Curcumin-in-epiβcyclodextrin double-loaded liposomes: selection of size reduction methodology

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Curcumin (cur) is a natural antioxidant, anti-inflammatory and anti-tumoral compound with extremely low solubility in water and bioavailability [1]. Two simple ways of improving these properties are liposomes and cyclodextrins, such as epichlorhydrin-β-cyclodextrin. In previous works, we have demonstrated that the optimal composition for double-cur-loaded liposomes is the combination of 1 mg of curcumin and 4 mg of estearylamine in the bilayer, and cur-epi-β-cyclodextrin in the aqueous compartment. However, the size reduction method was not clearly elucidated. Based on these premises, double-cur-loaded liposomes have been extruded or sonicated at three different levels. Firstly, multilamellar vesicles were prepared by thin-layer evaporation method described by López-Pinto et al. [2]. Extrusion was performed at 58ºC using polycarbonate filters with three different pore sizes (800, 400 and 200 nm). Samples were extruded 5, 9 or 13 times from each filter. Sonication was performed at 58ºC for 10, 20 and 30 minutes with an in-between pause of 1 min at room temperature every 10 min. A sample without size reduction treatment was made as control formulation. Techniques of photon correlation spectroscopy and DLS were applied for size and z-potential. Encapsulation efficiency (EE) and recovered PC were calculated, as previously reported González-Rodríguez et al. [3]. Results showed that liposomes sonicated more than 10 min (runs 2 and 3) have a tendency to leakage over time, while in those extruded (Run 4-11) EE decreases by 30% or more in all cases, except for those extruded 5 times using an 800 nm pore-sized filter (Run 4), which obtained similar EE than liposomes sonicated for 10 minutes (Fig 1.). Although the mechanical procedure of both techniques affect the integrity of the bilayer, also the thinning and loss of elasticity that curcumin provokes when it is imbibed in bilayers [4-6], could trigger this leakage. Thus, liposomes extruded 5 times using an 800 nm pore-sized filter was selected as optimal formulation for further studies.

References

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Figures

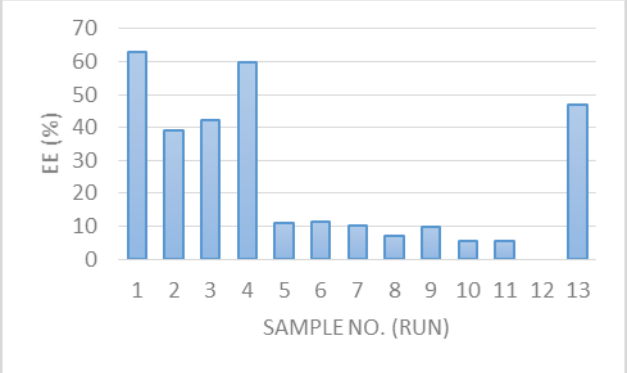

Figure 1: Encapsulation efficiency of each sample. Run 1 to 3 where sonicated. Run 4 to 11 where extruded. Run 13 is the control sample. Run 12 cannot be performed.