Milling

Is the mechanical process of reducing the particle size of solids.

Various terms (crushing –disintegration--dispersion – grinding---& pulverization)

Milling equipment is classified as coarse, intermediate, or fine according to the size of the milled product.

Size is expressed in terms of mesh (no. of openings per linear inch of a screen).

Pharmaceutical application

(The surface area per unit weight) which is known as

(the specific surface)

benefits of milling

1-This increased specific surface affects the therapeutic efficiency of medicinal compounds that possess a low solubility in body fluids by increasing the area of contact between the solid & the dissolving fluid.

2-The drying of wet masses may be facilitated by milling, which increases the surface area & reduces the distance the moisture must travel within the particle to reach the outer surface.

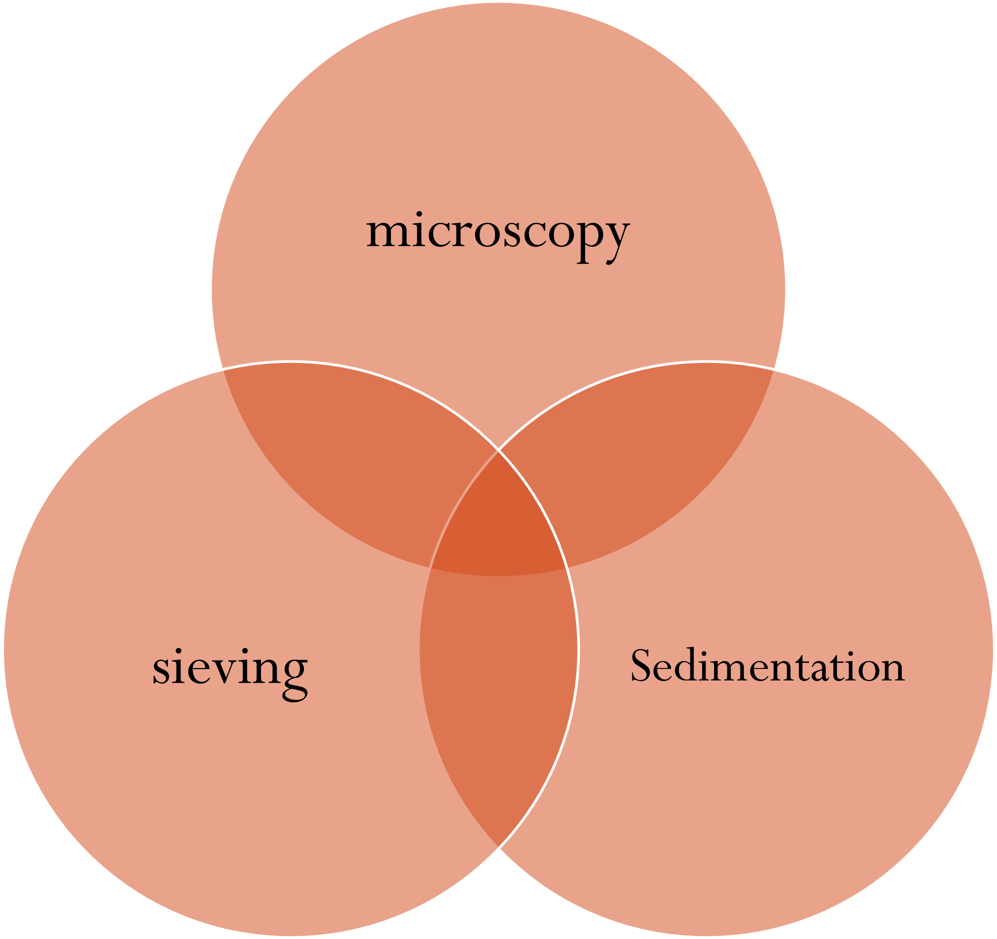
3- The mixing or blending of several solid ingredients of a pharmaceutical is easier & more uniform if the ingredients are approximately the same size. This provides a greater uniformity of dose. Solid pharmaceuticals that are artificially colored are often milled to distribute the coloring agent to ensure that the mixture is not mottled & is uniform from batch to batch.

Size distribution & measurement

- Naturally occurring particulate solids & milled solids, the shape of particles is irregular & the size of the particles varies within the range of the largest & smallest particles.
- There is no known method of defining an irregular particle in geometric terms ; however statistical methods have been developed to express the size of an irregular particle in terms of diameter.

for an irregular particle an equivalent particle with the same surface or volume may be substituted. For convenience of mathematical treatment, an irregular particle is considered in terms of an equivalent sphere. So the irregular particle expressed as diameter.

The main methods are used to measure particle size are



microscopy

- Is the most direct method for size distribution measurement. Its lower limit of application is determined by the resolving power of the lens.
- A particle cannot be resolved if its size is close to the wave length of the light source.

- **White light**
  - an ordinary microscope is used to measure particles from 0.4 to 150 microns.
- **ultraviolet**
  - The lower limit may be extended to 0.1 micron
- **ultramicroscope**
  - The resolution is improved by use of a darkfeild illumination& the size range is from 0.01 to 0.2 micron

The diameters of the particles on the slide are measured by means of a <u>calibrated filar micrometer eyepiece.</u>

the hairline of the eye piece is moved by the micrometer to one edge of a particle & the reading on the micrometer is recorded.

