UNIVERSITÀ DEGLI STUDI DI SALERNO

Department of Industrial Engineering

Master's Degree in Chemical Engineering

Characterization of a coaxial injection mixer for continuous production of nanoparticles

Thesis in

Transport Phenomena

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Abstract

This thesis aimed to investigate the fluid dynamics conditions in a coaxial injection mixer and to examine their impact on the resulting nanoparticles (liposomes). The objectives of the study were achieved through a series of experimental steps. Initially, the fluid dynamics conditions described by Lim et al. (2014) were replicated using a coaxial turbulent jet mixer. The mixing performance was studied by conducting an acid-base neutralization reaction, with the presence of an indicator, at several fluid dynamics regimes. From these experiments and through image analysis it was possible to calculate the mixing time from the measurement of the mixing length and from the knowledge of the total flow rate.

The mixing performance was also evaluated using the Villermaux-Dushman reaction (competitive consecutive reaction system). A linear relationship between the segregation index (Xs) calculated from the reaction yield and the mixing time was observed. These results allowed to confirm the goodness of the results obtained from the acid-base neutralization reaction and confirmed the importance of the micromixing phenomenon in this application.

Such a characterized system was used to produce liposomes containing a model drug (vitamin D3) at different flow rates and phosphatidylcholine concentrations. Moving from laminar to turbulent production conditions resulted in a significant decrease in the size of liposomes, maintaining high encapsulation efficiency. This demonstrated that the formation of liposome through nanoprecipitation is governed by the mixing time between the solvent and the antisolvent, which should be as fast as possible (micromixing time scale) to achieve narrow and low particle size distribution.

Chapter Four

Conclusions

In this chapter the conclusions of the work described in the previous chapter are summarized.

In conclusion, this thesis aimed to investigate and examine the influence of fluid dynamics conditions in a coaxial injection mixer on the characterization of liposomes. The objectives of the study were successfully achieved through a series of experimental steps.

Initially, the fluid dynamics conditions described in the study by Lim et al. (2014) were replicated using the coaxial turbulent jet mixer. By conducting an acid-base neutralization reaction and analysing the resulting flow behaviour zones, the accuracy of the coaxial injection mixing was verified. The experimental observations demonstrated a close correspondence between the results obtained with different needle sizes.

The mixing time, was calculated based on video analysis, using the measured mixing length (L) at the point of complete neutralization of the acid-base reaction. Indeed, the experimental results presented in the study demonstrated that the EDD model can effectively estimate the mixing time when the coaxial turbulent jet mixer is operated in the turbulent jet regime.

Furthermore, the study utilized the ε parameter from the EDD model, which represents the average turbulent kinetic energy dissipation, to calculate the τ_{ω} parameter. The ratio between τmix and τ_{ω} was found to be approximately one, regardless of the FVR and Reynolds number (NRe), indicating that the mixing time can be estimated accurately using the EDD model in the turbulent jet regime.

The mixing performance was evaluated using the Villermaux-Dushman reaction, and the segregation index (Xs) was measured for different concentrations of reagents. The results indicated that in the turbulent regime, the system approached almost a perfectly mixed state, where the common reagent was fully consumed by the quasi-instantaneous reaction. Additionally, a linear relationship between Xs and the mixing time (τ_{mix}) was observed, allowing for the quantification of micromixing independent of the chemical reaction.

Lastly, the impact of flow rates and phosphatidylcholine concentrations on the characteristics of liposomes was assessed. The study revealed that when moving from laminar to turbulent production conditions, there was a notable decrease in the size of liposomes. This transition led to the production of smaller liposomes under turbulent conditions. This finding highlights the importance of fluid dynamics conditions in controlling the size and properties of liposomes during their production process. This evidence was confirmed by evaluating the encapsulation efficiency, turbidity, z-average, load and numeric, volumetric, and intensity distribution, for different concentrations of extracted phosphatidylcholine.

Overall, this thesis successfully investigated the influence of fluid dynamics conditions on the resulting production of liposomes. The findings contribute to the understanding of the relationship between mixing conditions and liposome characteristics, offering insights for the optimization of liposome (and nanoparticles) production processes in coaxial-injection mixers.

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