Course Code : BPHT3004

Course Name: Pharmaceutical Engineering

TOPIC:SIZE REDUCATION

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Name of the Faculty: Dr. Shikha Yadav

Course Code : BPHT3004

Course Name: Pharmaceutical Engineering

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Size Reduction

Size Reduction means decreasing size of an object.

- It is a unit operation in which materials are reduced to smaller pieces/ to coarse particles, or to still finer powder, before they can be formulated into suitable dosage forms.
- Other terms: -

Comminution Grinding Milling Pulverizing Crushing

Course Name: Pharmaceutical Engineering Course Code : BPHT3004 **OBJECTIVES** Improve Appearance: -Add your content here Smooth appearance (Ointments, texture and elegant Pastes and Creams). Add your content here • Improve physical stability. Facilitate Absorption & Bioavailability: -Rate of absorption depends on particle size. Finer the particles faster the absorption of rate \bigcirc (Nasya dravya)

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- 4. <u>Improve Stability</u>: -
- Sp. for biphasic systems Suspension, Emulsion etc.
- Emulsion \downarrow Size of oil droplets \rightarrow Rate of creaming \downarrow
- Suspension \downarrow rate of sedimentation
- 5. <u>Extraction</u>: -
- More surface expose to solvent hence more extraction of drug (*Yavkuta* in *kwatha* formation).
- 6. <u>Mixing</u>: -
- Easy mixing
- Assure uniform dosage

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- 7. Aerosol and Inhalation preparations: -
- Size determines the position and retention of particles in bronchioles & less irritation.
- 8. Parenteral Suspension: -
- o Rheology
- Product Syringeability
- 9. Facilitate drying: -
- Drying of wet masses may be facilitated by milling.
- Milling \uparrow surface area Drying \uparrow .

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10. <u>Ophthalmic suspension</u>: -Very fine to avoid eye-irritation.

11. <u>To Increase Viscosity</u>: -Viscosity of Acacia increases on fine sub-division.

12. To decrease bulkiness of crude drugs

13. <u>Chemical reactivity</u>

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ADVANTAGES & DISADVANTAGES

DISADVANTAGES

- Change in colour (Ex. Red Mercuric oxide becomes yellow)
- Loss of Aromatic principles
- Drug degradation
- Problem of Preservation

ADVANTAGES

- Content uniformity
- Uniform flow
- Effective drying
- Increase surface area/ viscosity
- Uniform mixing & drying
- Improve rate of absorption
- Improve dissolution rate

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FACTORS AFFECTING SIZE REDUCTION

1.Hardness: -

- Harder the material difficult is the size reduction.
- 2. <u>Toughness</u>: -
- Ex. Fibrous drugs, Green fresh leaves etc. are soft but tough.
- Toughness can be reduced by lowering the temperature. The advantages of this method are:

Less decomposition of thermolabile material No loss of volatile material

No oxidation No explosion

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3. <u>Stickiness</u>: -

Cause difficulty in size reduction. Material may stick to the surface or mesh may get choked. Solution:

Dryness

Addition of inert materials such as Kaolin to sulphur

- Ex. Gums & Resinous materials (*Guggulu*, *Mochras* etc.)
- 4. <u>Slipperiness</u>: -

As material acts as lubricant.

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Moisture content: -

Influences properties such as Hardness, Toughness & Stickiness. Less than 5 % moisture – Dry grinding. More than 50 % - Wet grinding.

6. Melting or Softening point: -

Heat generated during grinding creates problems with materials which tend to melt/ stick/ decompose due to heat. Ex. Camphor, Thymol, Stearic acids, Waxes, Fats, Resins etc.

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Material Structure

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- 9. <u>Size of the starting material</u>
- 9. Quantity of material to be reduced
- 10. Size, Shape, Flow & Bulk density of the product

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FACTORS AFFECTING DEGREE SIZE REDUCTION Formulation: -

Pills, Powders (in suspension & in mixtures) – Fine powder. Suspension (to be injected) – Very fine powder.

- 2. <u>Extraction</u>: -
- a. Physical character of the drug: -
- Soft drug (fresh) Sliced/ Crushed.
- Hard drug (*yashti*) Coarse to Moderately Coarse.
- Solubility If constituents are less soluble fine powder.
- Localization of drug constituents

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- b. Solvent/ Menstruum used:
- Water (Causes more expansion of vegetable tissue and penetrates easily) Coarse powder.
- Alcohol (Hardens the vegetable drug tissues and so penetration is slow) Fine powder.
- c. Drug/ Menstruum ratio: -
- Menstruum large Coarse powder (Weak preparation).
- Small Fine powder (Strong preparation).

