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Short communication

Preparation of dried nanoemulsion formulation by electrospinning

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Introduction

An inherent challenge in ophthalmic drug delivery is the short drug residence time within the ocular region. Thus, the effectiveness of the treatment of eye diseases is often inadequate or limited. An appropriate drug delivery system is therefore crucial. Oil-in-water (o/w) nanoemulsions hold a great potential as a delivery system for effective treatment of different eye diseases. They can deliver drugs with limited aqueous solubility into the corneal segment resulting in delayed and/or sustained drug release (Dukovski et al., 2020). However, o/w nanoemulsions as liquid formulations have limited retention time on eye surface and can be susceptible to chemical and physical instabilities. Among various strategies to enhance the nanoemulsion stability, their transformation into a dry product has been shown as a promising approach. The dry product should dissolve rapidly on the ocular surface and form a transparent film to avoid disturbing the patient's vision. Recently, electrospinning has been shown as a promising drying method for nanoparticle dispersions, which enables the formation of easily redispersible non-powdered dry product without high amounts of additional excipients (Dragar, et al., 2022). The aim of this study was to adopt electrospinning as a drying method for nanoemulsions and thus to formulate a new solid ocular drug delivery system based on nanoemulsions.

Materials and methods

Nanoemulsions were prepared using microfluidizer. The oil phase was mixture of castor oil (Fagron), Capryol TM 90 (Gattefossé), and Kolliphor® EL (BASF) and the water phase was solution of Soluplus (BASF) in double-distilled water (DDW) (Table 1). The oil phase was added to the aqueous phase at room temperature under magnetic stirring and the obtained dispersion was further pre-homogenized with Ultra-Turrax® (IKA-Werke GmbH & Company). The coarse emulsion was further homogenized using microfluidizer LM20 equipped with a Y-type interaction chamber (Microfluidics) to obtain nanoemulsion.

Table 1. Composition of investigated nanoemulsions (castor oil (CO), Capryol™ 90 (C90), Kolliphor® EL (KOL), Soluplus (SP), double distilled water (DDW))

	CO (%)	**C90 (%)**	**KOL (%)**	**SP (%)**	**DDW (%)**
NE 1	20	1	1	0.5	77.5
NE 2	20	5	5	1	69
NE 3	10	1	5	1	83
NE 4	15	5	5	1	74

To prepare prior-drying samples the polymer solutions (Table 2) were firstly prepared by dissolving polyethylene oxide (PEO, Mw, 400,000 g/mol, Sigma-Aldrich), poloxamer 188 (P188, BASF) and Soluplus (BASF) in DDW at 80 °C. Next, the polymer solutions were cooled to room temperature and thoroughly mixed with nanoemulsions in a weight ratio of 1:1 just before the electrospinning.

The electrospinning was performed using Spinbox Systems electrospinning device (Bioinicia) at 25°C, relative humidity ≤ 45%, electrical voltage 15 kV, flow rate 1.77 mL/h, and needle to collector distance 15 cm. The obtained electrospun products were stored in a desiccator until further use.

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Table 2. Composition of polymer solutions for the preparation of prior-drying mixtures (polyethylene oxide (PEO), poloxamer 188 (P188), Soluplus (SP)).

Polymer solution	PEO (mg/mL)	P188 (mg/mL)	SP (mg/mL)
A	64	64	0
B	64	32	32
C	64	16	16

The reconstitution of nanoemulsions from the electrospun products was performed in DDW by vortex mixing (1-3 min). The droplet size in the prior-drying dispersions and in the reconstituted nanoemulsions was determined by dynamic light scattering using a Zetasizer Ultra (Malvern Panalytical). The morphology of the electrospun products was evaluated by scanning electron microscopy (Supra35 VP, Carl Zeiss).

Results and discussion

The electrospinning enabled transformation of investigated nanoemulsions in dry products with different morphologies (Fig. 1).

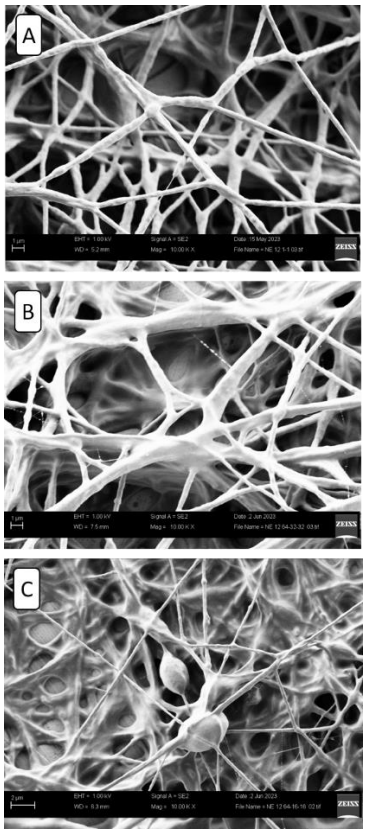

Figure 1. Representative SEM images of electrospun products of nanoemulsion 3: formulations A, B and C.

Their reconstitution in DDW resulted in nanoemulsions with increased droplet size compared to the initial nanoemulsion formulations. The higher amount of oil phase in the initial nanoemulsion resulted in the more pronounced increase in droplet size after reconstitution of the electrospun product (Fig. 2). NE 3 was revealed to have the most optimal composition, since the droplet size after drying and reconstitution has changed the least among investigated formulations. Moreover, it was shown that NE 3 can be reconstituted from the electrospun product in < 90 s, while the reconstitution for other nanoemulsions was longer.

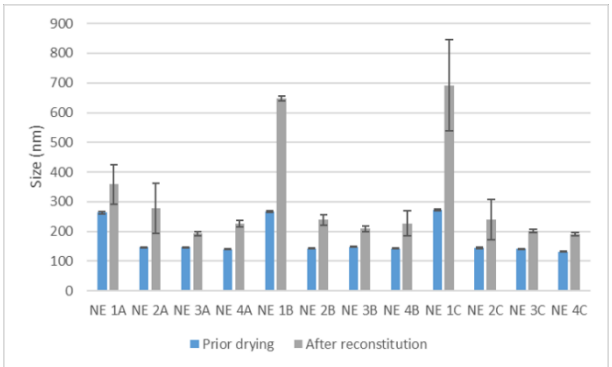

Figure 2. Average hydrodynamic size of droplets in dispersions prior drying and in dispersions after the reconstitution from the electrospun products (n = 3).

Conclusion

The results show that electrospinning enables transformation of nanoemulsions into dry products, which are easily and quickly transformed back into dispersion of nanodroplets upon contact with an aqueous medium. Thus, electrospun nanoemulsions represent a promising solid formulation for ocular delivery of nanoemulsions.

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