A proposal of innovative injectability assessment method for intravenous formulations – case study on PEGylated nanoemulsions

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CONCLUSION

The injectability testing method used in this research proved as a useful tool in screening formulations adequate for prospective intravenous use.

INTRODUCTION

Syringeability (ability of an injectable preparation to transfer from a vial through a hypodermic needle prior an injection) and **injectability** (force, or pressure, required to inject the formulation from a syringe-needle system into the tissue) are recognised as fundamental performance parameters / critical quality attributes of any parenteral dosage form, and should be tested to insure optimal performance upon administration.

AIM

The aim of this research was to develop a method that could be used for injectability assessment of the intravenous formulations and the application of this method on curcumin-loaded PEGylated nanoemulsions (NEs) in order to evaluate the impact of PEGylation on NEs' injectability.

MATERIALS AND METHODS

Nanoemulsion preparation and physicochemical characterization

NEs were prepared using high energy homogenization technique. In total, four formulations were prepared: the non-PEGylated (**CS**), and the PEGylated ones with 0.1% (**S1**), 0.3 % (**S3**) or 0.6 % (**S6**) of the PEGylated phospholipid – PEG2000-DSPE. The NEs were characterized regarding droplet size (Z-Ave) , droplet size distribution (PDI), and viscosity.

Injectability assessment

The injectability of the NEs was expressed as force needed to extrude the NE in the function of the extruded volume (ml). About 10 ml of the NE was loaded into the 10 ml syringe and extruded at 1 mm/s crosshead speed through the 25 G scalp vein infusion set into the blood mimicking solution (36.6 %, v/v, glycerol solution), circulating through pump at 4 ml/min, in order to assess the NEs' performance in the prospective intravenous administration for *in vivo* studies. (**Fig 1.**)

