WJPMR, 2025, 11(12), 156-163

Research Article

Impact Factor: 6.842

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

ISSN (O): 2455-3301
ISSN (P): 3051-2557
Coden USA: WJPMBB

SIZE REDUCTION IN PHARMACEUTICAL PROCESSING: MECHANISMS, MILLING EQUIPMENTS AND AYURVEDIC CORELATIONS

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DOI: https://doi.org/10.5281/zenodo.17746897

How to cite this Article: Dr. Malavika V. S.1*, Dr. Malavi Shayan2 and Dr. Vikram S.3 (2025). Size Reduction In Pharmaceutical Processing: Mechanisms, Milling Equipments And Ayurvedic Corelations. World Journal of Pharmaceutical and Medical Research, 11(12), 156–163.

Article Received on 30/10/2025 **Article Revised on 19/11/2025** **Article Published on 01/12/2025**

ABSTRACT

Size reduction is a fundamental unit operation widely utilized in pharmaceutical, chemical, and food industries to enhance material processing, improve bioavailability, and ensure uniformity of formulations. This paper provides a comprehensive overview of milling devices used for size reduction, detailing their principles, construction, working mechanisms, advantages, and limitations. Theoretical aspects including Kick's, Rittinger's, and Bond's laws are discussed to elucidate the energy requirements of comminution. Various milling techniques—such as cutting, compression, impact, and attrition—are analyzed with representative equipment like the ball mill, hammer mill, roller mill, and fluid energy mill. The paper also highlights the Ayurvedic correlation through traditional instruments like the *Khalva Yantra* and *Ullukala Yantra*, emphasizing their role in the preparation of fine powders and formulations. Factors influencing milling efficiency - such as material properties, moisture content, temperature, and polymorphism - are examined to optimize the process. Overall, milling devices are indispensable in modern and traditional pharmaceutical practices, ensuring controlled particle size, improved therapeutic efficacy, and consistent product quality.

KEYWORDS: Milling, Size reduction, Particle size.

INTRODUCTION

Size reduction is the process of decreasing large solid unit masses into smaller units. It is a fundamental operation used in various industries to improve the handling, processing, and effectiveness of materials. By reducing the size of solid materials, their surface area increases, enhancing reaction rates, dissolution and uniformity in subsequent processing steps.[1]

Milling refers to the mechanical process of reducing the particle size of solids through mechanical forces such as compression, impact or attrition.[1]

Depending on the material properties and desired fineness, methods like grinding, crushing, pulverization or disintegration are employed. In general, size reduction converts a polydisperse system(particle of various sizes) into a uniform mono-size particles.

Size reduction can be applied to both solids and liquids. In the case of solids, operations such as grinding and cutting are employed, whereas for liquids, techniques like emulsification and atomization are used to achieve the desired consistency and particle distribution.

MATERIALS AND METHODS

OBJECTIVES OF MILLING

- Production of fine particles.
- Specific Surface (surface area per unit weight) is increased.
- Increased therapeutic efficacy of certain drugs.

- Mixing/combinations becomes easier with similar size range.
- Finer size in suspensions reduces sedimentation.
- Stability of emulsions is increased.
- Rate of absorption increases.
- Improve physical appearance.

TYPES OF MILLING[1]

- Coarse (20 mesh)
- Intermediate (20 to 200 mesh)
- Fine (more than 200 mesh)

- Open Circuit Milling - Material is reduced to desired size by passing it once through the mill.
- Closed Circuit Milling - Discharge from the milling chamber is passed through a size separation device or classifier. Oversized particles are returned to the grinding chamber for further size reduction.Most valuable in reduction to fine and ultra fine size

THEORIES/ LAWS OF MILLING / COMMINUTION[2]

- GRIFFITH'S THEORY OF CRACKS & FLAWS

A crack will propagate when the reduction in potential energy that occurs due to crack growth is greater than or equal to the increase in surface energy due to the creation of new free surfaces.

- ENERGY FOR COMMINUTION - The energy required to reduce the size of particles is inversely proportional to the size raised to some power.
- KICK'S LAW - Kick assumes that the energy needed to reduce the size of the material by a certain proportion (say by half or by one order of magnitude) is constant (first order relationship).
- RITTINGER'S LAW - The energy required for reduction in particle size of a solid is directly proportional to the increase in surface area.
- BOND'S LAW - The work required to form particles of size from a very large particle size is proportional to the square root of the surface to volume ratio of the product.

MECHANISM OF COMMINUTION[3]

- CUTTING - Application of force to narrow area of material using a sharp edge of a cutting device.
- COMPRESSION - Material is gripped between 2 surfaces and crushed by application of pressure.
- IMPACT - 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.
- ATTRITION - Material is subjected to pressure as in compressure, but the surface are moving relative to each other, resulting in shear forces which break the particles.

EQUIPMENTS/ PARTS OF A MILLING DEVICE

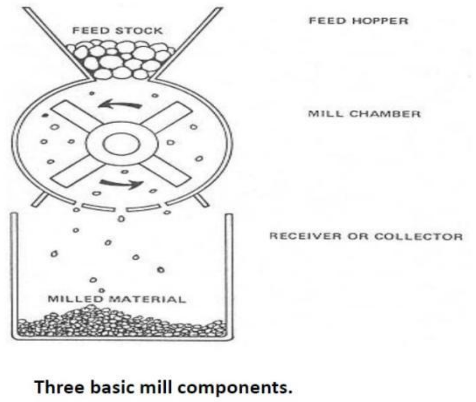

Fig 01: Components of a Milling device.

OTHERS - Seives / screens, Cyclone separator/ Centrifugation equipment, Dust Collector
SPECIAL FEATURES - Cooling Devices, Closed System with inert atmosphere & sterile environment

CLASSIFICATION OF MILLING DEVICES[4]

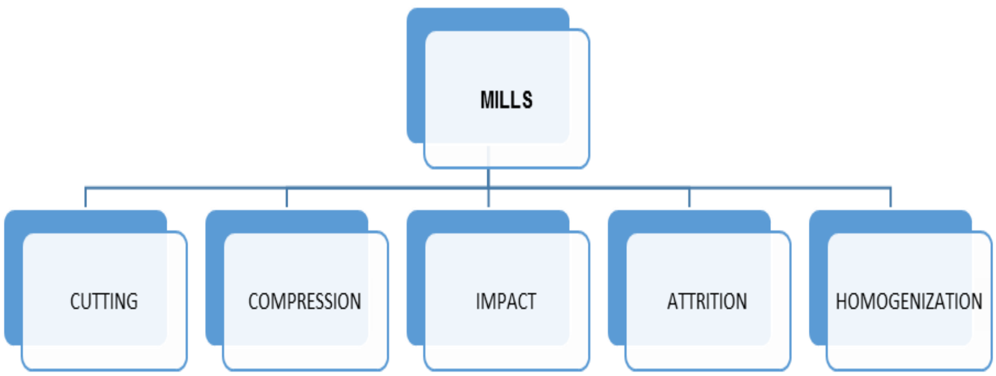

Fig 02: Classification of Milling Devices.

Examples

- Cutting - Cutter
- Compression - Roller, Colloid, Edge and End Runner
- Impact - Hammer
- Attrition - Pin, Ball, Vibro-Energy, Fluid-energy, Spiral Jet

- Homogenization - Simple, Silverson, Ultrasonic, High Pressure, Microfluidizer, Low-pressure cyclone.

1) ROTARY CUTTER MILL[4]

PRINCIPLE - Feed material is size reduced by continuous cutting and shearing by the help of sharp knives.

CONSTRUCTION

- 2 types of knives: stationary knives and rotating knives.
- A rotor disc is mounted horizontally which consist of 2 to 12 knives placed at equal distance.
- Several stationary knives and a hopper.
- Screen to control thesize present below.
- receiver

WORKING

The feed is loaded and it comes down due to gravity.→Feed material comes in close contact between the stationary and rotating knives which results in size reduction. →Small particles pass through the screen while the coarser particles are held again by the rotating knives →Repeated until desired size is obtained.

ADVANTAGES

✧ It results in particle size 80-100 mesh
✧ Used for tough and fibrous material
✧ Size reduction of drugs extracted from medicinal plants and animal tissues
✧ It is also used for the production of rubber, plastics and recycling of paper

DISADVANTAGES

✧ Consume more space
✧ Contamination
✧ Time consuming
✧ Cannot be used for sticky materials

VARIANTS - Double runner disc mill- It consist of two vertical discs which rotates in opposite direction

2) ROLLER MILL[4]

PRINCIPLE - Compression by applying stress. Stress is applied by rotating heavy wheels or rollers.

CONSTRUCTION

- Two cylindrical rollers made up of stone or metal (Size- few mm to meters)
- Rollers rotate on their longitudinal axis where one of the rollers is subjected to motor while the other one run freely.

WORKING

Material is fed from the hopper into the gap between the rollers→Rollers are also allowed to rotate at the same time→When the feed pass through the rollers under high pressure - Size reduction→Product is then collected in the receiver.

ADVANTAGES

✧ Used for crushing and cracking of seeds before extraction of fixed oils.
✧ To crush soft tissues to help in penetration of solvent during extraction process
✧ Less heat generated
✧ Less moisture loss
✧ energy efficient

DISADVANTAGES

✧ Not efficient on fibre products
✧ Additional operator inputs are required to suit grind requirements.

3) COLLOID MILL[4]

PRINCIPLE - Rotor stator priciple

CONSTRUCTION

To reduce particle size of a solid suspended in a fluid

- A rotor turns at high speed(2000-18000RPM)
- A high level of hydraulic shear[clarify] stress is applied on the fluid which results in disrupting and breaking down the structure.

WORKING

Material inserted through Hopper→It is then passed through to the narrow gap to the rotor and stator→The rugged edges shear the material into the tiniest particles depending on rotation speed→Passed through receiver

ADVANTAGES

✧ Particle size reduction
✧ Uniform dispersion
✧ Efficient Emulsification
✧ Versatality
✧ Reduced Heating
✧ Easy Maintainence
✧ Continuous Processing

DISADVANTAGES

✧ High Initial Cost
✧ Limited Particle Size Range
✧ Wear and Tear
✧ Product Contamination
✧ Energy Consumption

4) EDGE RUNNER MILL[4]

PRINCIPLE - size reduction by this mill is crushing due to the heavyweight of the stones or metal and shearing force

CONSTRUCTION

- 1 or 2 rollers made up of heavy steel or granite mounted on a horizontal shaft, which are turned around a vertical shaft attached to a steel or granite foundation.
- Runners are kept on course by scrapers which keep the material to be ground in front of them.

WORKING

Material placed on bed→Scrapper- keeps it in wheels path→Grinding.

ADVANTAGES

- Fine particles produced
- No attention is needed while operating

DISADVANTAGES

- occupies more space
- Possibility of contamination
- Time consuming
- Non- sticky materials cannot be milled
- Energy consumption

5) END RUNNER MILL[4]

PRINCIPLE - Crushing due to the heavyweight of the stones or metal pestle and shearing force as a result of the movement of these stones or meta

CONSTRUCTION

- Steel plate flanged on to a steel mortar.
- Horizontal shaft bearing the pulley is attached to a beveled cog fitting below the flanged plate.
- Pestle designed as a dumb-bell so that it can balance & grind effectively when its weight is applied.

WORKING

Feed is fed to the centre→Pestle rotates against bed of powders→Mortar revolves at high speed causing pestle to revolve→Scrappers - scrapes material constantly.

ADVANTAGES

- Easy cleaning & maintaining
- Less power usage
- Produces fine particles
- Less attention is needed while operating
- No problem of clogging or choking.

DISADVANTAGES

- Not suitable for sticky materials
- Unsuitable for hard, unbroken condition
- Noise pollution
- Requires scrapper adjustment intermittently
- Runs only on batch operation.

6) HAMMER MILL[5]

PRINCIPLE - Shred or crush aggregate material into smaller pieces by the repeated blows of small hammers

CONSTRUCTION

- A stout metal casing, enclosing a central shaft, to which 4 more swinging hammers are attached.
- Lower part consists of a screen.

WORKING

Material fed through hopper→Crushed in the chamber by hammers→Collected in the reciever.

ADVANTAGES

- Little space taken up
- Fractures Hard materials
- grinding of variety of materials
- Installation and operations are straight forward
- Easy maintance
- Reasonable price
- Produces reasonable no. of sizes

DISADVANTAGES

- Abrasive & very hard materials cannot be ground
- Excessive heat is generated
- Damage occurs if feed is not controlled
- Foreign materials
- Screen gets clogged.

7) BALL MILL[6]

PRINCIPLE - Impact and Attrition

CONSTRUCTION

- Hollow cylinder mounted on a metallic frame and rotates around its longitudinal axis.
- Balls occupy about 30-50% of mill volume.

WORKING

Feed material is introduced (60% of cylinder volume)→Fixed no. of balls introduced, closed and mill starts rotating. Speed adjusted→At optimum speed, due to centrifugal force, balls are picked by the walls, carried to top and then they fall to the bottom→This way Impact and attrition occur and size reduction becomes efficient.

ADVANTAGES

- Fine grinding
- At low speed - Milling dyes, pigments and insecticides.
- for very fine powder
- For both wet & dry grinding
- As its a closed system, Toxic substances can also be grounded.
- Sterility is achived

DISADVANTAGES

- Noisy
- Slow process
- Soft tacky, fibrous material cannot be milled.

8) PIN MILL[6]

PRINCIPLE - Centrifugal force pushes the powder to the periphery. The powder contacts with the cylindrical pins and are size reduced due to the impact.

CONSTRUCTION

- Feeding hopper
- Impact zone, Pin type or knife type rotor is used at a speed of few 100's to 5400 rpm.
- 3rd grinding done are periphery untill passes through the screens.

WORKING

Material fed→Centrifugal force pushed powder to periphery→Contacts with cylindrical pins and size reduced→Powder passes through sieve kept at bottom→Output collected.

ADVANTAGES

- Easy to clean and operate
- Components can be changes periodically
- Durable
- Higher efficacy
- Less power & time
- Solids as well as semi solids can be milled
- Low wastage

DISADVANTAGES

- Costly
- Risk of clogging in screen
- Screen & mill may get affected by abrasive materials.

9) FLUID ENERGY MILL / JET MILL[7]

PRINCIPLE - Impact and Attrition

CONSTRUCTION

- Consists of a loop pipe(dia 20-200mm, Ht - 2m)
- Inlet for feed & a series of nozzles for air, inert gas.
- Outlet with classifier which prevents the particles to pass until they become sufficiently fine.

WORKING

Pre treated feed(reduced to 100 meshes) is introduced→Air or inert gas is injected as a high pressure het through bottom nozzles→Powder particles accelerated to high velocity by gas pressure→Kinetic energy of air & resulting turbulence due to high pressure causes inter particle collisionand attritiondue to particle wall contact→Fluidized effect carries particle to classifier zone, where larger particles are retained→Fine particles collected through a collector.

ADVANTAGES

- Smaller particle size
- Expasion of gases at nozzle- cooling
- Little / no abrasion of mill - No contamination
- Inert gas- protect sensitive drugs
- Classifier- controls particle size
- Homogenous blend
- Equipment easily sterilized

DISADVANTAGES

- Energy consuming
- High headspace
- Coarse feed size is not suitable
- Clogging of feed device
- Formation of unwanted ultrafine products

10) VIBRO ENERGY MILL/ VIBRATION MILL[7]

PRINCIPLE - Applying high frequency, three dimensional vibrations to a chamber containing small cylindrical grinding media./ Continuous Impaction.

CONSTRUCTION - Annular grinding chambers with porcelain or stainles steel balls, accommodating cylinders, which align coaxially in a three-dimensional vibratory field to give close packing and line contact between the moving surfaces. The mill body is supported on springs which permit an oscillatory movement.

WORKING

Feed through Hopper→small but frequent vibration generated by a eccentric motor →Size reduction by repeated impact.

ADVANTAGES

- Suitable for Hard Abrasive grinding stock.
- Higher grinding rate.

DISADVANTAGES

- Not Suitable for thermoliable material

11) SPIRAL JET MILL (PANCAKE JET MILL)[7]

PRINCIPLE - Impact grinding, while also performing attrition and cutting

CONSTRUCTION - Flat cylindrical grinding chamber with several nozzles arranged tangentially in the peripheral wall, a pneumatic feed injector and a feed funnel

WORKING

Feed Injector→Force imparted on the particles by nozzles + drag force by airflow →Materials spirals towards the centre of the mill→As particles become finer, Drag force exters greater effect, Drawing particles to centre outlet.

ADVANTAGES

- Contamination free grinding.
- Easy to clean & sterilise
- High efficiency
- versatility
- Precise particle size control

DISADVANTAGES

- High energy consumption
- High wear at the point of impact while processing abrasive materials.
- Large equipment size.

12) DISINTEGRATOR

PRINCIPLE - The size reduction is done by Impact.

CONSTRUCTION - 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.

WORKING

Feed through hopper→Downsizing of particles→Seive→Output.

ADVANTAGES

- ✧ Powders all types of drugs including very hard drugs.
- ✧ Tacking of heavy load without vibration on high speed

DISADVANTAGES

- ✧ Possibilty of jamming of beater if large piece of material is inserted.

SIZE SEPARATION

Size separation is a unit operation that involves the separation of a mixture of various size particles into two or more portions by means of screening surfaces. Size separation is also known as sieving, sifting, screening.

Traditional methods of size separation include handpicking, threshing, winnowing, and sieving. The mechanisms involved in this process include agitation, brushing, and centrifugal methods. Agitation can be achieved through oscillation, vibration, or gyration, which help in effective separation of particles based on size.

Other techniques such as elutriation and the use of bag filters are also employed for efficient size separation in industrial and laboratory settings.

AYURVEDIC CO-RELATION

In Ayurveda, various Yantras or instruments are described for the preparation of medicines, reflecting the traditional methods of pharmaceutical processing. Among them, the Khalva Yantra and Ullukala Yantra hold great importance.

The **Khalva Yantra**, equivalent to the modern mortar and pestle, is primarily used for grinding and pounding raw materials to achieve a fine consistency. It plays a vital role in the preparation of various formulations such as Churna (powders), Kalka (pastes), Lepa and help enhance drug bio-availability by reducing particle size.[8]

The **Ullukala Yantra**, also known as the pounding apparatus or Kuttanaka Khalva, is used for coarse grinding and preliminary breaking of hard materials before fine milling.[9]

Classification of Sukshmatva of Churna in Ayurvedic Parameters

The fineness of powdered materials in ayurvedic formulations is categorized based on sieve size, which determines particle uniformity and suitablity for various dosage forms and pharmaceutical preparations.

Table no 01: Classification of churna size.

MATERIAL	EXAMPLE	SIEVE NUMBER
Sthula (Coarse)	Duma, Kashaya churna	10-40
Pruthu (Moderately coarse)	Phanta	20-60
Moderately fine	Kalka, Hima, Lepa	44 - 85
Sukshma (Finer)	Parpati, Gutika, Vati, Anjana, Pottali	85
Atyanta Sukshma (Very fine)	Bhasma	120

Pharmaceutical Application

Various milling equipments are employed in pharmaceutical manufacturing to achieve desired particle size reduction, improve homogeneity, and enhance the quality of formulations.

Each type of mill is selected based on the nature of the material and the specific processing requirement.

Table No 02: Use of Milling Devices in Ayurvedic Pharmaceuticals.

EQUIPMENTS	USES
Rotatry Cutter Mill	In tough and fibrous materials Eg. Plants parts
Roller Mill	Crush or grind materials Eg. grains
Colloid Mill	Reduce particle size of solis in suspensions Eg. emulsions.
Edge & End Runner Mill	Grinding semisolid preparations Eg. Ointments.
Hammer Mill	Shred or crush materials Eg- barks, roots etc
Ball Mill	Grinding/ blending Eg. Powders
Pin Mill	Grinding Eg. Powders
Fluid Energy Mill	Disintegration Eg.moderately hard & friable materials
Vibro Energy Mill	Fine powders
Spiral Jet Mill	Cosmetics etc
Disintegrator	Disintegration Eg.moderately hard & friable materials

RESULTS AND DISCUSSION

1. FACTORS INFLUENCING MILLING[10]

➢ **NATURE OF MATERIAL** - Hard, intermediate and soft. (Hard - those which are abrasive & cause rapid wear of mill parts immediately involved in size reduction. Ex - Fibrous material (Yasthimadhu, Sarpagandha, shunti) → cannot be crushed by pressure or impact and must be cut.
Friable material (sucrose etc) → they fracture around well defines planes and may be milled byattrition impact or compression.

