

Embrace reusable microfluidic mixing of LNPs on Sunshine

Introduction

Microfluidic mixing has become the go-to approach for LNP synthesis at scale, providing precise, reproducible control over how the aqueous payload and organic lipid streams meet. By tuning process parameters such as total flow rate (TFR), flow rate ratio (FRR), and mixer geometry, researchers can dial in particle sizes and achieve narrow size distributions for their chosen formulations.

Most commercial microfluidic mixing platforms rely on limited use cartridges. In their workflows, users need to install and discard cartridges, syringes, collection tubes, and waste tubes for each run. Every run adds consumable costs, setup time, and plastic waste. When experiments start stacking formulations, flow rates, payloads and replicates, the cost and hands-on time become significant concerns.

Sunshine takes a different approach (Figure 1A). It combines automated microfluidic LNP synthesis with reusable-by-design glass Sunny mixers (Figure 1B). The built-in automated flowpath washing lets you swap between formulations on the same Sunny while reducing carryover and contamination and maintaining particle quality and consistency.

Sunshine can further automate process optimization and particle size fine-tuning with batched runs of the same formulation but different TFRs and FRRs. Sunny mixers come in 9 different geometries, so you can tweak every parameter to make exactly the particles you need. Sunshine reduces cost, waste, and hands-on time and won't limit output volumes or reusability.

Once you have an optimized protocol, Sunshine has a path to GMP production and scale-up. Sunbather, another tool in the Sunny Suite, uses the same Sunny mixers as Sunshine and is GMP-ready.

Sunbather outputs up to 1.8 L/hour of particles with no maximum volume and can transfer

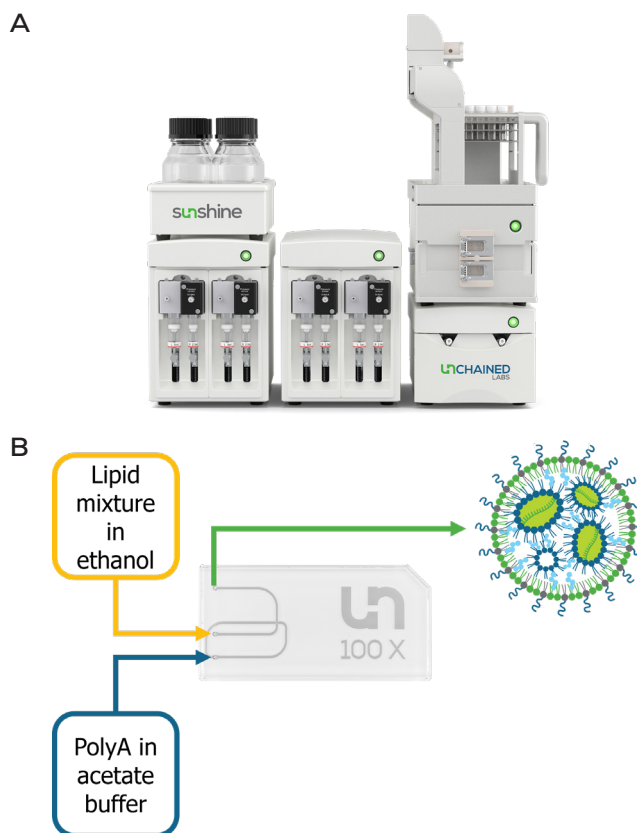


Figure 1: Sunshine (A) is the automated microfluidic nanoparticle mixing platform with reusable-by-design glass Sunny mixers (B) and minimum output volume of 400 µL, 0.1–30 mL/minute TFR, automated flowpath washing, and unlimited reusability.

processes directly from Sunshine without additional development time. When you're ready to move from bench to pre-clinical to clinical and even into commercialization, the Sunny Suite makes it a breeze.

In this application note, Sunshine was compared with a single-use cartridge-based instrument across 4 FDA-approved RNA-LNP formulations. Particle size and quality were assessed for each instrument and formulation while Sunshine delivered the additional benefits of reusable microfluidics, lower hands-on time, automated cleaning, and reduced running costs.

Methods

Three LNP formulations consisting of an ionizable lipid (SM-102, Dlin-MC3-DMA, or C12-200), 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC], cholesterol and DMG PEG-2000 were prepared at a 50:10:38.5:1.5 ratio. A fourth formulation of ALC-0315, DSPC, cholesterol, and ALC-0159 in a 46.3:9.4:42.7:1.6 ratio was also prepared. All formulations were used at 10 mM in ethanol. PolyA (Sigma Aldrich) was dissolved in 50 mM acetate buffer, pH 4, to give a Nitrogen/Phosphorus (N/P) ratio of 6.

1 mL of LNPs were prepared, in triplicate, on Sunshine using a 100X Sunny and a TFR of 8 mL/minute and a competitor single-use cartridge-based microfluidic instrument at a TFR of 12 mL/minute. Both instruments were used with an aqueous:organic FRR of 3:1. In Sunshine, acetate buffer and ethanol were used as the driver fluids for the aqueous and organic phases, respectively.

