Leveraging Microfluidic Technology as a Tool for Production of Lipid Nanoparticles for Nucleic Acids Delivery

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Abstract:
Lipid nanoparticles (LNPs) are essential for the effective delivery of nucleic acids in gene therapy and molecular medicine. Composed of ionizable, helper, and PEG-lipids, LNPs encapsulate and protect RNA and DNA, preventing degradation, enhancing cellular uptake, and facilitating intracellular release. This technology has greatly contributed to RNA-based therapeutics, playing a key role in vaccine development and treatments for cancer, infectious diseases, and genetic disorders. This research focuses on encapsulating non-coding RNAs and plasmid DNA using microfluidic techniques to achieve high encapsulation efficiency, uniform particle size, and stable formulations [1]. Microfluidics, which controls fluid movement in microscale channels, offers precise production of LNPs. This method allows for control over particle size and encapsulation efficiency, which are critical for the performance of nano delivery systems [2]. LNPs for RNA (siRNA and miRNA) were prepared by dissolving lipids in ethanol and mixing with an aqueous buffer using a herringbone microfluidic mixer. DNA plasmid LNPs followed a similar process with different lipid ratios and buffers. The resulting LNPs were purified and lyophilized. Characterization showed RNA LNPs ranged from 100-120 nm and DNA plasmid LNPs from 150-200 nm, achieving 60% to 80% encapsulation efficiency. Stability tests at 4°C showed that LNPs maintained size and encapsulation integrity. In vitro assays demonstrated effective cellular uptake, with siRNA achieving gene silencing in pancreatic beta-cells and plasmid DNA showing up to 90% transfection efficiency in HEK293T and HeLa cells. In summary microfluidic techniques enable efficient encapsulation of RNAs and plasmid DNA in lipid nanoparticles, enhancing the efficacy of nucleic acid-based therapeutics.

References

[1] Hou, Xucheng, et al. "Lipid nanoparticles for mRNA delivery." Nature Reviews Materials 6.12 (2021): 1078-1094.

[2] Maeki, Masatoshi, et al. "Microfluidic technologies and devices for lipid nanoparticle-based RNA delivery." Journal of Controlled Release 344 (2022): 80-96.

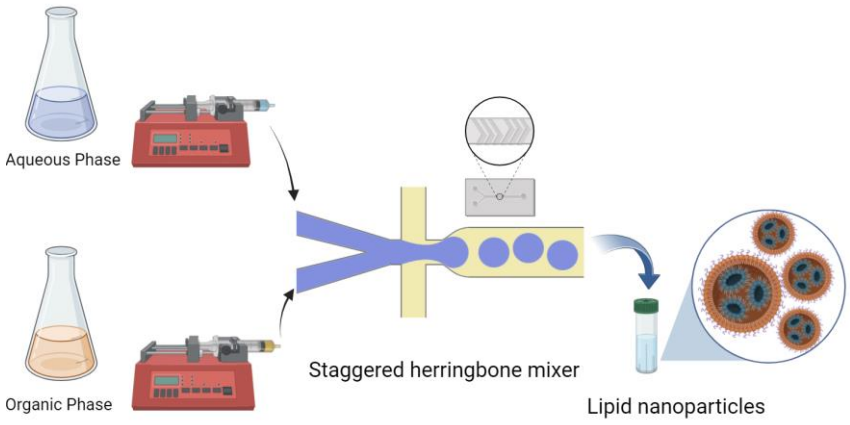

Figure 1: Graphical presentation of microfluidic production of LNPs encapsulating RNA and pDNA