The hairline is then moved to the opposite edge of the particle being measured & the micrometer is read.

The difference between the 2 readings is the diameter of the particle.

all of the particles are measured along an arbitrary fixed line.

Eyepieces with grids of circles & squares are used to compare the cross sectional area of each particle in the microscopic field with one of the numbered patterns. The number of particles that best fits one of the numbered particles is recorded. The process repeated until the size range is covered.

Total number of fields depends on the number of particles per field. Acc to British std at least 625 particles and thi sdepends on the particle size distribution. If it is wide so need to read more. If it is narrow so 200 particles are enough.

There is a considerable variation among operators using the microscopy technique.

Sieving is the most widely used because

- inexpensive
- simple
- rapid
- Little variation between operator
- The lower limit of application is to be 50 microns, micromish sieves are available for extending the lower limit to 10 microns

A sieve consist of a pan with a bottom of wire cloth with square openings.

In the united state 2 standards of sieves are used

1- the tyler std scale

2- u.s std scale

The procedure involves the mechanical shaking of a sample through a series of successively smaller sieves & the weighing of portion of the sample retained on each sieve.

Table 2-4. *Designations and Dimensions of U.S. Standard and Tyler Standard Sieves*

U.S. Standard		Tyler Standard	
Micron	Mesh	Micron	Mesh
5660	3½	5613	3½
4760	4	4699	4
4000	5	3965	5
3360	6	3327	6
2830	7	2794	7
2380	8	2362	8
2000	10	1651	10
1680	12	1397	12
1410	14	1168	14
1190	16	991	16
1000	18	883	20
840	20	701	24
710	25	589	28
590	30	495	32
500	35	417	35
420	40	351	42
350	45	295	48
297	50	246	60
250	60	208	65
210	70	175	80
177	80	147	100
149	100	124	115
125	120	104	150
105	140	88	170
88	170	74	200

Factors affect on sieving

1-the type of motion influences sieving: vibratory motion is most efficient followed successively by side-tap motion, bottom –tap motion, rotary motion.

2- time is an important factor in sieving

3-the load or thickness of powder per unit area of sieve influences the time of sieving .

The size of the particles retained is taken as the arithmetic or geometric mean of the 2 sieves

A powder passing a 30-mesh & retained on a 45-mesh sieve is assigned an arithmetic mean diameter of $(590+350)/2=470$ micron

sedimentation

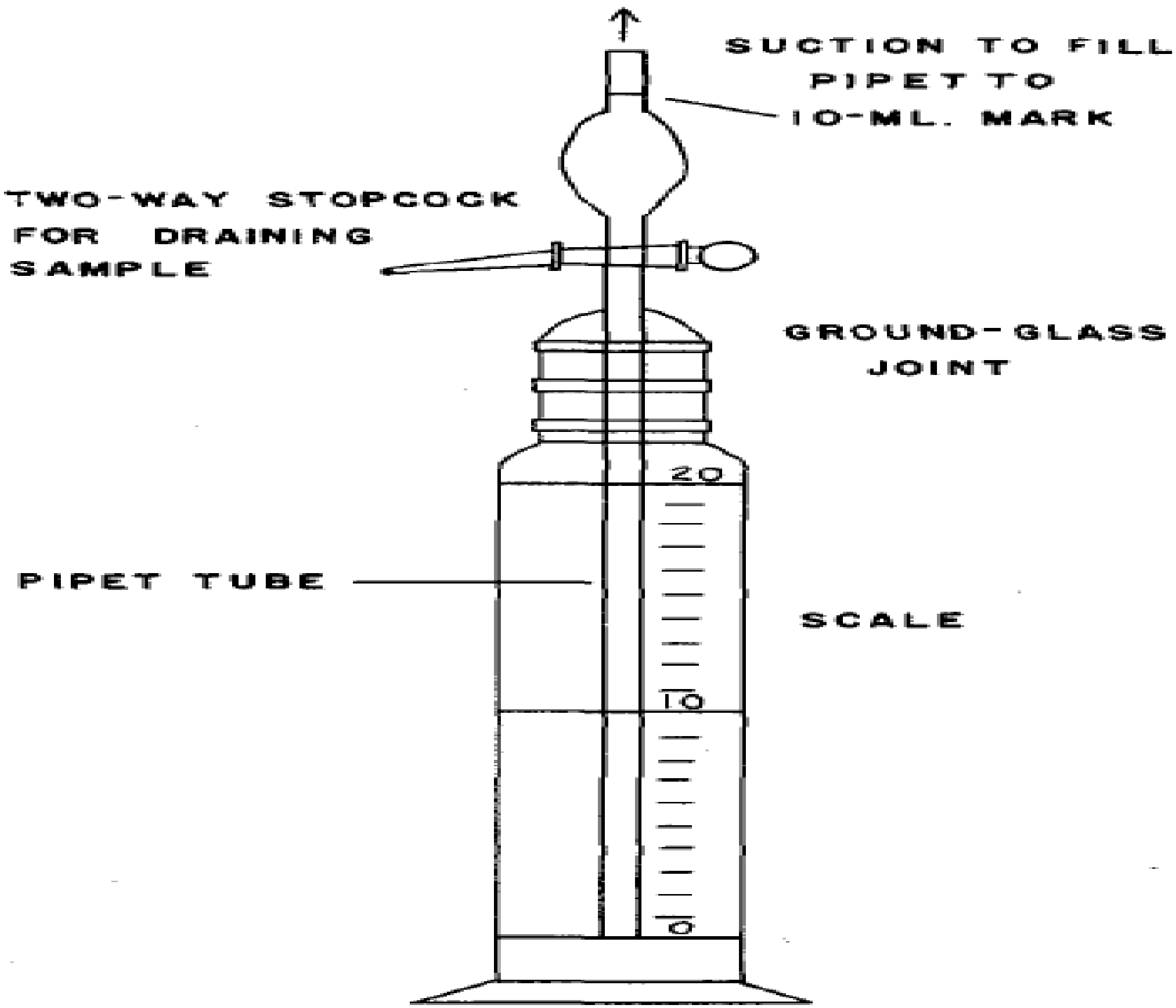
- May be used over a size range from 1 to 200 microns.
- The sedimentation method is based on the dependence of the rate of sedimentation of the particles on their size as expressed by stokes equation