➢ **MOISTURE CONTENT** - If more than 5% water is present, it hinders milling and produces a sticky mass. If more than 50%, then matter becomes a slurry or fluid suspension (WET MILLING). Increase in moisture decrease milling rate. Few drugs processing water of crystallisation liberate water at low temperature, causing clogging of mills. If Hygroscopic materials, they rapidly absorb moisture to the extend that the wet mass sticks and clog the mill.

➢ **TEMPERATURE** - Heat softens and melts materials with low MP. Synthethic gums, waxes and resins become soft and plastic. Heat sensitive drugs may bedegraded or even charred. Pigments may change their colour shade. Unstabe compounds and any finely powdered material (Dextrin, starch, sulphur)may ignite or even explode.

➢ **PARTICLE SIZE** - An impact mill produces sharp, irregular particles which may not flow readily. When specifications demand a milled product that will flow freely, it would be better to use an attrition mill, which produces free-flowing spheroidal particles.

Pre treatment of fibrous material with cutters and pressure rollers facilitaes further comminution.

➢ **POLYMORPHISM** - Meaning 'having multiple forms'. Milling may alter the crystalline structure and cause chemical changes. Wet milling helpful in producing a suspension containing a metastatis form of material causing crystal growth and caking. Starch, amylose and amylopectin may be broken down in a vibratory mill. Powdered povidine breaks down into lowers polymers in a Ball mill.

➢ **FEEDING RATE** - Rate of discharge should be equal to rate of feed. If feeding rate is slow, then readily discharge with minimized under size particles or fines is minimized. If mill is choke fed at a fast rate, material is in milling chamber for a longer time, as its discharge is impended by the mass of material→ greater reduction of particle size, but mill capacity is reduced and increased power consumption.

In most mills, force of gravity is sufficient for free discharge. For ultrafine grinding, force of gravity is replaced by a FLUID CARRIER. A current of steam, air or inert gas removes the product from attrition, fluid enery or high speed hammer mill. The powder is removed from the fluid by cyclone separators/bag filters.

2. TECHNIQUES OF MILLING[11]

➢ **SPECIAL ATMOSPHERE** - Hygroscopic materials in a closed atm with dehumidified air. Thermoliable or combustible in a closed system with an inert atm of CO2, or N.

➢ **TEMPERATURE CONTROL** - Energy converts into temperature. This may rise the temp of material → melt, decompose, explode. Avoid stalling of mill, use of cooling jackets, or a heat exchanger

➢ **PRE-TREATMENT** - Pre sizing & feed should enter at a uniform rate. Fibrous materials etc should be pre treated with cutters etc.

➢ **SUBSEQUENT TREATMENT** - If extreme control of size is needed- recycle **the larger particle (screening discharge & returning oversized particles)**

➢ **DUAL PROCESS** - Mixing and comminution. in fluid energy mill- size reduction and dispersion.

➢ **WET & DRY MILLING** - Choice of wet or dry mill depends on the product.

CONCLUSION

Milling devices play a vital role in various fields such as pharmaceutical manufacturing, fluid technology, drug delivery systems, and nanotechnology. In the pharmaceutical industry, these devices are essential for achieving desired particle size reduction, enhancing solubility, and improving the bioavailability of drugs. They ensure content uniformity, uniform flow, and efficient mixing of materials, which are critical factors in maintaining product quality and consistency.

The advantages of using milling equipment include better control over particle size distribution, enhanced homogeneity of blends, and improved process efficiency. The final selection of a milling device depends on the nature of the material being processed, the required fineness, and the specific quality requirements of the final dosage form. Hence, appropriate equipment selection and process optimization are key to achieving high-quality pharmaceutical formulations.

ACKNOWLEDGEMENTS

The author is grateful to the Department of Rasashastra and Bhaishajya Kalpana for the constant support and guidance.

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