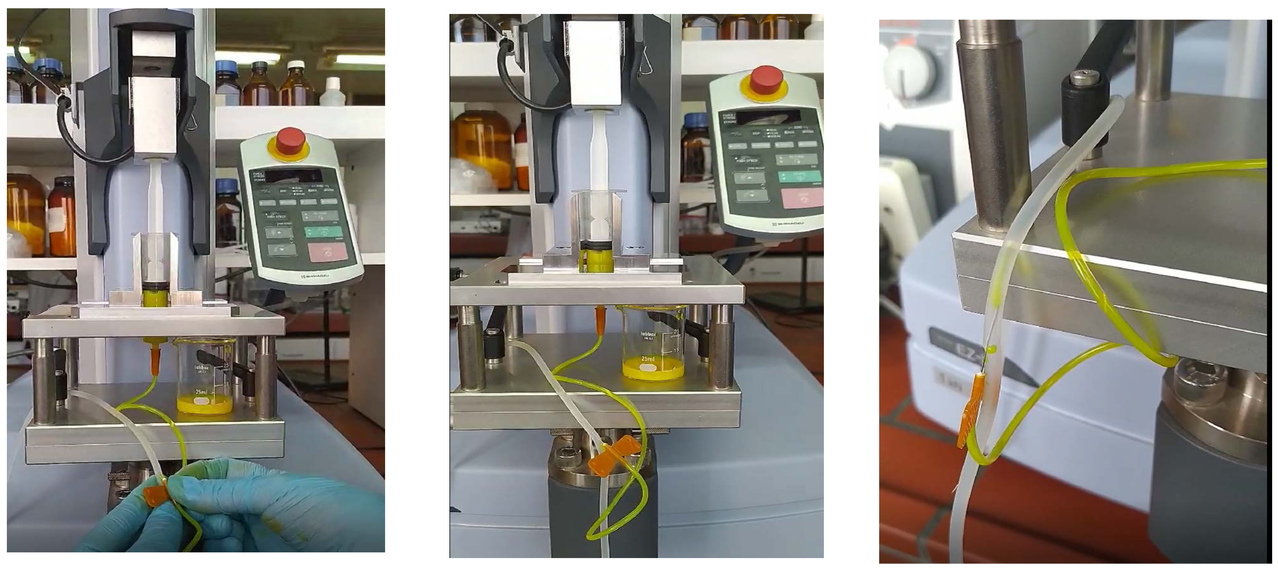

Figure 1. Injectability assessment setup

RESULTS AND DISCUSSION

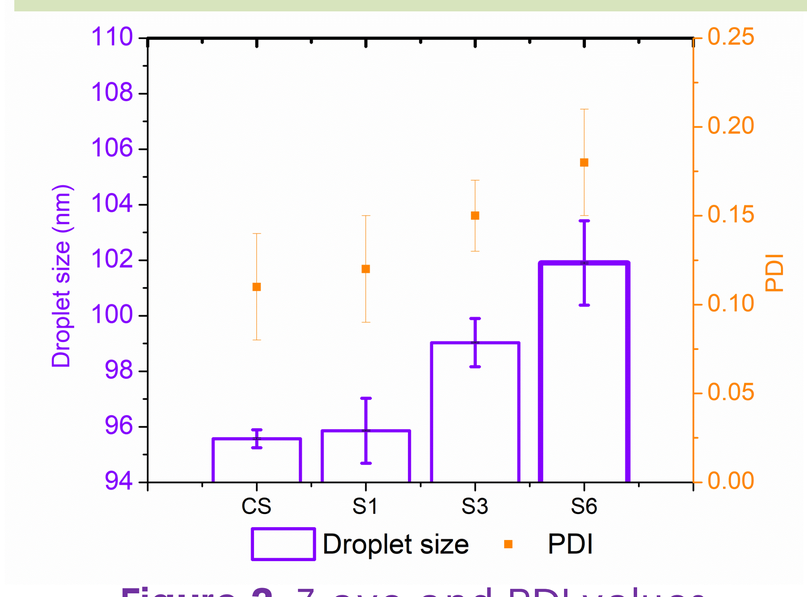

Figure 2. Z-ave and PDI values

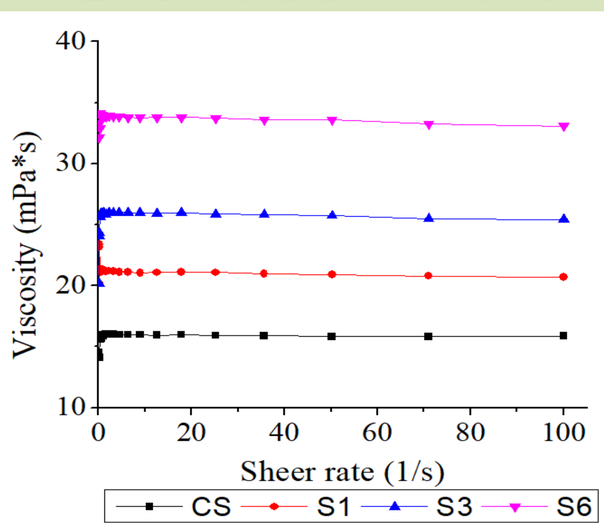

Figure 3. NE viscosity

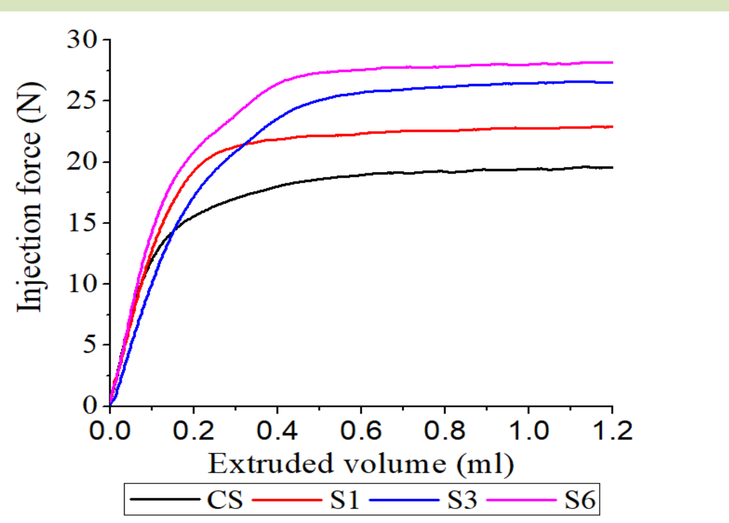

Figure 4. Injectability assessment

The Z-ave (about 100 nm) and the PDI values (below 0.2) suggested suitability for intravenous use (**Fig.2**). It could be observed from **Fig. 3** that the addition of PEGylated phospholipids caused an increase in NE viscosity, as could be expected given that the polyethylene glycols are used in parenteral suspensions as stabilizing / rheology modifying agents. Injectability of NEs depended on their viscosity, with the higher pressure needed to extrude the formulations with the higher PEG2000-DSPE concentration (**Fig. 4**). To the best of our knowledge, there are no studies investigating the injectability of the intravenous preparations, but based on some previous research on subcutaneous model, it is recommended the maximum force used to inject the formulations should be kept upto about 20 N, which would eliminate S3 and S6 from further investigation (**Fig. 4**).

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