$$d_{Stokes} = \sqrt{\frac{18\eta}{(\rho - \rho_0)g} \frac{x}{t}}$$

- This applicable to free spheres that are falling at constant rate.

If the concentration of the suspension does not exceed 2%, there is no significant interaction between the particles & they are settle independent of each other.

Anderson method



The pipet method (Andreasen) is the simplest means of incremental particle size analysis. A 1% suspension of the powder in a suitable liquid medium is placed in the pipet (Fig. 2-5). At given intervals of time, samples are withdrawn from a specified depth without disturbing the suspension, and they are dried so that the residue may be weighed. By means of Stokes' equation, the particle diameter corresponding to each interval of time is calculated, with x being the height of the liquid above the lower end of the pipet at time t when each sample is withdrawn. As the sizes of the particles are not uniform, the particles settle at different rates. The size-distribution and concentration of the particles vary along the length of the suspension as sedimentation occurs. The larger particles settle at a faster rate and fall below the pipet tip sooner

Theory of comminution

- The mechanical behavior of solids which under the stress are strained & deformed as shown below
- The initial linear portion of the curve is defined by Hooks law (stress is proportional to strain).
- Youngs modulus(slop of linear portion) expresses the stiffness or softness in dynes per square centimeter.
- The stress – strain curve becomes nonlinear at the yield point a measure of the resistance to permanent deformation.
- The area under the curve represents the energy of fructure.

measure of the impact strength of the material.

In all milling processes, it is a random matter if and when a given particle will be fractured. If a single particle is subjected to a sudden impact and is fractured, it yields a few relatively large particles and a number of fine particles, with relatively few particles of intermediate size. If the energy of the impact is increased, the larger particles are of a smaller size and more numerous, and although the number of fine particles is increased appreciably, their size is not greatly changed. It seems that the size of the finer particles is related to the internal structure of the material, and the size of the larger particles is more closely related to the process by which comminution is accomplished.

Size reduction begins with the opening of any small cracks that were initially present. Thus, larger particles with numerous cracks fracture more readily than smaller particles with fewer cracks. In general, fine grinding requires more energy, not only because of the increased new surface, but also because more energy is needed to initiate cracks.

