DANNALAB

Application note 0006

Particle size analysis in nanoscale range

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Introduction

The morphology of pharmaceutical excipients and API in nanoscale range may be of critical importance for the manufacturability, dissolution and bioavailability of a pharmaceutical product.

Small Angle X-Ray Scattering (SAXS) is applied at DANNALAB to determine the particle size, pore size and specific surface of nanomaterials, both in bulk and in dispersion.

Liquid dispersions of nanoscale particulates are currently used in many applications of drug delivery and labelling and as ingredients in pharmaceutical and cosmetic formulations. The development and validation of efficient methods for particle/pore sizing[1] together with evaluation of standard reference materials, is one of the areas of activity at DANNALAB.

Below we describe the test case of particle sizing for a fraction of silica nanoparticles in aqueous dispersion, conducted within a collaborative project. [2]

Several different definitions of particle-size distribution are currently in use: number-weighted, volume-weighted and intensity-weighted. Volume-weighted and intensity-weighted distributions are defined as $D_v(r) \sim D_n(r)V(r)$ and $D_I(r) \sim D_n(r)V^2(r)$, where $D_n(r)$ is a number-weighted particle size distribution and $V(r)$ is a function of particle volume. Function $D_n(r)$ is derived, for example, from TEM measurements.

Experiment

Prospective colloidal silica standard material FD100 developed by IRMM JRC EU was used for evaluation.

When investigated by TEM, particles form the single-mode distribution with an 18 nm modal diameter (number-weighted distribution).

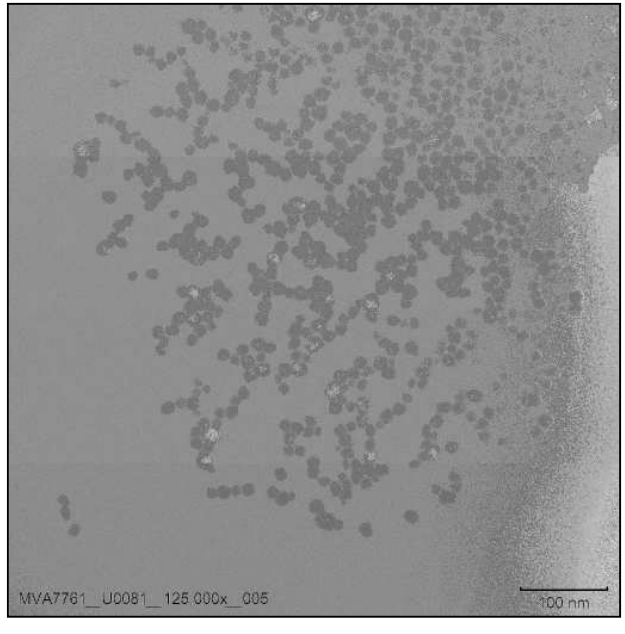

Figure 1. A mono-modal particle population with a modal diameter of 180 [A] estimated with number-weighted particle size distributions by TEM.[2]

During the SAXS characterisation, the samples from three ampoules containing an aqueous dispersion of FD100 were evaluated together with blanks, providing a total of 18 differential patterns.

Results

Several different methods of analysis were used to obtain parameters of number-, volume- and intensity-weighted distributions from the experimental SAXS data.

First, the volume-weighted size distribution function $D_v(r)$ was reconstructed by the inverse Fourier transform of differential scattering pattern. The typical form of the reconstructed distribution is shown in Figure 2.

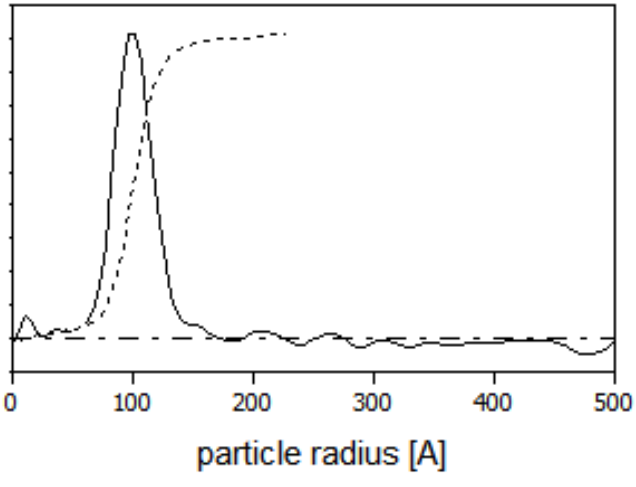

Figure 2. Volume-weighted particle size distribution $D_V(r)$ for aqueous dispersion of FD100 shows a well-defined single-mode distribution. Particle radius is shown as abscissa.

From the recovered $D_V(r)$ function, we reconstructed the functions of $D_I(r)$ and $D_n(R)$ and obtained the following values for the particle diameter taken as the maximum of distribution:

$D_I(D)$: maximum = 210±13 [A]
$D_V(D)$: maximum = 196±13 [A]
$D_n(D)$: maximum = 181±12 [A]

The value for number-weighted distribution obtained from the SAXS data closely match the data obtained by TEM.

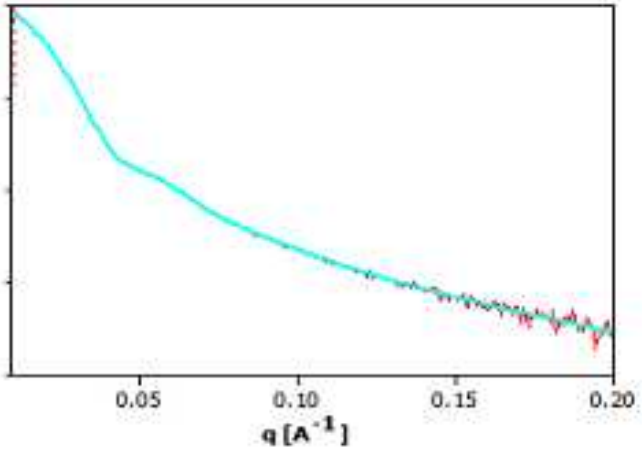

Figure 3. Theoretical, simulated based on the Gaussian distribution scattering curve (blue) is shown versus the experimental differential scattering curve (red)

The shape of particle size distribution was found to be close to the Gauss function. The simulated scattering curve based on the Gauss model closely fit the experimental differential curve, as shown in Figure 3.

Currently this silica dispersion is certified as ERM FD100 (European Reference Material)[3] and routinely used in our lab for quality control and methods validation.

References

[1] The EasySAXS software package is developed by PANalytical BV in cooperation with DANNALAB and EMBL
[2] Report: Certification of Equivalent Spherical Diameters of Silica Nanoparticles in Water ERM®-FD100, IRMM JRC EU
[3] Certificate of Analysis, ERM®-FD100