills.

Flammability : Almost any fine dust, such as dextrin, starch and sulphur, is a potential explosive mixture under certain conditions. All electrical switches should be explosive proof and the mill should be properly grounded (earthed).

Particle size of the feed : For a mill to operate satisfactorily, the feed should be of proper size. For example, pretreatment of fibrous materials with high pressure rollers or cutters facilitates further comminution.

Moisture content : Presence of more than 5% water hinders the milling process and produces a sticky mass. The effect is more pronounced, when the concentration of water is more. In general, materials with moisture content below 5% are suitable for dry grinding and above 50% are suitable for wet grinding.

Pretreatment : For the mill to operate satisfactorily, the feed should be of a proper size and enter the equipment at a fairly uniform rate. Therefore, a pretreatment step should be included. For example, fibrous material should be treated with cutter or roller, which can facilitate further comminution.

Factors Related to the Nature of Finished Product

The nature of finished (milled) product also influences the selection of the equipment.

Particle size : If extreme size control is necessary, it may be essential to recycle the larger particles. This can be achieved by screening the discharge material and returning the over size particles for a second time milling. Moderately coarse or coarse powders with a minimum of fine powder are easily obtained by using a high-speed impact mill. For example, cascara, liquorice, belladonna leaves and roots are easily broken down by impact mill.

For example, particle size of griseofulvin is critical in the production. Similarly the particle size is also critical in the suspension of penicillin G procaine for intra-muscular injection due to its syringeability.

Ease of sterilisation : When preparations are intended for parenteral and ophthalmic uses, size reduction should be conducted in a sterile environment. The equipment should be sterilisable. Ball mills and fluid energy mills are suitable for this purpose.

Contamination of milled materials : In case of potent drugs and low dose products, contamination of the product should be avoided. Use of equipment that is free from wearing of mill parts is preferred. Fluid energy mill is suitable for this purpose.

In addition to the end use of a product, subsequent processing steps mainly determine the choice of wet or dry milling. In the preparation of colloidal dispersions, suspensions, emulsions and ointments, wet grinding offers advantages in terms of size reduction of materials, elimination of dust hazards. Thus, wet grinding has become an integral part of the processing of the above dosage forms. The same mill can also be used as mixing equipment. Examples are triple roller mill and colloid mill.

Factors Related to Safety

The factors related to safety are explosivity, irritability and toxicity. During milling, fine dust of drug arises which may become flammable

under certain conditions. Explosion hazards of non-metallic materials, such as sulphur, starch and wood floor, are often appreciable. Metal powders pose a hazard because of their flammability. The useful precautions are:

(a) isolate the mill.

(b) use of non-sparking material of construction.

Stainless steel has less sparking tendency than ordinary steel or forging.

Factors Related to the Economy

Cost, power consumption, space occupied and labour costs are some of the economic factors that determine the selection of a mill.

Cost : Where the particle size control is not critical, the cost decides the type of equipment. In general, the cost of the size reduction increases, as the particle size decreases. Therefore, it is economically undesirable to reduce the particle size to a finer degree than necessary.

THEORIES OF COMMINUTION

Mechanical Behaviour of Solids

When various modes of stress are applied on a powder, the particles get strained. This stress-strain relationship is shown in Figure 6-14.

