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RESEARCH PAPER

Ultrafine Grinding Using a Fluidized Bed Opposed Jet Mill: Effects of Feed Load and Rotational Speed of Classifier Wheel on Particle Shape

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ABSTRACT

Circularity, aspect ratio, modelx, *and* pellips *were employed to study the effects of process parameters, namely varying feed loads and rotational speeds of the classifier wheel, of the fluidized bed opposed jet mill on the shape of the micronized particles produced. The Shapiro–Wilk statistical test showed that 80.0% of the shape distributions of the four descriptors were not normal. Therefore, the Kruskal–Wallis test, which is a nonparametric statistical test, was employed to analyze the data. Micronized particles were more spherical and less elongated, as indicated respectively by higher median* circularity *and lower median* modelx *values when compared to unmilled lactose. These descriptors were able to indicate that the particles had been micronized. When feed loads of 250 and 350 g were used, increasing the rotational speed of the classifier wheel was found to bring about a decrease in span values of all the shape descriptors, indicating that the micronized particles were more uniform in shape. Micronized particles produced had lower median* aspect ratio *values than the unmilled lactose, whereas a higher feed load of 450 g resulted in the production of micronized particles that were less uniform in shape and more elliptical in nature, as reflected by the lower median* pellips *values. A higher feed load of 450 g caused a high level of impingement of particles on to the rotating classifier wheel, causing decreased classifier wheel efficiency, and this resulted in a less well-controlled micronization process. Thus,* aspect ratio *and* pellips *were sensitive to the changes in performance of*

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the classifier wheel. The four shape descriptors were proposed to be used collectively as indicators for the monitoring of the micronization process.

Key Words: *Shape descriptors; Micronization; Fluidized bed opposed jet mill; Classifier wheel; Feed load*

INTRODUCTION

Powders are used in many industries for various purposes. In order to produce powder of the same quality, it has to be characterized with respect to certain parameters. The characterizing parameter frequently employed is the size of the constituting particles of the powder. However, there is growing interest in characterizing the shape of powder particles because shape has been found to affect bulk properties of powder like flow, packing, and compaction.[1–3] Solvation of sparingly soluble drugs could also be partially explained by shape parameter.[4] However, defining particle shape has always been problematical as there is no absolute shape system available.

A number of methods have been employed to assess the shape of particles. These methods are broadly classified as qualitative or quantitative in nature. Qualitative parameters derived from some of these methods include descriptive words like acicular, angular, and fibrous, which are ambiguous and lack quantitative measures. Many of the quantitative parameters are based on gross shape of the powder particles, neglecting the finer details of the particles. Hence, it becomes impossible to reconstruct the actual particle profile from these gross quantitative parameters. Speed and simplicity are the attractive features encouraging the utilization of such gross quantitative methods. Complex quantitative techniques like Fourier analysis can reconstruct the particle profile with a certain degree of accuracy from the Fourier coefficient. However, difficulty arises in handling the huge quantity of data generated per particle and this severely limits its application.[5]

Morphological characteristics of solid particles, such as size, shape, and surface irregularities, are greatly influenced by operational parameters. Small changes in operational parameters during crystallization,[6] pulverization, granulation, and drying can lead to remarkable changes in morphological characteristics of solid particles.[7] There are limited studies on the effect of the micronization process on the shape of particles.[8,9] Previous studies investigated the differences between micronized and unmilled particles without studying the effects of micronization process parameters. In view of the growing importance of shape as a characterizing parameter for powder, this study was initiated to investigate the effects of jet milling process parameters on the shape of micronized particles produced, using gross quantitative parameters.

EXPERIMENTAL

Materials

Lactose 100M (Pharmatose; DMV, Veghel, The Netherlands) was used as supplied. Lactose was chosen as a model crystalline substance for micronization studies.

Methods

Micronization Process

Lactose 100M was micronized using a fluidized bed opposed jet mill (100 AFG, Hosokawa Micron Corporation, Osaka, Japan). Lactose 100M was placed directly in the milling chamber and the mill was started using the automatic mode. As the grinding air entered the milling chamber via three nozzles, it propelled the lactose particles towards each other, breaking them down by impact and attrition.

