INTRODUCTION
Size reduction is a process of reducing large solid unit masses - vegetables or chemical substances into small unit masses, coarse particles or fine particles. Size reduction is commonly employed in pharmaceutical industries. It is the process of reduction of large solid units into small units. Size reduction process is also referred to as Comminution and Grinding. When the particle size of solids is reduced by mechanical means it is known as Milling. Pharmaceutical powders are polydisperse - Consisting particles of various size, which create considerable difficulty in production of dosage forms. Particles with equal size i.e., mono-size are ideal for pharmaceutical purpose. Size reduction along with size separation plays a very important role in producing mono-size powder. The size reduction operation can be divided into two major categories depending on whether the material is a solid or a liquid. If the material is solid, the process is called grinding and cutting, if it is liquid, emulsification or atomization. There are many types of size-reduction equipment, which are often developed empirically to handle specific materials and then are applied in other situations. Various factors like hardness, toughness, stickiness, slippingness, moisture content, melting or softening point, abrasiveness and others (material structure, size, shape, flow, and bulk density of product) ratio of feed size to product size, affect the size reduction. This literary study has been taken into consideration in order to understand different methods and the factors which effect size reduction.1-3

Objectives of Understanding Size Reduction
1. Size reduction leads to increase of surface area.
2. Pharmaceutical capsules, insufflations (i.e. powders inhaled directly into the lungs), suppositories and ointments require particles size to be below 60 mm size.
3. To increase the therapeutic effectiveness of certain drugs by reducing the particle size.
4. Size reduction produces particles in narrow size range. Mixing of powders with narrow size range is easier.
5. The mixing of several solid ingredients is easier and more uniform if the ingredients are reduced to same particle size.
7. The stability of emulsions is increased by decreasing the size of the oil globules.
8. All the ophthamical preparations and preparations meant for external application to the skin must be free from gritty particles to avoid irritation of the area to which they are applied.
9. The rate of absorption of a drug depends on the dosage form, route of administration and particle size. The smaller the particle size, quicker and greater will be rate of absorption.
10. The physical appearance of ointments, pastes and creams can be improved by reducing its particle size.4

MATERIALS AND METHODS
Materials
General Parts of Size Reduction Equipment
Any Size Reduction equipment contains 3 basic components, they are listed below and it has been highlighted in Figure No-1.5,6
- Hopper
- Milling chamber
- Discharge chute / Receiver

Other Accessories
- Sieves / Screens
- Cyclone separator / Centrifugation equipment
- Dust collector

Special Features
- Cooling device
- Closed system with inert atmosphere, sterile environment
Methodology
Mechanism of Size Reduction
Highlighted in Table 1 and Figure 2

Classification and Characteristic of Size Reduction Equipments
Highlighted in Table 2

An Over-view on Various Size Reduction Equipments
In order to understand the concept of size reduction, it is necessary to enumerate different instruments with their principle, parts and uses; they are as follows.

Rotary Cutter Mill
Principle
Size Reduction involves successive cutting / Shearing the feed material with help of sharp knife. Highlighted in Figure 3

Parts
- Hopper
- Milling chamber- Horizontally mounted rotor disc consisting 2 to 12 rotating knives spaced uniformly and Casing has stationary knives
- Screen
- Discharge chute

Determination of Particle Size and Shape
- Rotor size
- Gap between the 2 sets of knives
- Sieve

Uses
- Size reduction of tough - fibrous materials
- Medicinal plants, animal tissues are converted to small parts

Variants
- Double runner disc mill
- Single runner disc mill

Roller Mill
Principle
Material is compressed by application of stress and attrition. Stress is applied by rotating heavy wheels, Muller or Rollers. Highlighted in Figure 4

Parts
2 cylindrical rollers of stone / metal – mounted horizontally, having diameter ranging from few millimetres to a meter. They rotate in longitudinal axis; one roller is run by motor and other freely.

Determination of Particle Size and Shape
Gap between rollers controlled to obtain desired particle size

Uses
For crushing of seeds before extraction of fixed oils.

Variants
- Multiple / corrugated rollers
- Ribbed / saw-toothed rollers

Hammer Mill
Principle
It operates on the principle of impact between rapidly moving hammers mounted on rotor and the stationary powder material. Highlighted in Figure 5

Parts
Consists of a stout metal casing, enclosing a central shaft, to which 4 or more swinging hammers are attached. Lower part of casing consists of a screen, through which material can pass and collected in a suitable receiver.

