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PHARMACEUTICAL ENGINEERING

UNIT 1

TOPIC :

- **Size Reduction :** Objectives, Mechanisms & Laws governing size reduction, factors affecting size reduction, principles, construction, working, uses, merits and demerits of Hammer mill, ball mill, fluid energy mill, Edge runner mill & end runner mill.

SIZE REDUCTION

Size reduction is the process of breaking down large solid drug substances into smaller particles to increase surface area and improve pharmaceutical processing.

- In solids → done by grinding, cutting, crushing.
- In liquids → done by emulsification or atomization.
  It is also called Comminution **or** Pulverization.

Advantages of Size Reduction

1. **Content Uniformity** → Smaller particle size increases the number of particles, leading to better mixing and uniform drug distribution in dosage forms.
2. **Uniform Flow Properties** → Smaller and controlled particles improve flow of powders, aiding tablet compression and capsule filling.
3. **Increased Drying Rate** → Reduction in size increases surface area, enhancing the drying process.
4. **Improved Stability** → Smaller particles reduce sedimentation rate, thus increasing suspension stability.
5. **Better Absorption & Bioavailability** → Smaller particle size → faster dissolution → rapid absorption in the body.

Disadvantages of Size Reduction

1. **Drug Degradation** → Heat generated during milling may cause degradation of thermolabile drugs.
2. **Poor Mixing** → Extremely fine particles may agglomerate due to cohesive forces, reducing mixing efficiency.
3. **Contamination** → Particles may get contaminated from grinding surfaces and milling equipment.

Objectives of Size Reduction

- To increase surface area, which enhances the rate of physical or chemical processes (e.g., dissolution, solubility, reactions).
- To achieve ease of mixing in pharmaceutical formulations.
- To improve dissolution rate and bioavailability of poorly soluble drugs.
- To obtain particle size below 60 µm for dosage forms such as capsules, insufflations, and suppositories.
- To improve stability of emulsions by reducing the size of oil globules.
- To ensure ophthalmic and dermal preparations are free from gritty particles to avoid irritation.

Applications in Pharmacy

- Tablet and capsule formulations.
- Preparation of suspensions and emulsions.
- Enhancing dissolution rate of poorly soluble drugs.
- Improving flow properties of powders in industrial processing.
- Ophthalmic and topical dosage forms (to prevent irritation).

Mechanism of Size Reduction

Size reduction can be achieved by applying different types of mechanical forces. Each mechanism depends on the nature of the material (hard, fibrous, soft, brittle, etc.) and the equipment used. The main mechanisms are:

1. Impact

- **Principle**: In this method, particles are reduced in size by the force of high-speed moving objects striking them. The material shatters due to the sudden impact.
- **Best for**: Brittle materials.
- **Example Equipment**: **Hammer Mill, Ball Mill, Pin Mill.**

2. Attrition (Shearing)

- **Principle**: In this method, surfaces of particles slide or rub against each other, producing shear forces that reduce size.
- **Best for**: Fine powders and friable materials.
- **Example Equipment**: **Fluid Energy Mill, Colloidal Mill.**

3. Compression

- **Principle**: Material is crushed between two rigid surfaces (rollers or plates) by the application of pressure.
- **Best for**: Hard, tough, and crystalline materials.
- **Example Equipment**: **Roller Mill, Jaw Crusher.**

4. Cutting

- **Principle**: Material is reduced in size by sharp blades or knives that cut it into smaller pieces.
- **Best for**: Fibrous, soft, and tough materials (e.g., roots, leaves).
- **Example Equipment**: **Cutter Mill, Knife Cutter.**

Laws Governing Size Reduction

The process of size reduction (comminution) requires the input of **energy**. The relationship between energy consumption and particle size reduction is explained by three classical laws**:**

1. Kick's Law

- Statement: The energy required for size reduction is directly proportional to the ratio of size reduction (i.e., the ratio of initial to final particle diameter).
  - Equation:

$$E = k \cdot \ln\left(\frac{D_i}{D_f}\right)$$

Where:

- E = Energy required
- k = Kick's constant
- D_i = Initial diameter of particles
- D_f = Final diameter of particles

Application: Suitable for coarse crushing where there is small change in surface area.