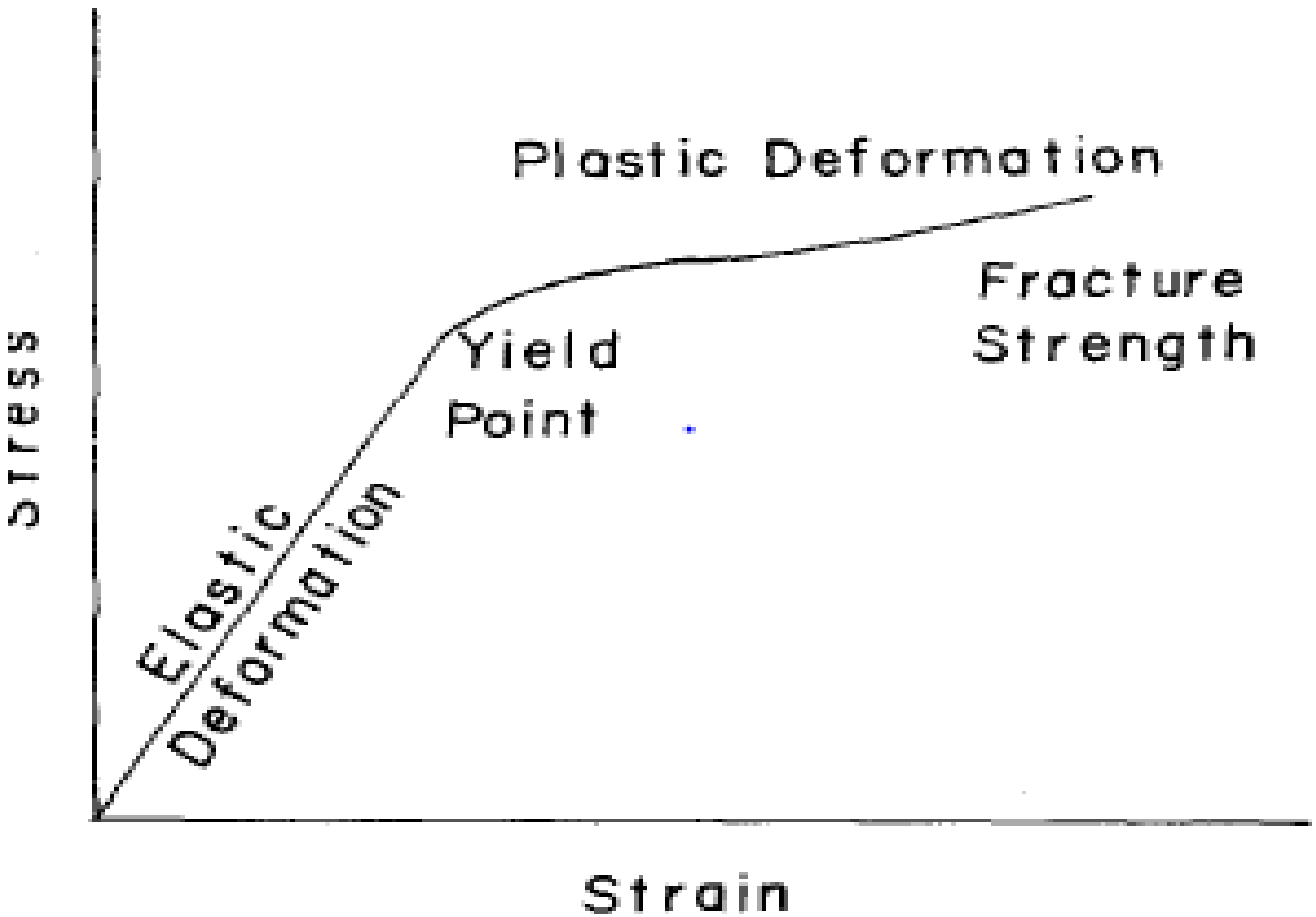


FIG. 2-6. *Stress-strain diagram for a solid.*

For any particle, there is a minimum energy that will fracture it; however, conditions are so haphazard that many particles receive impacts that are not sufficient to fracture them and are eventually fractured by some excessively forceful blow. As a result, the most efficient mills uti-

The most efficient mills utilizes less than 1% of the energy input to fracture. The rest of the energy is dissipated in

1- elastic deformation of unfractured particles

2-transport of material within the milling chamber

3-friction between particles

4-Friction between particles & mill

5- heat

6- vibration & noise

7-inefficiency of transmission & motor

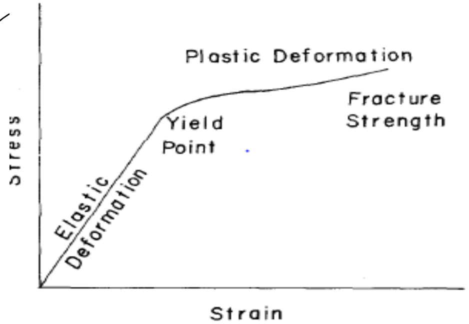


FIG. 2-6. *Stress-strain diagram for a solid.*

If the force of impact does not exceed the elastic limit (region of Hookes law) ,the material is reversibly deformed or stressed.

When the force is removed ,the particle returns to its original condition, & the mechanical energy of stress in the deformed particle appear as heat.

For polymeric material hysteresis is frequent occurs in the stress strain cycle the area of the loop represents the dissipation of stress energy(usually heat).

A force that exceeds the elastic limit fractures the particle. Usually, the surfaces of particles are irregular, so that the force is initially taken on the high portion of the surface, with the result that high stresses and temperatures may be set up locally in the material. As fracture occurs, the points of application of the force are shifted. The energy for the new surfaces is partially supplied by the release of stress energy. Crystalline materials fracture along crystal cleavage planes; noncrystalline materials fracture at random. If an ideal crystal were pressed with an increasing force, the force would be distributed uniformly throughout its structure until the crystal disintegrated into its individual units. A real crystal fractures under much less force into a few relatively large particles and several fine particles, with relatively few particles of intermediate size. Crystals of pure substances have internal weaknesses due to missing atoms or ions in their lattice structures and to flaws arising from mechanical or thermal stress.[20]

A flaw in a particle is any structural weakness that may develop into a crack under strain. It has been proposed that any force of milling produces a small flaw in the particle. The useful work in milling is proportional to the length of new cracks produced. A particle absorbs strain energy and is deformed under shear or compression until the energy exceeds the weakest flaw and causes fracture or cracking of the particle. The strain energy required for fracture is proportional to the length of the crack formed, since the additional energy required to extend the crack to fracture is supplied by the flow of the surrounding residual strain energy to the crack.

The Griffith theory of cracks and flaws assumes that all solids contain flaws and microscopic cracks, which increase the applied force according to the crack length and focus the stress at the atomic bond of the crack apex.[27,28] The Griffith theory may be expressed as:[29,30]

$$T = \sqrt{\frac{Y \epsilon}{c}} \tag{13}$$

where T is tensile stress, Y is Young's modulus, ϵ is the surface energy of the wall of the crack, and c is the critical crack depth required for fracture.