Determination of Particle Size and Shape
- Rotor speed
- Feed rate
- Clearance between hammers and grinding plates
- Size of discharging opening

Uses
- Brittle material is best fractured by impact from blunt hammers.
- Fibrous material is best reduced by cutting edges

Variants
- Fitzpatrick comminuting machine - Fitz mill
- Stokes Tornado mill

Disintegrator
Principle
The size reduction is done by impact. Highlighted in Figure 6

Parts
Consists of a steel drum enclosing a central shaft, which has a disc to which 4 beaters are fixed. The side and upper inner surface of drum is rough. Lower part of casing consists of a detachable screen.

Uses
To powder all types of drugs including very hard drugs.

Ball Mill
Principle
It operates on the principle of impact and attrition. Highlighted in Figure 7

Parts
- Consists of a hollow cylinder mounted on a metallic frame such that it can be rotated along its longitudinal axis.
- Cylinder contains balls occupying 30-50 % of mill volume. Weight of ball is constant; Size depends on the feed quantity and diameter of mill.

Determination of Particle Size and Shape
- Size of ball
- Feed rate
- Speed of rotation of cylinder

Uses
Produces fine powder. Can grind large variety of materials. As it is a closed system Toxic substances can be ground.

Fluid Energy Mill
Principle
It operates on the principle of impact and attrition. Highlighted in Figure 8

Parts
- Consists of a loop of pipe with diameter 20-200 mm. The overall height of the pipe is 2 m.
- Inlet for feed and a series of nozzles for air, inert gas. Outlet with classifier which prevents the particles to pass until they become sufficiently fine.

Determination of Particle Size and Shape
- The speed of air / inert gas
- The impact between the feed and air

Uses
To grind heat sensitive materials.
End- Runner and Edge- Runner Mill (Highlighted in Figure 9 and 10)

Other Important Techniques in Size Reduction
- Sonocrystallization - Utilizes ultrasound of frequency range 20 – 100 kHz for inducing crystallization. It is an effective means of size reduction and controls size distribution of active pharmaceutical ingredients.\(^9\)
- Spray drying - It is a common method of drying a liquid feed through a hot gas. This hot gas is air, but sensitive materials such as such as ethanol require oxygen free drying and nitrogen gas.\(^9\)
- Supercritical fluid process - It is a dense non-condensable fluid whose temperature and pressure are greater than its critical temperature and critical pressure. Drug particles are solubilised within super critical fluids and recrystallized to get greatly reduced particle sizes.\(^9\)

Advantages of Size Reduction
- Content uniformity
- Uniform flow
- Effective extraction of drug
- Effective drying
- Improves physical stability. The rate of sedimentation decreases by reducing particle size
- Improves dissolution rate
- Improves rate of absorption. Smaller the particle, greater is the absorption.
- Increases surface area and viscosity
- Facilitates bioavailability, uniform mixing and drying

Disadvantages of Size Reduction
- Drug degradation
- Poor Mixing
- Contamination

Factors affecting Size Reduction
Selection of mill - It is related to feed, milled product, safety and economics.\(^8,10\)

Factors related to nature of raw materials affecting size reduction
- Hardness - It is easier to break soft material than hard materials. Ex: For iodine hammer mill is used.
- Fibrous - These are tough in nature. A soft, tough material has more difficulty than a hard, brittle substance. Ex: Rauwolfia, Ginger. Here cutters can be used.
- Friable- These tend to fracture along well defined planes. Brittle substances can be easily converted into fine particles. Ex: Sucrose. Mechanism used is attrition, impact and pressure.
- Elastic / Sticky - Become soft during milling. Ex: synthetic gums, waxes, resins. Low melting substances should be chilled before milling. These are milled using hammer, colloid or fluid energy mill.
- Melting point - Waxy substances, fats and oils are softened during size reduction due to heat generated. This is avoided by cooling the mill and the substance.
- Hygroscopic - Certain substances absorb moisture content rapidly. This wet mass hampers the milling process. Ex: Potassium carbonate. Closed system such as porcelain ball mill is used.
- Solvated- Hydrates liberate water during milling, causes clogging of mill. Ex: sodium sulphate.
- Thermolability- Certain Substances are degraded by hydrolysis and oxidation, due to moisture and atmospheric oxygen. Heat produced on milling enhances these reactions. Closed system is used here with an inert atmosphere of CO\(_2\) and N. Vitamins and antibiotics are milled using fluid energy and ball mills.\(^10,11\)

