EFFECT OF PSA300 POWDER DISPERSER ON SIZE

As in all particle analysis, sample selection and sample preparation remain critical to obtaining accurate results. This note addresses one aspect of sample preparation by showing the effects of varying disperser conditions on the obtained particle size distribution. In addition, we take advantage of the unique features of static image analysis to evaluate sample preparation strategies.

Introduction

Image analysis is often considered a referee technique for particle sizing. The intuitive appeal of seeing particle pictures is compelling. In addition, the ability to extract more than size information, that is, shape, from images means that image analysis meets requirements not covered by other techniques. Naturally, methods to improve image analysis results are important to extracting full value from this technique.

The steps discussed here are examples of the steps used in developing a final method for analyzing a particular product. The HORIBA PSA300 Powder Disperser option is used to prepare microscope slides for static image analysis. With this device, sample particles are dispersed with a controlled blast of air and allowed to settle on a microscope slide. In general, this method is quite gentle and distributes the particles evenly across the microscope slide in a tightly controlled environment. It should be noted that not all static image analysis samples are best dispersed in this manner. For example, particle suspensions are often cast or spin coated onto the slide (1). Gels are spread onto a slide with a cover slip or razor blade (2). Some samples such as glass beads are first dispersed in a glycerin paste and then spread. But, for dry powders, the Powder Disperser is often the most convenient choice.

In order to allow a single unit to be used with multiple sample types, the PSA300 Powder Disperser is quite flexible. In order to take advantage of this flexibility, the effect of various operating conditions on a particular sample type should be investigated. And, the effect of varying one operating condition, the starting pressure, is described here.

Materials and Methods

A narrow size distribution fraction of Avicel PH-101 microcrystalline cellulose was isolated by sieving. By using a narrow size fraction, one can ignore issues of sampling and counting a sufficient number of particles. The sample used here passed through 53 micron sieve openings, but not 45 micron sieve openings. For a discussion on reconciling sieving results with image analysis data (or dispensing with sieve analysis altogether), see (3).
Two slides were prepared with the Powder Disperser. The only difference between the two slides was the starting pressure condition. The dispersion conditions are tabulated on the following page.

Condition	**High PD**	**Low PD**
Starting Pressure (torr)	*100*	*500*
Dispersion Flow	Normal	Normal
Dispersion Time (*msec*)	500	500
Air Restoration Delay (*sec*)	30	30
Nozzles	Medium, Large	Medium, Large

The starting pressure reflects the pressure of the chamber into which the particles are dispersed. The velocity of the blast of air can be controlled by lowering the chamber pressure since the air velocity is controlled by the difference between atmospheric pressure (760 torr) and chamber pressure. Of course, the dispersion flow setting is a different way to manipulate velocity. A more complete study would examine the effect of multiple disperser conditions. The slides are designated High PD and Low PD to reflect the pressure difference.

A third slide, denoted "Manual," was prepared by using a spatula and dropping the powder onto the slide without applying any dispersion energy.

The three slides were then examined with the HORIBA PSA 300 Static Image Analysis System using the 5x objective.

Results

Qualitative Analysis

The qualitative conclusions discussed here are based on reviewing images from each slide at a number of positions on the slide. The single photos presented here are for illustrative purposes even though qualitative analysis should be performed over multiple regions of a slide.

A representative image from the High PD slide is shown below in Figure 1. From this image, one sees that the particles are not touching and therefore particle separation during image processing is unnecessary. Most notably for the discussion at hand, there are a substantial number of fine particles (less 20 microns) that are much smaller than the main particles.

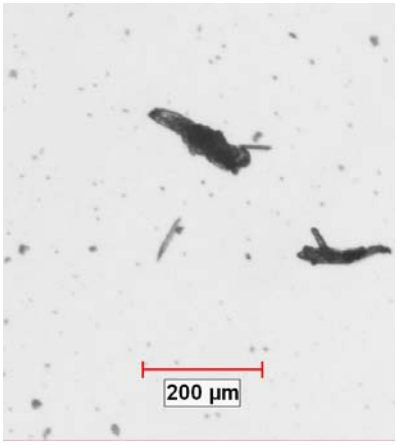

Figure 1 Representative image of particles dispersed under high pressure difference conditions (high PD). Note the presence of a substantial number of fine particles that are an artifact of the dispersion process.

Here one can take advantage of the nature of image analysis to confirm the presence of the fine particles in the original sample. An image from the Manual slide is shown in Figure 2. In this image, the particles tend to overlap significantly; better dispersion will provide superior results to any numerical algorithm for particle separation. Therefore, this slide is not optimal for automated image analysis. Note the near absence of fine particles. It is clear that the fine particles observed in the High PD slide are not part of the original sample. This is consistent with the fact that the sample was prepared by sieving which would tend to remove any fine particles. From this image along with two or three others from the same slide, one can develop a qualitative idea of the particle

size and shape for comparison with images obtained from other slides prepared with the HORIBA Sample Disperser.

