Research on Particle Size Measurement of Lactose by Laser Particle Size Analyzer

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Abstract: Objective: To establish a method for the determination of lactose powder particle size by laser diffraction. Method: Using Bettersizer 2600 with a fully automatic dry dispersion system, to systematically study the particle size measurement of lactose powders. Investigated the effect of different dispersive pressures on the particle size distribution measurement and researched the precision of dry dispersion method. Conclusion: By comparing the test results, it is concluded that dry dispersion can better control risks and provide more reasonable data correlation.

Key words: Laser diffraction; Particle size analyzer; Lactose

The powder properties of excipients have important effects on the preparation process and quality. In order to guide the selection of the excipients of the tablet prescription, the prescription and process design of the tablet can be developed from the traditional "experience" to the scientific and quantitative level by measuring the powder study index of the excipient. At the same time, the quantitative control of the excipients also helps to ensure the quality and stability of the tablets.

Lactose is one of the most common kinds of tablet excipients. The USP has clear regulations on raw materials particle sizing by laser diffraction method, such as the structure and principle of the instrument, the specific method of dry and wet dispersions, the factors in the measurement process, etc. However, for specific lactose, there is no related instruction on how to choose the dispersive pressure and how to evaluate the results of dry and wet methods. This paper carried out a systematic research on lactose particle size distribution measurement in accordance with the USP and the ISO 13320.

1. Experiment

1.1 Instruments

- Bettersizer 2600 laser particle size analyzer from Dandong Bettersize Instrument Ltd;
- MS303S electronic scale from Mettler Toledo;

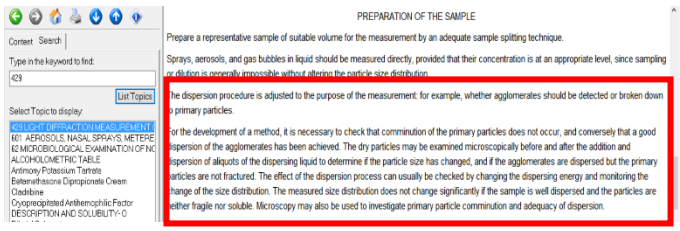
1.2 Sample and reagent

- No.1: non-micronized lactose sample (batch No.00116-17);
- No.2: micronized lactose sample.

2. Particle size distribution measurement and method evaluation

2.1 Study on the methodology of dry dispersion method

Dry dispersion is to transport powder particles by compressed air, disperse powder particles by collision of particles and particles, collision of particles and pipe, and airflow shear. Lactose powder was composed by small organic molecules particles, which could break under the shear stress and collision. In order to ensure the dispersal of large agglomerate without breaking the original particles, the USP requires investigating the effect of different dispersive intensity on test results (USP 429):



In dry dispersion experiments, we investigated the effect of dispersed pressure on the particle sizing results. The dispersed pressure ranged from 0.05 Mpa to 4 Mpa, and a set of data was tested every 0.5 bar or 1 bar.

Abscissa: dispersion pressure; Ordinate: particle size; Blue curve: D10; Orange curve: D50; Grey curve: D90.

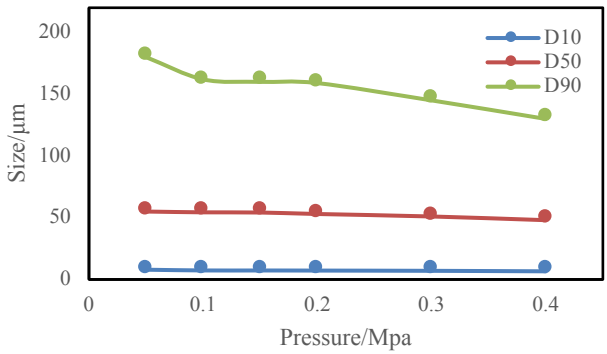


Figure 1. Particle size pressure titration data of No.2 micronized lactose sample

The ideal pressure titration curve, as the dispersed pressure increases, the particle size gradually decreases, and the curve gradually reaches a stable period. If pressure increases further, the curve will go further downward, which corresponds to the gradual dispersal of large

agglomerate to single particles. If the pressure is further increased, the drug particles could break.

Through the above pressure titration curve, lactose sample appeared an obvious "stable platform", which represented the results between 0.1 Mpa and 0.2 Mpa. For further diagnosis, we captured the image of micronized lactose sample (Figure 2 & 3), which shown that the sample was semitransparent irregular crystal particles. Judging from the state, the sample was easy to break. When increasing the dry dispersion pressure, the risk of particle breakage would increase consequently.