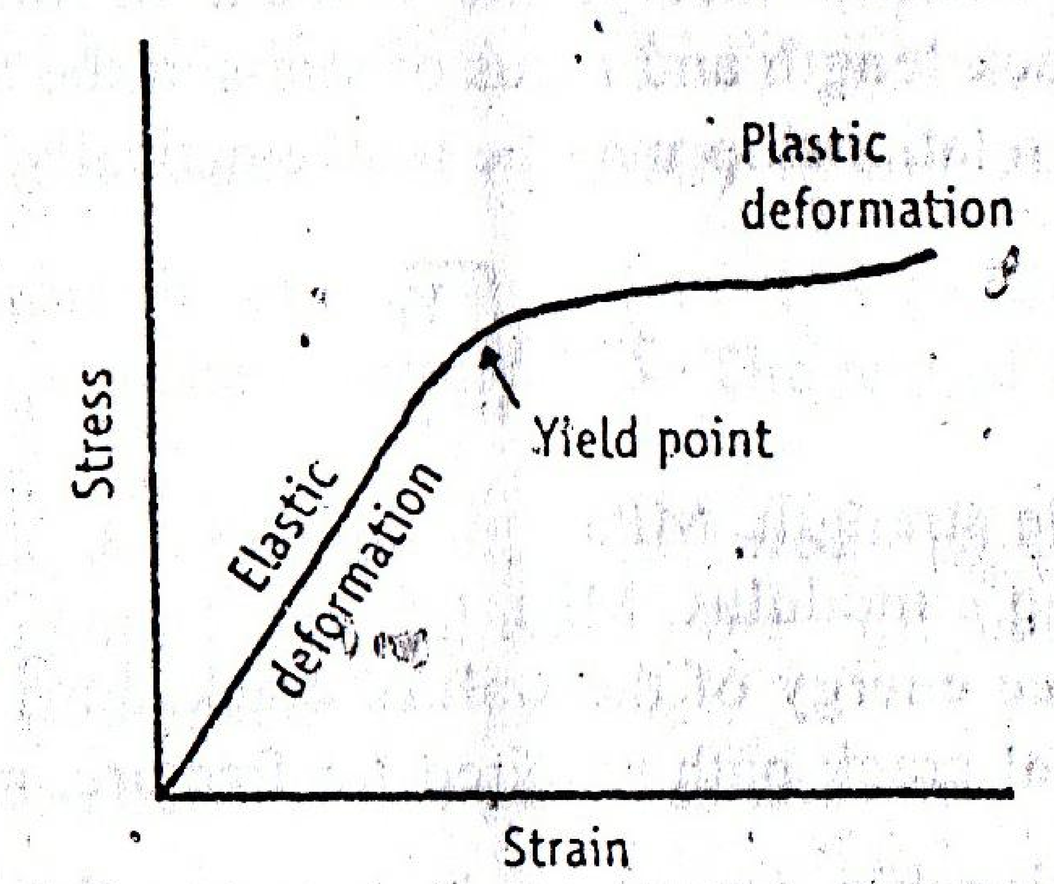


Figure 6-14. Stress-strain curve for a solid.

- In Figure 6-14, the initial linear portion is defined by Hooke's law. It states that stress is proportional to strain. The slope of linear portion represents *Young's modulus*. It expresses the stiffness or softness in megapascals.
- If the force of impact (stress) does not exceed the elastic limit (region of Hooke's law), the material is reversibly deformed.

When the force is removed, the particle returns to original condition. The elastic limit is known as *yield value*. The stress energy in the deformed particle appears as heat. Example is plastic material such as polymer.

- The stress-strain curve becomes nonlinear at the yield point. This is a measure of the resistance to permanent deformation.
- Beyond the yield point, the region represents irreversible plastic deformation.
- The area under the curve represents the fracture toughness (or modulus of toughness). This is an approximate measure of the impact strength of the material. Fracture of a particle can be obtained when the force exceeds the elastic limit.

Theories of Size Reduction

(1) According to Griffith theory, all solids contain flaws and microscopic cracks. A *flaw* is any structural weakness that may develop into a crack under strain. The weakest flaw in a particle determines its fracture strength. It controls the number of particles produced by fracture. The particles with the weakest flaw fractures most easily and produce largest possible pieces. In the next step, another weakest flaw fractures. This process continues until all flaws are fractured. The particle size produced in this process may not be the desirable one. However, Griffith theory is simple and explains the size reduction process reasonably.

According to Griffith theory, the amount of force to be applied depends on the crack length and focus of stress at the atomic bond of the crack apex. This relationship may be mathematically expressed as:

$$T = \sqrt{\frac{Y\varepsilon}{c}} \qquad (1)$$

where T = tensile strength, MPa
Y = Young's modulus, MPa
ε = surface energy of the wall of crack, J/m^2
c = critical crack path required for fracture, m

A linear relationship (equation 1) between the square of tensile strength of minerals and the critical height for drop weight impact suggests that the square of tensile strength is a useful criterion of impact fracture.

(2) If flaws are not present in a particle, the force of milling produces new flaws. The useful work in milling is proportional to the length of new crack formed. The mechanism of creating new flaws in a particle is as follows.

