

Lipid Nanoparticles Formulations from Bench Scale To Industrial Scale

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Abstract

Purpose:

Lipid nanoparticles are self-assembling vesicles obtained by hydrating a mixture of non-lipids and cholesterol and are suitable as carriers of drugs and biopharmaceuticals. It is desirable to be able to accurately control size and polydispersity of the vesicles as this can impact on biological outcome. Moreover, it is crucial to formulate these nanoparticles in a scalable method that can be used in industrial settings. One approach that has been successful for lipid-based systems is the use of microfluidics (MF). In this study we compared a MF-based method with traditional methods such as thin film hydration (TFH) method and heating method using niosomes as a model nanoparticles.

Method:

Niosomes using MF were prepared on a NanoAssembler. Monopalmitin, cholesterol and dicetyl phosphate were dissolved in ethanol at specific molar ratios. The lipids and aqueous buffer were injected into separate chamber inlets of the micromixer. The flow rate ratio (FRR; ratio between aqueous and solvent streams) and the total flow rate (TFR) of both streams were controlled by syringe pumps. An established TFH and heating methods were used to prepare niosomes followed by extrusion through an Avanti-polar miniextruder. The particles generated from these methods were compared for their size and potential by dynamic light scattering and morphology using atomic force microscopy.

Results and Discussion:

The size of niosomes produced by MF was controlled by altering the FRR and TFR in both the lipid and aqueous phases (Table 1). In contrast, niosomes prepared by the TFH method and heating method were large, polydisperse and required a post-manufacturing extrusion size reduction step (around $4\mu\text{m} \pm 0.2$ before extrusion). A stability study was performed on NISV generated by both methods, at four temperatures (4, 25, 37 and 50°C) for 4 weeks, and the

vesicles were shown to be stable in terms of size and polydispersity index (PDI) (Table 2).

Table 1: Characteristics of NISV prepared at different flow ratios between the aqueous and the lipid phase through MF.

*Progressed to stability studies. n=3

FRR

Aqueous/solvent	Size (nm)	PDI	Z potential (mV)
1:1	187.8	0.12	-27.2
3:1*	166.1	0.05	-21.4
5:1	120.6	0.16	-19.2

Table 2: Characteristics of NISV prepared by TFH and MF stored at 4°C for four weeks. n=3

Time (weeks)	Microfluidics		TFH	
	Size (nm)	PDI	Size (nm)	PDI
0	166.1	0.05	110.6	0.18
1	170.7	0.05	110.8	0.18
2	171.8	0.06	111.5	0.21
3	171.9	0.07	111.4	0.24
4	172.0	0.06	111.2	0.23

Conclusion:

Stable, controlled size niosomes, were manufactured by MF in seconds. The TFH method and heating method also produced stable niosomes, but the process took several hours and the resulting vesicles were polydisperse and required an extrusion step to control the size. Studies are on-going to determine the drug entrapment efficiency and biological impact of controlled size vesicles.



Biography:

Mohammad Obeid is an Assistant professor at the Faculty of pharmacy, Yarmouk University, Irbid, Jordan. He is the head of pharmaceuticals and pharmaceutical technology department and specialized in designing lipid based nanoparticles as a delivery system. He was successfully developed stable nanoparticles and tested their efficacy in the delivery of different therapeutic agents such as siRNA, curcumin, doxorubicin and various types of antibiotics and vaccines. The aim of his work is to prepare these nanoparticles at industrial scale for large batches production.

Speaker Publications:

1. Mohammad A. Obeid (2017) Comparison of the Physical Characteristics of Monodisperse Non-Ionic Surfactant Vesicles (NISV) Prepared Using Different Manufacturing Methods. International Journal of Pharmaceutics 521(1-2) 10.1016/j.ijpharm.2017.02.007.
2. Mohammad A. Obeid (2020) Development of novel nanoparticles based formulation for the treatment of antibiotic resistance. International Journal of Nanotechnology and Nanoscience, Volume 6, 2020, 26-30.
3. Mohammad A. Obeid (2020) Correction to: Application of Nanomaterials in the Diagnosis and Treatment of Genetic Disorders. Applications of Nanomaterials in Human Health 10.1007/978-981-15-4802-4_16.
4. Mohammad A. Obeid (2020) Chemical engineering of protein cages and nanoparticles for pharmaceutical applications. Nanofabrication for Smart Nanosensor Applications (pp.415).

5. Mohammad A. Obeid (2019) Gold-coated plant virus as computed tomography imaging contrast agent. Beilstein Journal of Nanotechnology 10(1):1983-1993.

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