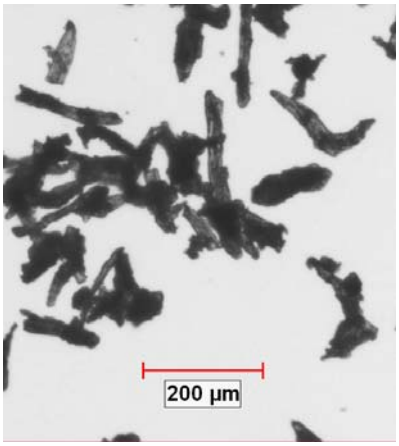

Figure 2 Representative image of manually dispersed particles. Note the lack of fine particles and the significant overlap of analyte particles that preclude good automated image analysis.

Finally, a typical image from the Low PD slide is shown in Figure 3. Note that in this case, unlike the High PD slide but similar to the Manual slide there are almost no fine particles. In addition, unlike the particles in the Manual slide, the particles are well separated; automated particle separation during image processing is unnecessary. It should be pointed out that the number of particles in each image could be increased. And, optimizing the number of particles in each frame would be the next step in method development.

From these photographs, it is clear that the High PD dispersion conditions are affecting the particles under study. The particles prepared under the Low PD dispersion conditions are unaffected by dispersion. Therefore, quantitative image analysis should be performed on the particles prepared under the Low PD dispersion conditions.

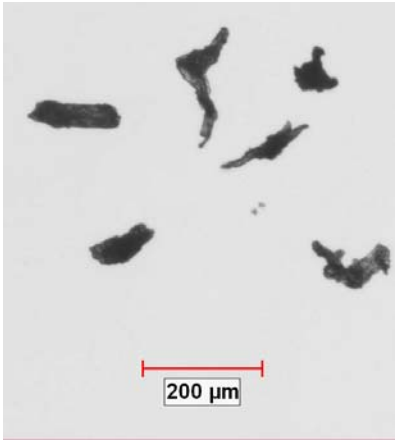

Figure 3 Representative image of particles dispersed under low pressure difference conditions (low PD). Note the lack of fine particles and the distinct analyte particles. This sample is most appropriate for accurate automated image analysis.

Quantitative Analysis

Let us now compare the results of static image analysis from each sample. We consider two different distribution weightings: number weighted and volume weighted. For the volume weighted distribution, the particle volume is estimated based on the area of the particle in the image and an assumed spherical form. Spherical volume is chosen since it is specified in ISO 13322-1 (4). The ellipsoidal volume calculation from the PSA 300 could be more appropriate. However, the choice of model does not affect the conclusions drawn here.

	High PD	**Low PD**	**Manual**
Number Median Size (*microns*)	12	70	66
Volume Median Size (*microns*)	81	80	662

Here it is clear that the number median sizes (D50) obtained from the Manual

slide, 66 microns, and the Low PD slide, 70 microns are similar. For the High PD slide, the large number of fine particles brought the median size down to 12 microns. The small number of large agglomerates which are really overlapping or touching particles did not substantially change the obtained median size of the Manual slide. So, that value was still accurate.

On the other hand, the volume median sizes (D50) obtained from the High PD slide, 81 microns and Low PD slide, 80 microns, were quite similar. This is because the volume fraction of fine particles is small. But the volume of large agglomerates was substantial enough to significantly perturb the measured volume median particle size from the Manual slide.

The small difference between the number median and volume median particle sizes for the Low PD slide is a direct consequence of using a sample with a narrow size distribution.

Since these numerical results were obtained by analyzing 392 images, and from 4000 to 20000 particles, the statistics are certainly better than those from manually inspecting four or five images. For a discussion on the effect of the number of analyzed particles on the accuracy of the determined size distribution parameters such as the median size, see references (4) and (5). Review of only the numerical results does not clearly show which set of results is correct. But manual inspection of only a few images did clearly show which set of numbers is most accurate.

Conclusions

Image analysis allows inspection of the results of different dispersion settings and this feature should be exploited in order to evaluate the quality of the slides prepared for image analysis. Comparing images from an undispersed sample to images from a dispersed sample rapidly verifies the appropriateness of dispersion conditions.

References

(1) AN193 Measuring 10 Micron PSL on the PSA300, available from www.horiba.com/us/particle
(2) AN190 Particle Characterization of Ointments and Creams Using Image Analysis, available from www.horiba.com/us/particle
(3) AN142 Determination of the Roundness of Globules in the Pharmaceutical Industry, available from www.horiba.com/us/particle
(4) ISO 13322-1, Particle Size Analysis– Image Analysis Methods – Part 1: Static Image Analysis Methods
(5) TN155 The Effect of Sample Size on Result Accuracy using Static Image Analysis, available from www.horiba.com/us/particle

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