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Selection of Size Reduction Technique in API (Pharmaceutical) Industry

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A B S T R A C T

The size reduction generally induced amorphization and/or structural disordering of the drug crystal (mechanochemical activation). The size reduction enhances drug dissolution and solubility include alterations in the size, specific surface area and shape of the drug particles. Size reduction technology such as milling now enable the production of drug micro- and nano-particles on a commercial scale with relative ease. This review will provide a background on milling followed by the introduction of common milling techniques employed for the size reduction of drugs. Salient information contained in the cited examples are further extracted and summarized for ease of reference by researchers keen on employing these techniques for drug solubility and ease in formulation preparation

Keywords: Micronisation, Milling, Size reduction, Bulk drug, Particle size, Active pharmaceutical ingredient

1. Introduction

1.1Context

The size reduction of APIs is increasingly becoming a key capability of industries like pharmaceutical, food, pigments, minerals, chemical etc.Micronization is a term used to describe size reduction of solid material where the resulting particle-size distribution is less than 10 microns. In many cases, the micronization process is often considered as a black box that produces fine powder and coarse particles enter. The basic mechanism of size reduction is based on impact, compression, shear and attrition.Although it may vary with the nature of material. The particle properties of material like shape, size, static charge, agglomeration, roughness, adhesiveness, morphology, wettability, density, surface chemistry, plasticity, hardness, brittleness and hygroscopicity play an important role during micronization.

Within this paper several size reduction techniques together with principle, working and applicability of equipment is presented for the first time. while from this study we conclude that the effective technique for essential particle size range. the conclusion is corroborated by experimental evidence and previously reported data in the academic literature and provides an insight into the interaction between fine grinding techniques and its usage.

Size reduction laws:

1. Kicks lawstates that the energy required to reduce the size of particles is directly proportional to the ratio of the initial size to the final size of the material [1].
2. Rittinger’s lawstates that the energy required for size reduction is proportional to the change in surface area of the pieces [1].
3. Bond’s lawstates that the work required to form particles of size Dp from very large feed is proportional to the square root of the surface to volume ratio of the product [1].
4. Griffith theorythe amount of force to be applied depends on the crack length and focus of stress at the atomic bond of the crack apex [10].

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1.2 Need of particle size reduction

The demand for milling or jet milling of API is growing steadily to achieve crystal level particle size.Micronisation ensures the safe and effective delivery of APIs in new formats with increase in surface area.It helps particles to enable the solubility of Active Pharmaceutical Ingredients (APIs) which directed to effectiveness of a drug. The solubility is a key factor in bioavailability, micronization reduces particles down to the micrometer or in some cases nanometer size, that can be used to improve the bioavailability of poorly soluble APIs by increasing particle surface area and accelerating dissolution rates. The mixing of several solid ingredients easier and more uniform if reduces the particle size and it also resulted to reduce rate of sedimentation. The rate of adsorption of any drug depends on three things i.e. the dosage form, rout of administration and particle size. The smaller the particle size, quicker and greater will be the rate of adsorption.The demand for pharmaceutical materials including finely ground active substances and excipients is growing. Injectable drugs and dry powder inhalants require particle-size distributions in the range of 2-20 microns with a steep distribution curve and a minimum of fine and over-sized particles. Milling is a highly effective technology for reducing particle size of inhalation.

2. Types of Size Reduction Techniques used in API industries

Size reduction is a unit operation process and the operations include grinding, compression and impact forces.The traditional techniques for micronization have been based on friction to reduce the particle size and this is accomplished by milling or grinding particles.Modern techniques also known as supercritical fluids, which make the API soluble.Micronization is most often used to describe processes that reduce particle size by using fluid energy, such as a jet mill, rather than by mechanical means. During particle size reduction operation knowing the properties of the material to be processed is essential. 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. Size reduction process is also termed as comminution or diminution or pulverization. Normally, size reduction may be achieved by two methods, namely crystallization or mechanical process. In the crystallization method, the substance is dissolved in an appropriate solvent. In the mechanical process, the substance is subjected to mechanical forces using grinding equipment (ball mill, roller mill, colloid mill etc.)

