Optimisation of Multifunctional Nanostructured Lipid Carriers for Dry Eye Disease: Influence of Solid to Liquid Lipid Ratios, Preparation Methods, and Process Parameters

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Introduction

- Dry eye disease (DED) is a chronic and multifactorial disorder characterised by tear film instability, hyperosmolarity, ocular surface inflammation, neurosensory abnormalities, and a loss of tear film homeostasis [1].
- Despite the availability of treatments including artificial tears, corticosteroids, antibiotics, topical ocular immunomodulatory drops, and other prescription therapies, current options are often insufficient and leave many patients with unmet needs [2].
- A multifactorial nanoparticle system that can better deliver therapeutic agents to the target site, as well as provide natural relief to the eye, is needed to address the eye-related symptoms of DED [3].

Aims

- To explore the fabrication of multifunctional nanostructured lipid carriers (NLCs) that contain components which can address the multifactorial nature of dry eye while replenishing tear film layers.
- To optimise the solid to liquid lipid (S:L) ratios (ranging from 1:10 to 10:1), preparation method, and processing parameters for the development of a Design of Experiments (DOE) plan aimed at fabricating a multifunctional NLC-based artificial tear formulation.

Methodology

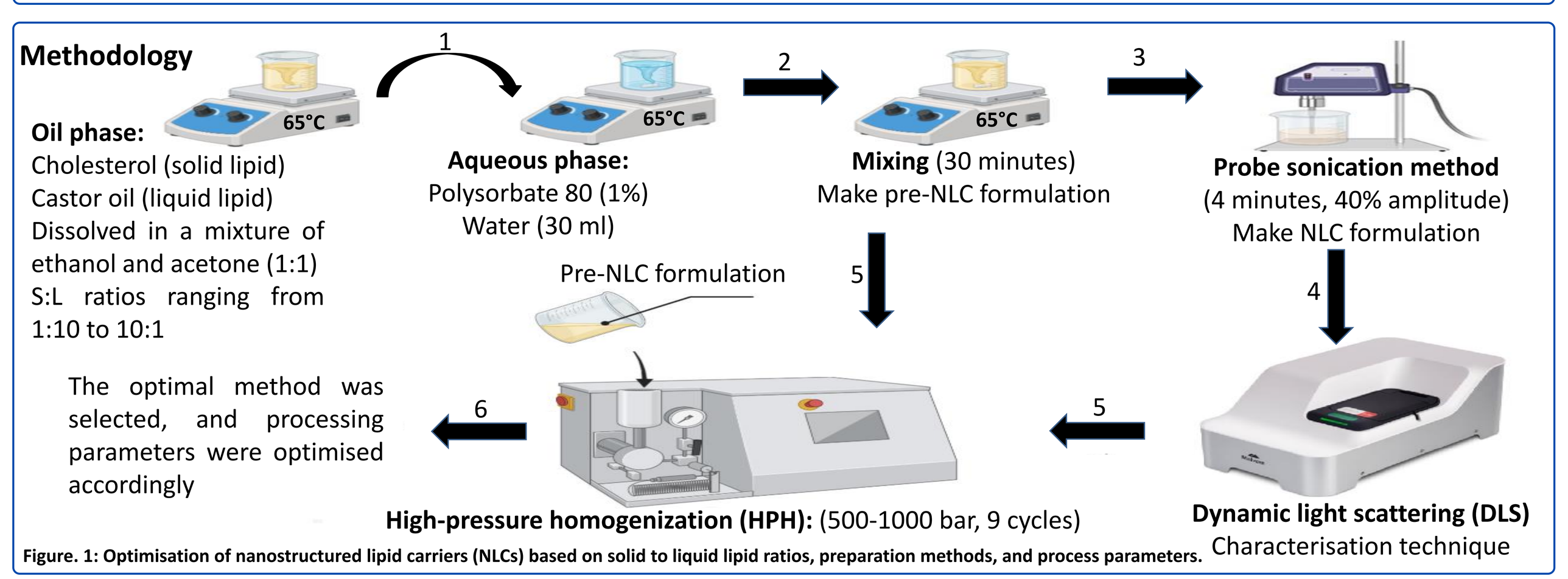

Figure. 1: Optimisation of nanostructured lipid carriers (NLCs) based on solid to liquid lipid ratios, preparation methods, and process parameters.