2. Rittinger's Law

- **Statement:** The energy required for size reduction is directly proportional to the new surface area produced
  - Equation:

$$E = k_R(S_a - S_i)$$

Where:

- E = Energy required
- k_R = Rittinger's constant
- S_a = Final surface area
- S_i = Initial surface area

- **Application**: Suitable for fine grinding where surface area increase is significant.

3. Bond's Law

- **Statement**: The energy required for size reduction is proportional to the new crack length produced.
    - Equation:

$$E = W_i \left(\frac{1}{\sqrt{D_f}} - \frac{1}{\sqrt{D_i}} \right)$$

Where:

- E = Energy required
- W_i = Bond Work Index (energy required to reduce 1 ton of material from an infinite size to 100 μm)
- D_i = 80% passing size of feed
- D_f = 80% passing size of product

- **Application**: Provides a practical estimate of energy requirement for size reduction in industry; intermediate between Kick's and Rittinger's laws.

Factors Affecting Size Reduction

The process of size reduction (comminution) is influenced by several material and equipment-related factors. These factors determine the efficiency, energy requirement, and quality of the final product.

1. Hardness

- Hardness is the resistance of a material to deformation or scratching.
- **Effect**:
  - Soft materials are easy to reduce in size.
  - Hard materials require more energy and wear down the grinding surfaces.
- **Example**: It is easier to grind chalk (soft) compared to quartz (hard).

2. Toughness

- Toughness refers to the ability of a material to absorb energy and deform without breaking.
- **Effect**:
  - Tough materials are more difficult to break, even if they are not very hard.
  - This property often causes greater problems than hardness.
- **Example**: Rubber (tough) is harder to grind than chalk (brittle).

3. Abrasiveness

- Abrasiveness is the tendency of materials to cause wear on grinding surfaces.
- **Effect**:
  - Grinding of abrasive materials damages the milling equipment.
  - Contamination of the final product may occur due to worn-off particles from the mill.
- **Example**: Silica and minerals cause high abrasiveness.

4. Stickiness

- Stickiness is the tendency of a substance to adhere to surfaces.
- **Effect**:
  - Sticky materials clog sieves and adhere to grinding surfaces, reducing efficiency.
- **Example**: Gummy or resinous substances.

5. Slipperiness

- Slipperiness is the opposite of stickiness, where materials slide easily.
- **Effect**:
  - Slippery materials act as lubricants, preventing effective grinding.
  - This lowers the efficiency of size reduction.

6. Melting Point

- Solids with a low melting point can soften or melt due to heat generated during milling.
- **Effect**:
  - Causes clogging and aggregation of particles.
- **Solution**: Grinding can be carried out under cooling conditions (e.g., cryogenic grinding).
- **Example**: Waxes and fatty substances.

7. Explosiveness

- Some materials are explosive in nature and may ignite due to heat or sparks during grinding.
- **Effect**:
  - Dangerous explosions can occur if proper precautions are not taken.
- **Solution**: Grinding should be done wet or in an inert atmosphere.
- **Example**: Coal dust, nitro compounds.

Equipment Used for Size Reduction

In the pharmaceutical industry, size reduction is achieved using various machines that apply principles of impact, attrition, shear, and compression. Commonly used equipment are:

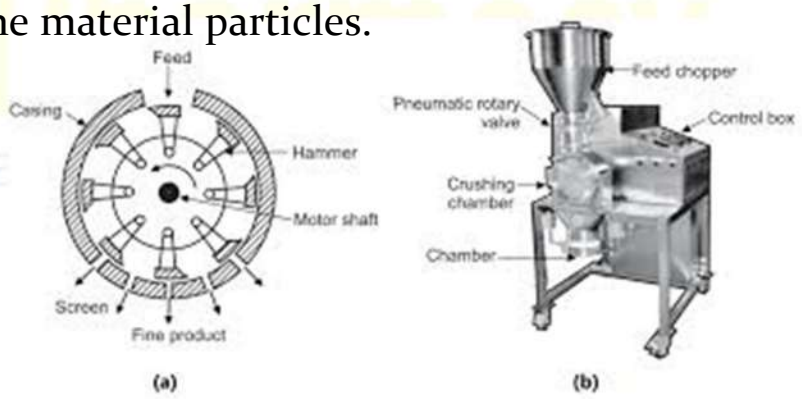
- **Hammer Mill**
- **Ball Mill**
- **Fluid Energy Mill (Jet Mill)**
- **Edge Runner Mill**
- **End Runner Mill**