Other Factors affecting size reduction
- Purity required - The size reduction of such hard substances leads to the abrasive wear of milling parts, causing contamination. Such mills are to be avoided. The mills should be thoroughly cleansed between different batches.
- Flammability - Under certain conditions fine dust such as dextrin, starch, sulphur are potential explosive mixtures. All electrical switches should be explosive proof and mill should be well grounded.
- Particle size - The feed should be of proper size and enter the equipment at a uniform rate to get a fine powder. Several stages are carried out in size reduction process. Pre treatment of fibrous materials with pressure rollers and cutters facilitates further Comminution.
- Moisture content- Presence of more than 5 % moisture influences hardness, toughness, stickiness of substance. In general, materials with moisture content below 5 % are suitable for dry grinding and above 50 % for wet grinding.\(^10,11\)

Advances in Size Reduction Technologies
- Micron technologies - Micronizing is defined as particles smaller than 20 microns. It enhances solubility and improves bioavailability, optimizes the formulation of the product and reduces therapeutic dose. High pressure air / gas are introduced causing particle collision and micronization.
- Gran-U-Lizer Technology - It is designed to maximize yield and minimize the size of particles. In this process there is regrinding of already ground particle, resulting in very tight particle size.
- Jet-O-Mizer particle size reduction - This mill is designed with distinct features to consume less power, provide greater range of output and ensures exceptional finished product quality. It is efficient in fine grinding and classification, no attritional heat, adjustable classification zone.
- Micro fluidizer particle size reduction - The ultra-high shear developed by the micro fluidizer processor reduces the particle size and high turbulence prevents agglomeration. This method produces a very stable product with long shelf life.\(^12-14\)

DISCUSSION
The size reduction sector in pharmaceutics is so complex and extensive that only a brief overview of the most important size reduction methods can be given here. Ever-new applications from the research and development divisions of different target markets lead to the continual further development of size reduction machines and grinding tools.\(^15\) There are many types of size-reduction equipment, which are often developed empirically to handle specific materials and then are applied in other situations. Knowing the properties of the material to be processed is essential.
Figure 1: General Parts of Size Reduction Equipment (Three basic Components)

Figure 2: Mechanism of Size Reduction

Figure 3: Rotary Cutter Mill
Figure 4: Roller Mill

Figure 5: Hammer Mill

Figure 6: Disintegrator
Figure 7: Ball Mill

Figure 8: Fluid Energy Mill

Figure 9: Edge Runner Mill
Figure 10: End Runner Mill

Table 1: Mechanism of Size Reduction-Methodology

<table>
<thead>
<tr>
<th>Methods</th>
<th>Examples</th>
<th>Approx. particle size (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutting</td>
<td>Scissors, Shears, Cutter Mill</td>
<td>100-80,000</td>
</tr>
<tr>
<td>Compression</td>
<td>Roller Mill, Pestle-Mortar</td>
<td>50-10,000</td>
</tr>
<tr>
<td>Impact</td>
<td>Hammer Mill, Disintegrator</td>
<td>50-8000</td>
</tr>
<tr>
<td>Attrition</td>
<td>Colloidal Mill, Roller Mill</td>
<td>1-50</td>
</tr>
</tbody>
</table>

Table 2: Classification and Characteristic of Size Reduction Equipments

<table>
<thead>
<tr>
<th>Equipments</th>
<th>Techniques</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutter Mill</td>
<td>Cutting Machine</td>
<td>Used for almost all the drugs, Soft materials</td>
</tr>
<tr>
<td>Impact Mill (Hammer Mill)</td>
<td>Grinders</td>
<td>Used for almost all the drugs Brittle drugs</td>
</tr>
<tr>
<td>Rolling Compression (Roller Mill)</td>
<td>Ultra Fine Grinders</td>
<td>Moderately hard and friable materials</td>
</tr>
<tr>
<td>Attrition Mill</td>
<td>Crushers</td>
<td>Soft materials</td>
</tr>
<tr>
<td>Fluid Energy Mill</td>
<td></td>
<td></td>
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<tr>
<td>Edge Runner Mill</td>
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<tr>
<td>End Runner Mill</td>
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</table>

Probably the most important characteristic governing size reduction is hardness because almost all size-reduction techniques involve somehow creating new surface area and this requires adding energy proportional to the bonds holding the feed particles together. Nearly all size-reduction techniques result in some degree of fines. So unless producing very fine particles is the objective, it usually is more efficient to perform size reduction in stages, with removal of the desired product after each operation.16

CONCLUSION

The chemical, pharmaceutical, food and mining industries all rely on size reduction. Size reduction technology has considerable importance in the pharmaceutical field. Size reduction technology has application in different fields like pharmaceutical manufacturing of novel and conventional dosage forms, supercritical fluid technology, drug delivery, nanotechnology, etc. It offers several advantages such as content uniformity, uniform flow, facilitates mixing etc. The final selection of the equipment is based on the material and the quality requirements of the product.

REFERENCES


Cite this article as: