Size Reduction by a Microfluidizer

Nicomp® DLS System

OVERVIEW

Particle size analysis is often performed to track the unit operation of size reduction. One very efficient technology used to reduce the size of emulsions/suspensions is a Microfluidizer®. An emulsion and liposomes formulation were processed using a lab scale Microfluidizer and the size reduction process was analyzed using a Nicomp® dynamic light scattering (DLS) system.

MICROFLUIDIZER TECHNOLOGY

Size reduction and/or homogenization can be accomplished using various technologies. In this study, a Microfluidizer from the company Microfluidics was used to process the samples of interest. As shown in Figure 1, the Microfluidizer takes a sample from an inlet reservoir and an intensifier pump generates pressures up to 40,000 psi to force the sample through the interaction chamber. The interaction chamber (Figure 2) exposes the sample to consistent intense impact and high shear rates. Next the sample is cooled and the nanometer scale particles can be recovered for use or recirculated for multiple passes, to achieve the desired uniform particle size distribution. The Microfluidizer approach is repeatable and can be scaled up from laboratory to commercial processing volumes.

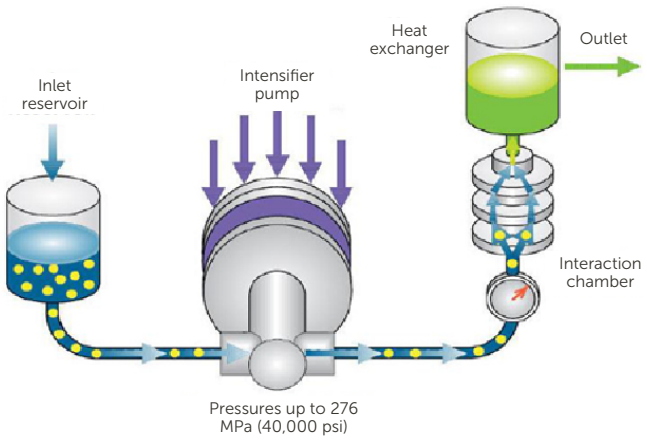

Figure 1. The Microfluidizer process.

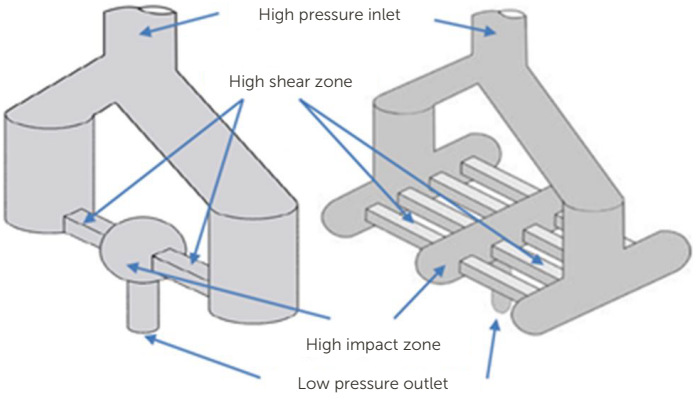

Figure 2. Y single slotted (left) and multi-slotted (right) interaction chambers.

MATERIALS AND EQUIPMENT USED

The samples discussed in this study were all processed on the LV1 Microfluidizer as seen in Figure 3. This is a bench top unit developed to bring Microfluidizer quality nanotechnology processing to the milliliter scale with applications in the pharmaceutical, biotechnology, and other industries.

Figure 3. The LV1 Microfluidizer.

Laser diffraction was used to analyze the samples before size reduction and the Nicomp DLS system was used to measure the samples post processing.

Figure 4. The Nicomp DLS system.

The first sample was an oil-in-water emulsion which mimics a drug delivery vehicle. The dispersed phase consists of 5 wt% Squalane and 1.5 wt% surfactant. The dispersion was created using the following formula:

- DI water = 93.5%
- Tween 80 = 0.75%
- Squalane = 5%
- Span 85 = 0.75%

Prior to processing on the Microfluidizer the sample was mixed for 5 minutes using a rotor-stator mixer (IKA T25). The nanoemulsions were generated using the LV1 Microfluidizer processor. Sample 329A was processed using the F12Y chamber operating at 20k psi and Sample 329B was processed using the F12Y chamber operating at 30k psi. Each sample was processed at the chosen pressure for 1 and 5 passes through the Microfluidizer.

The second sample was liposomes[1] created using the following formula:

- DI water = 93.5%
- Lipoid S 100 = 1.5%
- Soybean oil = 5%

Prior to processing on the Microfluidizer the sample was mixed for 5 minutes using a rotor-stator mixer (IKA T25). The liposomes were generated using the LV1 Microfluidizer processor using the F12Y chamber operating at 20k psi for sample 329C and at 30k psi for Sample 329D. Each sample was processed at the chosen pressure for 1, 2, and 5 passes through the Microfluidizer.