Ground particles that were sufficiently small in size passed through the rotating vanes of the classifier wheel with the air current, while larger particles were rejected and returned to the grinding zone. A blower at the outlet of the equipment maintained a constant airflow for conveying particles passing through the classifier wheel to a collection cyclone, where the micronized particles were removed via a product collection bin. The superfine particles not arrested in the cyclone were removed by the filtering system before the air was exhausted.[10]

Three levels of loads and rotational speeds of the classifier wheel were studied at milling pressure of 0.5 MPa (Table 1). Altogether, nine runs were conducted and the particle shapes of the products obtained were evaluated.

Table 1

Operational Parameters Employed in the Micronization Process

Batch Code	Lactose Feed Load (g)	Rotational Speed of the Classifier Wheel (rpm)
A1	250	5,000
A2	250	9,000
A3	250	15,000
B1	350	5,000
B2	350	9,000
B3	350	15,000
C1	450	5,000
C2	450	9,000
C3	450	15,000

Table 2

Mean Pre-calibration Factors and Median Mean Feret Diameter (F_{mean}) Values of the 10 Batches of Unmilled and Micronized Lactose

Batch Code	Mean Pre-calibration Factor (μm/Pixel)	Median F_{mean} (μm)
Unmilled lactose	2.215	99.125
A1	0.138	2.714
A2	0.074	1.509
A3	0.031	0.914
B1	0.093	1.692
B2	0.057	1.188
B3	0.032	0.678
C1	0.112	2.051
C2	0.057	1.066
C3	0.033	0.614

Scanning Electron Microscopy

The particles were gold-coated under an argon atmosphere (Bio-Rad, SC502, Cambridge, UK) and subsequently examined under the scanning electron microscope (JEOL, JSM-5200, Tokyo, Japan). Scanning electron photomicrographs of particles were employed for image analysis to ensure magnified images of the micronized particles such that the shape of the smaller size particles would be measured with greater accuracy. The use of larger images prevents a compromise where smaller images would lead to reduced resolution and fewer pixels mapping the micronized particle, thus sacrificing details. The pre-calibrated factors and sizes of the various batches of unmilled and micronized lactose are presented in Table 2.

Image Analysis

Scanning electron photomicrographs of the particles were digitized using a video camera (CCD-IRIS, Sony, Tokyo, Japan) and parameters such as area, perimeter, length, breadth, maximum Feret diameter (F_{max}), and mean Feret diameter (F_{mean}) of each particle were determined using computer software (PC Image, version 2.2.01, Foster Findlay, Newcastle, UK). At least 300 particles were measured for each batch of micronized particles.

The area was measured by determining the number of square pixels within the image, including the boundary, and converting measurements into scaled units using a pre-calibrated factor (Table 2). Perimeter was the cumulative distance between calibrated pixels lining the smoothened outer edge of the digitized image. Length was the maximum chord length of the image regardless of orientation and breadth was the width perpendicular to the length (Fig. 1). The value of F_{max} was the maximum distance out of 64 Feret diameters measured at intervals of 2.8125°, while F_{mean} was the mean of the 64 measurements.

Various shape descriptors for the micronized particles were calculated from the measured parameters of the particles according to the following

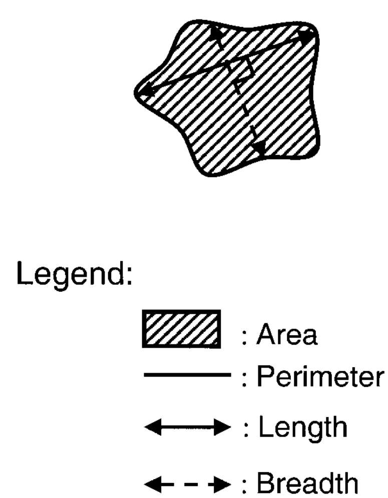

Figure 1. Pictorial representation of area, perimeter, length, and breadth.

