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# Application News

## No. Q122

## Characterization of Particles in Suspension Eye Drops: Detection of Maximum Length of Irregular Particles

Eye drops can be classified as aqueous (nonaqueous) eye drops in which the ingredients are dissolved in water (oil), and aqueous (nonaqueous) suspension eye drops in which the ingredients are not dissolved but the particles are suspended. The Japanese Pharmacopoeia states that the maximum particle size of particles in suspension eye drops is generally 75 $\mu$m or less.

The laser diffraction method is widely used as a technique for measurement of particle size distribution because measurement time is short and the measurement range is wide. However, this technique also has certain problems in cases where it is necessary to obtain the maximum length, as it is difficult to detect coarse particles that exist in very small quantities relative to the total amount of particles, and it is not possible to measure the maximum length of aspherical particles because the particle size is calculated as the sphere equivalent diameter.

This article introduces an example of characterization of the maximum length of particles in a suspension eye drop product and a mixed sample containing both spherical and acicular particles by acquiring particle images and analyzing the particle shape, size distribution, and concentration with the iSpect™ DIA-10 dynamic particle image analysis system (Fig. 1).

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### ■ Samples

Two types of samples were analyzed, the first being a suspension eye drop product which is available in the market, and the second, a dispersion containing a mixed sample of polystyrene particles and glass fibers as an example of an admixture containing aspherical coarse particles. The dispersion medium of both samples was water.
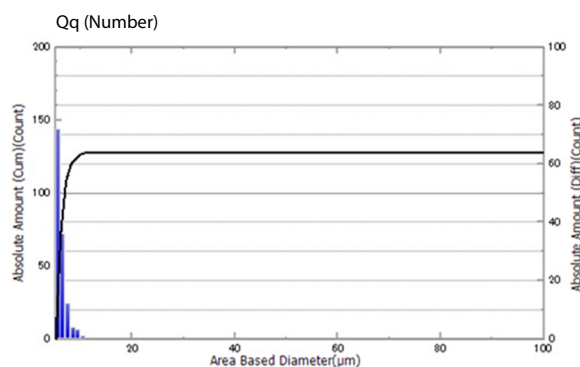
### ■ Measurement Results

Fig. 2 shows the measurement results for the suspension eye drop product. The thumbnail image shows that the particle shape is nearly circular, but each particle has a different shape. From the particle size distribution, no particles with sizes of approximately 15 $\mu$m or larger were detected. The concentration of particles with sizes of 5 $\mu$m or larger was 2,652 particles/mL.



**Fig. 1 iSpect™ DIA-10 Dynamic Particle Image Analysis System**
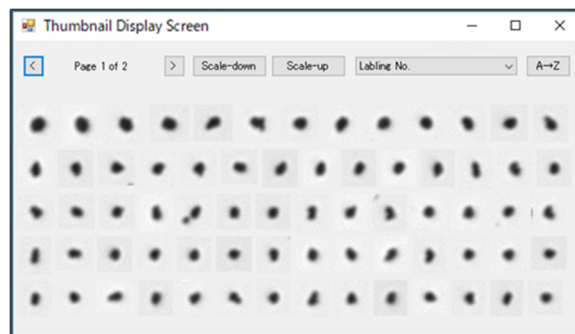


a) Thumbnail images



b) Particle size distribution

**Fig. 2 Measurement Results of Suspension Eye Drop Product**

Some particle size distribution analysis systems can obtain the measurement results of the particle diameter in the form of the equivalent diameter of a sphere of the same volume (volume based diameter) or a circle of the same area (area based diameter). When considering the maximum length, values near the area based diameter and maximum length can be obtained if the particle shape is spherical. However, the maximum length of acicular (needle-shaped) particles and other non-spherical shapes is generally larger than the area based diameter. Fig. 3 shows the definitions of particle size.

As a concrete example, Fig. 4 shows the results of measurement of a mixed sample containing polystyrene particles and glass fibers. From the thumbnail images, it can be understood that this is a mixture of spherical particles and acicular particles.
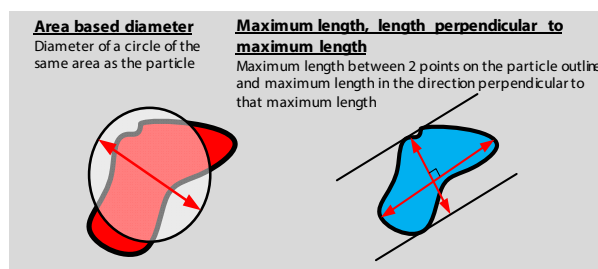


**Area based diameter**
Diameter of a circle of the same area as the particle

**Maximum length, length perpendicular to maximum length**
Maximum length between 2 points on the particle outline and maximum length in the direction perpendicular to that maximum length