RESULTS: NANOEMULSION

The nanoemulsion sample was measured after mixing by rotor-stator but before processing through the Microfluidizer by laser diffraction to have a median size (Dv50) = 8.5 µm, or 8500 nm. The sample was then processed by the Microfluidizer at 20k psi and measured by the Nicomp DLS system after one and five passes. These results are shown in Figure 5 and 6 and Table 1. Note: Figure 5 shows the unprocessed to processed size reduction in orange (left Y axis) and the processed results in light blue (right Y axis). The table reports the intensity weighted mean diameter and polydispersity index PI.

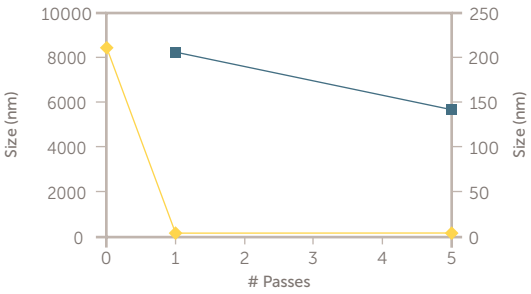

Figure 5. Nanoemulsion sample 329A, unprocessed and 1 and 5 passes, 20k psi.

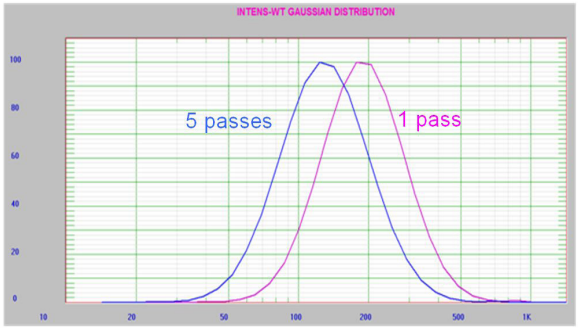

Figure 6. Nanoemulsion sample 329A, 1 and 5 passes, 20k psi.

Passes	Size (nm)	PI
1	205.5	0.166
5	141.8	0.139

Table 1. Nanoemulsion sample 329A, 1 and 5 passes, 20k psi.

The sample was next processed by the Microfluidizer at 30k psi and measured by the Nicomp DLS system after one and five passes. These results are shown in Figures 7 and 8 and Table 2.

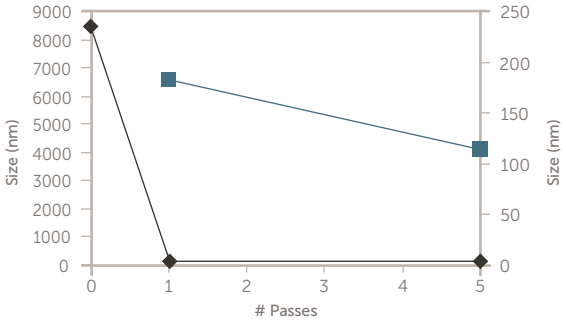

Figure 7. Nanoemulsion sample 329B, unprocessed and 1 and 5 passes, 30k psi.

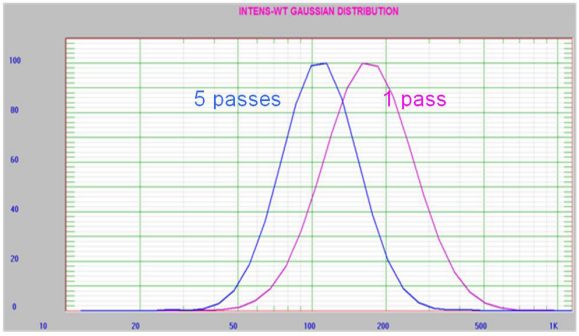

Figure 8. Nanoemulsion sample 329B, 1 and 5 passes, 30k psi.

Passes	Size (nm)	PI
1	185.1	0.174
5	114.4	0.127

Table 2. Nanoemulsion sample 329B, 1 and 5 passes, 30k psi.

RESULTS: LIPOSOMES

The liposome sample was measured after mixing by rotor-stator but before processing through the Microfluidizer by laser diffraction to have a median size (Dv50) = 8.9 µm. The sample 329C was then processed by the Micro-fluidizer at 20k psi and measured by the Nicomp DLS system after one, two and five passes. These results are shown in Figure 9 and 10 and Table 3. Note: Figure 8 shows the unprocessed to processed size reduction in blue (left Y axis) and the processed results in maroon (right Y axis).