Results

- **Preliminary screening of S:L ratios for NLC Fabrication Using Probe Sonication:** 10:1 and 5:1 S:L ratio formulations showed immediate and within 2 hours precipitation, respectively. 1:10 and 1:5 S:L ratio formulations resulted in large particle sizes (500–2000 nm). These ratios were excluded for further tests.
- **Probe sonication vs HPH for included S:L ratios:** Ratios of 1:3, 1:1, and 3:1 were selected for further evaluation using both probe sonication and HPH methods.

Table. 1: Characterisation of included Solid to liquid lipid ratios using two methods (n=2).

Method	S: L (ratio)	Particle size (nm)	PDI
Probe sonication	3:1	774.90 ± 332.48	0.78 ± 0.12
Probe sonication	1:1	299.35 ± 44.19	0.41 ± 0.01
Probe sonication	1:3	796.65 ± 399.30	0.63 ± 0.14
HPH	3:1	310.70 ± 4.81	0.52 ± 0.02
HPH	1:1	278.35 ± 13.65	0.38 ± 0.06
HPH	1:3	504.00 ± 82.73	0.46 ± 0.06

- **Optimisation of process parameters in HPH:** 1:1 S:L ratio was chosen as the optimal formulation for HPH process optimisation.

Table. 2: Characterisation of included Solid to liquid lipid ratios using the HPH method (n=2).

Number of cycles	Pressure (bar)	Particle size (nm)	PDI
3	500-1000	373.30 ± 4.95	0.55 ± 0.01
6	500-1000	284.60 ± 41.01	0.40 ± 0.02
9	500-1000	280.65 ± 12.94	0.38 ± 0.06
12	500-1000	300.55 ± 25.24	0.46 ± 0.06
6	1000-1500	547.90 ± 33.09	0.52 ± 0.05
3	1000-1500	446.80 ± 69.58	0.57 ± 0.13

Conclusions

- HPH was selected over the probe sonication method for its ability to produce smaller particle sizes and lower PDIs.
- S:L ratios of 10:1, 5:1, 3:1, 1:3, 1:5, and 1:10 precipitated or produced particle sizes >300 nm, which is above the optimal range for ocular delivery. Therefore, 2:1, 1:1, and 1:2 S:L ratios were selected for the future DOE plan.
- HPH with 6 cycles at 500-1000 bar was identified as the optimal processing condition, due to its ability to fabricate smaller particle sizes in an efficient time.
- Among the current formulations, 1:1 S:L ratio was identified as the optimised formulation, as it achieved a particle size of ~285 nm with a PDI of 0.4.

References:

[1] Craig JP, Nelson JD, Azar DT, Belmonte C, Bron AJ, Chauhan SK, et al. TFOS DEWS II Report Executive Summary. Ocul Surf. Size of 2017; 15(4): 802–12.

[2] Shen Lee, B., Kabat ,Alan G, Bacharach ,Jason, Karpecki ,Paul, and Luchs, J., 2020. Managing Dry Eye Disease and Facilitating Realistic Patient Expectations: A Review and Appraisal of Current Therapies. Clin. Ophthalmol. 14, 119–126.

[3] Sarfraz, M., Behl, G., Rani, S., O'Reilly, N., McLoughlin, P., O'Donovan, O., Reynolds, A.L., Lynch, J., Fitzhenry, L., 2025. Development and in vitro and ex vivo characterization of a twin nanoparticulate system to enhance ocular absorption and prolong retention of dexamethasone in the eye: from lab to pilot scale optimization. Nanoscale Adv. 7, 3125–3142.

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Poster

OTRG Group

Acknowledgement: This project is funded by South East Technological University. The Scholarship is funded through WIT 2023 Presidents Scholarship programme (NFQ level 10).