Research on Particle Size Measurement of Chinese Medicine Powder by Laser Particle Size Analyzer

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Abstract: Objective: To establish a laser diffraction method for the determination of particle size distribution of Chinese medicine powders. Method: Using Bettersizer 2600, an automatic laser particle size analyzer with both dry and wet dispersion system, to systematically study the particle size distribution of different Chinese medicine powders. The research investigated the impact of dispersing intensity on the particle size analysis, including different air pressures of dry dispersion and different stirring speeds and ultrasonic dispersing time of wet dispersion. 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; Chinese medicine

Traditional Chinese medicine powder is one of the most important forms of Chinese medicinal materials. For example, pills and powders are forms mixed by one or more medicinal powder. According to particle size, Chinese medicine powder can be divided into traditional powder, micron powder, and nano-powder. With the continuous improvement of drug processing and detection technology, the research of Chinese medicine powder has been developed rapidly. The traditional Chinese medicine is prepared into herbal medicine granule, micron medicine and nanometer medicine. By reducing the particle size, the specific surface area of drug particles can be increased and the solubility and bioavailability of traditional Chinese medicine are improved.

The properties of Chinese medicine powder have great influence on the forming process. The particle size and particle size distribution, which are related to the quality of the products and the safety of the drugs, are the important physical properties of the Chinese medicine powder. However, because of the irregularity and inhomogeneity of particle size, the results obtained by different measurement methods are different. Laser particle size measurement has been widely used in the determination of traditional Chinese medicine by its fast measuring speed, wide testing range, and good reproducibility. This paper focused on the principles and characteristics of laser particle size measurement and its application of Chinese medicine powder.

The ChP and the USP have 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 Chinese medicine, there is no related instruction on how to choose between dry and wet dispersion methods and how to evaluate the measurement results. This paper carried out a systematic research on Chinese medicine 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;
- SC ultrasonic cleaner from Shanghai Shengyan Ultrasonic Instrument Co., Ltd.

1.2 Sample and reagent

Seven kinds of Chinese medicine powder samples:

- Poria cocos
- Astragalus membranaceus
- Angelica sinensis
- Salvia miltiorrhiza
- Codonopsis pilosula
- Dendrobe
- Momordica grosvenori

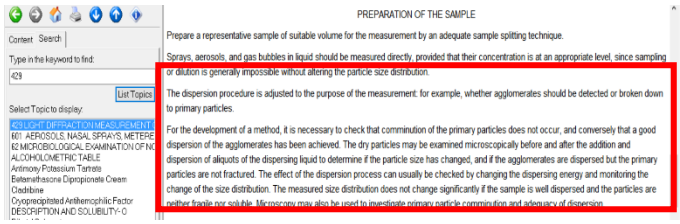
2. Particle size distribution measurement and method evaluation

2.1 Dry dispersion method

2.1.1 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.

Drug 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 0.25 Mpa (Figure 1-7).

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

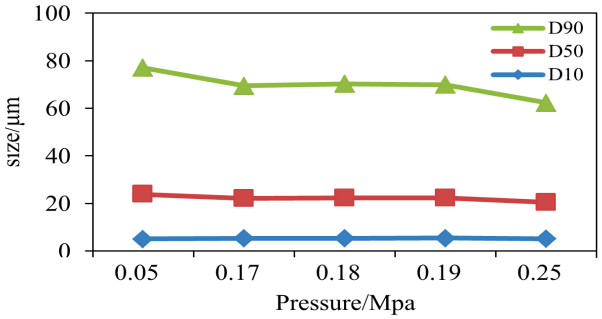


Figure 1. Particle size pressure titration data of Poria cocos sample (dry dispersion)

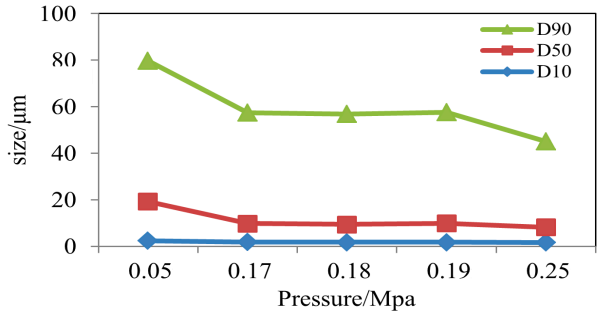


Figure 2. Particle size pressure titration data of Astragalus membranaceus sample (dry dispersion)