equations:

$$Circularity^{[11]} = 4 \times \Pi \times \text{area} / \text{perimeter}^2$$
$$Aspect\ ratio^{[12]} = \text{length} / \text{breadth}$$
$$Modelx^{[13,14]} = \text{perimeter} \times F_{max} / 4 \times \text{area}$$
$$Pellips^{[13,14]} = \text{perimeter} / \Pi \times F_{max}$$

These four descriptors were used to illustrate the spherical (*circularity*), elongated (*aspect ratio*, *modelx*), and elliptical (*pellips*) nature of the micronized particles. For a perfectly spherical particle, these four shape descriptors would have values of unity. Values <1 for *circularity* and *pellips* would respectively mean that the particles are less spherical and more elliptical. As for *aspect ratio* and *modelx*, values >1 would mean that the particles are more elongated. Gross quantitative shape descriptors representing the spherical and elliptical nature of the particles were specially chosen for this study because earlier investigators had shown that micronized particles were smoother and rounder by using a more complicated shape system.[8,9] The advantage of employing them over a complicated shape system was that they could be easily measured using any standard image analysis package. Speed and ease of measuring are important considerations, especially if these descriptors are of any value for monitoring the micronization process.

The shape descriptors of the particles were calculated and the span and median values are listed in Table 3. The median is the value at the 50th percentile point of the cumulative distribution of increasing shape descriptor value, whereas the span is the difference between the 90th and 10th percentile points divided by the median. Plots of the shape descriptors vs. F_{mean} did not reveal any size-dependent shape descriptors for the unmilled and micronized lactose batches, indicating that the magnifications and precalibrated factors were sufficient.

Statistical Software

The statistical software SAS v6.12 was used for the computation and analysis of the data.

RESULTS AND DISCUSSION

Statistical Analysis

Nonparametric statistics were chosen to analyze the data because the Shapiro–Wilk statistical test for normality had indicated that out of the 40 shape distributions of the descriptors, comprising four distributions for the unmilled lactose and 36 for the micronized lactose, 32 did not conform to the normal distribution. This was calculated to be 80.0% of 40 shape distributions (Table 4).

Effects of Varying Rotational Speed

It was observed that an increase in the rotational speed of the classifier wheel from 5,000 to 15,000 rpm was accompanied by a general decrease in the span values of the shape descriptors for feed loads of 250 g (A1 to A3) and 350 g (B1 to B3)

Table 3

Descriptive Statistics of the Shape Descriptors for the 10 Batches of Unmilled and Micronized Lactose

	Circularity		*Aspect ratio*		*Modelx*		*Pellips*	
Batch Code	Span	Median	Span	Median	Span	Median	Span	Median
Unmilled lactose	0.226	0.788	0.627	1.512	0.400	1.507	0.164	0.838
A1	0.276	0.829	0.552	1.401	0.392	1.436	0.166	0.836
A2	0.247	0.860	0.511	1.389	0.385	1.385	0.154	0.836
A3	0.218	0.851	0.518	1.394	0.352	1.383	0.156	0.845
B1	0.287	0.843	0.586	1.422	0.443	1.416	0.180	0.826
B2	0.267	0.846	0.578	1.416	0.432	1.417	0.160	0.829
B3	0.247	0.870	0.524	1.387	0.369	1.376	0.158	0.844
C1	0.282	0.835	0.627	1.493	0.442	1.465	0.185	0.820
C2	0.302	0.852	0.605	1.409	0.492	1.417	0.189	0.828
C3	0.320	0.849	0.592	1.467	0.492	1.434	0.176	0.818

Table 4

Results of the Shapiro–Wilk Statistical Test on the Distributions of Particle Shape Descriptors

	Conformance of Shape Descriptor to Normal Distribution	
Shape Descriptor	Unmilled Lactose	Micronized Lactose[a]
Circularity	Yes	0
Aspect ratio	No	0
Modelx	No	0
Pellips	Yes	6

[a]For each shape descriptor, nine batches of micronized lactose obtained using different operational parameters were analyzed.