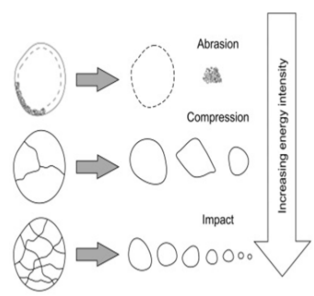


Fig. 1. Energy Intensity Vs Size Reduction Mechanism

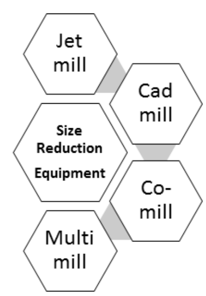


Fig. 2. Size Reduction Equipment

The mechanisms used for particle size reduction are,

i. Impact: Particle is stationary and hit by an object moving at high speed(hammer).
ii. Compression: Particle is crushed by two rigid forces.
iii. Shear or cutting:the material is crushed by means of a sharp blade.
iv. Attrition: Breaking the edges of the solid either by impact or particle collision or arising from particles scraping against one another or against the rigid surface [9].

Table 1: Mechanisms of Size Reduction[10]

Method	Approximate Particle size (µm)
Cutting	100-80,000
Compression	50-10,000
Impact	50-8000
Attrition	1-50
Impact and attrition Fluid energy mill	1-2000

Fig.1 shows the Energy intensity or consumption as a function of size reduction. As energy intensity increases finer product particle size accomplish [9].There is wide variety of miller amiable for wet and dry material size reduction in Pharmaceuticals, Chemicals, Cosmetics, Ceramics, Colors etc. industries. Making the best choice of equipment has significant impacts on product quality and costs. The majorly used equipment are explained with their principle, operation and significance.

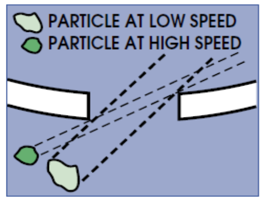


Fig. A

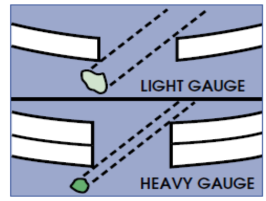
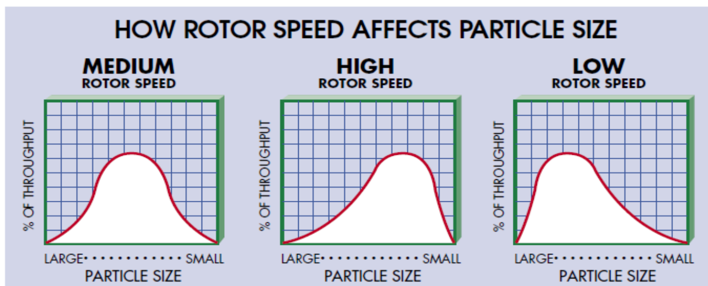


Fig. B



For every combination of rotor speed and screen, particles in a certain size range are permitted to pass through screen and exit the machine. Higher rotor speeds flatten the approach angle of a particle relative to a screens surface effectively reducing the screen hole size(fig A) [4]. A circular hole, for example appears elliptical, thereby allowing only smaller particles to pass through. At slower speeds, the approach angle increases, allowing lager particle to pass through. As screen gauge increases, opening size must also increases to maintain desired particle size (Fig B) [4]. Variable rotor speed and screen interchangeability make it easy for a single mill to produce a variety of results [4]. Some of the common techniques for size reduction are listed as follows:

2.1 Multi Mill

The Multi mill working principle involves a variable force rotate blades having both knife and sharp edges with validated screen size to reduce particle in a controlled manner. The mechanism of multi mill is based on pulverization process, knife is used to cut the large particles into small size particle, these big particles are made from granules during the crystallization or drying operation. Multi mill is used for high speed Granulating, Pulverizing, Mixing, Shredding and Chopping etc. of a wide range of wet and dry materials without special attachments.

Material fed in the hopper, goes down to the processing chamber where it moves to the periphery and passes through the screen radially and tangentially. Finally, the processed material gets collected in the container kept below the processing chamber. The direction of beaters can be changed by reversible switch from knife to impact forward and vice versa. Output and quality of the final product depends on three main factors shape of beaters (knife/impact edges), speed and screen size.

