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Effects of preparation methods on the characteristics of niosomes

Li Key Yeo*, Cheng Shu Chaw, Amal Ali Elkordy

School of Pharmacy and Pharmaceutical Sciences, Faculty of Health Sciences and Wellbeing, University of Sunderland, United Kingdom

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*Corresponding author.
Tel.: +44 (0)774 162 3198
E-mail: li-key.yeo@research.sunderland.ac.uk

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SUMMARY

Niosomes are colloidal vesicles capable of encapsulating drugs as a carrier for drug delivery systems. They are formed by self-assembly of a non-ionic surfactant with cholesterol and co-surfactant. In this work, cinnarizine-containing niosomes comprised of sorbitan monostearate (Span® 60), cholesterol and co-surfactants (Cremophor® ELP, Cremophor® RH40 or Solutol® HS15) were prepared using conventional thin film hydration and microfluidic methods. The effects on the characteristics of the niosomes, with the presence of poorly water-soluble drug, cinnarizine in the niosomal formulations prepared using different methods and incorporation of different co-surfactants, were studied and compared for their particle size, polydispersity index (PDI) and encapsulation efficiency. Dynamic light scattering was employed for particle size measurements and drug loading studies were analysed using high performance liquid chromatography (HPLC). The morphology of the niosomes was characterized using optical light microscopy.

INTRODUCTION

Niosomes are non-ionic single-chain surfactant-based bilayer membrane vesicles that are formed by self-assembly upon hydration (Obeid et al., 2017). They are capable of entrapping both hydrophobic and lipophilic drugs such as cinnarizine. Cinnarizine is a class II drug according to the BCS Classification (Brittain, 2015). The poorly water-soluble drug has variable absorption and bioavailability which requires multiple dosing each day. Conventional thin film hydration (bulk) and microfluidic methods were used. The aim of this study was to develop niosomes containing cinnarizine using different preparation methods to assess their characteristics and encapsulation efficiency to enhance the drug characteristics and bioavailability.

MATERIALS AND METHODS

For both thin film hydration (TFH) and microfluidic (MF) methods, Span® 60, cholesterol and co-surfactants (Cremophor® ELP, Cremophor® RH40 and Solutol® HS15) at a molar ratio of 45: 45: 10 and cinnarizine were weighed and dissolved in solvent. Phosphate buffered saline (PBS, pH 7.4) was used as the aqueous phase. TFH was performed using a Buchi rotavapor R-210 (Buchi, Chadderton, UK). For the microfluidic method, a NanoAssemblr™ Benchtop system (Precision NanoSystems Inc., Vancouver, Canada) was employed with a microfluidic cartridge and a heat block controller set at 60 °C. Niosome suspensions prepared were dialysed against 0.1M hydrochloric acid solution for 24 hours to remove free drug. Purified niosomes were disrupted using isopropanol and the drug concentrations were measured using HPLC system (Agilent Technologies, Germany). Zetasizer Nano ZSP (Malvern Instruments, Worcestershire, UK) was used to measure particle size and polydispersity index.

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RESULTS AND DISCUSSION

Formation of distinctive round circular shaped niosomes was observed under optical light microscope (Figures 1 and 2).

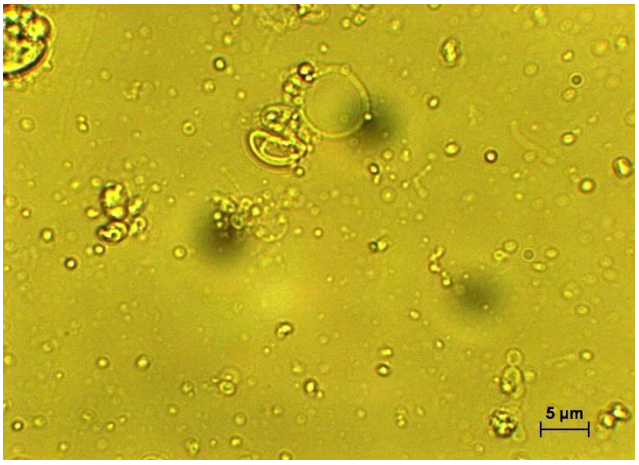

Fig. 1. *Span® 60: cholesterol: Cremophor® ELP niosomes prepared by TFH method (magnification x40).*

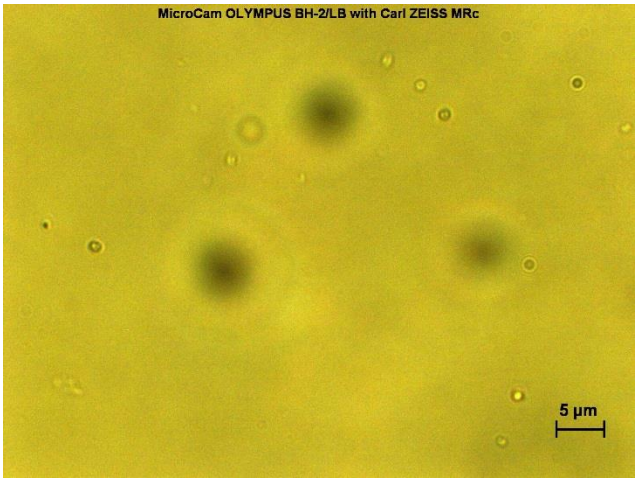

Fig. 2. *Span® 60: cholesterol: Cremophor® ELP niosomes prepared by MF method (magnification x40).*

Particle sizes and polydispersity index were generally small in microfluidic-prepared niosomes as compared to the bulk method (Tables 1 and 2). The microfluidic method produced homogenously uniform niosomes without a further size reduction step required. This is in agreement with Kastner el al., 2015. On the other hand, the encapsulation efficiencies (%EE) of the microfluidic-prepared niosomes were noticeably low compared to the multi-lamellar vesicles formed by the thin film hydration method.

Table 1. *Niosomes prepared by thin film hydration method.*

Formulation	z-average (nm)	PDI	% EE
S60: Cho: ELP*	3701 ± 414	0.52	26.3
S60: Cho: RH40*	1244 ± 314	0.71	10.8
S60: Cho: HS15*	7320 ± 675	0.93	**

*Span® 60 (S60); Cholesterol (Cho); Cremophor® ELP (ELP); Cremophor® RH40 (RH40); Solutol® HS15 (HS15). **undetermined.

Table 2. *Niosomes prepared by microfluidic method.*

Formulation	z-average (nm)	PDI	% EE
S60: Cho: ELP*	355 ± 1.5	0.20	**
S60: Cho: RH40*	172 ± 0.5	0.21	0.37
S60: Cho: HS15*	304 ± 2.0	0.01	0.53

*Span® 60 (S60); Cholesterol (Cho); Cremophor® ELP (ELP); Cremophor® RH40 (RH40); Solutol® HS15 (HS15). **undetermined.

CONCLUSIONS

In this work, different preparation methods (bulk and microfluidic) of niosomes have been shown to have an impact on the characteristics of niosomes containing cinnarizine. A microfluidic method produced small, monodisperse niosomes in a single step, however with very low %EE. (For this reason in the future the drug will be incorporated into microfluidic prepared niosomes by using a different pH buffer to increase %EE by the difference in concentration gradient). In contrast, multi-lamellar vesicles produced by the bulk method enabled higher entrapment of the hydrophobic drug (cinnarizine).

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