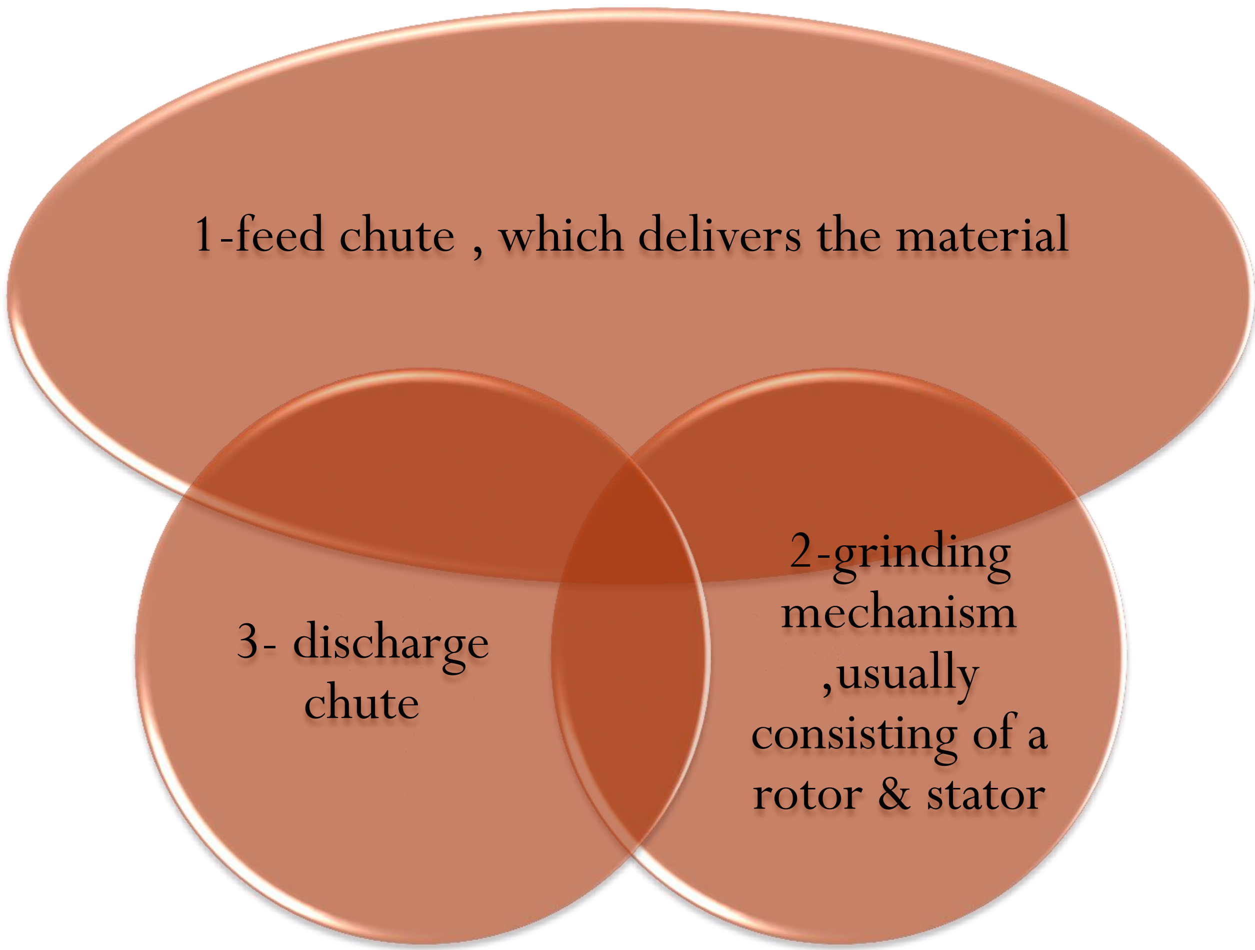
Energy of comminution

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

$$\frac{dE}{dD} = -\frac{C}{D^n} \qquad (15)$$

Where dE is the amount of energy required to produce a change in size , dD, of unit mass of material & where C &n are constants.

Types of mills
a mill consist of 3 basic parts



- The principle of operation depends on direct pressure ,impact from a sharp blow, attrition or cutting .
- In most mills the grinding effect is a combination of these actions.
- The manner in which the operator feeds a mill markedly affects the product.
- 1- if the rate is of feed is slow, the product discharged readily & the amount of undersize or fines is minimized.
- 2- If the mill is choke fed at a fast rate , the material is in the milling chamber for along time as its discharge

- Is impeded by the mass of material. <u>This provide a greater reduction of particle size but the capacity of the mill is reduced & power consumption is increased.</u>
- <u>Choke feed is used when a small amount of material is to be milled in one operation.</u>
- **The rate of discharge should be equal to the rate of feed, which is such that the milling parts can operate most effectively.**

Hammer mill

- The hammer mill is an impact mill using a high speed rotor to which a no. of swinging hammers are fixed.
- The material is fed at the top or center, thrown out centrifugally,& ground by impact of the hammers or against the plates around the periphery of the casing.
- The clearance between the housing and the hammers contributes to the size reduction. The matrrial retained until it is small enough to fall through the screen.
- Particles fine enough to pass through the screen.
- The hammer mill versatility makes it use to mil dry materials, wet filter press cakes, ointments & slurries .
- The size of the product size is controlled by selecting the speed of hammers & the size & type of screen.

most materials behave as if they were brittle. Brittle material is best fractured by impact from a blunt hammer; fibrous material is best reduced in size by cutting edges. Some models of hammer mills have a rotor that may be turned 180 degrees to allow use of either the blunt edge for fine grinding or the knife edge for cutting or granulating.

