Microfluidic cIJM Technology for Robust, CMC-Aligned Manufacturing of Therapeutic Nanoparticles

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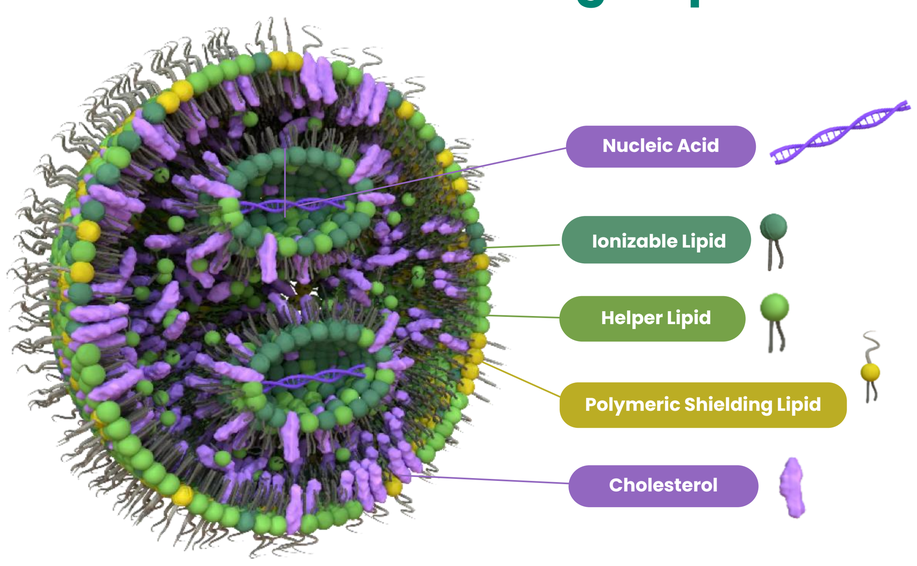
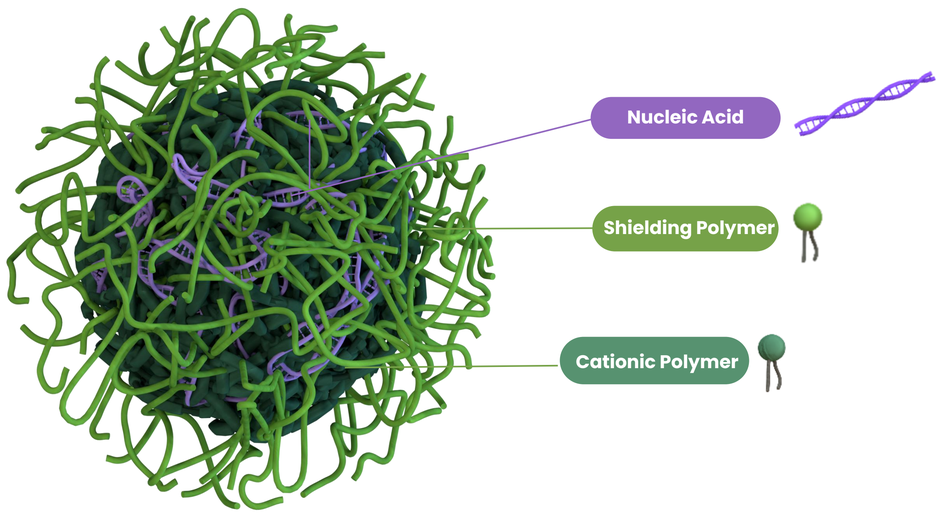
Addressing CMC Challenges in Nanoparticle Manufacturing Through cIJM

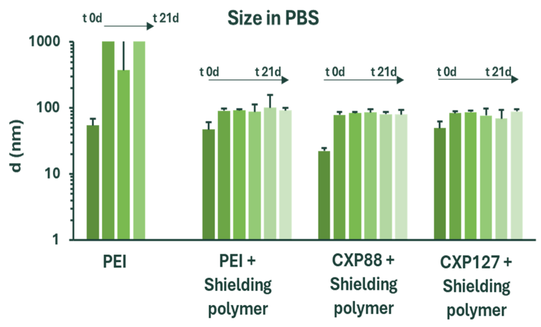
Nanoparticle-based drug delivery systems offer significant potential for improving the solubility, stability, and delivery of therapeutic molecules, including poorly soluble APIs, biologics, and nucleic acid-based drugs. Despite their promise, successful clinical and commercial translation requires robust manufacturing platforms capable of meeting stringent CMC expectations, particularly regarding reproducibility, scalability, and control of critical quality attributes such as particle size, PDI, ζ-potential, and encapsulation efficiency [1]. As formulation complexity increases across polymeric nanoparticles, PLGA nanoparticles, liposomes, and lipid nanoparticles, controlled continuous manufacturing approaches are becoming essential. Continuous Impinging Jet Mixing (cIJM) enables rapid and reproducible nanoprecipitation through precise mixing of solvent and anti-solvent streams, providing consistent particle formation and predictable scale-up. When combined with fit-for-purpose purification strategies, including centrifugal concentration and tangential flow filtration, cIJM represents a versatile and scalable workflow for the manufacturing of high-quality nanoparticle therapeutics [2,3].