Process: -

- Infusion & decoction Drug/ Menstruum ratio is high & Menstruum is water Coarse to Moderately coarse.
- Maceration & percolation Drug/ Menstruum ratio is small & Menstruum may or may not be water Fine.

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MECHANISM OF SIZE REDUCTION

- Consists of two parts: -
- 1. First opening up of any small fissures (cracks) which are already present.
- 2. Secondly formation of new surfaces.
- Large particles with several cracks More rapid size reduction.
- Small particles with less no. of cracks Slow size reduction.
- Ex. Coal contains no. of small cracks Large particles are broken more rapidly than the small ones.

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- Fine grinding needs more energy to initiate cracks.
- So, from Energy utilization point of view Size reduction is an inefficient process.
- Efficiency of the process depends on: -
- a. Load applied
- b. Magnitude
- c. Nature of force exerted (Compressive/Impact/Shear)
- If applied force must be more than the elastic limit.
- If not on removing the load the expanded particle again returns to its original size.
- The energy is stored in the particles in form of heat & no size reduction is done.

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METHODS OF SIZE REDUCTION

- There are four reduction: -
- 1. Cutting (Slicing)
- 2. Compression (Bruising)
- 3. Impact
- 4. Attrition

5. Impact and Attrition

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- 1. Cutting (Slicing): -
- The material is cut into pieces.
- It may be effected by a sharp pen knife, a pair of scissors, or a root cutter.
- Equipment: Cutter mill
- 2. Compression (Bruising): -
- Material is crushed by application of a pressure.
- Particle disintegration by two rigid forces.
- Equipment: Mortar and Pestle (Laboratory) and Roller mill (Industry)

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Impact: -

- The material is stationary and is hit by an object moving at high speed or Moving particles strikes a stationary surface.
- Size reduction occurs by a single rigid force.
- Equipment: Mortar and Pestle (Laboratory) and Hammer mill & Disintegrator (Industry)

4. Attrition: -

- Arising from particles scraping against one another or against a rigid surface.
- Here, the material is subjected to pressure as in compression, but the surfaces are moving relative to each other.
- Equipment: Roller mill

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- 5. Impact and Attrition: -
- Here, both impact and attrition are combined.
- Equipment: Ball mill and Fluid energy mill

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ENERGY LAWS

- <u>Rittinger's Law</u>: -
- "Energy required (cons

(consumed)

is proportional

to the fresh surface produced (sheared)".

if p=-2

$$E = C\left(\frac{1}{L_2} - \frac{1}{L_1}\right)$$

 $C = K_R f_c,$

fc is the crushing strength of the material

energy required for size reduction is directly proportional to the increase in surface

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More applicable to fine powders

- Kick's Law: -
- the logarithm of the ratio between initial and final "Energy necessary for crushing material is proportional to diameters".

if p=- 1 $E = C \ln \frac{L_1}{L_2}$ $C = K_k f_c,$

fc is the crushing strength of the material

$$E = K_K f_c \ln \frac{L_1}{L_2}$$

energy required to crush a given amount of material from 50 mm to 25mm in size is same as that required to reduce 12 mm to 6mm

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- **Bond's Law:** (Intermediate between Rittinger's & Kick's law)
- "The useful work is directly proportional to the new surface area, & since the crack length is proportional to the square root of the new surface area produced, the useful energy or work in inversely proportional to the square root of the product diameter minus the feed diameter".

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Methods

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CUTTER MILL PRINCIPLE: - Cutting