1. Hammer Mill

Principle

- Works on the principle of impact.
- Size reduction occurs due to the high-speed impact between rapidly moving hammers and the material particles.

Construction & Working



- The mill consists of a steel drum containing a rotating shaft.
- Hammers (fixed or swinging) are mounted on the shaft.
- The shaft rotates at high speed inside the drum.
- Material is introduced through a hopper into the grinding chamber.
- The hammers strike the material, shattering it into smaller particles.
- Powdered material passes through a screen at the bottom and is collected at the outlet.
- Particle size can be controlled by changing the screen size.

Uses

- Grinding pharmaceutical raw materials (e.g., drugs, chemicals, and excipients).
- Size reduction of herbal medicines and sugar.
- Preparation of powders in chemical and pharmaceutical industries.
- Produces particles in the size range of **10–400** µm.

Advantages

- Rapid and efficient in action.
- Can grind a wide variety of materials.
- Simple design, easy to install and operate.
- Requires moderate energy.
- Low maintenance cost.

Disadvantages

- Not suitable for materials with low melting point (may soften/melt due to heat generation).
- Not suitable for sticky materials (they clog screens and adhere to surfaces).
- Equipment may get damaged by very hard or foreign materials in the feed.

2. Ball Mill

Principle

- The Ball Mill works on the principle of impact and attrition.
- Size reduction occurs when balls collide with the particles and with each other inside the rotating cylindrical chamber.
- The impact breaks larger particles, while attrition (rubbing action) helps in fine grinding.

Construction & Working

- A hollow cylindrical shell is mounted horizontally and rotates on its axis.
- The shell is partly filled with steel balls, porcelain balls, or hard rubber balls (grinding media).
- The material to be ground is introduced into the cylinder.
- As the cylinder rotates, the balls are lifted on the rising side due to friction, then fall back, striking the material.
- Continuous rotation causes repeated impact and attrition, reducing particle size.
- The ground material is collected from the outlet after a specified milling time.
- Ball mills may be operated in:
  - **Batch process** (fixed quantity is ground and collected).
  - **Continuous process** (material continuously fed and discharged).

Uses

- Used for fine grinding of powders in pharmaceutical and chemical industries.
- Preparation of suspensions, emulsions, and ointments.
- Suitable for grinding brittle materials like drugs, minerals, and pigments.
- Used in the production of nano-sized particles (with advanced designs).
- Common particle size obtained: 10–20 µm.

Advantages

- Suitable for both wet and dry grinding.
- Can handle large quantities of material.
- Continuous operation is possible.
- Can grind very hard substances.
- Simple design and reliable operation.

Disadvantages

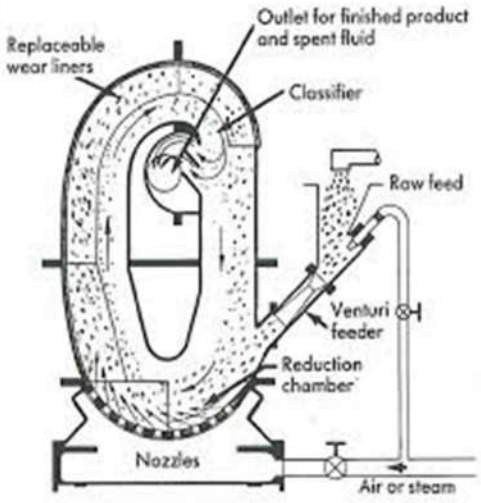
- Time-consuming process (takes longer compared to hammer mill).
- Bulky equipment → requires large space.
- High power consumption.
- Not suitable for sticky or soft materials (they may coat balls and chamber).
- Possibility of contamination from balls or lining material.