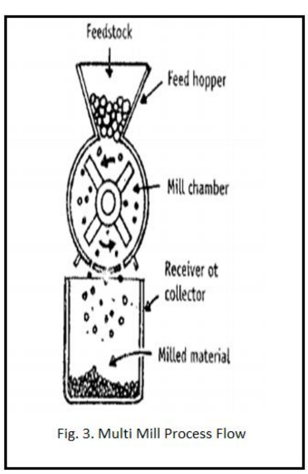


Fig. 3. Multi Mill Process Flow

Fig. 4. Multi Mill Equipment

The Industrial Multi Mill consists of hopper, processing chamber & hammer blades, suitable screen, reversible switch, DOL starter, four-speed arrangement, container & pillar mounted on the base plate with castor wheels for easy mobility. Machine is designed for continuous operation with wide option of operated speed from 720 to 2880 RPM and capacity 50 Kgs to 200 Kgs/hr.Screen hole size ranges are approx. 0.5 mm up to 25 mm diameter this screen is also available in wire mesh for specific requirement. The material passes through the screen, radially & tangentially, thus avoiding the chocking of material in the chamber & rise in temperature. Product particle size range may vary with feed rate, RPM of blade, No. of blade, No. of collision and sharpness of blade etc.

2.2 Jet Mill:

The Air jet mill works on fluid energy precisely aligned jets create a vortex inside the milling chamber. Material is entered in vortex and high-speed rotation subjects the material to particle-on-particle impact, creating increasingly smaller fines. While centrifugal force drives large particles toward the perimeter, fine particles move toward the center where they exit through the vortex finder. Jet mill is one-step grinding in a continuous or batch process with no dead zones to trap material, no moving parts to wear, no grinding media or lubrication to contaminate milled products.Jet milling uses pressurized gas to create high particle velocity and high-energy impact betweenparticles. Compared with mechanical milling, jet milling reduces metal contamination and because process temperature is relatively constant, it can be used for heat-sensitive products. Jet milling has relatively low productivity, large equipment size and high process-gas flow requirements. Using Jet mill particles size can be reduces to below 5 microns.

During operation of jet mill, the material is fed into this vortex along an engineered tangent circle and accelerates. Strong velocity gradients near the jet cause the suspended particles of the material to collide with each other and reduce themselves by attrition and collision. Size reduction is the result of the high-velocity collisions between particles of the process material itself. No grinding media is involved. The jet fluid exits through an outlet at the center of the chamber either from top and draws the micronized the particles with it to the cyclone collection system. Heavier oversized particles are held in the grinding chamber by centrifugal force, until micronized to a desired size.

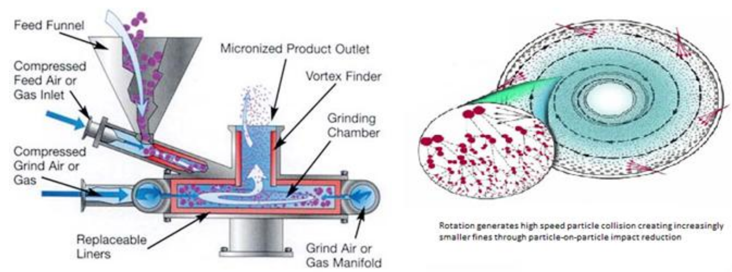
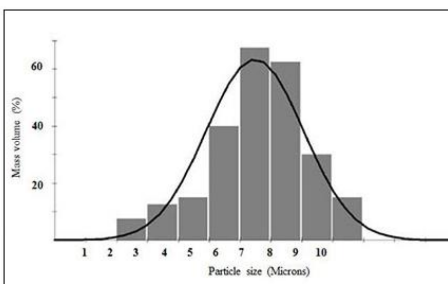


Fig. 5. Jet Mill schematic diagram

There are several factors, both operational and physical, which affect the fineness of the product, such as feed rate, nozzle size, nozzle pressure, nozzle angle, airflow rate, feed particle size, chamber diameter and width, and product outlet diameter. All these variables can be adjusted during operation, but it is more likely that once operation has begun, only feed rate will be varied to meet the required particle-size distribution.Feed particle size is critical, restricted by the size of the feed injector. For mills of 200-300 mm, the feed size can be a maximum of 1.5 mm. For smaller-size mills, the feed size is correspondingly finer.The surface area achieves increase in potency of drugs, which reduces the dosage of the drugs. Product of 30 mesh size when jet milled to 5 microns, has more than 160,000 particles & surface area increases more than 115 times. This results into faster reaction time for chemicals, faster ignition time in the case of solid fuels of rockets.