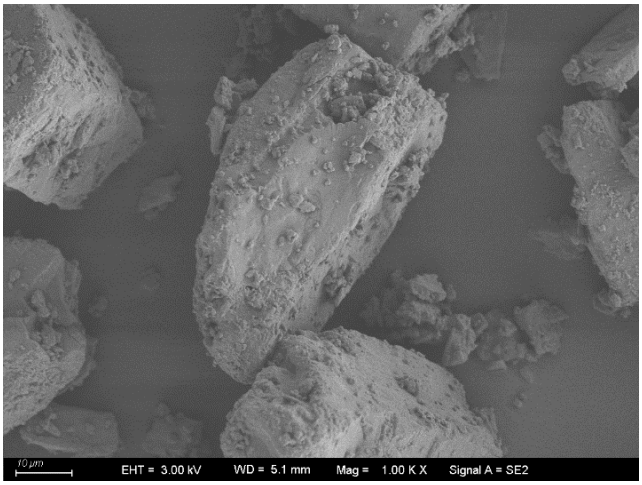


Figure 2. Particle image of No.2 micronized lactose sample

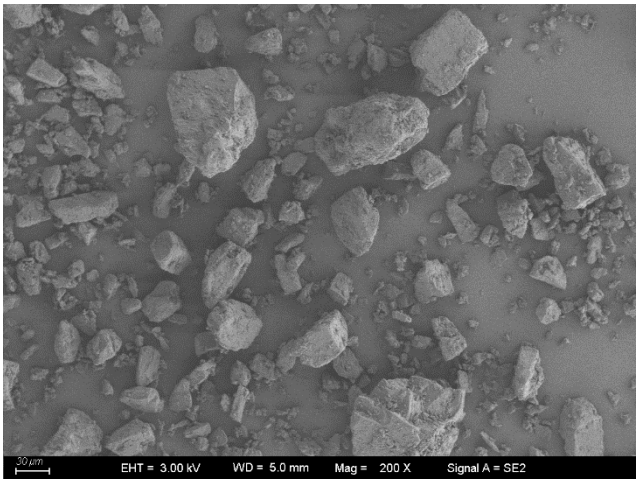
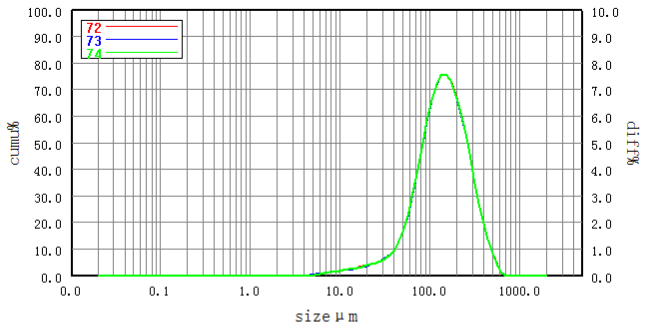


Figure 3. Particle image of No.2 micronized lactose sample

2.2 Research of the precision of dry dispersion method

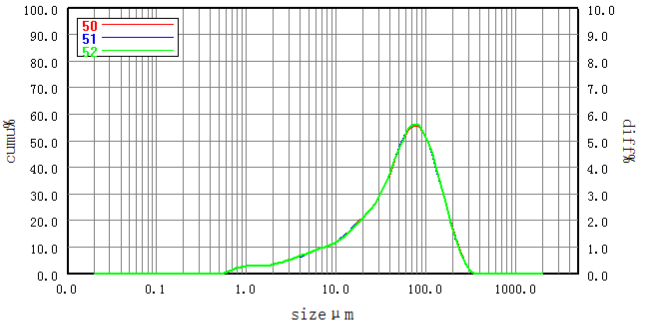
Considering the fragile property of lactose, the precision of the sample size was investigated under dispersion pressure 0.1 Mpa. Figure 4 and 5 shown the particle size distribution curves and repeatability data of p-micronized and micronized samples.

The repeatability results for both samples far exceeded the requirements of the USP: the fluctuation of D50 data was less than 0.5%, and the relative standard deviation of the D10 and D90 data was below 1%, indicating the high accuracy of the dry dispersion method.



Number	Sample	D10/μm	D50/μm	D90/μm
72	No.1 lactose	57.40	141.4	304.1
73	No.1 lactose	57.15	141.2	304.0
74	No.1 lactose	57.32	141.2	304.1
RSD		0.22%	0.08%	0.02%

Figure 4. Particle size distribution and RSD of non-micronized lactose sample (dry dispersion)



Number	Sample	D10/μm	D50/μm	D90/μm
50	No.2 lactose	7.822	55.80	144.7
51	No.2 lactose	7.840	55.76	144.0
52	No.2 lactose	7.813	55.81	144.2
RSD		0.18%	0.05%	0.25%

Figure 5. Particle size distribution and RSD of micronized lactose sample (dry dispersion)

3. Conclusion

Dry dispersion is an adaptive way to measure particle size distribution of lactose. But considering the fragility of lactose, the test pressure should be as small as possible to prevent the break of the lactose original particles. In the above test, we chose 0.1 MPa and obtained satisfied results.