PHA 389 PHARMACEUTICAL TECHNOLOGY- I

7th week

Milling (Grinding)

- Milling or grinding is a mechanical process of reducing the particle size of solids.

- *Also known as* ***comminution, cutting, chopping, crushing, micronizing or pulverization***

Milling is important for :

- Decreasing particle size increase specific surface of the substance.
- Increase the free surface energy of milled substance.
- significantly increase the speed of substance and diffusion processes.
- strengthen the pharmacological activity of substances

Milling

advantages

- Mixing is more uniform if ingredients are roughly the same size
- Milling of wet granules can promote uniform and efficient drying
- Increased surface area can improve dissolution rate and bioavailability
- Improved content uniformity of dosage units

disadvantages:

- Excessive heat generation can lead to degradation, change in polymorphic form
- Increase in surface energy can lead to agglomeration
- May result in excessive production of fines or overly broad particle size distribution

Reducing particle size can strengthen the pharmacological activity of substances

- Specific surface (surface area per unit weight) increase by size reduction which affect the therapeutic efficiency of medical substance.

❑ especially if the material have low solubility.

Examples,

- Griseofulvin
- Penicillin G procaine
- Aspirin suppository
- Calomel ointment
- Aerosol
- Suspensions

- ✓ At all stages of milling process there will be a **size distribution** of particles,
- ✓ No machine can produce completely the same size for all particles in the bulk.
- ✓ So the particle size distribution must be measured.

Three method involved in size distribution measurement:

a. Microscopy
b. Sieving
c. Sedimentation

Microscopy

- Particles are sized directly and individually
- A calibrated scale can be used
- White light can resolve particles between 0.2-100 micron
- Ultraviolet light can resolve with a lower limit of 0.1 micron
- Ultra microscope lower limit is 0.01micron
- Elecron microscope limit range is 0.2-0.0010 micron (SEM-TEM)

Sieving

- Sieve is a pan with a bottom of wired cloth with square openings
- The procedure involve shaking, weighing of portion retained, and taping
- Particle shape is important, mostly sphere-like shapes passes through sieves much easily

✓Most widely used method

✓Inexpensive

✓Rapid

✓Little variation

✓Lower limit is 50 micron

Sedimentation

- Used over size range from 1 to 200 microns.
- Based on the dependence of the rate of sedimentation of the particle on their size expressed by stoke’s equation.
- Pipette method (Ex. Andreasen pipette)is the simplest means of incremental particle size analysis.

Mills

✓A mill consist of three part:

1. Feed chute
2. Grinding mechanism
3. Discharge chute

✓The principle of operation depends on:

1. Cutting
2. Attrition
3. Rolling/Compression
4. Impact

Milling forces

Attrition
involves breaking down of the material by rubbing action between surfaces

Rolling/compression
uses a heavy rolling member to crush and pulverize the material

Impact
involves the operation of hammers at high speeds. These strike the lumps of material and throw them against each other or container walls.

Classification of equipment for milling:

Due to the machine type

1. Cutting machine
2. Attrition machine
3. Compression machine (Roller machine)
4. Impact machine
5. Impact - Centrifugal machine

Due to the mechanism used to break the particles:

1. Disc
2. Ball
3. Rotor
4. Hammer
5. Rollers and others

Classification equipment for milling:

Due to degree of milling:

- Coarse crushers (>20 mesh; >840 micron)
  roll and impact crushers
- Intermediate grinders (200-20 mesh; 74-840 micron)
  Hammer mills, roller mills
- Fine grinding mills (<200 mesh; <74 micron)
  Colloid, fluid energy centrifugal mills

Factors influence milling

1. Properties of a solid (Hard (iodine), soft and intermediate solid).
2. Specification of the product.
3. Physical nature of material (fibrous, friable)
4. Water content
5. Heat during milling (low melting point, heat sensitive drug, pigment, unstable compound)
6. Shape of milled particle (flow specifications)
7. Milling may alter crystalline structure and causes chemical change in some materials

Machine requirements

- The substances must retain their initial composition and pharmacological properties during the milling process;
- They must remove enough milled particles periodically from the sphere of comminution ;
- Prevent formation of dust (sealed enclosures);
- Must keep moisture of material
- The use of sequence connected crushing-milling machines are preferred.