(Table 3). A lower span value indicates less variation in the shape of the micronized particles. This was due to a stronger centrifugal force being subjected on the micronized particles at higher rotational speed of the classifier wheel. Only particles of sufficiently small size could overcome this force to pass through the classifier wheel and be collected in the product collection bin. Hence, better classifying efficiency was obtained by a higher rotational speed of the classifier wheel, resulting in the production of batches of micronized particles with narrower size distributions. The narrower size distribution caused the observed smaller variation in shape of the micronized particles. However, the above trend was not observed for a feed load of 450 g (C1 to C3). There was no reduction in span values of the four shape descriptors despite increasing the rotational speed of the classifier wheel. At a high feed load of 450 g, more particles were thrown against the rotating classifier wheel, resulting in particles that were insufficiently micronized leaving the milling chamber. The micronization process was less well controlled as a result of the adverse effect of an increase in feed load on the classifying efficiency of the classifier wheel. Consequently, a clear reduction in the span values of the shape descriptors was not observed. Thus, it could be concluded that the variation in shape decreased with increasing rotational speed of the classifier wheel, from 5,000 to 15,000 rpm, for feed loads less than 450 g.

The second observation that could be made is that the unmilled lactose was found to have the lowest *circularity* and the highest *aspect ratio* and *modelx* median values, indicating that its particles were less spherical and more elongated than the micronized particles (Table 3). Micronized particles are rounder and smoother than unmilled particles because the irregularities of the particles would have been abraded under the harsh micronizing condition.[8,9] These observations were tested statistically with the aid of the Kruskal–Wallis test, which is the nonparametric equivalent of one-way analysis of variance. This test examines whether the sampled batches produced by varying the rotational speed of the classifier wheel come from a population with a common median.[15] The alternative hypothesis states that at least one of the batches does not come from a population with the same median. For each shape descriptor, this statistical test was performed on the three sets of data obtained. The three sets of data are unmilled lactose, A1, A2, and A3; unmilled lactose, B1, B2, and B3; and unmilled lactose, C1, C2, and C3. These sets of data were found to be significantly different, indicating that varying rotational speed of the classifier wheel resulted in the production of at least one batch of particles that were different from the other three in the set. The Dunn multiple comparisons procedure was subsequently carried out to identify the batch or batches that contributed to the observed significant difference in the Kruskal–Wallis test. The procedure was computed with $\alpha = 0.1$, adjusted for inflated Type 1 error using Bonferroni's inequality.[16] The results of the Dunn multiple comparisons procedure for the effects of varying rotational speed of the classifier wheel are summarized in Table 5.

Table 5 indicates that as the rotational speed of the classifier wheel increased, at feed loads of 250 g (unmilled lactose, A1, A2, and A3) and 350 g (unmilled lactose, B1, B2, and B3), all the shape descriptors except *pellips* showed significant differences between the unmilled and micronized lactose. This confirms the earlier observations (Table 3) that these micronized particles were more rounded and less elongated than those of the unmilled lactose. The insignificant difference between the *pellips* values of the unmilled and micronized lactose suggested that *pellips* was not as sensitive as the other indicators for detecting changes in shape under these operating conditions. The results obtained using this relatively simple shape system were in agreement with those found by other investigators.[8,9] However, the latter employed a more complex shape system involving Fourier descriptors to compare the shapes of micronized and control salbutamol particles, and they did not study the effects of the micronization process parameters on the shape of particles produced.

The results displayed in Table 5 also show that there was no significant difference between batches A2 and A3; B1 and B2; C1 and C2; C1 and C3; and C2 and C3. If a feed load of 250 g was used (A2 and A3), it was sufficient to employ a classifier wheel rotational speed of 9,000 rpm instead of 15,000 rpm, as both speeds produced micronized particles of similar shape. It is always advantageous to operate the micronization process at a lower rotational speed, as less energy is consumed and this also reduces wear and tear, hence prolonging the life span of the classifier wheel assembly. For feed load of 350 g (B1 and B2), it was sufficient to employ a classifier wheel rotational speed of 5,000 rpm. A feed load of 450 g (C1 and C2; C1 and C3; and C2 and C3) resulted in a loss of efficiency of the classifier wheel and the shapes of the micronized particles obtained were similar, unaffected by the rotational speed employed.