Fig.6. Jet Mill Equipment



Graph 1. Particle size Vs Mass volume

2.3 Cad Mill:

Cad mill works on the principle of variable force that mill material in between beaters and screen to the required mesh/micron size which can be collected at the bottom of the container.Quality and output depend upon the three main variables beaters shape (knife/impact forward), speed and screen size. While the knife edge for coarse or large particles and impact or flat edge for finer particles. The speed of beater varies from 1000-2250-4500.Highspeed for fine grinding, low speed for coarser particles. Cad mill consist of quality hopper, feed throat and processing chamber with beaters assembly, heavy duty motor, star delta starter with overload relay, three speed step pulley, suitable screen, cladded base having tubular legs with castors, optional jacket for the feed throat and processing chamber for cooling.

Fig. 7. Cad Mill Machine and flow

During operation of Cad Mill the product is poured from the top through in feed hopper and material falls on the rotor blades beater assembly for milling or pulverization. Due to the knife edges mounted on rotor, the downsizing of particle takes place and through sieve material gets pushed outward from the bottom opening. Knife edges can be removed for cleaning very easily.High speed milling, granulating, pulverizing, mixing and size reduction of wet & dry material. Simply to change knife to impact forward vice-versa by reversible chamber.The dynamically balanced rotor mounted on pillow back at outside of the chamber with effectively sealed in a fabricated housing.

2.4 Co Mill:

Co-Mill is designed for low heat, low sound, low energy consumption operation and speed variation. Particles fall from the hopper into the blades of the mill which are moving at a very high RPM. The impact of the blades on the particles is the cause of the sizing. The blade has sharp edge on one side and blunt on the other.

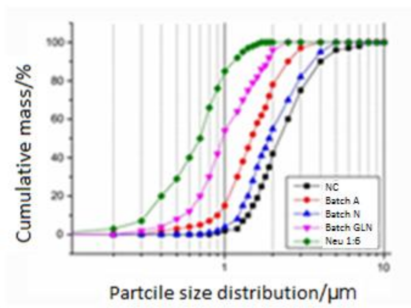
During Co mill operation product is poured into the feed hopper of the Co Mill. In the conical screen chamber, a rotating impeller imparts a vortex flow pattern to the in-feed product. The product is forced outward to the screen surface by centrifugal acceleration, ensuring continuous delivery into the "action zone" between the screen and impeller. No heating of product during granulation, due to better air circulation and lesser impact action. In the "action zone" the material is uniformly sized and instantaneously passed tangentially through the screen openings. The finished product is discharged at the bottom of the milling chamber. Cone mills used for achieving de-lumping, dispersion, Deagglomeration, fine grinding, dry and wet milling uniform size reduction, sieving and mixing in the pharmaceutical, food, fine chemical, personal care and cosmetics industries.The output of co mill is near to the size of sieve used approx. 80%-90%.Adjustable clearance between rotor and cone sieve.

Fig. 8. Co Mill Equipment

Co Mills extend the Gericke range for producing fine to very fine powders (6 mm - 150 µ). Cone Mills are used for granulation processes with small particle size distribution at the end of production processes and before filling plants.

3. Trends of Particle Size After Crystallization

Crystallizationis the process of atoms or molecules arranging into a well-defined, rigid crystal lattice in order to minimize their energetic state.While crystals have many important attributes the crystal size distribution probably has the greatest impact on the quality and effectiveness of the final product. Crystal size and shape directly influence key steps downstream from the crystallizer, with filtration and drying performance being particularly susceptible to changes in these important attributes. Similarly, the final crystal size can also directly influence the quality of the final product. In a pharmaceutical compound, bioavailability and efficacy are often related to particle size with smaller particles often desired for their enhanced solubility and dissolution characteristics. Crystal size distribution can be optimized and controlled by carefully choosing the correct crystallization conditions and process parameters. Understanding how process parameters influence key transformations, such as nucleation, growth, and breakage, allow scientists to develop and manufacture crystals that will have the desired attributes and be efficient to bring to the market.Developing the science to "Dial-In" particle size



Comparison of particle size distribution of nimesulide batches: native crystals (NCs), Batch A obtained by solvent evaporation in a nanospray dryer, Batch N and Batch GLN obtained by grinding in the absence and in the presence of liquid nitrogen, respectively, and Batch Neu 1:6 obtained by coprecipitation in the presence of Neusilin® UFL2

through control of the crystallization or precipitation processes will significantly enhance productivity and impact the bottom line. To accomplish this goal in a scale-transparent way, we must be able to measure and understand the competing rate mechanisms between mixing, nucleation and growth and their scale dependencies in order to properly design processes to control particle size.Process development of final form crystallization typically focuses on impurity purging with primary goalsof achieving high purity API of the desired crystal form. Additional consideration is typically given to ensure filtration rated are acceptable and thus large crystals are typically manufactured. A controlled crystallization technique was developed to obtain well-defined, large crystals with a narrow particle size distribution.

