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Effect of sucrose in freeze-dried liposomes encapsulating drugs

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The use of liposomes as drug delivery system is very promising due to their ability to encapsulate hydrophilic and hydrophobic drugs [1]. However, the long-term storage of liposomes reveals physical and chemical instabilities which limits the use in therapeutic applications [2]. The development of a dry powder formulation can be a solution to improve these problems. The production of a freeze-dried liposomes encapsulating drugs is considered a key challenge, since the drugs can leak out from the liposomes during the freeze-drying process, occurring drug leakage [3]. The stress caused by the main steps of the process may affect the structure of liposomes. Therefore, cryoprotectants can be used to prevent damage in the integrity of the liposome bilayer [2].

The aim of this study was to optimize a liposomal formulation that after freeze-drying continues to be stable and able to maintain drugs with few leakages. The protective effect of five sugars at different concentration was tested in terms of size distribution, morphology and concentration.

Results showed that sucrose, in a concentration dependent manner, effectively prevents liposomal fusion or aggregation and protects the integrity of freeze-dried liposomes (Figure 1). This liposomal formulation encapsulating a hydrophobic drug Tamoxifen can be freeze-dried and stored without significant drug leakage. The biological activity of drug after freeze-drying was also evaluated. In sum, the results indicated that this optimized liposomal formulation can be a good approach to long-term storage.

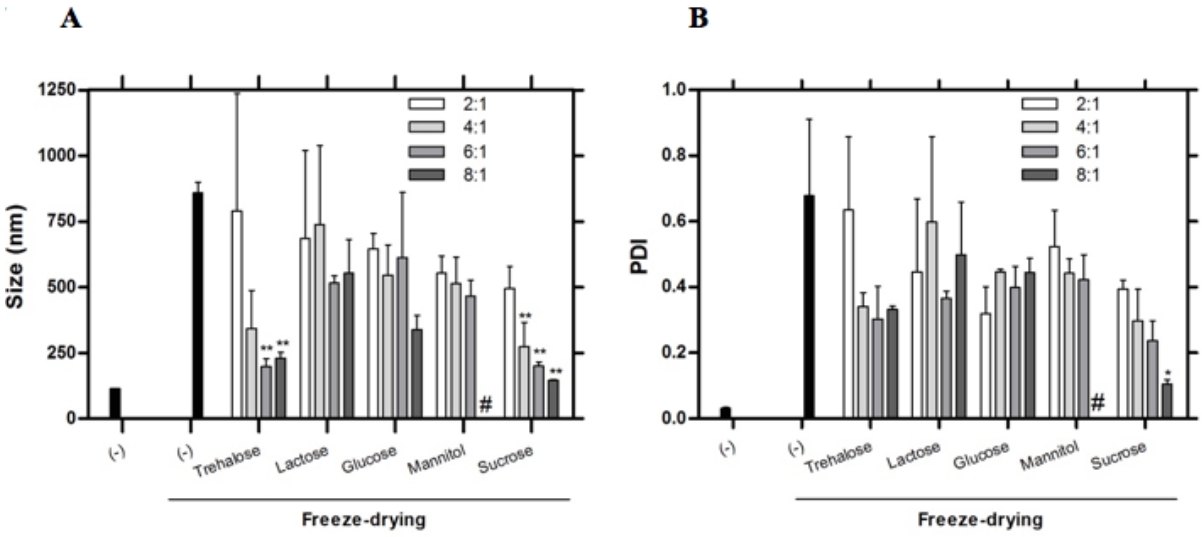

Figure 1. Influence of several sugars in size distribution after freeze-drying of liposomes. Determination of (A) size and (B) PdI of liposomes with and without (-) cryoprotectants, before and after freeze-drying, by DLS. # Values not determined due to non-homogenous dispersion obtained. Values represent the mean +SD of 2 independent experiments. Significant differences were detected as shown by an * ($P<0.05$) and ** ($P<0.005$).

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