PHARMACEUTICAL

Particle size measurement with S-MLS in **higly viscous media**

Introduction

Size determination of objects embedded in highly viscous media, such as gels, is very limited with Dynamic Light Scattering (DLS). This application note shows how Turbiscan® technology based on Static Multiple Light Scattering (SMLS) can easily and quickly determine the mean diameter of objects in a highly viscous medium in a range of 10nm to 1000µm. The example presented here, focuses on vesicles introduced into a biopolymer gel for pharmaceutical or cosmetic application (skin application).

KEY **BENEFITS**

- FAST
- NO DILUTION
- SENSITIVE

Context

Thanks to the Stokes-Einstein relationship, the diffusion coefficient D_t of a particle can be measured with DLS. This coefficient is inversely proportional to the particle size d and the viscosity of the dispersant η.

$$D_t = \frac{k_b T}{3\pi\eta d}$$

with T, the absolute temperature and k_b the Boltzmann's constant.

For a constant size d, the diffusion coefficient strongly decreases with the increase of viscosity η. Thus, the particle size measurement duration with DLS becomes prohibitive for highly viscous media.

Therefore, the maximum measurable particle size with DLS strongly decreases while the viscosity increases as shown in Figure 1.

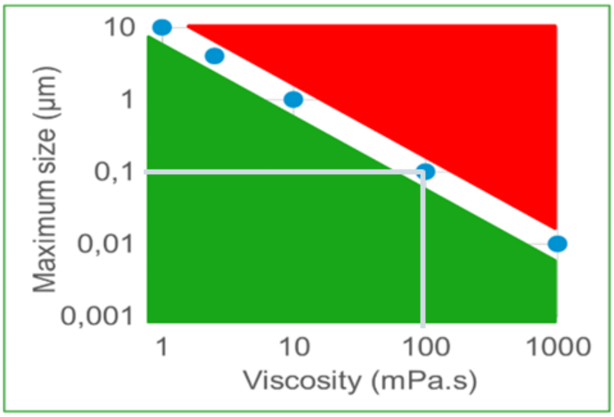

Figure 1: Maximum measurable particle size with DLS in function of the viscosity and for diluted media.

For example, in a 100 mPa.s solvent, the maximum measurable particle size is 100 nm as depicted by the white line in Figure 1.

For a viscosity equal to 1000 mPa.s, the DLS measurements are limited to only 10nm sized particles.

Reminder on SMLS technique

Turbiscan® technology, based on S-MLS, consists on illuminating a sample with an infrared light source and acquiring backscattered (BS) and transmitted (T) signals over the whole sample height.
By repeating this measurement over time, the instrument enables to monitor physical stability.

The BS and T signals are directly linked to the particles' concentration φ and size d according to the Mie theory.

Materials & Methods

Vesicles (0.06 v/v%) which are drug delivery systems were introduced into bio-polymer dispersions of hydroxyethylcellulose (HEC) of 0.5, 0.75, 1.0 and 1.25 wt% and solutions were stirred overnight. The viscosity of these polymer systems is ranging from 150 to 30 000 mPa.s. The samples were analyzed at 25°C and the particle size results were obtained in 25s.

The vesicles size was also measured by DLS in water solvent and at low viscosity only, as the measurement duration was prohibitive for higher viscosity. The particle size value obtained is in the range between 150-200 nm.

Results

Table 1 summarizes the vesicle size measured by SMLS for the 4 different polymer concentrations.

[HEC]	η (mPa.s)	d_{SMLS} (nm)
0%	1	**180**
0,50%	150	**248**
0,75%	1 500	**272**
1,00%	4 200	**245**
1,25%	30 000	**262**

Table 1 : Mean particle size measured for vesicles dispersed in HEC at different concentrations.

As shown in Table 1, the solvent is highly viscous (30 000 mPa.s) for a HEC concentration of 1.25% and measurements with DLS would be impossible in this case.

The measured average size with SMLS is in the same range for all HEC concentration regardless of the viscosity. The measurement in the native viscous media enables to observe that the vesicle size in HEC is larger than in water.

CONCLUSION

Turbiscan LAB technology based on SMLS enables to measure sizes from 10 nm to 1000 µm, in a concentration range between 10^{-4} v/v% to 95v/v% in native samples and in only 25s. It has been proved that, in contrary to DLS, SMLS can provide a reliable measurement of particle sizes in highly viscous media.