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P-79

Preformulation Studies of Polymeric Nanocapsules

LUCA ÉVA UHLJAR[1]; PÉTER GIESZINGER[1]; PIROSKA SZABÓ-RÉVÉSZ[1]; RITA AMBRUS[1]

[1] *University of Szeged, Institute of Pharmaceutical Technology and Regulatory Affairs, 6 Eötvös Street, H-6720, Szeged, Hungary*

Correspondence: ambrus.rita@szte.hu

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1. Introduction

Nowadays, nanotechnology-based approaches are in the focus of pharmaceutical research. These nanometer-scale size formulations carrying the active pharmaceutical ingredient, give more benefits than conventional drugs. Generally, the main benefits are the improvement of the solubility of highly hydrophobic compounds and the enhancement of their permeability across the biological barriers. In this way, increased bioavailability can be achieved which leads to the reduction of the drug dose and, in most cases, also the decrease of the side-effects [1].

The nanocarriers can be separated into colloidal systems such as liposomes, solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC) and polymeric nanoparticles such as nanospheres, nanofibers and nanocapsules. This article focuses on the polymeric lipid nanocapsules. Nanocapsules can be considered as hollow polymer nanostructures where the API is dispersed in the oil-filled core surrounded by a biodegradable polymer shell [Figure 1]. Encapsulation in nanocapsules can provide further advantages e.g., protecting the drugs against harsh physiological environments and enzymatic degradation. Moreover, these nanocarriers have high drug encapsulation efficiency and low polymer content compared to other polymeric nanoparticles [2,3].

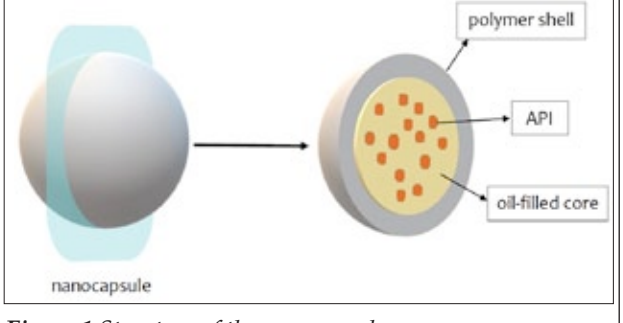

Figure 1 *Structure of the nanocapsule*

This preformulation study aimed to prepare nanocapsules from various compounds of the core to get general information and find optimal formulations for further investigation.

2. Materials and methods

Materials

Meloxicam (MEL) was used as a model drug (EGIS Ltd., Budapest, Hungary). Glyceryl monooleate (Type 40) (Peceol®) and Diethylene glycol monoethyl ether (Transcutol HP®) were kind gifts from Gattefossé (St. Preist, France). Polyoxyethylene (40) monostearate (PEGst 40) was obtained from Croda (East Yorkshire, United Kingdom). Chitosan hydrochloride salt was used as a shell-making polymer from HMC+ (Halle, Germany).

Preparation method

The solvent displacement technique was used for the preparation of the polymeric nanocapsules [4]. Generally, it is a simple three-step method shown in Figure 2. The first step was spontaneous emulsification which took place by mixing an organic phase with an aqueous phase under magnetic stirring. In the next step, the nanocapsules were prepared by adding the shell-making polymer. The last step was the purification via ultracentrifugation. The MEL solution, the surfactant and the liquid lipid were used in different ratios.

Characterization of the nanocapsules

As a preformulation study, three notable properties of the formulations were chosen for the characterization. The particle size and polydispersity index (PDI) were analyzed by photon correlation spectroscopy while Zeta potential was determined by laser Doppler anemometry (Zetasizer NanoZS®, Malvern Instruments; Malvern, United Kingdom).

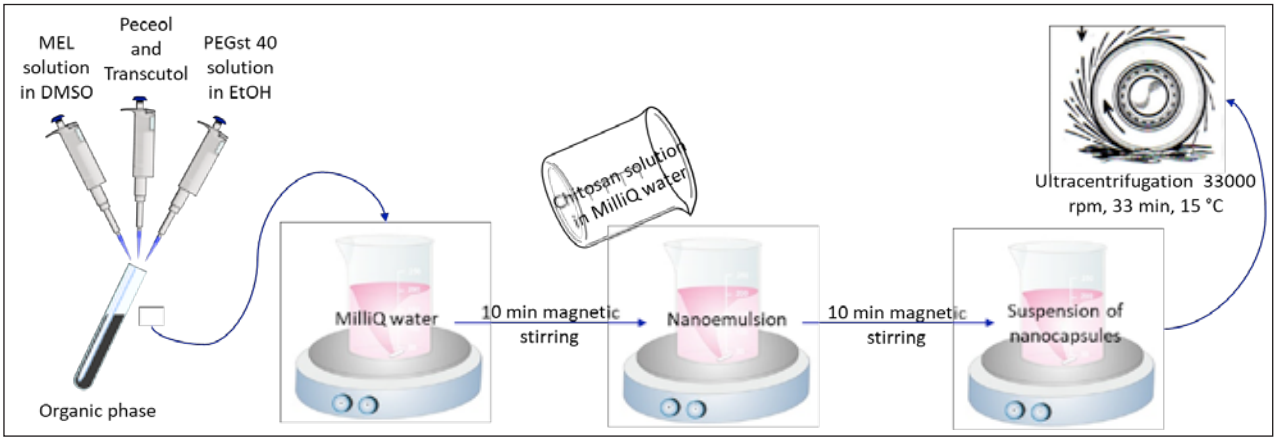

Figure 2 *Solvent displacement technique used for the preparation of nanocapsules*

Table 1 *Main properties of different nanoemulsion (em.) and nanocapsule (NC)formulations*

MEL sol.: Peceol:Transcutol (µL ad 1 mL organic phase)	Type	Particle size (nm)	PDI	Zeta potential (mV)
100:20:40	em.	1259.0	0.308	-2.00
	NC	793.5	0.216	0.92
100:40:40	em.	717.1	0.273	-0.86
	NC	404.2	0.231	0.52
100:60:40	em.	769.0	0.240	-2.21
	NC	680.0	0.226	0.35
100:40:20	em.	677.7	0.239	-1.83
	NC	507.4	0.157	0.49
100:40:60	em.	857.7	0.270	-0.52
	NC	651.2	0.271	-0.21

3. Results

Different formulations of MEL loaded nanocapsules were prepared. The organic phases containing MEL solution (15 mg/mL), Peceol®, Transcutol® and PEGst 40 solution were prepared first with different ratios of the surfactant and the liquid lipid (Table 1).

Then, this solution was mixed with 2 mL of ultrapure water under 10 minutes of continuous magnetic stirring. Finally, the shells of the nanocapsules were formed from the added 2 mL of chitosan solution (1 mg/mL). The characterization was executed with each formulation as nanoemulsion and as nanocapsule form (Table 1).

4. Conclusions

Based on the results it can be recognized that the particle size and the PDI are reduced while the zeta potential is increased in the case of the nanocapsules compared with the adequate nanoemulsions. The latter probably caused by the formation of the positively charged chitosan shell. Zeta potential is predictive of colloidal stability. Therefore, it is important to enhance it more.

To meet with the particle size and the PDI criteria of nanosystems according to regulatory guidelines two formulations (100:40:40 and 100:40:20) have been chosen for further measurements.

5. Acknowledgements

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