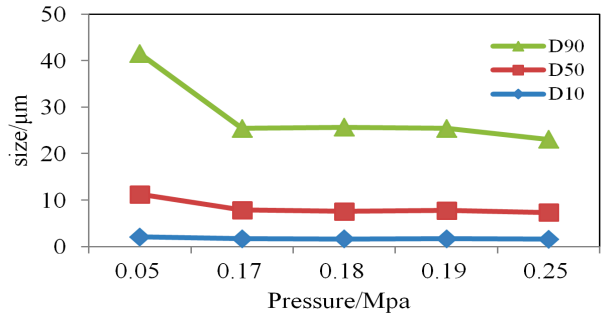


Figure 3. Particle size pressure titration data of Angelica sinensis sample (dry dispersion)

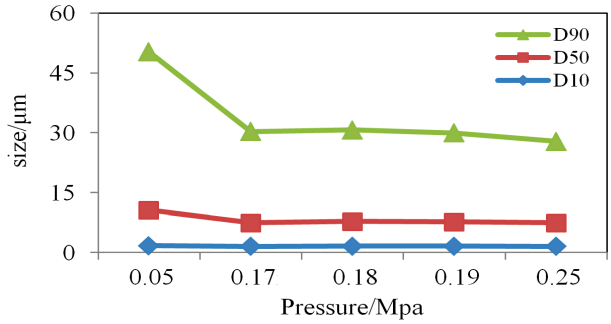


Figure 4. Particle size pressure titration data of Salvia miltiorrhiza sample (dry dispersion)

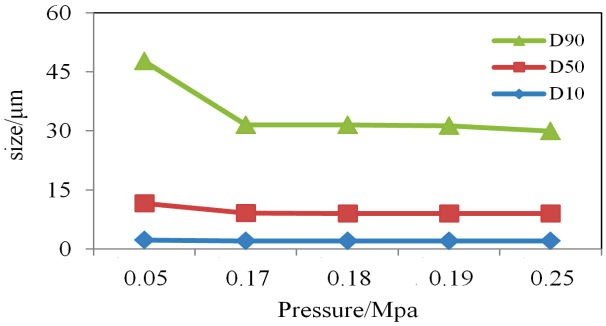


Figure 5. Particle size pressure titration data of Codonopsis pilosula sample (dry dispersion)

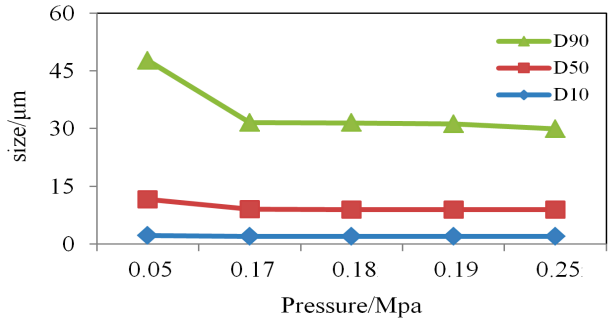


Figure 6. Particle size pressure titration data of Dendrobe sample (dry dispersion)

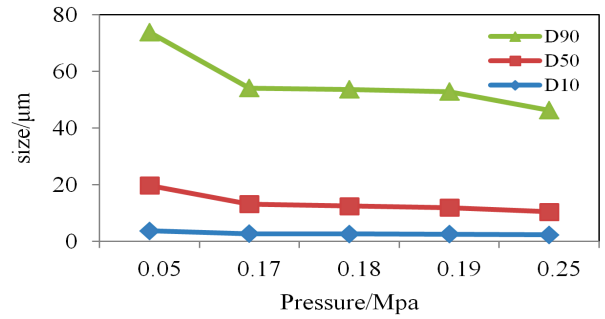


Figure 7. Particle size pressure titration data of Momordica grosvenor sample (dry dispersion)

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.

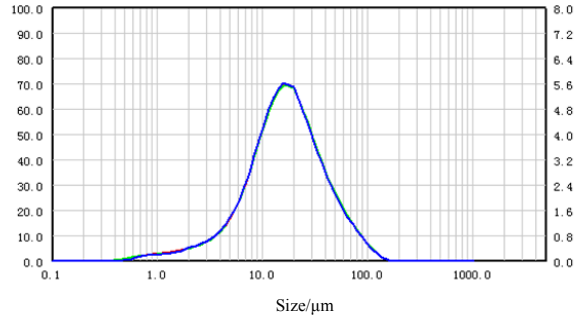
Through the pressure titration of the seven kinds of Chinese medicine, we can see that the overall data conformed to the above rules, all of which were decreased with the pressure increase first, then gradually reached a "stable platform", and the second decline might occur at the end. Although some drugs did not have the second drop, such as Dendrobe, we could basically determine that the risk of data was low under the 0.18 Mpa dispersion pressure.