4. Criteria of Selection

Food, pharmaceutical, pigment manufacturers and ingredient suppliers have access to a wide range of high-tech milling methods. Each one offers advantages for achieving product characteristics such as particle size and moisture content, along with other considerations such as cost, footprint and the need for ancillary equipment. Each method has also given rise to a diverse range of size reduction equipment. In fact, there may be more than one solution when selecting milling equipment [12].According to SuhaOzsoylu, director of operations at Hosokawa Micron Powder Systems, the most important step in selecting size reduction equipment is establishing the target size reduction of the product. This target is typically based on the particle size and particle size distribution desired, typically expressed in terms of milling the material down to a given particle size distribution in microns.End products that demand the vast majority of particles consistently measure the same size. For example, cake flour, often requires a different approach to milling than end products that include a range of different sizes. The particle size directly affects the amount of surface area and the interactions among other ingredients [12].

4.1 Testing and particle size analysis:

Despite the importance of determining the required particle size, many product developers do not know the size of their existing products or the particle size needed for new products. When asked about the target particle size, “something like flour,” “as fine as possible” or “just likecereal” are common responses [12]. In these cases, develops should consider checking with a milling machinery manufacturer that has a track record with the product.By far the most important physical property of particulate samples is particle

size. Particle size measurement is routinely carried out across a wide range of industries and is often a critical parameter in the manufacture of many products. Particle size has a direct influence on material properties. Measuring particle size and understanding how it affects your products and processes can be critical to the success of many manufacturing businesses. Identifying systems that are proven to work with a given product can accelerate the specification process by weeks or months.Whether the product matches existing test data, or you are starting from scratch, today's milling equipment manufacturers offer configurations and custom options that can meet tight specifications. Testing the actual product on lab-size and/or full-size machinery is recommended. The first step in testing often involves evaluating a sample on a particle size analyzer that uses pneumatic sieving to determine the particle size distribution and provides a target end point. Other product characteristics can be addressed such as the size at the infeed, bulk density, flowability, hardness, moisture content, heat sensitivity, toxicity and even explosivity [12].Particles are 3-dimensional objects, and unless they are perfect spheres (e.g.emulsions or bubbles), they cannot be fully described by a single dimension such as a radius ordiameter. In order to simplify the measurement process, it is often convenient to define the particle size using the concept of equivalent spheres. In this case the particle size is defined by the diameter of an equivalent sphere having the same property as the actual particle such as volume or mass for example. It is important to realize that different measurement techniques use different equivalent sphere models and therefore will not necessarily give exactly the same result for the particle diameter. The equivalent sphere concept works very well for regular shaped particles. However, it may not always be appropriate for irregular shaped particles, such as needles or plates, where the size in at least one dimension can differ significantly from that of the other dimensions [11]. In the case of the rod-shaped particle shown in the image figure 2, a volume equivalent sphere would give a particle diameter of 198µm, which is not a very accurate description of its true dimensions [11]. However, we can also define the particle as a cylinder with the same volume which has a length of 360µm and a width of 120µm. This approach moreaccurately describes the size of the particle and may provide a better understanding of the behavior of this particle during processing or handling for example. Many particle sizing techniques are based on a simple 1-dimensional sphere equivalent measuring concept, and this is often perfectly adequate for the required application [11]. Measuring particle size in two or more dimensions can sometimes be desirable but can also present some significant measurement and data analysis challenges. Therefore, careful consideration is advisable when choosing the most appropriate particle sizing technique for your application like Particle size distribution, weighted distribution, number weighted distribution, volume weighted distribution, intensity weighted distribution [11].

