Understanding the criterion of sampling technique and selection of dispersant in attaining better results during wet method development for particle size analysis .

By: Kanuri Sreenivasa Raja

Abstract

This article deliberates on the measurement of crystal growth rates using laser diffraction technique. The paper discussed how the method was developed and experiments carried out in a fluidized bed apparatus, a specifically designed measuring chamber typical in solid and liquid crystallization dealing with both spherical and non-spherically shaped particles. The particles were exposed to high suspension densities. The outcome indicated that particle size distributions are subject to the volume concentration. The experimental results used both different volume concentrations and constant particle sizes. Timely detection and correction of errors in the volume concentration helped to obtain reproducible and understandable particle size distribution. The experiment led to the introduction of an essential correlation function for the particle size measurements at great suspension densities.

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1. **Introduction**

The quality of various collections of pharmaceutical products ranging from powders for pulmonary delivery to topical ointments is attributed to the particle size. In the recent past, the exceptional qualities of laser-diffraction examination have led to the selection of this particle-sizing technique for the outcome of a variety of pharmaceutical uses. Laser diffraction, being nondestructive, fast, and suitable for a wide size array (0.1 to 3000 µm) is good for full automation. Consequently, particle-size measurement has made it easier for most routine users because it just involves putting the sample and clicking a key or button. But, reforming particle measurement to this size requires the creation of a safe and sound technique can steadily provide reproducible and reliable data. In the past decade, the

understanding and application of this technique have grown immensely (1). There is a lot of published literature that can support method development, but its realization largely depends on a systematic and rigorous analysis of the factors proven to impact on the study outcome.

1.1 Ideologies of Laser Diffraction

For any successful method development to take place, it is essential to know the simple ideologies of laser diffraction. The technique of laser diffraction can be defined as a collaborative particle-sizing method. It provides a whole sample research outcome as opposed to creating distributions generated from individual particle data, similar to how microscopy or image analysis does.

Lit up collimated laser-beam particles distribute light over many angles. Highly scattered light intensity is generated by large particles to the incident beam at comparatively close angles. Smaller particles, on the other hand, are known to produce a signal of lower intensity, but at angles that are much wider. Laser-diffraction analyzers, using several detectors record the sample's arrangement of the scattered light.

1.2 Particle Size Scatterings Ranging from Nanometers to Millimeters

In applying the right light behavior model, the scattered data from the sample particle-size distribution can be defined through deconvolution step (2). The Mie theory, as well as the Fraunhofer approximation approach, is both regularly used to estimate the particle size distribution. Mie theory is especially for making measurements of wide-ranging dynamics. One gets identical results from the two models for particles of large sizes. However, improved accuracy is offered by the Mie model when measuring finer materials.

Furthermore, you cannot predict the resultant inaccuracies when using Fraunhofer. The assumption one makes when using the two models is that you are dealing with spherically measured particles. For that reason, particle-size distribution acquired when handling non-spherical samples is linked to spherical correspondence.

1.3 Optical Properties

Like mentioned before, effective use of Mie theory needs some understanding about optical material goods (imaginary component and refractive index) of both the measured sample as well as the dispersant's refractive index. Typically, the dispersant's optical properties are rather easy to get from available data.

A majority of contemporary measurement tools has inbuilt databases that include common dispersants. In case there are no known optical properties of samples, the researcher can either estimate them or measure them with an iterative method, relying on the fit goodness between the real data gathered from the sample and the modeled data.

The Fraunhofer approximation is an easy measurement method used in such cases because it does not need in-depth knowledge about the sample's optical properties. Accurate results can be acquired on large particles using this method. Though, it must be used with a lot of restraint every time you are working with samples where particles are comparatively transparent or with particles measuring less than 50µm

2. Method Development

This comprises finding a solution to a broader set of real-world problems generated from this fundamental description of the elementary ideology of operation. According to the *United States Pharmacopeia* (*USP*), laser diffraction includes the measurement of a typical

sample, distributed at a proper concentration level in an appropriate gas or liquid (4). The most critical features are neatly highlighted from this definition of laser-diffraction analysis development, which are dispersion, and sampling parameters.

