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محتوى المحاضرة

Milling
Milling Concept

Few materials used in pharmaceuticals exist in the optimum size, and most must be comminuted at some stage or the other during the production of a dosage form.

Milling is the mechanical process of reducing the particle size of solids.

Various terms (comminution, crushing, disintegration, dispersion, grinding, and pulverization) have been used synonymously with milling depending on the product, equipment, and the process

Milling equipment is classified as coarse, intermediate and fine

according to the size of the final product. Size is conventionally expressed in terms of mesh (number of opening per inch square)

1. Coarse for particles size larger than 20-mesh
2. Intermediate (20-200) mesh (74 -840 micron)
3. Fine for particles size smaller than 200-mesh

A given mill can be used successfully to prepare particles in more than one class. (ex. Hammer mill used for granulation (16-mesh) and for milling crystalline API to a 120-mesh powder)

PHARMACEUTICAL APPLICATIONS

Numerous examples have been quoted to stress the importance of fine particles in pharmacy and milling or grinding offers a method by which these particles can be produced. The surface area per unit weight, which is known as the *specific surface*, is increased by size reduction. In general, a 10-fold increase in surface area has been given by a 10-fold decrease in particle size. This increased surface area affects:

1)Dissolution and therapeutic efficacy: Dissolution and therapeutic efficiency of medicinal compounds that possess low solubility in body fluids are increased due to increase in the area of contact between the solid and the dissolving fluid

2) **Extraction:** Extraction or leaching from animal glands (liver and pancreas) and crude vegetable drugs is facilitated by comminution. The time required for extraction is shortened by the increased area of contact between the solvent and the solid and the reduced distance the solvent has to penetrate into the material.

3)Drying: The drying of wet masses may be facilitated by milling, which increases the surface area and reduces the distance that the moisture must travel within the particle to reach the outer surface. In the manufacture of compressed tablets by wet granulation process, the sieving of the wet mass is done to ensure more rapid and uniform drying

PHARMACEUTICAL APPLICATIONS

4)Flowability: The flow property of powders and granules is affected by particle size and size distribution. The freely flowing powders and granules in high-speed filling equipment and tablet presses produce a uniform

product.

5)Mixing or blending: The mixing or blending of several solid ingredients of a pharmaceutical is easier and more uniform if the ingredients are of approximately the same size. This provides a greater uniformity of dose. Solid pharmaceuticals that are artificially coloured are often milled to distribute the colouring agent to ensure that the mixture is not mottled and uniform from batch-to-batch.

6)Formulation: Lubricants used in compressed tablets and capsules function by virtue of their ability to coat the surface of the granulation or powder. A fine particle size is essential if the lubricant is to function properly. The milling of ointments, creams, and pastes provides a smooth texture and better appearance in addition to improved physical stability. Also, the sedimentation rate of suspensions and emulsions is a function of particle size and is reduced by milling

SIZE DISTRIBUTION AND MEASUREMENTS

1. **Microscopy**
2. **Sieving**
3. **Sedimentation**

THEORY OF COMMINUTION

The mechanical behavior of solids, under stress are strained and deformed, is shown in the stress-strain curve which

The initial linear portion of the curve is defined by Hooke's law(stress is directly proportional to strain), and Young's modulus (slope of the linear portion) expresses the stiffness or softness of a solid in dynes per square centimeter. The stress-strain curve becomes nonlinear at the yield point, which is a measure of the resistance to permanent deformation. With still greater stress, the region of irreversible plastic deformation is reached. The area under the curve represents the energy of fracture and is an approximate 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 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 greater number, 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.

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If the force of impact does not exceed the elastic limit, the material is reversibly deformed or stressed. When the force is removed, the particle returns to its original form, and the mechanical energy of stress in the deformed particle appears as heat

A force that exceeds the elastic limit fractures the particle, 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

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.

Mechanisms of Comminution

Mills are Equipments designed to impart energy to the material and cause its size reduction. There are four main methods of effecting size reduction, involving different mechanisms:

1)Cutting: It involves application of force over a very narrow area of material using a sharp edge of a cutting device.

2)Compression: In compression, the material is gripped between the two surfaces and crushed by application of pressure.

3)Impact: It involves the contact of material with a fast moving part which imparts some of its kinetic energy to the material. This causes creation of internal stresses in the particle, there by breaking it.

4)Attrition: In attrition, the material is subjected to pressure as in compression, but the surfaces are moving relative to each other, resulting in shear forces which break the particles.