**Fig. 3 Definitions of Particle Size**

a) Thumbnail images

b) Scatter diagram
(*x*-axis: Area based diameter)
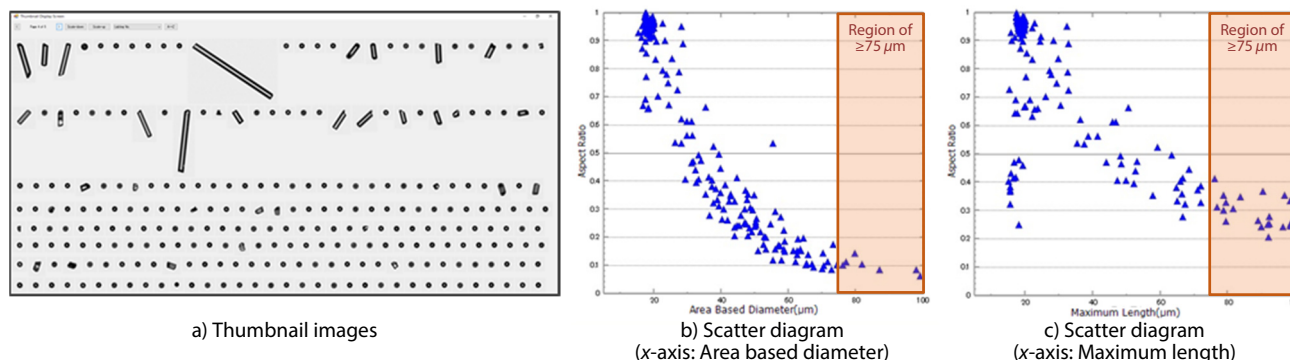
c) Scatter diagram
(*x*-axis: Maximum length)

**Fig. 4  Measurement Results of Mixed Sample of Polystyrene Particles and Glass Fibers**

For example, the hatched regions on the right side of the scatter diagrams in Fig. 4b and c are the regions of particle sizes of 75 µm and larger. The concentration of particles included in this region is 47 particles/mL when calculated by the area based diameter (Fig. 4b), but 420 particles/mL when calculated by the maximum length (Fig. 4c). Thus, in comparison with the maximum length method, the number of particles with sizes of 75 µm and larger is smaller when the area based diameter method is used. Based on this, calculation of the maximum length from particle images, and not the area based diameter, is effective when it is necessary to evaluate the maximum length.

As shown in Fig. 5, classification of the particles in mixtures of particles with different shape parameters (in Fig. 5, Aspect ratio = Length perpendicular to maximum length ÷ Maximum length) is possible by using those parameters, and it is also possible to obtain the ratios of the respective particles. (Here, the relative contents are spherical particles 69.4% and acicular particles 30.6%.)

### ■ Conclusion

In an analysis of a suspension eye drop product with an iSpect DIA-10, it was possible to confirm that all detected particles had sizes of less than 75 µm (actual result with this sample <15 µm). In analyses of mixed samples containing particles with different shape parameters, such as polystyrene particles and glass fibers, it is also possible to obtain the ratios of the respective particles by classifying the particles by their shape parameter. As demonstrated in these experiments, characterization of the maximum particle length and classification of particles in particle groups that had been difficult to characterize by the laser diffraction method is possible by using the iSpect DIA-10.

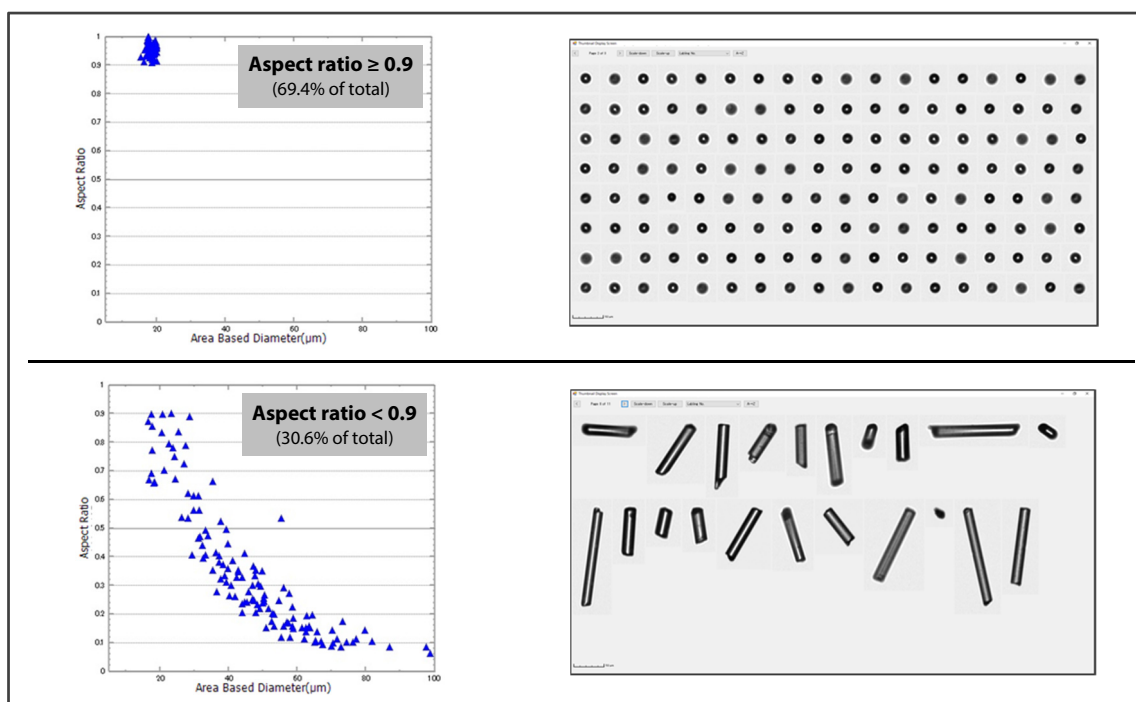iSpect is a trademark of Shimadzu Corporation in Japan and/or other countries.



**Aspect ratio ≥ 0.9**
(69.4% of total)

**Aspect ratio < 0.9**
(30.6% of total)

**Fig. 5  Example of Particle Classification**

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