Dr. Arvind Kumar Gupta
(M.Pharm, PDCR, PGDMM & Ph.D)
GATE 2003 Qualified with 97.2 percentile
Dr. S. N. Dev College of Pharmacy
Shamli (U.P.)

OFFICE: BUILDING No. 3/314, OFFICE-1, GAUSHALA ROAD, SHAMLI DISTRICT SHAMLI (U.P.) – 247776
Mobile: +91-9719638415
Email: arvindrkgit@gmail.com

Course Name	**: D. Pharm**
Year	**: First Year**
Subject Name	**: Pharmaceutics**
Topic Name	**: Size Reduction**

Ch - 4

Size Reduction

Size reduction (or Comminution): *Size reduction* or *comminution* is the process of reducing substances to smaller particles.

Objectives of size reduction:

1. Size reduction leads to increase of surface area.

***Example-I*:** The rate of dissolution of solid drug particles increases many folds after size reduction. Griseofulvin, an antifungal drug, when administered in its micronized form shows around five times better absorption.

***Example-II*:** The absorptive power of charcoal and kaolin increases after size reduction due to increase in surface area.

2. Size reduction produces particles in narrow size range. Mixing of powders with narrow size range is easier.
3. Pharmaceutical suspensions require finer particle size. It reduces rate of sedimentation.
4. Pharmaceutical capsules, insufflations (i.e. powders inhaled directly into the lungs), suppositories and ointments require particles size to be below 60µm size.

Factors affecting size-reduction

The pharmaceutical industry uses a great variety of materials, including chemical substances, animal tissues and vegetable drugs.

A. Factors related to the nature of raw materials:

- **Hard materials**: Hard materials like pumice and iodine are most difficult to comminute. During size reduction these types of materials will produce abrasive wear of milling surfaces, which will then contaminate the material.
- **Fibrous materials**: Crude drugs obtained from plants like glycyrrhiza, rauwolfia, ginger etc. are fibrous in nature and cannot be crushed by pressure. So they may be size-reduced by cutter mill.
- **Friable materials:** Sucrose and dried filter cakes are friable (i.e. brittle) hence they are easy to comminute by hammer mill or fluid energy mill.
- **Plastic materials**: Synthetic gums, waxes and resins become soft and plastic during milling. These low melting substances should be chilled (made cold) before milling. These types of materials are milled by using hammer mill and fluid energy mill.
- **Hygroscopic materials**: Hygroscopic materials absorbs moisture rapidly hence they must be comminuted inside a closed equipment like ball-mill.

- **Thermolabile materials**: Thermolabile materials like vitamins and antibiotics are milled inside chilled equipment.
- **Inflammable materials**: 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 earthed properly.
- **Particle size of the feed**: For a mill to operate satisfactorily, the feed should be of proper size.
- **Moisture content**: Presence of more than 5% moisture hinders the milling process and produces a sticky mass.

B. Factors related to the nature of the finished product

- **Particle size**:
- **Ease of sterilization**:
- **Contamination of milled materials**:

Methods of size reduction: Mechanism of size reduction varies the nature of the particle. Hence different modes of stress are required for different substances.

S. No.	Principle	Mill following the given mode	Description	Type of material
1.	Cutting	Cutter mill	Material is cut by the means of sharp blades	Fibrous and waxy substances
2.	compression	Roller mill Crusher mill	Material is crushed between the rollers by applying pressure	Soft materials
3.	Impact	Hammer mill Fluid energy mill	· In this, the substance is subjected to hammers or bars at high speed · Impact also occur when a forceful particle is strike against a stationary object	Almost all drugs are size reduced by hammer mill. Fluid energy mill is used for moderately hard and friable materials
4.	Attrition (Pressure and friction)	Fluid energy mill	In this, breaking of material occur y rubbing it between two surfaces	Brittle drugs

Theories of milling:

1. Rittinger's theory

2. Bond's theory

3. Kick's theory

4. Walker's theory

HAMMER MILL

Method of size reduction: Impact

Construction and working principle:

Hammer mill consists of a stout metal casing, enclosing a central shaft to which four or more *hammers* are attached. These are mounted with *swivel* joints, so that the hammers swing out to a radial position when the shaft is rotated. The lower part of the casing consists of screen through which materials can escape, when sufficiently size reduced. The material is collected in a container placed below the screen.

- The screen can be changed according to the particle size required.
- According to the purpose of operation the hammers may be square-faced, tapered to a cutting form or have a stepped-form.
- The interior of the casing may be undulating in shape, instead of smooth circular form for better impact.
- The rotor operates at a speed of 80cycles per second.

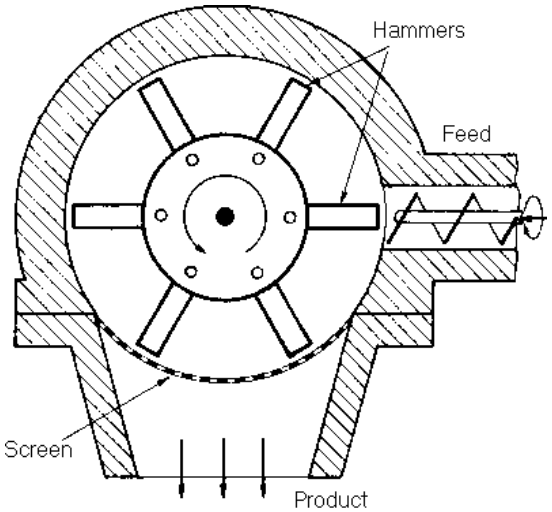

Fig. Hammer Mill

***Advantages*:**

(a) It is rapid in action, and is capable of grinding many different types of materials.