Effects of Varying Feed Load

As the feed load was increased from 250 to 450 g for rotational speeds of 5,000 rpm (A1, B1, and C1), 9,000 rpm (A2, B2, and C2), and 15,000 rpm (A3, B3, and C3), a general increase in the span values was observed for all four shape descriptors (Table 3). This increase in span values indicates a higher variation in the shape of the micronized particles produced. As the feed load increased, more particles were thrown against the rotating classifier wheel, resulting in a lowering of the classifier wheel efficiency, as already discussed.

The *pellips* median values of unmilled lactose were larger than those for the batches of micronized lactose produced when a feed load of 450 g was used

Table 5

Results of the Dunn Multiple Comparisons Procedure for the Analysis of the Effects of Varying Rotational Speed of the Classifier Wheel

	Unmilled Lactose[a]				A1				A2			
Batch Code	C	AR	M	P	C	AR	M	P	C	AR	M	P
A1	*[b]	*	*	[c]	—	—	—	—	—	—	—	—
A2	*	*	*		*	*	*		—	—	—	—
A3	*	*	*		*	*	*	*				
	Unmilled Lactose				B1				B2			
	C	AR	M	P	C	AR	M	P	C	AR	M	P
B1	*	*	*		—	—[d]	—	—	—	—	—[e]	—
B2	*	*	*						—	—	—	—
B3	*	*	*		*		*	*			*	*
	Unmilled Lactose				C1				C2			
	C	AR	M	P	C	AR	M	P	C	AR	M	P
C1	*		*	*	—	—	—	—	—	—	—	—
C2	*	*	*	*					—	—	—	—
C3	*		*	*								

[a]C = *Circularity*; AR = *Aspect ratio*; M = *Modelx*; P = *Pellips*.
*Indicates that there is a significant difference between the batches examined, with $p < 0.05$. For example, *[b]shows a significant difference between unmilled lactose and batch A1 for *circularity*.
An unfilled cell indicates that there is no significant difference between the batches examined, with $p > 0.05$. For example, [c]shows that there is no significant difference between unmilled lactose and batch A1 for *pellips*.
—Indicates either an invalid comparison or that the comparison has already been made between the batches examined. For example, —[d]shows that the comparison between batches B1 and B1 for *aspect ratio* is invalid; —[e]shows that comparison has been made earlier between batches B2 and B1 for *modelx*.

(C1 to C3) (Table 3). This would mean that the unmilled lactose was less elliptical than these batches of micronized lactose. According to previous investigators, micronized particles are rounder and smoother than unmilled particles.[8,9] Since the micronized particles in batches C1, C2, and C3 were more elliptical than the unmilled lactose, it indicates that the micronization process with a high feed load was less well controlled. The influence of varying feed load on particle shape was similarly tested with the aid of the Kruskal–Wallis test. For each shape descriptor, the three sets tested were unmilled lactose, A1, B1, and C1; unmilled lactose, A2, B2, and C2; and unmilled lactose, A3, B3, and C3. All the shape descriptors in the three sets were significantly different, and the results of the Dunn multiple comparisons procedure were subsequently calculated and tabulated in Table 6. When a higher feed load of 450 g (C1, C2, and C3) was applied, the *circularity*, *pellips*, and *modelx* median values of the micronized particles were significantly different from those of the unmilled lactose (Table 6), confirming earlier observations (Table 3) that these micronized particles were more spherical and elliptical and less elongated in nature. Even though the *aspect ratio* median values of these three batches were lower than that of unmilled lactose, the statistical tests showed that only batch C2 was significantly different from the unmilled lactose. It could be deduced that *aspect ratio* was not as sensitive as *pellips* for these less well-micronized particles. There was no significant difference observed between batches A1 and B1; A2 and B2; and A3 and B3, indicating that feed loads of 250 and 350 g consistently produced micronized particles of similar shape at the same classifier wheel rotational speed (Table 6). Thus, this further verifies that feed loads of 250 and 350 g were within the processing capability of the fluidized bed opposed jet mill.