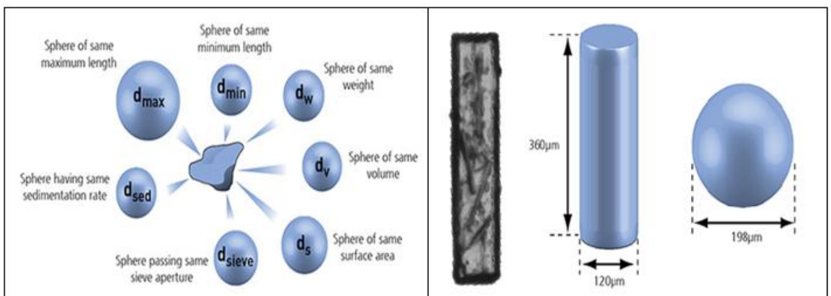


Figure 1: Illustration of the concept of equivalent spheres.

Figure 2: Illustration of the volume equivalent rod and sphere of a needle shaped particle.

4.2 Milling Selection

4.2.1 Hammer and screen mill

Check to see if a low-cost technology can meet the requirements. One of the least costly types of milling machinery for food products is also the most frequently used. The hammer and screen mill style use the impact of swinging hammers that rotate at high speeds inside a round housing to reduce the particle size. When the particles meet the targeted size, they fall through a screen and into collection. Screens are available in a variety of sizes and configurations to suit dry, sticky, fibrous or abrasive ingredients. Today's most effective hammer mills grind down to D90 <75 µm. If a finer end product is required, a more advanced impact systems may be considered.

4.2.2 Pins, knife and attrition mills

Advanced systems achieve fine grinding down to D97 <35 µm. They replace the hammer rotor with a pin disc style rotor and force the material to collide with a series of pins set in concentric circles protruding from high-speed rotating discs. This style excels in milling crystalline, fatty and oily products such as spices that may build-up and blind screens [12]. The latest models allow these fatty, oily and other heat-sensitive products to be processed without separate cooling equipment.Other systems replace the hammers with knife rotors that granulate the material. These perform well for coarse granulation to medium fine size reduction and excel with softer products [12].For finer milling of soft and/or heat-sensitive products, attrition mills offer an alternative. These mills grind the product between two, tapered plates that rotate at high speeds, reducing the particle size as the product moves from the infeed at the center to the periphery for discharge and collection [12].

4.2.3Air classifying mills

When the target demands very narrow particle size distributions with grinding down to D97 at <20 µm, air classification mills may be considered. Bringing a higher level of engineering to the process, the latest air classification mills combine impact milling with dynamic air classification. Material is fed from a silo or fed into the hopper and automatically conveyed first into a milling chamber where hammers rotate at high speeds for size reduction [12].In this design, particles are constantly recirculated from the outer liner back into the rotating hammers. When the particles meet the desired size, air carries them to an internal classifier. On-spec particles exit the mill for collection, and any oversized particles are rejected and captured for further milling."Air classifying mills can reduce very large particles such as 6 mm grains of rice to very small particles under 50 µm in a single pass with minimal fines when other mills would take several passes," says Ozsoylu. This type of mill is quickly becoming the preferred system for companies that focus on efficiency and lean operations [12]. "It's easy-to-clean design and flexibility for processing multiple products on the same system make it a good choice for the food processing industry."Other types of milling equipment such as traditional ball mills and advanced fluidized jet mills perform similar ultra-fine size reduction, but rarely offer the same combination of capabilities and low cost for processing food products [12].

4.3 Making the right call

More than one of the systems described may effectively meet the target specifications. Initial cost must be considered, along with secondary factors such as footprint, maintenance needs and versatility. In many cases, the initial cost needs to be weighed against the gains in product quality, production speed, dust control and worker safety along with energy savings and the payback period [12].

With numerous milling options available, food processors face a challenging landscape when sifting through the range of methods and machines. Further, many mills require an array of ancillary components upstream and downstream of the actual mill from storage silos and feeders to conveyors and dust collectors. In these cases, consider whether the milling equipment manufacturer has experience integrating all the elements as an integrated mill system [12].

