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Viscosity Measurement of mRNA Encapsulated in Lipid Nanoparticles (LNPs) Using VROC® Technology

Key Words: Viscosity, Lipid Nanoparticles, mRNA, Shear Rate, Temperature, m-VROC® II

Goal: RheoSense viscometers are powerful tools for advanced rheological analysis of biological fluids. One of the latest biologics attracting attention is LNP-mRNA. In this application note, we demonstrate how the RheoSense **m-VROC® II** is used to measure the viscosity of LNP-mRNA during shear rate and temperature sweep experiments. Our goal is to show the accuracy and repeatability of low viscosity measurements using the **VROC®** instrument.

Introduction

Lipid nanoparticles (LNPs) encapsulating messenger RNA (mRNA) have emerged as a critical delivery system in biopharmaceutical applications, particularly in vaccines, gene therapy, and cancer treatment. These LNPs protect mRNA from degradation and enhance its uptake into target cells. The success of LNP-mRNA technology is clearly demonstrated by the development of COVID-19 vaccines, such as those by Pfizer and Moderna.

One key parameter in the formulation of LNP-mRNA systems is viscosity, which plays a crucial role in manufacturability, stability, and injectability. For instance, maintaining an optimal viscosity range enhances the stability of the formulation, and ensures ease of injection into patients. Consequently, accurate viscosity measurement is essential for the design and optimization of lipid-based drug delivery systems.

This application note demonstrates the capabilities of the next-generation m-VROC II viscometer for precisely measuring the viscosity of LNP-mRNA formulations. With its advanced features, including superior repeatability, reduced sample volume requirements (15 µL), and sample retrieval capability, the m-VROC II offers an ideal solution for characterizing the viscosity of biological samples across a wide range of shear rates and temperatures.

Methodology

In this study, we tested three LNP-mRNA formulations with varying lipid-to-mRNA ratios (n/p ratios) of 6, 15, and 30 at two temperatures, 25°C and 37°C. These samples were prepared in Dr. Bobbala's lab at West Virginia University. The objective was to assess the viscosity differences of these formulations and demonstrate how the m-VROC II can effectively distinguish even small viscosity variations.

Viscosity measurements were performed using a combination of two microfluidic chips: the B05 chip (depth = 50 µm, Pmax = 40 kPa) and the E02 chip (depth = 20 µm, Pmax = 1.8 MPa). These chips were chosen based on the expected viscosity range of the samples. For each measurement, 80 µL of the LNP-mRNA formulation was back-loaded into the syringe.

A Level generated measurement protocol was created using the m-VROC II software, which automatically adjusts flow rates to achieve pressure readings between 5% and 95% of full-scale pressure. The sample

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retrieval feature was activated, enabling extensive testing with a single loaded volume for enhanced data accuracy.

Viscosity Results and Analysis

Our results **(Figure 1)** indicated that the LNP-mRNA system with an n/p ratio of 6 exhibited the highest viscosity, followed by the formulations with n/p ratios of 15 and 30, respectively. Although the differences in viscosity were small, m-VROC II was able to reliably distinguish these variations. These findings suggest that slight changes in the lipid-to-mRNA ratio can have an impact on the viscosity, although the overall viscosities of the three formulations were similar and within the same general range.

In LNP-mRNA systems, the n/p ratio represents the number of lipid molecules (n) relative to the amount of mRNA (p) used in the formulation. At lower n/p ratios, there is typically a higher proportion of free mRNA, which may lead to a more viscous formulation. However, in this study, while n/p = 6 showed a higher viscosity than n/p = 15 and n/p = 30, the differences were not pronounced enough to establish a clear trend across the samples.

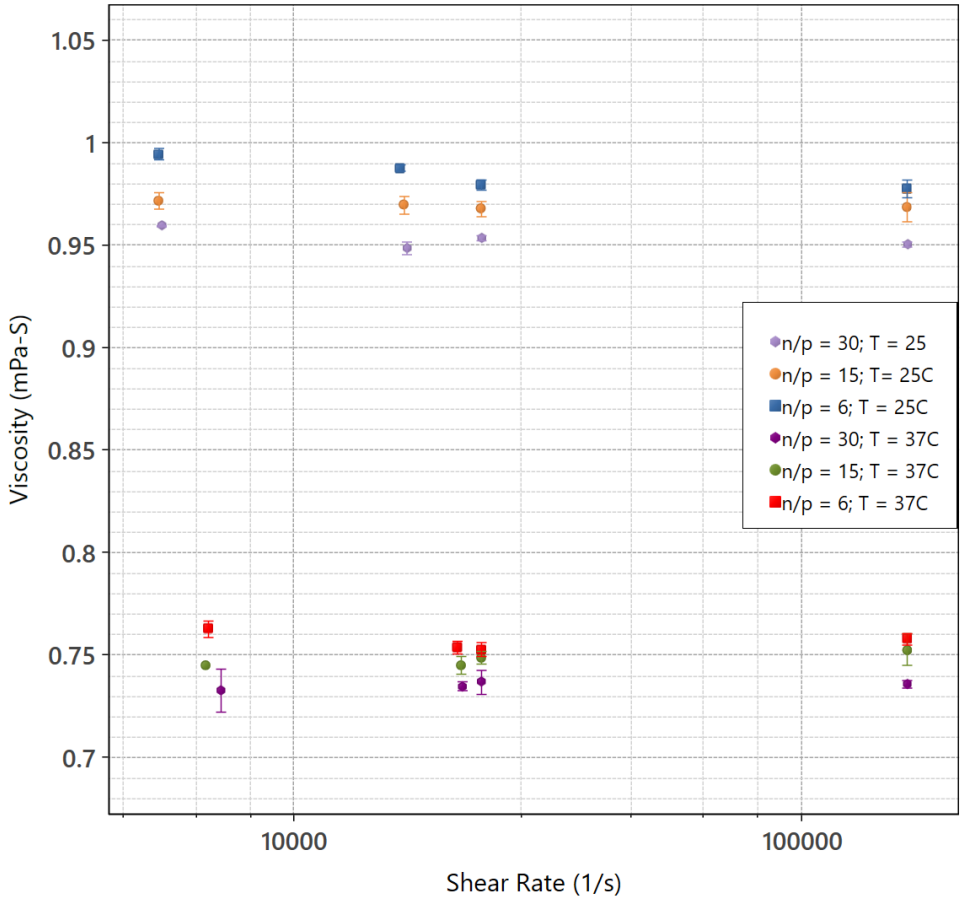

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Figure 1: Viscosity vs. shear rate for three LNP-mRNA formulations measured on m-VROC II at temperatures, 25˚C and 37˚C. The graph was generated using RheoSense's **Clariti®** software.

Conclusion

This study illustrates the effectiveness of the m-VROC II viscometer in measuring the viscosity of LNP-mRNA formulations across a wide range of shear rates and temperatures. The results demonstrate the ability of the m-VROC II to distinguish small viscosity differences in LNP-mRNA systems, even when the formulations are within similar viscosity ranges. Measuring viscosity with m-VROC II provides valuable insights into the behavior of lipid-based drug delivery systems, supporting their development for a variety of therapeutic applications.

If this note is helpful, please let us know! 👍 If you have questions or need more information about this product or other applications, please contact us:

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