Usually, the surface of particles is irregular. The applied force is initially taken on the high portion of the surface. As a result, high stress and increased temperature may be set up locally in the particle. The bonds at this place become weak, which may be responsible for creating flaws. The particle further absorbs applied strain energy and is deformed. The strain energy required to extend the crack to fracture is proportional to the length of the crack formed. This energy is supplied by the flow of the residual strain energy to the crack.

3. Not all materials exhibit this type of brittle behaviour. They resist fracture even at much larger stresses, because these are tougher. They undergo plastic flow, which allows strain energy relaxation without crack propagation. When plastic flow occurs, atoms or molecules slip over one another and this process of deformation requires energy.

ENERGY FOR COMMINUTION

Size reduction begins with the opening of small flaws that were initially present. Based on the probability, larger particles may have numerous flaws and readily fracture when compared to smaller particles with fewer flaws. The supplied energy is used to:

- Increase new surface area from flaws.
- Initiate flaws or cracks in the particle.

This phenomenon is observed generally in fine grinding.

Most efficient mills utilise less than 1% of the energy input to fracture particles or create new surfaces. The rest of energy is dissipated in:

1. Elastic deformation of unfractured particles.
2. Transport of material within the milling chamber.
3. Friction between the particles.
4. Friction between the particles and mill.
5. Heat.
6. Vibration and noise.
7. Inefficiency of transmission and motor.

Energy input and utilisation are important factors to estimate the efficiency of a mill for a given material. A number of theories has been proposed to establish a relationship between energy input and the degree of size reduction produced.

The energy required to reduce the size of the particles is inversely proportional to the size raised to some power. This may be expressed mathematically as;

$$\frac{dE}{dD} = \frac{-C}{D^n} \quad (2)$$

where E = amount of energy (work done) required to produce a change, kW·h
D = size of unit mass, µm
C = constant, W·h
n = constant

Equation (2) may be written (when n = 1) as:

$$E = C\, ln\, (\frac{d_i}{d_n}) \quad (3)$$

where d_i = size of the feed, µm
d_n = size of the product, µm

In equation (3), (d_i/d_n) is known as *reduction ratio*. The usefulness of equation (3) is that it satisfies various laws proposed. These are:
For n = 1.0, equation (3) becomes Kick's law
For n = 1.5, equation (3) becomes Bond's law
For n = 2.0, equation (3) becomes Rittinger's law

Rittinger's Theory

According to the Rittinger's hypothesis, energy, E required for size reduction of unit mass is directly proportional to the new surface area produced. It is expressed as:

$$E = K_R\,(S_n - S_i) \quad (4)$$

where S_i = initial specific surface area, $\mu m^2/\mu m^3$
S_n = new specific surface area, $\mu m^2/\mu m^3$
K_R = Rittinger's constant, energy per unit area, $kW{\cdot}h./\mu m^3$
E = amount of energy (work done), kW·h

It is mostly applicable to brittle materials undergoing fine milling. Rittinger's theory ignores particle deformation before fracture.

Bond's Theory

According to the Bond's theory, the energy used in crack propagation is proportional to the new crack length produced. It states that the energy used for deforming or fracturing a set of particle of equivalent

shape is proportional to the change in particle dimensions. According to Bond's theory, the equation can be written as:

$$E = 2K_B\,(\frac{1}{\sqrt{d_n}} - \frac{1}{\sqrt{d_i}}) \quad (5)$$

where K_B = Bond's work index, energy per unit mass, $kW{\cdot}h{\cdot}\sqrt{\mu m}$
d_i = initial diameter of particles, µm
d_n = new diameter of particles, µm

Bond's work index is the work required to reduce a unit weight from a theoretical infinite size to 80% passing 100 µm. According to this theory, the energy used in crack propagation is proportional to the new crack length produced. This law is useful for rough mill sizing. The work index is useful for comparing the efficiency of milling operations.

Kick's Theory

According to the Kick's theory, the energy used in deforming or fracturing a set of particles of equivalent shape is proportional to the ratio of the change in size. It may be expressed as:

$$E = K_K\, ln\, \frac{d_i}{d_n} \quad (6)$$

where K_K = Kick's constant, energy per unit mass, kW·h
d_i = diameter of the particle in the initial stage, µm
d_n = diameter of the new particle, µm

The Kick's proposal was developed on a stress-strain diagram for cubes under compression. It assumes that the material has flaws distributed throughout its internal structure. For crushing (compression) of large particles, Kick's equation (equation 6) is more useful.

