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Effects of Cryoprotectants on Freeze-drying of Nanoemulsion

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Freeze-drying has become the method of choice for transformation of instable liquid formulations into stable solid products at sterile conditions. The purpose of this study was to develop dry powder formulation of oil in water nanoemulsion (NE) based on vegetable oil via freeze-drying. However, limitation was noted due to large oil droplets in the formulationthat elegant lyophilized cake of the freeze-dried product could not be achieved. Therefore, 3 different cryoprotectants such as lactose, glycine and mannitol were employed at the concentrations of 3% 5%, 10% and 15% to maintain stability of nanoemulsion from aggregation during freeze-drying [1]. The oil in water nanoemulsion was formulated by using polysorbate 80 and Span 85 as surfactants along with different percentages of cryoprotectants and freeze-dried. To regard their appearance, lyophilized products were investigated by scanning electron microscopy (SEM). Zeta potential and the particle sizes were determined by nanozetasizer before freezing and after reconstitution of freeze-dried samples. In order to achieve good results, minimum concentration of 10% cryoprotectant was required. In this study, the results of three cryprotectants, lactose, glycine and mannitol according to their different percentages were compared. The morphological images of lyophilized cakes by SEM indicated that most mannitol crystals occurred as the nearly rod-shaped structures in the continuous phase (Fig. 1(A)) [2]. Zeta potential of each reconstituted formulation increased after freeze-drying to satisfactory level (-9.87 vs. -23.4 mV; -8.01 vs. -22.7 mV, -8.47 vs. -23.1 mV; -9.04vs.-27.7mV and -13.4 vs. -21.9 mV; -7.01 - 6.68 mV for formulation with 10 and 15% lactose, glycine and mannitol, respectively).

In addition, the mean droplet sizes of the nanoemulsions with these cryoprotectants were also slightly increased after freeze-drying (145 vs. 162 nm; 148 vs. 150 nm, 145 vs. 170 nm; 155 vs 199 nm and 156 vs. 185 nm; 160 vs 192 nm) (Fig. 1(B).The overall results represented that selected cryoprotectants at the concentrations of 10% and 15% could be reliable as good candidates for the protection of the vegetable oil based nanoemulsion during exposure to freezing in the freeze-drying cycle.

Keywords: Lactose; Glycine; Mannitol; Nanoemulsion; Freeze-drying

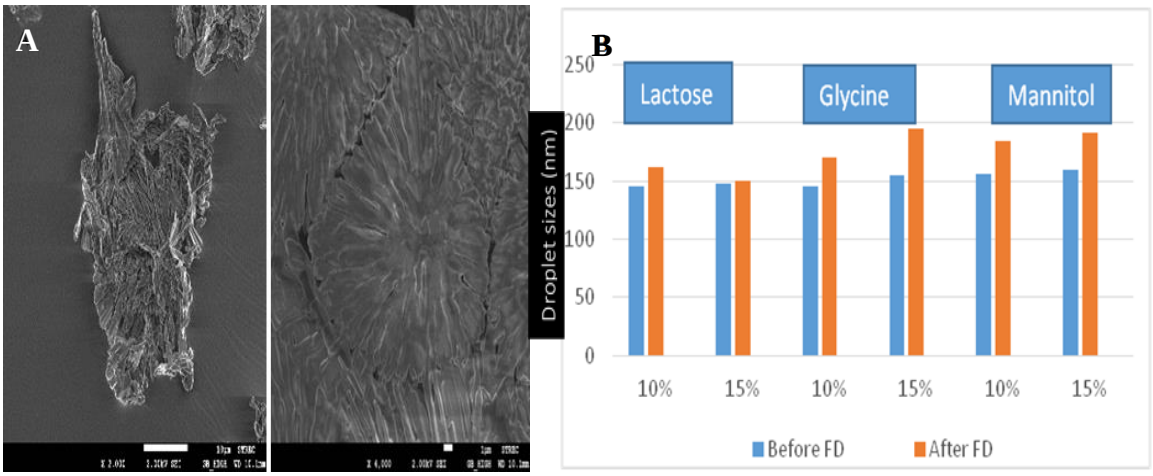

Fig.1 (A); SEM images of lyophilized product containing mannitol as cryoprotectant (B); comparisons of droplet sizes before freezing and after reconstitution of freeze-dried cakes.

References

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