2.1.2 Research of the precision of dry dispersion method

Based on the above conditions, we investigated the

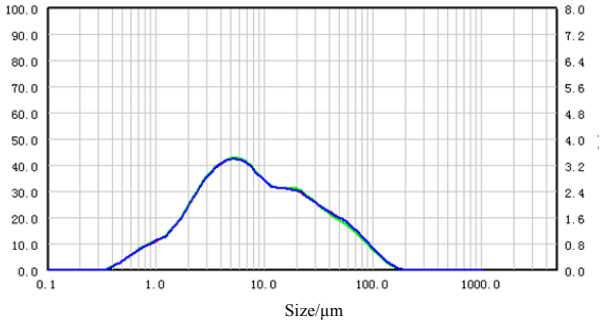
precision of the particle size under dispersion pressure of 0.18Mpa. The repeatability results for seven samples were excellent: the relative standard deviation of D50 was less than 1%, and those of D10 and D90 data were also below 2%, which is far exceeded the requirements of the ChP and the USP, indicating that the dry dispersion results were relatively reliable.

According to the results of particle size distribution, the difference of each Chinese medicine is relatively large. The smallest D50 is about 5 μm, and the largest one can reach 16 μm; the minimum of D90 is 19 μm, and the maximum is nearly 50 μm.



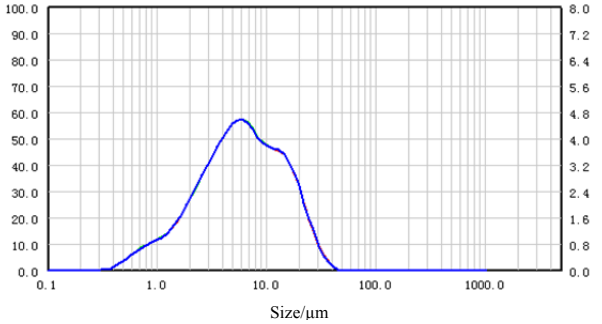
Sample	D10/μm	D50/μm	D90/μm	D95/μm
Poria cocos-0.18-3	5.396	16.95	47.9	64.61
Poria cocos-0.18-2	5.449	16.99	48.11	64.87
Poria cocos-0.18-1	5.462	16.83	47.66	64.29
RSD	0.64%	0.49%	0.47%	0.45%

Figure 8. Particle size distribution and RSD of Poria cocos sample (dry dispersion)



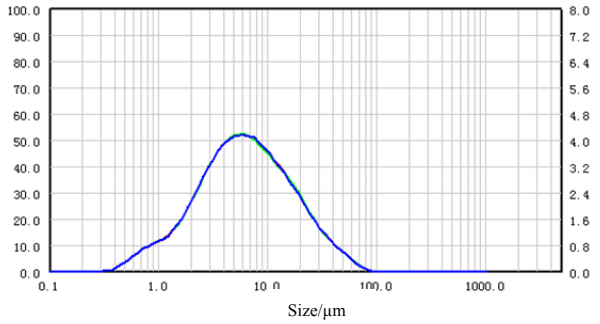
Sample	D10/μm	D50/μm	D90/μm	D95/μm
Astragalus-0.18-3	1.709	7.671	47.530	68.74
Astragalus-0.18-2	1.692	7.521	45.410	66.50
Astragalus-0.18-1	1.708	7.669	47.560	68.74
RSD	0.56%	1.13%	2.63%	1.90%

Figure 9. Particle size distribution and RSD of Astragalus membranaceus sample (dry dispersion)