Equations (1 to 6) apply precisely only under the condition that all the energy is transferred into surface energy.

Size reduction of a material is alone not sufficient to obtain powder of desired size. It is followed by separation. Several equipment described earlier also include sieves or screens as integral parts. However, size separation is discussed separately in the following chapter.

Glossary of Symbols

C = Constant or coefficient.
c = Critical crack path required for fracture, m.

D = Size of unit mass, μm.
E = Amount of energy required to produce a change in unit mass, kW·h.
d_i = Size of the feed or initial diameter of particles, μm.
d_n = Size of the product or new diameter of the particles, μm.
ε = Surface energy of the wall of crack, J/m^2.
K_B = Bond's work index, energy per unit mass, kW·h·$\sqrt{\mu m}$.
K_K = Kick's constant, kW·h.
K_R = Rittinger's constant, kW·h/μm^2.
n = Constant.
S_i = Initial specific surface area, μm^2/μm^3.
S_n = New specific surface area, μm^2/μm^3.
T = Tensile strength, MPa.
Y = Young's modulus, MPa.

QUESTION BANK

Each question carries 2 marks

1. It is essential to include a sieve in the size reduction equipment. Why?
2. In a hammer mill, the particle size of the powders is far less than the mesh size of the screen. How is it possible?
3. Screen type of sieves gives more fine powder than the wire woven sieves. Why?
4. Size reduction of vegetable matter is essential for the extraction of crude drugs. Explain.
5. It is difficult to obtain uniform sized product during milling without the use of sieves. Why?
6. Fluid energy mill is better equipment for size reduction of thermo-labile substances compared to hammer mill. Substantiate.
7. Ball mill is not useful for size reduction of fibrous material. Explain
8. It is possible to prevent the heat generated during milling using colloid mill. How?
9. Size reduction of a material enhances the action of drugs. Explain.
10. When ball mill is used, size reduction is not obtained. Under what condition size reduction is not effective.
11. How do you prevent the problems of sticking and clogging of sieves in the size reduction?
12. List special precautions to be taken while thermolabile substances are subjected to size reduction process.
13. The powder must contain fewer amounts of fines when it is meant for percolation process of extraction. Why?
14. What are the advantages of swinging type of hammer compared to rigid hammers?

15. Powders of same particle size that are obtained by different equipment have same physicochemical characteristics. True or false. Justify.
16. List the areas in which size reduction equipment is used in tablet production.
17. A large number of size reduction equipment is available currently. Why do we require so many types of mills?
18. Size reduction of powders is not possible, if particles do not contain flaws or cracks. Explain.
19. The classical equipment mortar and pestle uses the mechanism of impact in size reduction. True or False. Explain.
20. Fluid energy mill is meant for wet grinding. True or false. Explain.
21. Reducing the size of the particles to fines leads to particle aggregation. True or false. Explain.
22. Size reduction mill can also be used as mixing or dispersion equipment. True or false. Explain.
23. How does stickiness affect the process of size reduction?
24. How does the presence of moisture interfere with the process of size reduction?
25. Differentiate the mechanisms, attrition and impact in size reduction.

Each question carries 5 marks

1. Describe five factors that influence the selection of milling equipment for size reduction.
2. Explain with the help of a diagram the construction and working of a ball mill.
3. Explain with the help of diagram the construction and working of a hammer mill.
4. Describe the mechanisms of size reduction with suitable examples of equipment.
5. What is ultra-fine grinder? Explain the concept of ultra-fine grinding.
6. Describe 'micronizer'. Describe aseptic grinding process of antibiotics.
7. List the laws governing size reduction. What is work index?
8. How is size reduction affected in ultra-fine grinders? Describe the mechanism.
9. How is energy utilised in size reduction accounted for?

Each question carries 10 marks

1. Explain the factors related to feed-material influencing size reduction.
2. Describe the construction, working, advantages and disadvantages of fluid energy mill.

3. Describe the milling equipment with the help of a neat diagram that uses the principle of shear and impac
4. Explain the theories related to the size reduction of a powder.
5. Explain the advantages and disadvantages of size reduction process.
6. State and explain the laws governing size reduction.
7. Describe the mechanisms and modes of size reduction of solid drugs.