Potential Monitoring Indicators for the Micronization Process

Tables 5 and 6 show that *circularity* and *modelx* were able to indicate that the unmilled lactose had undergone a micronization process. However, other studies had shown that these two shape descriptors were not sensitive to describe the shape of particles.[14,17] The differences in sensitivity could be due to the fact that in the reported literature investigations, these shape descriptors were employed to characterize the pellets rather than crystals. In pelletization, sensitive descriptors are required as the process produces spherical pellets and highly sensitive descriptors are needed to detect very small differences

Table 6

Results of the Dunn Multiple Comparisons Procedure for the Analysis of the Effects of Varying Feed Loads[a]

	Unmilled Lactose				A1				B1			
Batch Code	C	AR	M	P	C	AR	M	P	C	AR	M	P
A1	*	*	*		—	—	—	—	—	—	—	—
B1	*	*	*						—	—	—	—
C1	*		*	*		*		*		*		*
	Unmilled Lactose				A2				B2			
	C	AR	M	P	C	AR	M	P	C	AR	M	P
A2	*	*	*		—	—	—	—	—	—	—	—
B2	*	*	*						—	—	—	—
C2	*	*	*	*				*				
	Unmilled Lactose				A3				B3			
	C	AR	M	P	C	AR	M	P	C	AR	M	P
A3	*	*	*		—	—	—	—	—	—	—	—
B3	*	*	*						—	—	—	—
C3	*		*	*		*	*	*	*	*	*	*

[a]Please refer to Table 4 for the interpretation of this table.

among the spherical batches. In the present study, the unmilled lactose particles were quite different in shape compared to the micronized lactose particles. Thus, these gross quantitative measures are adequate shape descriptors to distinguish their difference and, hence, sufficiently sensitive for the purpose of indicating the particles had undergone micronization.

From Tables 5 and 6, *pellips* appeared to be a more sensitive shape descriptor for particles produced by a decrease in the classifying wheel efficiency, whereas *aspect ratio* was more sensitive to the changes in particle shape when there was no loss in efficiency of the classifier wheel. Even though these two batches of micronized lactose were very similar in size, the two shape descriptors were both sensitive enough to detect the differences between them and the unmilled lactose (Table 2). This finding shows that the magnification and pre-calibrated factors employed in this study were sufficient, and the shape descriptors were accurately measured. Thus, two shape descriptors are useful as indicators for monitoring the micronization process, since they indicate the performance of the classifying wheel. Hence, the four gross descriptors, when employed collectively, were able to monitor the process parameters of the micronization process.

CONCLUSION

Circularity, *aspect ratio*, *modelx*, and *pellips* were chosen to study the effects of the fluidized bed opposed jet mill process parameters, namely varying feed load and rotational speed of the classifier wheel, on the particle shape of the micronized particles produced. The Kruskal–Wallis test, which is the nonparametric equivalent of the one-way analysis of variance, was employed to analyze the data because the Shapiro–Wilk statistical test revealed that 80.0% of the shape distributions of these descriptors were not normal.

Feed loads of 250 and 350 g did not exceed the processing capability of the fluidized bed opposed jet mill. Hence, the micronized particles produced were more spherical and less elongated in nature compared to the unmilled lactose as the micronization process was well controlled. A higher feed load of 450 g resulted in the production of elliptical particles because of the decrease in classifier wheel efficiency resulting in a less well-controlled micronization process. When the fluidized bed opposed jet mill was operated with well-controlled feed loads of 250 and 350 g, increasing the rotational speed of the classifier wheel from 5,000 to 15,000 rpm would result in the production of micronized particles that were less variable in shape. The four gross quantitative shape descriptors chosen were found to be applicable as monitoring indicators in the micronization process. It is important to monitor jet milling process parameters, as the quality of end products could be compromised by poor process control. Clearly, excessive feed load is to be avoided. Changes in the shape of particles can be used to assess the efficiency of the milling process.

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