4.4 Case study:

Milling trail taken for one of the pharmaceutical API using different milling technique and monitor the results for selection of best suit size reduction technique for API.The initial particle size of the API is 35 µm which wasmilled at different RPM and air pressure, the results obtained are as,

Appendix A. Sr. No.	**Appendix B. Machin/ Equipment**	**Appendix C. Input Quantity** **Appendix D. (Kg)**	**Appendix E. Milling parameters**	**Appendix F. Results by Malvern master sizer 2000**
Appendix G. Multi Mill				
Appendix H. 1	**Appendix I.** Expt. 1	**Appendix J.** 1.0	**Appendix K.** RPM – 2800	**Appendix L.** D90 = 23.2µm
Appendix M. 2	**Appendix N.** Expt. 2	**Appendix O.** 1.0	**Appendix P.** RPM – 2800	**Appendix Q.** D90 = 24.1µm
Appendix R. Jet Mill				
Appendix S. 1	**Appendix T.** Expt. 1	**Appendix U.** 0.5 **Appendix V.**	**Appendix W.** Grinding – 1 kg/cm2 **Appendix X.** Venturi – 0.6 kg/cm2 **Appendix Y.** RPM – 80	**Appendix Z.** D90 = 9.2 µm
Appendix AA. 2	**Appendix BB.** Expt. 2	**Appendix CC.** 0.5	**Appendix DD.** Grinding – 0.8 kg/cm2 **Appendix EE.** Venturi – 0.4 kg/cm2 **Appendix FF.** RPM – 120 **Appendix GG.** Dispenser full open	**Appendix HH.** D90 = 11.5 µm
Appendix II. Cad Mill				
Appendix JJ. 1	**Appendix KK.** Expt. 1	**Appendix LL.** 1.0	**Appendix MM.** RPM – 4500 **Appendix NN.** Screen – 0.5 mm	**Appendix OO.** D90= 22.5 µm
Appendix PP. 2	**Appendix QQ.** Expt. 2	**Appendix RR.** 1.0	**Appendix SS.** RPM – 4500 **Appendix TT.** Screen – 0.5 mm	**Appendix UU.** D90= 19.6 µm

The comparable results obtained after completion of trail with decided parameters. Experimental study comes to conclusion that jet mill is preferable to achieving fine particle size up to 11 µm while to achieve coarser particle ranges from 15 to 25 µm multi mill or cad mill uses with RPM as suited.

5. Discussion

Size reduction offers several advantages such as content uniformity, uniform flow, facilities mixing, and drying, etc. Moreover, due to advance technologies the concept of size reduction become wider and has application in different field like pharmaceutical manufacturing of novel and conventional dosage forms, drug delivery, supercritical fluid technology, nanotechnology, etc.At the most basic level, we can define a particle as being a discrete sub-portion of a substance. For the purposes of this guide, we shall narrow the definition to include solid particles, liquid droplets or gas bubbles with physical dimensions ranging from sub-nanometer to several millimeters in size. The most common types of materials consisting of particles are [11]:

- Powders and granules e.g. pigments, cement, pharmaceutical ingredients
- Suspensions, emulsions and slurries e.g. vaccines, milk, mining muds
- Aerosols and sprays e.g. asthma inhalers, crop protection sprays.

In an increasingly competitive global economy, better control of product quality delivers real economic benefits such as [11]:

- Ability to charge a higher premium for your product
- Reduce customer rejection rates and lost orders
- Demonstrate compliance in regulated markets.

All particle size reduction technologies have addressed the certain drawbacks of the standard techniques. The processes lead, in general, to faster top-down process steps, improved physical stability, and smaller particle sizes than the standard comminution processes such as high-pressure homogenization or wet bead milling. The small particle sizes have a direct impact on the dissolution rate and bioavailability of poorly soluble drugs after oral, topic. The research performed to solve the technical challenges of the different technologies in order to achieve improved particle size reduction effectiveness and better formulations for new, problematic compounds. In the future, it is expected that more screenings will be performed employing the principle of design of experiments to systematically analyze the critical factors for the production of nanosuspensions. In this way, it will be possible to establish optimal process parameters to achieve final mean particle sizes below 100 nm for a wide variety of compounds.A plethora of size reduction equipment of varying sizes and capacity are available currently and have ability to handle a wide variety of feeds. The nature of feed to be processed is also as critical as the choice of size reduction equipment. Overall, size reduction helps in achieving uniform mixing, homogeneity and ideal flow of the materials.

6. Conclusion

The selection of the most appropriate milling technology for anapplication requires experience and trials. Achieving particle size below d90 200 µ multi mill with above 2800 rpm, for particle size below d90 100 µ cad mill above 4800 rpm and particle size below d90 20 µ jet mill is crucial. Before application of these machines powder safety data should be evaluated.

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