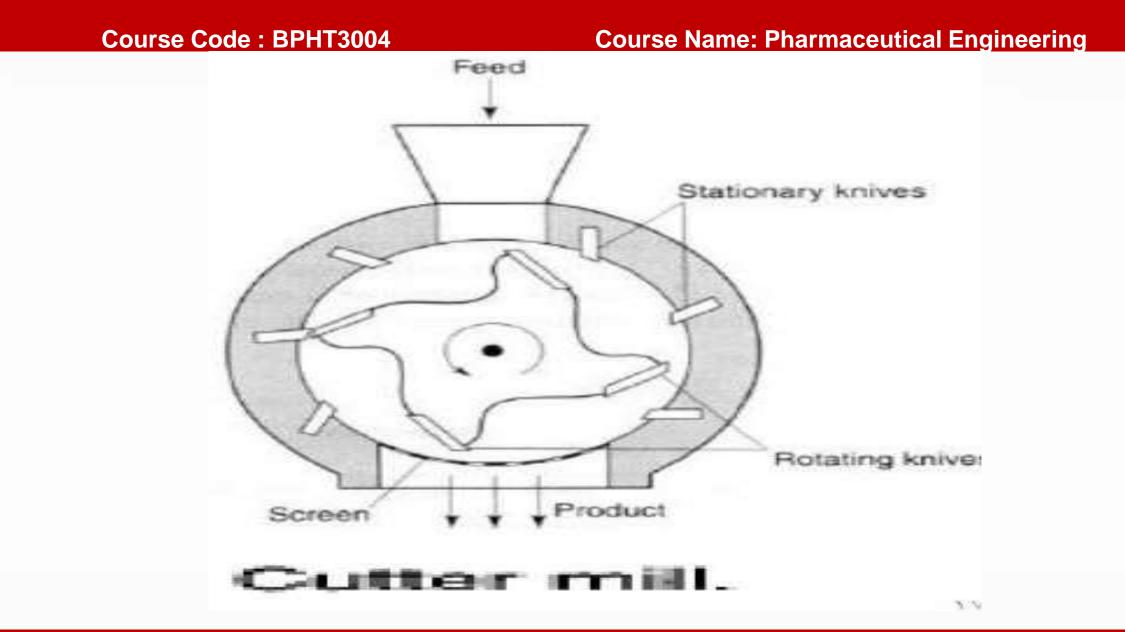
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• CONSTRUCTION: -

- Cutter mill has two type of knives
 - Stationary & Rotatory.
- Stationary knives are mounted in the casing of the machine.
- Rotating knives are attached to a horizontal rotor which rotate at high speed. Upper part has a hopper for the feed and lower part has a detachable screen.



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• WORKING: -

- Rotor disc rotate at 200-900 revolution per minute.
- Feed material is loaded through hopper.
- Size reduction occurs by fracture of particles between two knives (rotating and stationary) which have a clearance of few millimetres.
- Particles pass through the screen product which is collected into receiver.

• ADVANTAGES: -

- Simple set-up.
- Easy to clean, operate and maintenance cost is less due to less complicated machinery involved.
- Operation is continuous.
- Less wear and tear.
- Good for coarse grinding.
- Wide range of materials (soft-hard-fibrous-tough).
- Sieve being detachable different sizes can be used as per need.

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size

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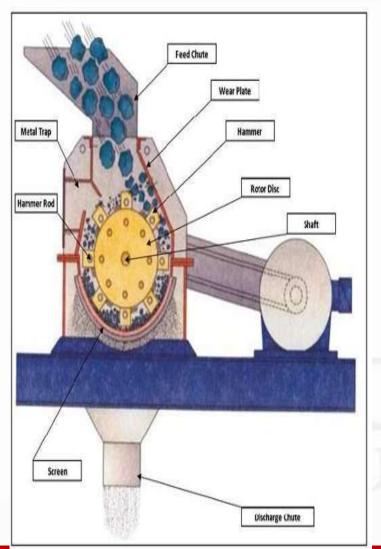
• DISADVANTAGES: -

- Not suitable for fine grinding.
- Very hard material cannot be grinded.
- In case of fine particle thus increases the cost of production.
- Sticky materials cannot be used.
- O HAMMER MILL
- **PRINCIPLE: -** Impact
- CONSTRUCTION: -
- \circ Stout metal (S.S.) casing.
- Metal casing enclosing central shaft.
- Four or more hammers attached to central shaft.
- Hammers are mounted with swivel joints. Hammers swing out to a radial position when shaft is rotated.
- $\circ~$ Hammers may be either square, tapered or stepped form.

further processing needed

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• CONSTRUCTION: -

- Upper part Feed hopper.
- Lower part Screen of desired size.
- Screen is replaceable as per size required.
- Mill is connected with fan and cyclone separator.