A hammer mill can be used for granulation and close control of the particle size of powders. The size of the product is controlled by selecting the speed of the hammers and the size and type of the screen. Speed is crucial. Below a critical impact speed, the rotor turns so slowly that a blending action rather than comminution is obtained. This results in overloading and a rise in temperature. Microscopic examination of the particles formed when the mill is operating below the critical speed shows them to be spheroidal, indicating not an impact action, but an attrition action, which produces irregularly shaped particles. At very high speeds, there is possibly insufficient time between hammers for the material to fall from the grinding zone. In wet milling of dispersed systems with higher speeds, the swing hammers may lay back with an increased clearance; for such systems, fixed hammers would be more effective.

Figure 2-12 shows the influence of speed on the particle size-frequency curves for boric acid milled at 1000, 2450, and 4600 rpm in a hammer mill fitted with a screen having 6.35-mm circular holes.

The screens that retain the material in the milling chamber are not woven but perforated. The particle size of the discharged material is smaller than the screen hole or slot, as the particles exit through the perforation on a path approximately tangential to the rotor. For a given screen, a smaller particle size is obtained at a higher speed, as is shown in Figure 2-13. Efforts to strengthen a screen by increasing its thickness influence particle size. For a given rotor speed and screen opening, a thicker screen produces a smaller particle, which is also illustrated in Figure 2-13.

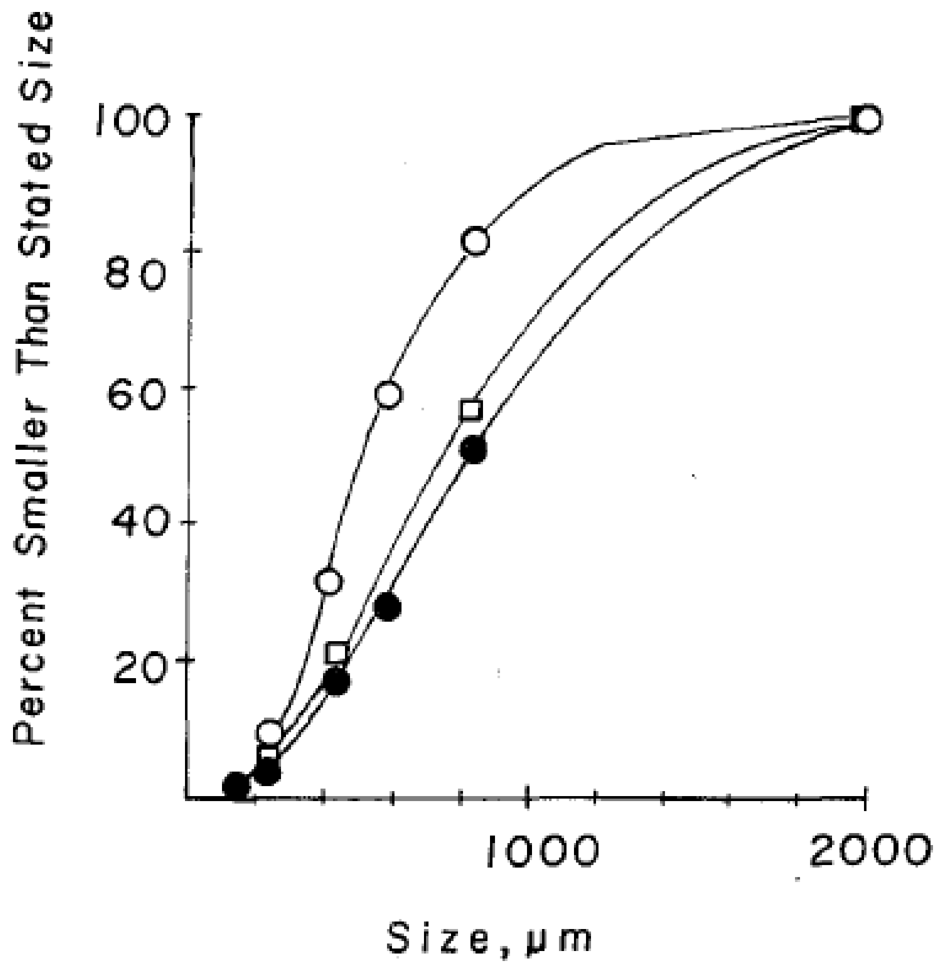


FIG. 2-12. *Influence of speed on the size-frequency distribution of boric acid flakes milled by a hammer mill operating with impact edge forward and fitted with a round hole No. 4 screen (hole diameter: 6.35 mm). Key:* ●, *1000 rpm;* □, *2450 rpm; and* ○, *4600 rpm.*