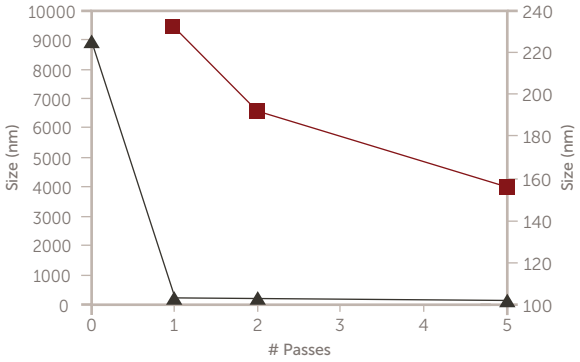

Figure 9. Liposome sample 329C, unprocessed, and processed at 1, 2, and 5 passes, 20k psi.

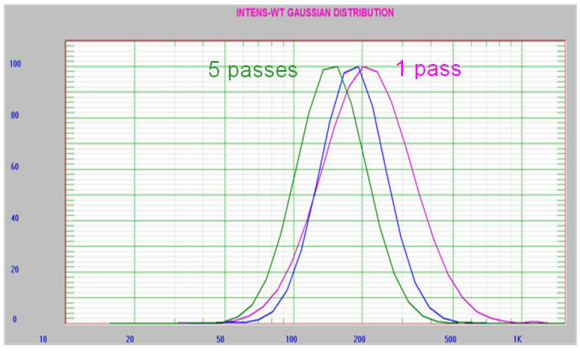

Figure 10. Liposome sample 329C, 1, 2, and 5 passes.

Passes	Size (nm)	PI
1	232.2	0.202
2	191.6	0.127
5	155.3	0.122

Table 3. Liposome sample 329C after 1, 2 and 5 passes, 20k psi.

The liposome sample 329D was then processed by the Microfluidizer at 30k psi and measured by the Nicomp DLS system after one, two and five passes. These results are shown in Figures 11, 12, and Table 4.

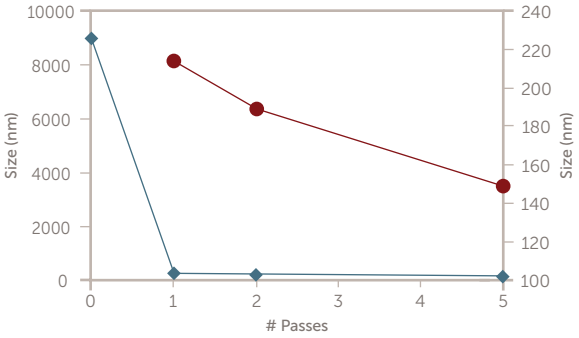

Figure 11. Liposome sample 329D, unprocessed, 1, 2, and 5 passes, 30k psi.

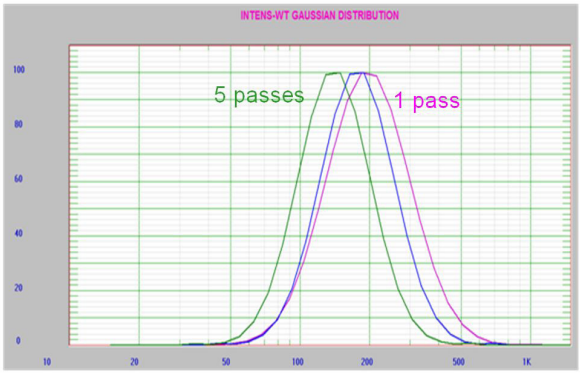

Figure 12. Liposome sample 329D, 1, 2, and 5 passes, 30k psi.

Passes	Size (nm)	PI
1	214.2	0.172
2	189.1	0.133
5	149.4	0.129

Table 4. Liposome sample 329D, 1, 2, and 5 passes, 30k psi.

CONCLUSIONS

The LV1 Microfluidizer proved to be an easy, efficient technology to create the nanoemulsion and liposome samples. Size distributions became smaller and tighter after processing through the Microfluidizer. A unique benefit of performing formulation and processing experiments at the lab scale using the Microfluidizer is knowing that the process can be scaled up to commercial scale without any difficulty or additional development work. The Nicomp DLS system proved an easy, effective instrument for tracking the size reduction by the Microfluidizer.

References

[1] Entegris Application Note - Liposomes

Note: The word Microfluidics has the complication of being both a company name and a term used to describe the multidisciplinary field intersecting engineering, and several fields in science with practical applications to the design of systems in which low volumes of fluids are processed to achieve measurement, automation, and high-throughput screening. Microfluidizer® is a registered trademark of Microfluidics, an Idex Company.

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