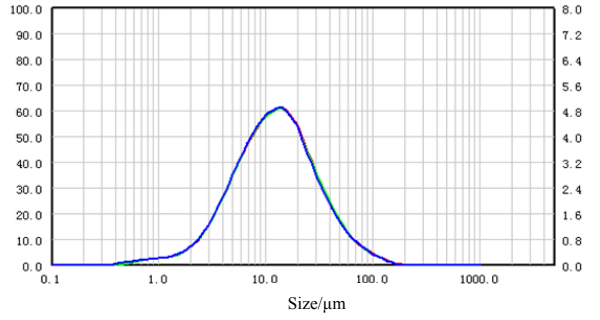
Sample	D10/μm	D50/μm	D90/μm	D95/μm
Angelica sinensis -0.18-3	1.627	5.963	18.070	22.41
Angelica sinensis -0.18-2	1.624	5.965	18.070	22.41
Angelica sinensis -0.18-1	1.627	5.960	18.070	22.41
RSD	0.11%	0.04%	0.00%	0.00%

Figure 10. Particle size distribution and RSD of Angelica sinensis sample (dry dispersion)



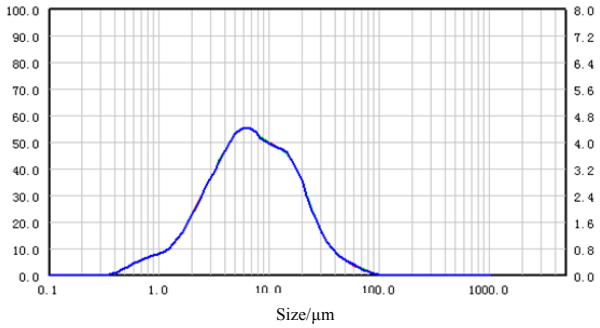
Sample	D10/μm	D50/μm	D90/μm	D95/μm
Salvia miltiorrhiza-0.18-3	1.634	6.186	22.880	32.180
Salvia miltiorrhiza-0.18-2	1.638	6.193	23.000	32.250
Salvia miltiorrhiza-0.18-1	1.637	6.190	22.920	32.250
RSD	0.13%	0.06%	0.27%	0.13%

Figure 11. Particle size distribution and RSD of Salvia miltiorrhiza sample (dry dispersion)



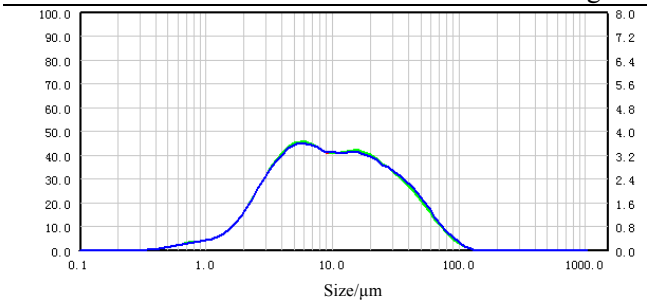
Sample	D10/μm	D50/μm	D90/μm	D95/μm
Codonopsis pilosula -0.18-3	3.888	12.500	38.030	53.250
Codonopsis pilosula -0.18-2	3.887	12.470	38.210	53.240
Codonopsis pilosula -0.18-1	3.813	12.300	37.750	53.050
RSD	1.11%	0.87%	0.61%	0.21%

Figure 12. Particle size distribution and RSD of Codonopsis pilosula sample (dry dispersion)



Sample	D10/μm	D50/μm	D90/μm	D95/μm
Dendrobe-0.18-3	1.994	6.995	22.470	29.970
Dendrobe -0.18-2	1.992	6.992	22.460	29.930
Dendrobe-0.18-1	1.994	7.000	22.500	30.020
RSD	0.06%	0.06%	0.09%	0.15%

Figure 13. Particle size distribution and RSD of Dendrobe sample (dry dispersion)



Sample	D10/μm	D50/μm	D90/μm	D95/μm
Momordica grosvenori-0.18-3	2.589	9.787	40.58	53.98
Momordica grosvenori-0.18-2	2.581	9.694	39.96	53.43
Momordica grosvenori-0.18-1	2.596	9.836	41.23	54.66
RSD	0.29%	0.74%	1.56%	1.14%

Figure 14. Particle size distribution and RSD of Momordica grosvenori sample (dry dispersion)

2.2 Wet dispersion method

The solubility of the Chinese medicine is poor with water. Besides, its powder density is small and tends to float on water. Therefore, we adopted a compound surface-active agent to improve the dispersity of the powder in the water. The dispersion effect was as follows:

