Pharmaceuticals

Instrument: CAMSIZER X2

Introduction

Particle characterization is a standard analytical procedure in the pharmaceutical industry. Traditionally, sieve analysis and laser diffraction have been used to determine the size distribution of active ingredients and excipients. However, these methods suffer from several disadvantages. Sieving is time consuming, provides a limited amount of data points, the results are often user dependent and not very reproducible. Laser diffraction is a "black box" procedure, the results strongly depend on the evaluation model used. Comparability between different manufacturers or laboratories is therefore difficult to achieve. Image analysis with the CAMSIZER X2 (Fig. 1) provides an alternative which overcomes most disadvantages of other sizing methods. The wide measurement range from 0.8 µm to 3000 µm (standard configuration with X-Jet dry dispersion module) allows the characterization of granulates and powders within less than 3 minutes. The operation is easy and the high sample throughput makes the CAMSIZER X2 a perfect tool for routine analysis in quality control. However, the software offers a vast amount of possibilities in the data evaluation, making the instrument suitable for R&D applications as well.
The following materials can conveniently be analyzed with the CAMSIZER X2:

- Granulated material & powders
- Active pharmaceutical ingredients
- Excipients (Starch, Cellulose, Sugars etc...)
- Crystalline Material (e.g. citric acid)

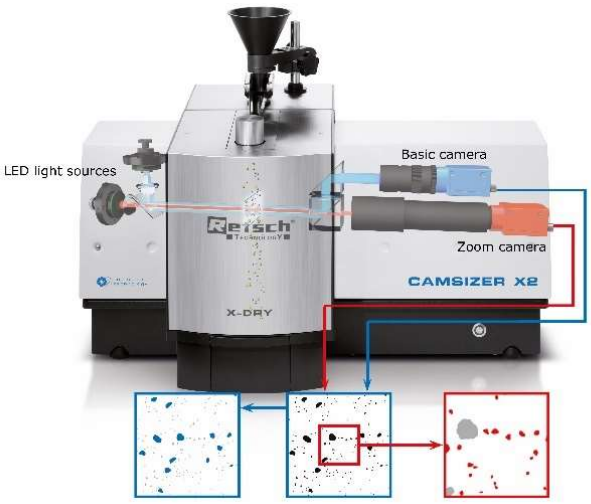

***Fig. 1**: The CAMSIZER X2 dynamic image analysis system.*

Example: starch

Starch and starch derivatives are widely used excipients in the pharmaceutical industry. They are found in many solid oral dosage forms like tablets or capsules.
Our example shows the CAMSIZER X2 measurement result of two different starch samples. The two samples are very similar in size but show significant difference in particle shape (Fig. 2 and 3). Three consecutive measurements of one of the starch samples show the great repeatability of the measurements. This is one major advantage of dynamic image analysis over many other techniques.

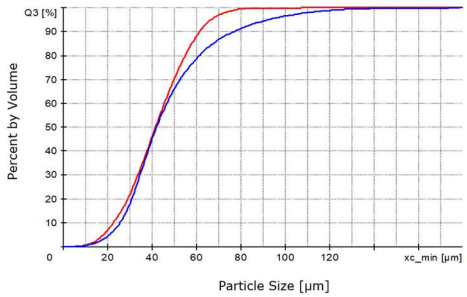

Fig. 2: *Two starch samples, Sample 1 (**red**), Sample 2 (**blue**). CAMSIZER X2 size measurement shows that the size distribution is quite similar, the d50 is exactly the same! The size definition is $x_{c\ min}$ (particle width), which gives a similar result as sieve analysis.*

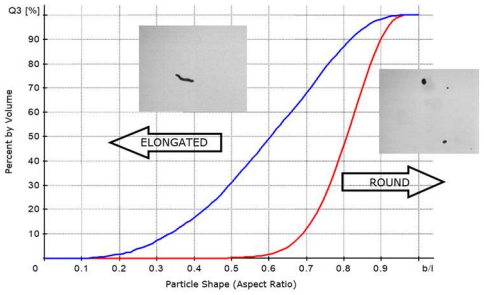

Fig. 3: *The same two starch samples, shape parameter b/l (width/length, aspect ratio). Sample 1 has compact, round particles which is reflected by high values of b/l. Sample 2 has significantly lower aspect ratio. The images clearly show that sample 2 is fibrous material.*