Mill selection depends on:

- Initial particle shape, size and size distribution of the material,
- Physical and chemical properties of material for milling (such as brittleness, hardness, moisture content, melting point..)
- Desired final product specifications
- The total amount of material for milling, capacity of the mill and milling rate
- Versatility of operation
    - wet and dry milling,
    - rapid change of speed and screen
    - and safety requirement

Cutting machines

- They are used to comminution herbal drug that has a fiber structure
- Grass cutting and straw cutting (grass, stalks).
- Root cutting with the guillotine knife - for grinding roots.
- Drum straw cutting - for grinding dry medicines.
- Knife mill - for milling volume materials, containing cellulose
- Motorized soft meat grinder - for fresh herbal drugs, animal raw materials

Crusher machines

They are used for milling solid materials:

- Cheek and jaw mill
- Rollers mill
- Cone mill
- Hammer mill
- Disk mill (Excelsior)

Hammer mills

- They contain a high speed rotating shaft on which is mounted either rigid or swing hammers. This unit is enclosed with a chamber containing a grid/removable screen which the material passes.
- Feeding hopper is on the upper part.

- Hammer mills are impact - attrition mills.
- Particle size is regulated by
  - rotor speed
  - feed rate
  - type/number of hammers,
  - clearance between hammers

Advantages of hammer mills

- The size of product is controlled by speed of hammers and type and size of the screen
- Narrow size distribution
- Can be used for dry, wet, cakes, ointment, slurries.
- Simple to install and operate
- Speed and screen can be rapidly changed
- Comminution is affected by impact of peripheral hammer speed (up to 7600m/minute).
- Easy to clean
- May be operate as closed system.

Centrifugal-impact mills

- Their design combines sieving and milling in one unit operation.
- Mill consist of non-rotating stator with a basket sieve basket.
- Particles smaller than sieve hole size passes through the mill and larger particles directed to a centrifugal force to impact with the stator.

Ball mills

- It’s combined of attrition and impact mills.
- Consist of horizontally rotating hollow vessel of cylindric shape.
- The mills filled with balls of steel or pebbles (grinding medium).
- Pebbles, rods, and tube mills
- According to the speed of balls, At low speed attrition force
  At sufficient speed centrifugal force
  At high speed impact force is used
- Degree of particle size reduction depends on: size of the balls,
  ratio of ball and powder
  speed of the mill

Factors affecting ball milling process

1. size of ball
2. Charge of balls in mills
3. Amount of material to be milled
4. Weight of balls
5. Wet an dry milling
6. Viscosity
7. Wetting agent

Advantages of ball mill

- Used either for dry or wet
- Batch or continuous operations
- Sterile grounding possible
- Installation, operation, and labor costs are low
- Unsurpassed for fine grinding of abrasive and hard material

Fluid energy mill (Micronizer)

- Mills have no moving parts
- Grinding is achieved by subjecting solid material to stream of high velocity elastic fluids like air, inert gas or steam.
- Particles are accelerated to high speed, when they collide with each other the impact causes a fracture of these particles.
- Original material is generally pre-milled so milling begins from 20-100mesh and
- Reduction of particle size is between 1-20 microns
- Fine powder is removed centrifugally so there is always danger of dust explosions. Thus, dust collector is required
- Fluid energy source is also required.

Cutting mills

- Used for tough and fibrous material
- Cutting and shearing
- They consist of horizontal rotor with rotary knife cutter (with 2-12 knives) which turns with a cylindrical housing.
- This housing also involves stationary knives.
- The feeding hopper is at the upper part and feed should not exceed the length of knife
- There is a screen at the bottom not more than 1 inch thick for finished product.

Roller mill

- Consist of two smooth rollers (could up to five) operating at different speed in the same direction
- Reduction power is combination of compression (crushing) and shearing forces
- The gap between the rollers control the particle size.

Colloid mill

- Consist of high speed rotor and stator with adjustable clearance range.
- Rotor speed up to 20.000 rpm
- Premilling is required
- Used to process suspension and emulsion
- Not for dry material
- Pre mixing with liquid
- May be smooth or rough surface regarding rotor and stator