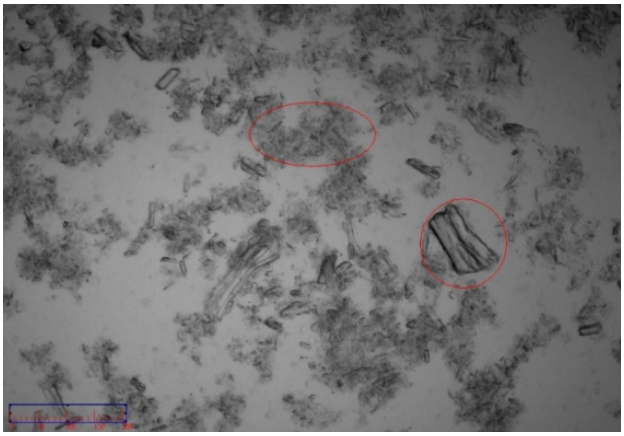


Figure 15. Dispersing state of Astragalus membranaceus in water

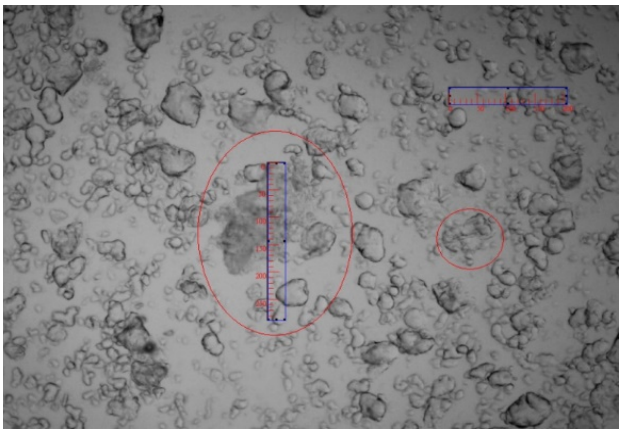


Figure 16. Dispersing state of Poria cocos in water

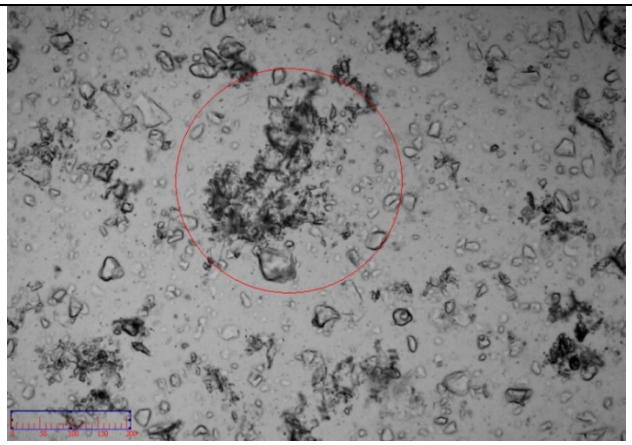


Figure 17. Dispersing state of Gastrodia elata in water

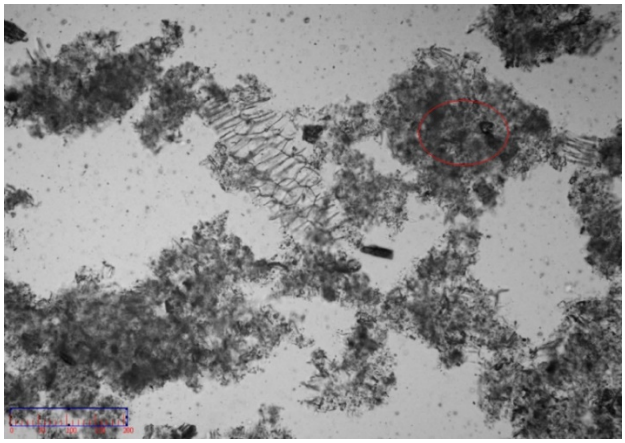


Figure 18. Dispersing state of Codonopsis pilosula in water

Although the compatibility of the Chinese medicine powder could be improved by wetting the surfactant and the dispersion of the powder could be improved by ultrasonic, due to the characteristics of the Chinese medicine, the dispersion of the powder in water was in forms of mass and flocculation. Although some special solvents could improve the dispersing effect, it is difficult to find one kind of solvent to disperse a variety of Chinese medicine powder.

3. Conclusion

Generally, the laser particle size analyzer with dry dispersion method can provide high precision particle size distribution result of Chinese medicine powder. Although wet dispersion method can disperse the powder through surfactants and ultrasonic, the effect is not satisfied. Therefore, dry dispersion method is relatively reasonable to analyze particle size distribution of Chinese medicine powder.