3. Fluid Energy Mill (Jet Mill)

Principle

- Works on the principle of impact and attrition.
- High-velocity compressed air, steam, or inert gas is introduced into a chamber at supersonic speed.
- Particles collide with one another and with the walls of the chamber → this causes size reduction.
- The centrifugal force classifies particles:
  - Fine particles → carried away with the air stream.
  - Coarse particles → remain in the chamber for further grinding.

Construction & Working



- The mill consists of a grinding chamber (circular or oval-shaped) with no moving parts.
- Compressed air or steam nozzles are placed tangentially at the base of the chamber.
- Material is fed into the chamber through a venturi injector.
- High-velocity air jets cause particles to:
  1. Accelerate and collide with each other (impact).
  2. Rub against each other (attrition).
- A classifier is attached at the outlet which allows only fine particles to escape, while coarse ones circulate back for further grinding.
- Achieves very fine powder: up to micron (1–10 µm) or submicron size.

Uses

- Production of very fine powders for pharmaceutical industries.
- Preparation of thermolabile substances (antibiotics, vitamins, enzymes) since no heat is generated.
- Used in inhalation products (e.g., aerosols, dry powder inhalers) where extremely fine size is needed.
- Also used for grinding toxic and explosive materials under inert atmosphere.

Advantages

- Can produce ultrafine particles (1–10 μm).
- No moving parts → low maintenance.
- No significant temperature rise, suitable for heat-sensitive drugs.
- Contamination is minimal.
- Continuous and automatic operation possible.

Disadvantages

- Very high energy consumption (requires compressed air/steam).
- High installation and running cost.
- Not suitable for sticky and soft materials.
- Needs skilled supervision.
- Limited capacity → not ideal for large-scale grinding of all types of drugs.

4. Edge Runner Mill

Principle

- Works on the principle of compression and attrition.
- Size reduction occurs by the pressure applied by heavy rollers (edge runners) as they rotate over the material and simultaneously cause shearing/attrition.

Construction & Working

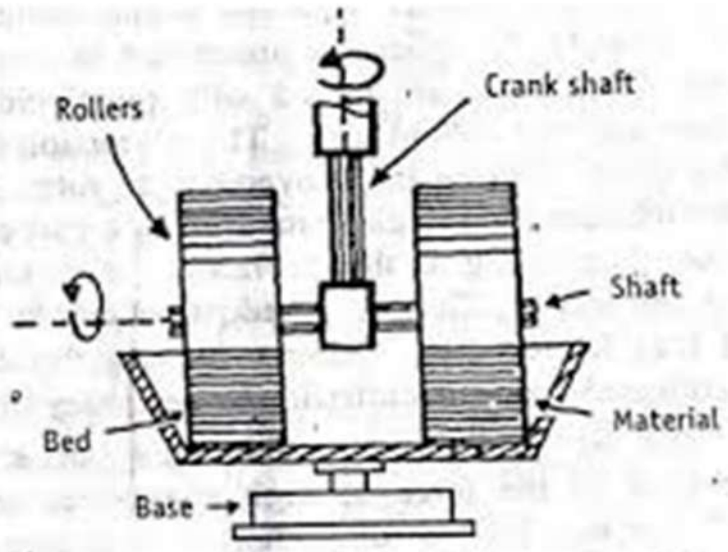


Figure 6-11. Construction of edge runner mill.

- Consists of a circular pan (granite or cast iron) fixed on a horizontal shaft.
- Inside the pan → two or more heavy wheels/rollers (edge runners) are mounted vertically.
- Rollers are made of granite/metal and are mounted on a horizontal shaft.
- The rollers rotate around the pan and also revolve on their own axis.
- Material is placed in the pan, and rollers crush, grind, and mix it by heavy pressure and rubbing action.

- Scrapers may be attached to prevent sticking of material and ensure uniform grinding.

