

Ionizable LNP Lipid Purification by CPC

Lipid nanoparticles (LNPs) are novel powerful pharmaceutical drug delivery vehicles, intensively utilized in the formulation (i.e., encapsulation) of mRNA vaccines. These systems primarily rely on four lipid components: a PEG lipid, amino (cationic) lipid, structural lipid, and cholesterol [1]. The ionizable (cationic) lipids are key components in LNPs, since they can form aggregate complexes with nucleic acids through a charge-charge interaction (**Fig. 1**).

In an ongoing feasibility study an alkane/alcohol/water solvent system-based multiple dual mode (MDM) CPC method was developed to isolate a cationic lipid with a proprietary structure from a synthetic reaction mixture (containing unreacted

starting material and over-alkylated byproducts as major impurities).

The CPC method outperformed the currently used normal-phase flash chromatography in terms of yield. The alkane/alcohol/water solvent system also managed to keep the stability of the target lipid, which is often an issue experienced on solid stationary phase column chromatography with dichloromethane-methanol solvents.

By the end of the purification, 320 mg of lipid crude was processed in 35 min to produce the target lipid in 93% yield and with 98% purity on a lab-scale CPC system (**Fig. 2**).

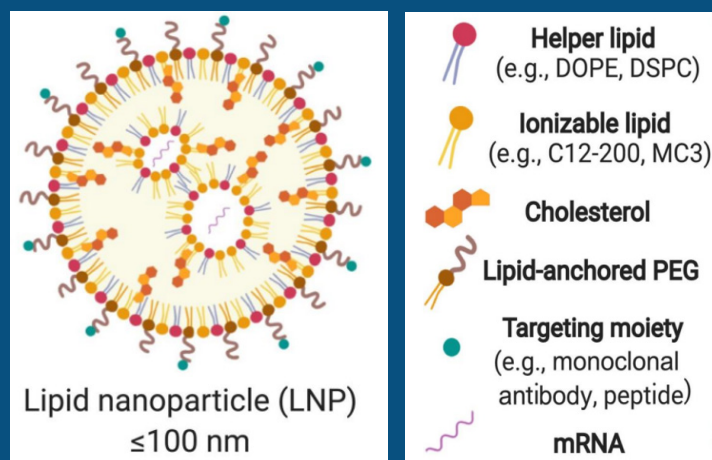


Fig. 1. Schematic structure and components of a lipid nanoparticle encapsulated mRNA.

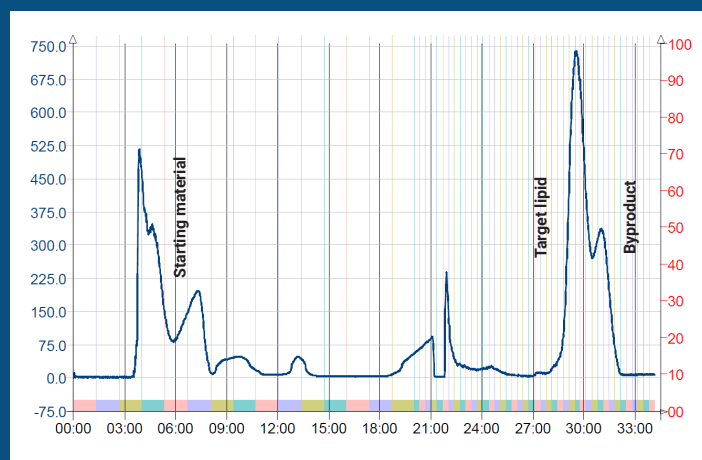







Fig. 2. Lab-scale MDM CPC elution profile of the synthetic crude lipid mixture in alkane/alcohol/water solvent system.

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References

[1] K.L. Swingle, et al., Lipid Nanoparticle-Mediated Delivery of mRNA Therapeutics and Vaccines, Trends in Molecular Medicine, 2021, <https://doi.org/10.1016/j.molmed.2021.03.003>