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• WORKING: -

- Material is fed in the grinding zone.
- In the grinding zone the hammers revolve at very high speed (5000-10000 RPM).
- Material is thrown out centrifugally and is grinded by impact of hammers or against the plates along the periphery of mill casing.
- If the particle-size of the material (feed) is less than that of the mesh size it will pass. Oversize particles will retain which will be recycled.
- ADVANTAGES: -
- Rapid size reduction.
- Different types of materials can be grinded Dry, Wet filter press cake, ointments & slurries.
- Product size can be controlled by variation of Rotor speed
 - Hammer type & no. Size of
 - mesh
 - Feed rate
 - Clearance between hammer & casing

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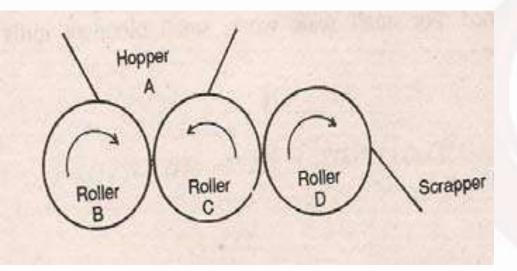
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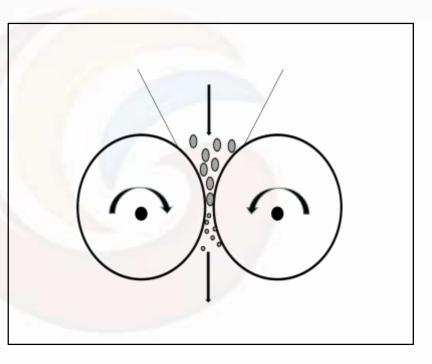
- DISADVANTAGES: -
- Not suitable for thermolabile material as high speed causes heat generation.
- Sticky material cannot be grinded as it may choke the screen.
- If rate of feed not controlled mill may choke.
- Not useful for abrasive material.
- APPLICATIONS: -
- Used for producing intermediate grades of particle size.
- Powdering of barks, roots, leaves (dry), crystals and filter cakes.
- For preparation of wet granules for tablets.
- MODIFICATIONS: -
- Different types of screen.
- Water jacketed for thermolabile material. **ROLLER MILL**

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- Also known as Crushing rolls.
- **PRINCIPLE:** Compression & Attrition





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- CONSTRUCTION: -
- Consists of two cylindrical rolls of stone or metal, mounted horizontally & rotate along their axis.
- The gap between the rolls is adjustable to control the size of product.
- The rollers are from few centimetres to a meter or more in diameter.
- The surface of the rollers may be smooth, furrowed or toothed.
- Upper part hopper and lower part collector/screen.
- WORKING: -
- Material is fed into the hopper and then it is dropped into the gap.
- The rolls rotate at different speeds, so that the material is sheared as it passes through the gap and is transferred from the slower to the faster roll, from which it is removed by means of a scraper.
- The speed of the rollers & the gap between the rollers determine the product size.
- ADVANTAGES: -
- Simple construction.
- Easy to clean and operate.
- Gives uniform product.
- Suitable for abrasive material.

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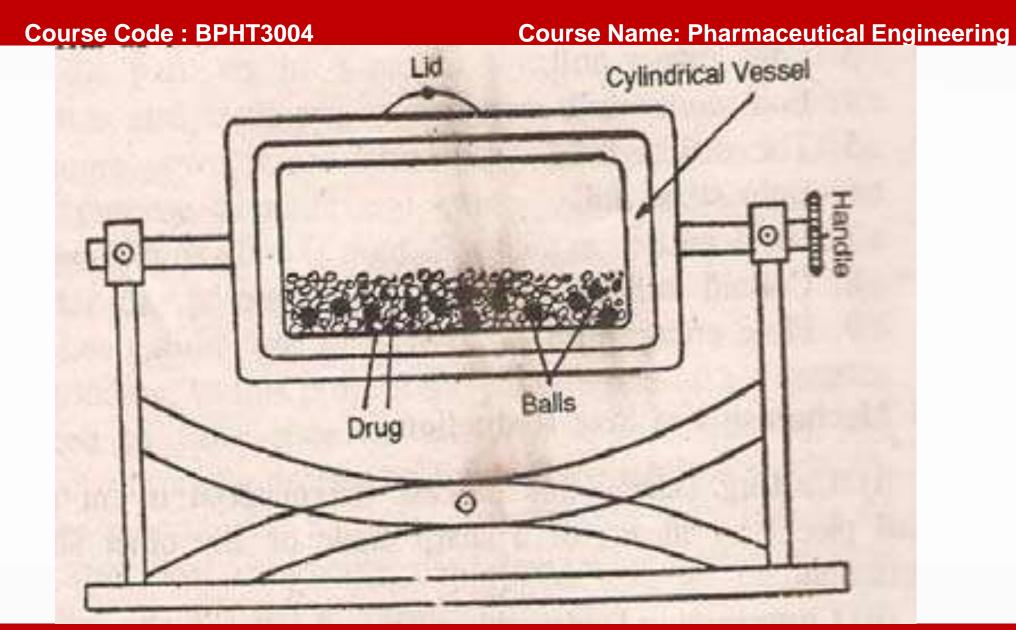
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- DISADVANTAGES: -
- \circ Do not produce very fine powder.
- High Wear & Tear.