Uses

- Used for crushing and grinding tough materials.
- In pharmaceutical industry:
  - For mixing and size reduction of ointments, pastes, and semi-solids.
  - To prepare triturations and herbal extracts.
- Also used in ayurvedic and traditional medicine preparation.
- Common in production of paints, pigments, and chocolates (outside pharma).

Advantages

- Simple in construction and easy to operate.
- Can handle both dry and wet materials.
- Suitable for tough and fibrous substances.
- Good for mixing and grinding simultaneously.

Disadvantages

- Requires large floor space.
- Slow process, not suitable for high output.
- Heavy rollers cause high wear and tear.
- Not suitable for very hard materials.
- Risk of contamination from metal rollers.

5. End Runner Mill

Principle

- Works on the principle of compression and shear (attrition).
- The heavy pestle applies pressure on the material against the hard mortar surface, causing size reduction and mixing.

Construction & Working

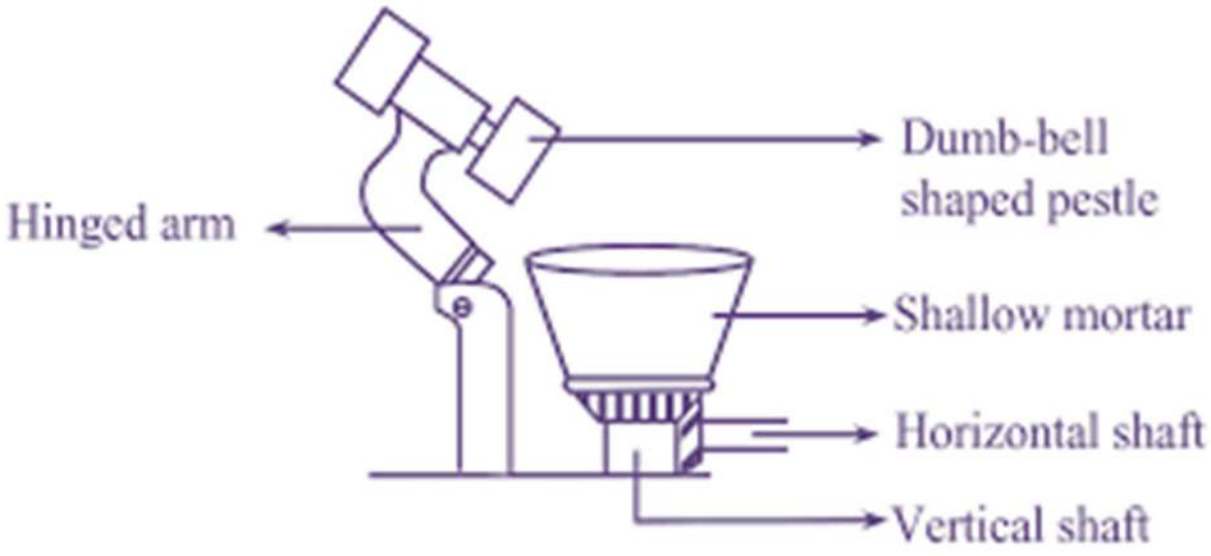


Figure: End Runner Mill

- Consists of a granite or porcelain mortar (circular pan) fixed on a base.
- A vertical shaft with a heavy pestle is mounted at the center.
- The pestle is attached to the shaft and rotates with the help of power (motor/gear system).
- Material is placed in the mortar.
- When the pestle rotates, it crushes and grinds the material by rolling and shearing action against the mortar surface.
- Scrapers may be fitted to prevent sticking of material and to improve mixing.

Uses

- Commonly used for grinding and mixing of pastes, ointments, and semi-solid preparations.
- Suitable for wet grinding.
- Used in preparation of ayurvedic medicines, herbal extracts, and traditional formulations.
- Also used for pigments, paints, and food industry applications.

Advantages

- Simple design, easy to use.
- Can handle both wet and dry grinding.
- Good for fine grinding and thorough mixing.
- Suitable for small-scale production (pharmacy labs, research).

Disadvantages

- Slow and time-consuming process.
- Requires manual feeding and supervision.
- Not suitable for large-scale production.
- High wear and tear of mortar and pestle.
- Risk of contamination from the grinding surface.