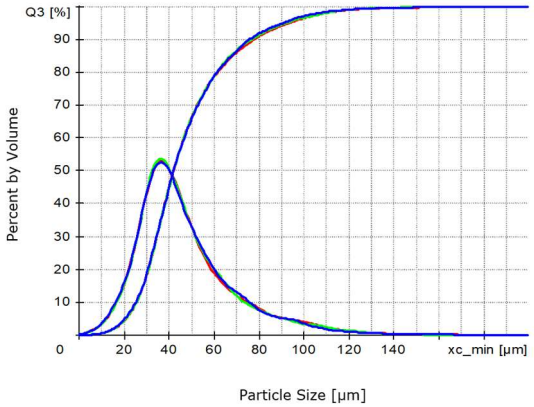

Fig. 4: *Three consecutive measurements of sample 2. The repeatability is excellent. This shows the reliability of the CAMSIZER X2 measurements*

Example: active ingredient

Many active ingredients used in the pharmaceutical industry are highly agglomerated powders. Handling these materials in the laboratory is difficult, especially when it comes to particle size analysis. Sieving is not a very meaningful type of analysis if the particles do not separate to pass the apertures. Air-jet sieving might be a solution for some materials, but many substances will still be too sticky (Fig. 5). The CAMSIZER X2 offers a powerful dispersion system that disrupts agglomerates using a venturi nozzle. The dispersion pressure can be adjusted from 20kPa to 460kPa.

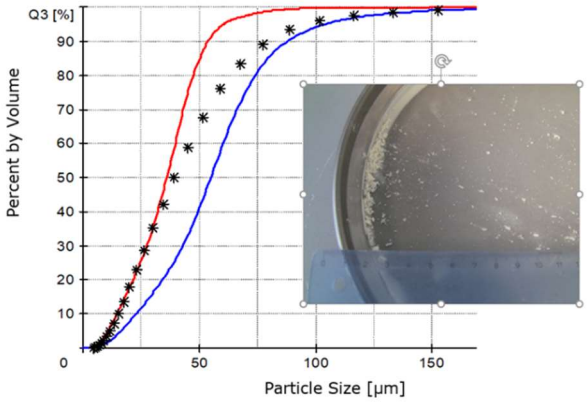

Fig. 5*: Active ingredient sample, CAMSIZER X2 result, size definition $x_{c\ min}$ (particle width, **red**), size definition $x_{Fe\ max}$ (particle length, **blue**). The black asterisks represent the result from laser diffraction. CAMSIZER X2 and Laser analyzers can disperse the particles better than sieving, but laser data do not discriminate between length and width, the result is therefore between CAMSIZER $x_{c\ min}$ and $x_{Fe\ max}$. Thus, the image analysis delivers more detailed information about the sample.*
Right side: Active ingredient particles on a 50 µm sieve after air-jet sieving. The particles stick to the wall of the sieve due to static charge. Agglomerates are clearly visible.

Summary

The CAMSIZER X2 is perfectly suitable for the routine analysis of pharmaceutical granulates, powders and excipients. The method of dynamic image analysis is more reliable and provides higher information content than sieve analysis or laser diffraction. Thanks to the modular design, the CAMSIZER X2 can analyze large pellets up to the millimeter range as well as fine powders and even suspensions.

CAMSIZER P4 - Benefits at a glance

- Flexible dispersion options (air-pressure, liquid, free-fall). Analysis of highly agglomerated APIs
- Very high sensitivity to oversize particles
- High sample throughput: only 2-5 minutes per measurement
- Very repeatable results with excellent instrument to instrument agreement
- Shape analysis is possible: roundness, circularity, aspect ratio, etc.
- Dry measurement with air-jet dispersion 20-460kPa, free-fall option
- More reliable results than sieving due to better dispersion
- higher resolution than sieving or laser diffraction
- more objective, independent of operator
- Full compliance with 21CFR part 11

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