Reusable Sunny mixers were cleaned using Sunshine's automated flowpath washing workflow as part of the experiment sequence.

All particle size and PDI data were collected by rotating angle DLS (RADLS) using Stunner at 7 different angles.

A buffer viscosity and refractive index of 1.002 cP and 1.334, respectively, at 20°C and the default acquisitions of 7 angles, 5 acquisitions, and 1 second each were used. The hydrodynamic diameters were taken from the peak-of-interest of the mass distributions. Samples were diluted 10-fold in PBS and measured in triplicate.

Results

When deciding to move from one mixer technology to another, the new method should make the particles you need AND bring additional benefits. Bridging and comparability studies are a key part of this validation. Sunshine and a single-use cartridge-based system made LNPs with 4 FDA-approved RNA-LNP formulations at TFRs of 8 and 12 mL/minute, respectively (Figure 2). Sunshine produced LNPs with particle sizes that were within 8% of those generated using the alternative method across the formulation panel. Sunshine LNPs had PDIs of less than 0.1 for all formulations, indicating the particles were monodisperse. Particles can undergo finer tuning on Sunshine by varying TFR or FRR during a single run, taking advantage of Sunshine's multi-experiment automation capabilities.

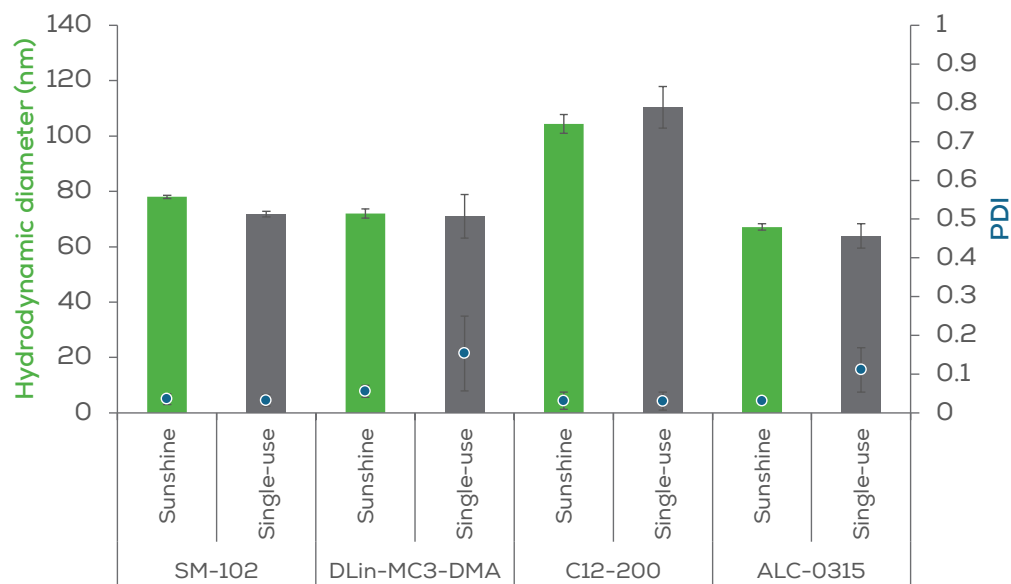


Figure 2: Hydrodynamic diameter (bars, left y-axis) and PDI (dots, right y-axis) of polyA-LNPs using 4 formulations made on Sunshine and a single-use, cartridge-based microfluidic mixer. Values are the average of triplicates; error bars are 1 standard deviation.

Sunshine offers significant time and cost savings compared to the disposable cartridge-based system. The automated workflow with built-in flowpath wash only took 33 minutes with 10 minutes of hands-on time for all 12 experiments while the alternative needed 60 minutes, all of which was hands-on (Table 1). The reusable Sunny also generated less waste, only needing the LNP reagents and about 50 mL of the driving fluids. The single-use system needed the same reagents and 12 cartridges which had to be thrown away.

For labs running multiple formulations or process optimizations, these time and consumable savings can add up quickly. Sunshine keeps the focus on the particles, not the prep work.

Conclusion

Sunshine produced high-quality LNPs with narrow distributions, excellent reproducibility, and sizes similar to the single-use cartridge-based platform across all 4 formulations of the panel. The reusable glass Sunny, automated flowpath washing and low-waste workflow helped reduce consumable costs, minimized plastic waste and freed researchers from repetitive cartridge handling. Sunshine can fine-tune particles to make exactly what you need while also reducing hands-on time so scientists can focus on the hard work that brings new nanoparticle medicines from the bench to patients.

	Sunshine	Single-use
Hands-On Time	10 minutes	60 minutes
Total Time	33 minutes	60 minutes
Waste Generated	~50 mL driving fluid	12 disposable cartridges
System/Chip Wash	Included in Experimental Time	NA
Consumables cost	Reagents only	Reagents + cartridges

Table 1: Time, waste, and consumables used by 12 LNP synthesis experiments (4 formulations x 3 runs) on Sunshine and a single-use, cartridge-based microfluidic mixer.



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