BALL MILL

PRINCIPLE: - Impact & Attrition

- CONSTRUCTION: -
- Consists of a hollow, cylindrical shape vessel- jar or POT rotating horizontally.
- \circ Pot may be made up of metal (S.S.), porcelain, or rubber lined.
- Length of cylinder is slightly greater than its diameter.



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- CONSTRUCTION: -
- The mill is filled with "balls" or "pebbles" of flint, porcelain, steel or S.S. which act as grinding medium.
- For effective grinding 30 50
 % volume of the mill should be filled with balls (Ball charge).
- Ball size depends on the size of the feed & diameter of the mill.
- Smaller balls give slower but fine grinding.
- Varying sizes of balls gives a better product, since large balls crush the feed & smaller ones give fine product.
- WORKING: -
- The material to be reduced is fed into the cylindrical vessel (pot).
- The vessel rotates horizontally on its long axis.
- Balls move causing combined Attrition & Impact thereby doing size reduction.

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- ADVANTAGES: -
- Simple construction.
- Easy to clean and operate.
- Economical and Cheap.
- Afford large grinding surface within a limited space.
- Useful for Batch or Continuous operation.
- Being a closed system useful for toxic substances.
- May be sterilized and sealed for sterile milling in the production of ophthalmic & parenteral products.
- Wide degree of materials can be grinded with different degrees of hardness.
- \circ Very fine powder (100 #) can be produced.
- Useful for grinding explosive due an inert atmosphere being created.
- Used for both wet & dry grinding.

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• DISADVANTAGES: -

- High Wear and Tear.
- Not suitable for soft & sticky materials.
- Very noisy.
- Slow process.
- APPLICATIONS: -
- For grinding of drugs & suspensions.
- For dry or wet grinding.
- For sterile grinding.
- 0

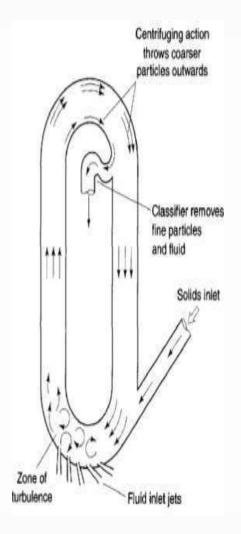
FLUID ENERGY MILL

PRINCIPLE: - Impact & interparticulate Attrition

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- CONSTRUCTION: -
- Loop of pipe (20 to 200 mm in diameter & upto 2 m in height) form cylindrical grinding chamber made up of S.S. or alloy steel.
- Fluid (air/ steam/ inert gas) introduced through nozzles at the bottom of the loop under pressure (25 to 300 PSI (pounds per square inch).
 WORKING: -
- Material is fed near the bottom of the mill.
- Material is then exposed to high pressure stream of air or gas & is swept into violent turbulence by the sonic & supersonic velocity of the streams.
- The particles are accelerated to high speed & they collide with each other, which causes fracture of the particles.
- The high degree of turbulence causes impact & attritional forces between the particles, which reduce the material to finer state.
- The finer particles are employed by the drag of gas leaving the mill, while larger, heavy particles are carried downward & back to the grinding chamber.



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• ADVANTAGES: -

- Simple construction and Easy to operate.
- Fine particle size can be obtained.
- There is no moving part in the mill, so no abrasion hence no contamination of the product.
- The classifier, permits close control of the particle size thereby narrow size distribution.
- Expansion of gases leads to cooling, so useful for thermolabile pharmaceuticals such as Vitamins, Antibiotics, Enzymes & Hormones.
- For sensitive materials inert gas can also be used.
- Product is smoother than by any other method.
- **DISADVANTAGES:** -
- High cost.
- If feed is not controlled the material may choke.
- If the air fluid is not clean it causes contamination of the product.
- Premilling is required.

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- APPLICATIONS: -
- Fine powdering
- Thermolabile materials
- Dehydration of wet materials
- Coating of fine particles



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