Optimization of mesoscale nanoparticle formulation process through the design of experiments approach

Anastasiia Vasylaki [1]*, Arantxa Roach [1], Ryan Williams [1]

[1] *Department of Biomedical Engineering, The City College of New York, New York, NY 10031, USA*

Correspondence: avasyla000@citymail.cuny.edu

Polymeric nanoparticles with a diameter of 350 – 400 nm (mesoscale) have been shown to selectively accumulate in the kidneys, thus presenting a promising delivery system for kidney disease therapeutics. This kidney-targeting property is specifically attributed to the nanoparticle size in the mesoscale range. Therefore, it is crucial to be able to precisely control the nanoparticle characteristics via the formulation process. In this work, we aim to optimize the formulation conditions of the mesoscale nanoparticles to achieve desired characteristics using the design of experiments (DoE) approach.

Mesoscale PLGA-PEG nanoparticles encapsulating edaravone as a model drug were prepared using the nanoprecipitation method. Different formulation parameters have been screened to establish the significance of their influence on the nanoparticle characteristics such as size, polydispersity index, zeta potential, drug loading, and yield. Fractional factorial 2^{8-4} resolution IV design was used for the screening step. Further experiments were aimed at building a model for the nanoparticle formulation process and finding optimum levels of the formulation parameters that allow for obtaining desired nanoparticle characteristics. This step employed response surface methodology.

Formulation parameters that have a significant effect on mesoscale nanoparticle characteristics (size, polydispersity index, zeta potential, drug loading, and yield) were identified. Then the mathematical model of the formulation process was established and represented in the form of a response surface plot. Based on this data, formulation parameter levels were optimized to achieve nanoparticle size in the range of 350 – 400 nm, as well as minimize polydispersity index, and maximize drug loading and yield.

This study has systematically evaluated and mathematically described the impact of various formulation process variables on the resulting mesoscale nanoparticle characteristics. Such a thorough understanding of the formulation process is fundamental for consistently obtaining desired nanoparticle specifications and, hence, successful drug delivery to the disease site.