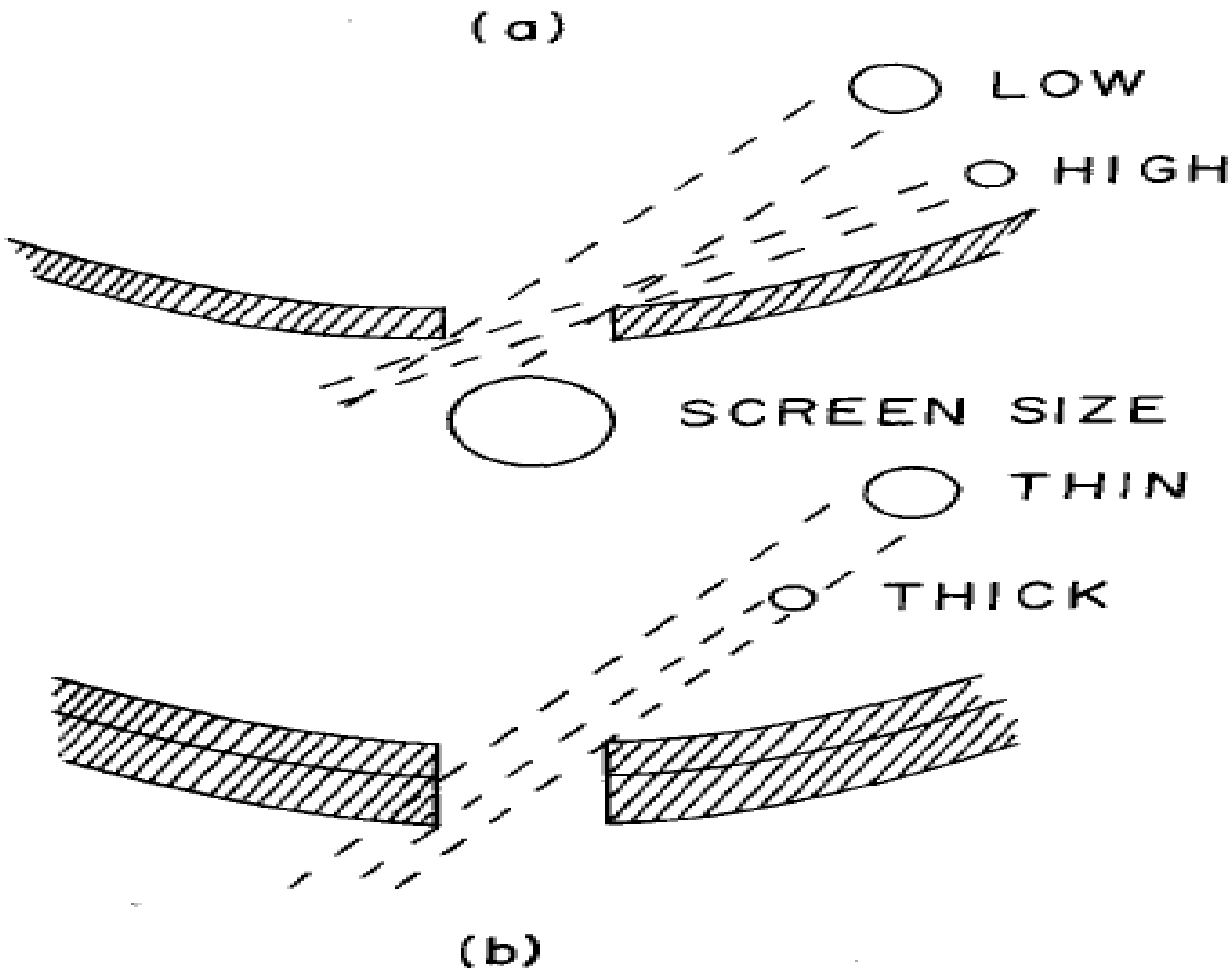


FIG. 2-13. *In a hammer mill, particle size is influenced by speed (a) and thickness of screen (b).*

narrow size distribution. Hammer mills are simple to install and operate. The speed and screen can be rapidly changed. They are easy to clean and may be operated as a closed system to reduce dust and explosion hazards.

Ball mill

- The ball mill consists of a horizontally rotating hollow vessel of cylindrical shape with the length slightly greater than its diameter. The mill is partially filled with balls of steel or pebbles are used, it is known as rod or bars are used, it is known as a rod mill.
- The rod mill is particularly useful with sticky material that would hold the balls together ,because the greater weight of the rods causes them to pull apart.
- Ball milling is combination of impact & attrition.

to pull apart. The tube mill is a modified ball mill in which the length if about four times that of the diameter and in which the balls are somewhat smaller than in a ball mill. Because the material remains in the longer tube mill for a greater length of time, the tube mill grinds more finely than the ball mill. The ball mill may be modified to a conical shape and tapered at the discharge end. If balls of different size are used in a conical ball mill, they segregate according to size and provide progressively finer grinding as the material flows axially through the mill. Recently, small-scale vibration ball mills, which produce particles of a few microns, have been introduced.[60] These oscillate 1500 to 2500 cy-

Most ball mills utilized in pharmacy are batch-operated; however, there are available continuous ball mills, which are fed through a hollow trunnion at one end, with the product discharged through a similar trunnion at the opposite end. The outlet is covered with a coarse screen to prevent the loss of the balls.