(b) The product can be controlled by variation of rotor speed, hammer type and size and shape of mesh.

(c) Operation is continuous.

(d) No surface moves against each other so very little problem of contamination of mill materials.

***Disadvantages*:**

(a) High speed of operation generates heat that may affect thermolabile materials or drugs containing gum, fat or resin.

(b) The rate of feed should be controlled otherwise the mill may be choked.

(c) Because of high speed of operation, the hammer mill may be damaged if some foreign materials like stone, metal pieces etc. are present in the feed.

Applications: Powdering of crystals and filter cakes.

BALL MILL

Construction

The ball mill consists of a hollow cylinder rotated on its horizontal axis. Inside the cylinderballs or pebbles are placed.

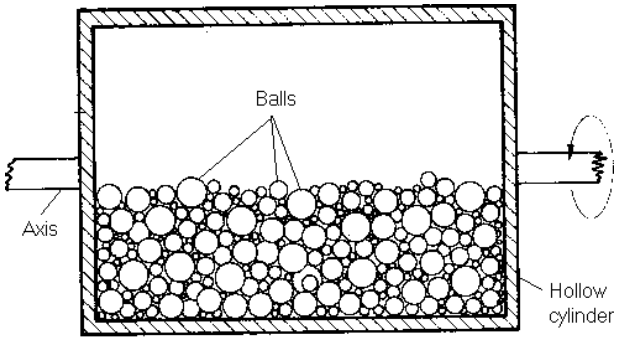

Fig. Ball mill

Cylinder:

- Cylinder may be made up of metal, porcelain or rubber.
- Rubber reduces the abrasion. Diameter of the cylinder ranges from 1 to 3m in pharmaceutical practice.

Balls:

- Balls occupy about 30 to 50% of the volume of the cylinder.
- Diameter of the balls depends on the feed size and diameter of the cylinder. The diameter of balls ranges from 2cm to 15cm.
- Balls may be of metal, porcelain or pebbles.

Working Principle:

Larger particles are fed through an opening of the cylinder. The opening is closed. The cylinder is rotated at the critical speed of ball mill. The optimum size reduction in a ball mill depends o the following factors:

Feed quantity:

Too much feed will produce cushioning effect and too little feed will produce loss of efficiency of the mill.

Speed of rotation of the cylinder:

- At low speed the mass of balls will slide or roll over each other and only a negligible amount of size reduction will take place.
- At high speeds, balls will be thrown out to the wall of the cylinder due to centrifugal force and no grinding will occur.

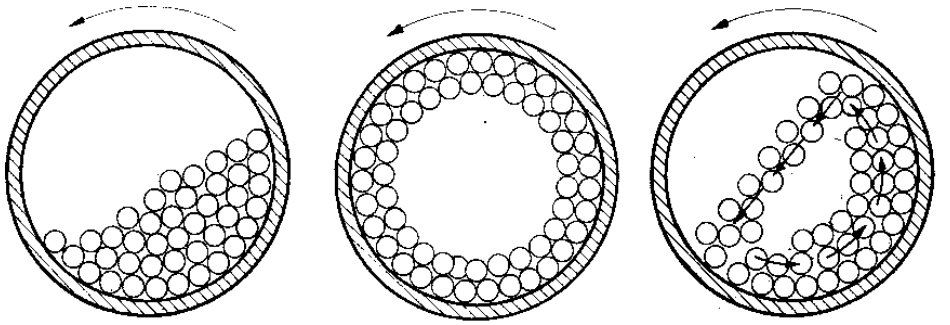
(a) Low speed with sliding (b) High speed with centrifuging (c) Correct speed with cascading

Fig. Ball mill operation

- At 2/3rd speed at which centrifugation just occurs is called the critical speed of the ball mill. At this speed the balls are carried almost to the top of the mill and then fall in a cascade across the diameter of the mill. By this means the maximum size reduction is obtained by impact of the particles between the balls and by attrition between the balls. Generally it is 0.5 cycles per seconds (cps).

Advantages

1. It is capable of grinding a wide variety of materials of differing hardness.
2. It can be used in completely enclosed form, which makes it suitable for use with toxic materials.
3. It can produce very fine powders.
4. It is suitable both for dry and wet milling. Wet milling is required for preparation of pharmaceutical suspensions.

Disadvantages

1. Wear occurs from the balls and the inside surface of the cylinder hence there is possibility of contamination of product with mill material. Abrasive materials increase wear.
2. Soft or sticky materials may cause problems by caking on the sides of the mill or by holding the balls in aggregates.
3. The ball mill is a very noisy machine, particularly if the cylinder is made of metal.

Applications:

Large ball mills are used to grinding ores prior to manufacture of pharmaceutical chemicals. Smaller ball mills are used for grinding of drugs or excipients or for grinding suspensions.

Type of ball mills:

1. Hardinge mill
2. Tube mill
3. Rod mill
4. Vibration mill

Uses of size reduction methods

S. No.	Degree of size reduction	Typical methods	Examples
1.	Large pieces	Cutter or compression mills	Rhubarb
2.	Coarse powders	Impact mills	Liquorice, cascara
3.	Fine powders	Combined impact and attrition mills	Rhubarb , belladonna
4.	Very fine powders	Fluid energy mills	Vitamins and antibiotics