2.1 Sampling

Using a larger bulk to generate a representative sample is one of the primary challenges encountered with any particle characterization technique applied in a laboratory. The greatest errors are generated from issues encountered in sampling in laser-diffraction analysis, particularly under the circumstances where large particles are measured.

Similarly, mistakes can be easily made when the specification is founded on size limits adjacent to the distribution extremes. For instance, the Dv95 refers to particle sizes under which exists 95% of the particle measurements. The reason being a volume-based technique of laser diffraction is very sensitive to slight alterations in some bristly particles within the chosen sample. The same reason is behind the dissuasion regarding the use of specifications founded on the Dv100 by ISO 13320:2009. The outcome of the test group on reproducibility upsurges with the width and particle size distribution. This determined by the required sample volume that can guarantee descriptive sampling of the fraction of the abrasive particle increases.

Given such a condition, it may be essential to work on a large sample, every so often, larger than 1–2 g to have reproducible outcomes. For measurements on wet-dispersion, it may require the application of a dispersion volume that is large to make sure that material concentration range within the established standard and accurate measurements,

particularly avoid multiple scattering (5). The best way of sampling is to collect the sample at different levels from entire entity. With a constraint of being sensitive analysis it is quite difficult to finalize the particle size distribution of the entire product by analyzing a single sample collected from the same entity. It is always better to analyze more samples with the same method until the consistency is found.

To know the actual size of the sample it should never undergo any stress before analyzing unless confirmed with aggregation.

2.2 Dispersant:

The selection of dispersant impacts the results directly, a bad dispersant could also perplex in understanding the results. There are some points as followed that should be considered while selecting a dispersant are as followed:

- The dispersant media should be clear from particulate matter.
- The refractive index of the dispersant should be known but in case of mixture it has to be found.
- The sample should not be soluble in the selected dispersion selected.
- The dispersant should be selected in such a way that the sample when added should not get deposited at the bottom immediately.
- The refractive index of dispersant selected should be different from the sample.
- The dispersant selected should not react with the sample.
- It should not create static charge where the sample might stick to the glass wall of the test tube taken.
- It should not be more viscous as there might be chances of bubble formation when introduced to the sonication or stirring.
- The dispersant should not change the form of the sample.

Selecting the dispersion by visual observation:

1. 20 mL of Water was taken into 50 mL flat bottomed test tubes and added with approximately 20 mg of different types of sample as categorized above and observed their nature in the dispersion media. It was clearly observed that each type of sample behaved differently in the media. This gives us a conclusion that even sample has to be analyzed with different types of dispersant depending upon their chemical nature.
2. We have taken Sample A with less particle size that was attained by sieving through a suitable mesh and considered it as A_1 the sample as it is as A_2. We have used silicone oil 100 cst as dispersant. The sample A_2 is observed to disperse in the dispersant evenly and upon waiting for gradual time it started depositing at the bottom. But sample A_1 was not evenly dispersed in the same dispersant and upon waiting for gradual time it was observed that some of the material is floating in the surface and some of the sample is dispersed into the dispersant. So we have changed the dispersant to silicone oil 50 cst and observed that the sample A_1 is evenly dispersed in the dispersant same like the sample A_2. By this it was concluded that the viscosity of the dispersant should also be considered depending on the size and density of the sample to be analyzed. So the viscosity of the dispersant should be directly proportional to the density of the sample.

$$\text{Viscosity of dispersant} \propto \text{Density of the particles}$$

Summary:

To attain a robust method, different sampling techniques will help in identification of variations in the results during the development stage itself rather than getting surprises after finalizing the method. The selection of perfect dispersion would help in attaining constant or less variant and accurate results. Along with these two parameters there are also other variable that effect the particle size distribution like refractive index, absorption, and also cleanliness of the instrument.

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