In a ball mill rotating at a slow speed, the balls roll and cascade over one another, providing an *attrition action*. As the speed is increased, the balls are carried up the sides of the mill and fall freely onto the material with an impact action, which is responsible for most size reduction. Ball milling is a combination of impact and attrition. If the speed is increased sufficiently, the balls are held against the mill casing by centrifugal force and revolve with the mill. The critical speed of a ball mill is the speed at which the balls just begin to centrifuge with the mill. Thus, The charge of balls can be expressed in terms of percentage of volume of the mill (a bulk volume of balls filling one half of a mill is a 50% ball charge). To operate effectively, a ball charge from 30 to 50% of the volume of the mill is required.

The amount of material to be milled in a ball mill may be expressed as a material-to-void ratio (ratio of the volume of material to that of the void in the ball charge). The efficiency of a ball mill is increased as the amount of material is increased until the void space in the bulk volume of ball charge is filled; then, the efficiency of milling is decreased by further addition of material.

Increasing the total weight of balls of a given size increases the fineness of the powder. The weight of the ball charge can be increased by increasing the number of balls or by using a ball composed of a material with a higher density. Since optimum milling conditions are usually obtained when the bulk volume of the balls is equal to 50% of the volume of the mill, variation in weight of the balls is normally effected by the use of materials of different densities. Thus, steel balls grind faster than porcelain balls, as they are three times more dense. Stainless steel balls are also preferred in the production of ophthalmic and parenteral products, as there is less attrition and less subsequent contamination with particulate matter.

In dry milling, the moisture should be less than 2%. With batch processing, dry ball milling produces a very fine particle size. With wet milling, a ball mill produces 200-mesh particles from slurries containing 30 to 60% solids. From the viewpoint of power consumption, wet grinding is more efficient than dry grinding. A slower speed is used in wet milling than in dry milling to prevent the mass from being carried around with the mill. A high viscosity restricts the motion of the grinding medium, and the impact is reduced. With 1.27-cm steel balls, a viscosity from 1000 to 2400 centipoises (cp) is satisfactory for wet milling.

Wetting agents may increase the efficiency of milling and the physical stability of the product by nullifying electrostatic forces produced during comminution. For those products containing wetting agents, the addition of the wetting agent at the milling stage may aid size reduction and reduce aggregation.

In addition to being used for either wet or dry milling, the ball mill has the advantage of being used for batch or continuous operation. In a batch operation, unstable or explosive materials may be sealed with an inert atmosphere and satisfactorily ground. Ball mills may be sterilized and sealed for sterile milling in the production of ophthalmic and parenteral products. The installation, operation, and labor costs involved in ball milling are low. Finally, the ball mill is unsurpassed for fine grinding of hard, abrasive materials.

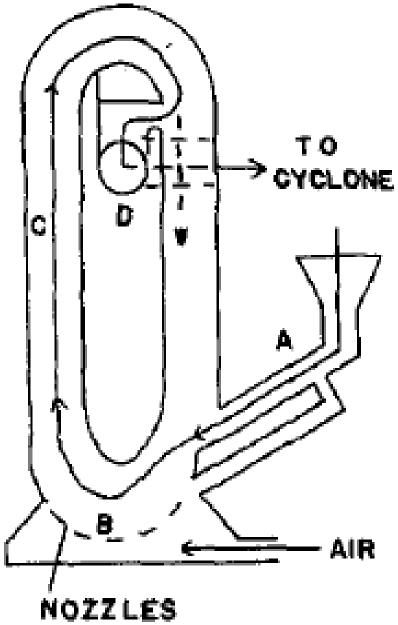
Fluid energy mill

in the fluid energy mill or (micronizer) the material is suspended & conveyed at high velocity by air steam

The violent turbulence air& steam reduces the particle size by interparticular attrition

Air is usually used because most pharmaceuticals have a low melting point or are thermoliable.

As the compressed air expands at the orifice ,the cooling effect counteracts the heat generated by milling.



FLUID-ENERGY

As shown in Figure 2-11, the material is fed near the bottom of the mill through a venturi injector (A). As the compressed air passes through the nozzles (B), the material is thrown outward against the wall of the grinding chamber (C) and other particles. The air moves at high speed in an elliptical path carrying with it the fine particles that pass out of the discharge outlet (D) into a cyclone separator and a bag collector. The large particles are carried by centrifugal force to the periphery, where they are further exposed to the attrition action. The design of the fluid-energy mill provides internal classification, which permits the finer and lighter particles to be discharged and the heavier oversized particles, under the effect of centrifugal force, to be retained until reduced to a small size.

Fluid-energy mills reduce the particle to 1 to 20 microns. The feed should be premilled to approximately a 20- to 100-mesh size to facilitate milling. A 2-inch laboratory model using 20 to 25 cubic feet per minute of air at 100 psi mills 5 to 10 grams per minute. In selecting fluid-energy mills for production, the cost of a fluid-energy source and dust collection equipment must be considered in addition to the cost of the mill.