Curapath's cIJM Manufacturing Capabilities



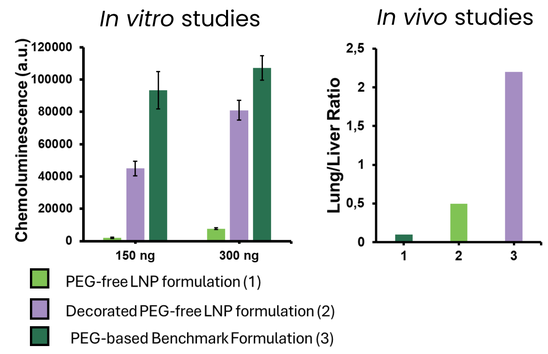


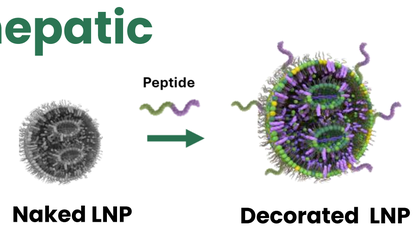
cIJM Application for PNPs formulation



cIJM enables the production of polymeric nanoparticles with tight size control and excellent stability over time. As shown, shielded formulations [4] consistently maintain particle sizes in the ~70–120 nm range from day 0 to day 21 in PBS, in contrast to unstable and heterogeneous PEI-only systems. This robust physicochemical stability translates into preserved transfection performance, highlighting cIJM as a reliable and scalable platform for generating high-quality PNPs.

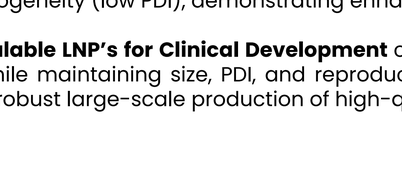
Targetable LNPs for Extrahepatic Delivery





In vitro tests (left) shows chemoluminiscence (transfection) of HEK293 cells after being treated with 3 mRNA-LNPs. In vivo studies (right) were conducted in male BALB/c mice via intravenous injection of mRNA encoding Firefly luciferase (mFLuc), followed by organ dissection and image acquisition using the IVIS Spectrum system [5].

cIJM PLGA NPs Manufacturing

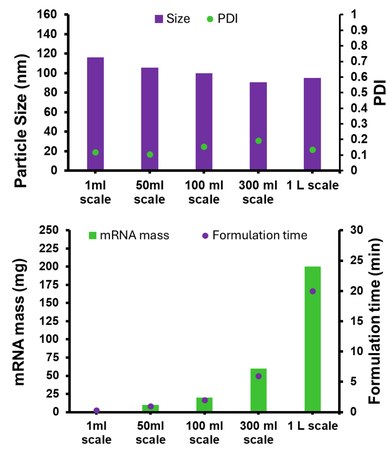


Formulation	Particle size (d.nm)	PDI	Z-pot (mV)	EE%
PLGA-NPs	101	0.06	2.6	35

cIJM enables the production of polymeric nanoparticles with enhanced functional performance and controlled physicochemical properties. As shown, cIJM-processed PLGA nanoparticles exhibit significantly faster and higher peptide release (~40% at 24–30 h) compared to conventional PLGA (~7–8%), while maintaining well-defined characteristics (≈100 nm size, low PDI of 0.06, and moderate surface charge). This highlights cIJM as a robust and scalable platform for generating uniform nanoparticles with improved release kinetics and reliable formulation quality.

Scalable LNP's for Clinical Development

- Scaling up from 1 ml to 1L GMP batches.
- This system exhibited remarkable proficiency in generating LNPs of optimal size and Polydispersity Index (PDI) between 80 and 120 nm, with high reproducibility, during the Process Development stage, allowing the creation of a robust protocol for the following GMP tech transfer.
- Notably, the technology has demonstrated its efficacy in formulating LNPs for large-scale production.



Conclusions

✓ **cIJM Application for PNPs formulation** cIJM enables the production of PNPs with tight size control and excellent stability in PBS up to 21 days. Shielded formulations maintain narrow distributions (~70–120 nm) and improve reproducibility and transfection performance compared to PEI-only systems.

✓**Targetable LNPs for Extrahepatic Delivery** LNP functionalization enhances in vitro transfection and promotes redistribution toward extrahepatic tissues in vivo. Decorated LNPs show clearly improved biological activity compared to standard formulations.

✓**cIJM PLGA NPs Manufacturing** cIJM significantly improves peptide release kinetics in PLGA NPs, reaching higher release levels (~40%) without compromising size (~100 nm) or homogeneity (low PDI), demonstrating enhanced functional performance.

✓**Scalable LNP's for Clinical Development** cIJM technology is highly scalable (from mL to L) while maintaining size, PDI, and reproducibility. This enables efficient GMP translation and robust large-scale production of high-quality LNPs.

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