Stability of liposomal particles with encapsulated coumarin derivate

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INTRODUCTION: Coumarin derivates possess several biological effects, including anti-inflammatory, antioxidant, anticoagulant, antitumor, insecticidal, anthelminthic, hypnotic, antifungal, and HIV protease inhibition properties [1,2]. Due to their solubility in organic solvents and insolubility in water and body fluids, their bioavailability is significantly low. Thus, they can be encapsulated into liposomal particles with the aim of overcoming the mentioned disadvantage [3]. Hence, in the present study, coumarin derivate was encapsulated in phospholipid liposomes and their stability was monitored for 60 days in terms of vesicle size, polydispersity index (PDI), zeta potential, and mobility.

EXPERIMENTAL: Coumarin derivate-loaded liposomes were prepared by mixing 0.1 g of coumarin derivate, 1 mL of dimethyl sulfoxide, 2 mL ethanol, 1 g of phospholipids, and 7.5 mL of water in the proliposome technique [4]. Vesicle size, PDI, zeta potential, and mobility were determined during 60 days of storage at 4°C using the photon correlation spectroscopy and Zetasizer Nano Series, Nano ZS (Malvern Instruments, United Kingdom). Every measurement was performed in triplicates at room temperature. The statistical analysis was performed by using the analysis of variance and Duncan's *post hoc* test (STATISTICA 7.0). The differences were considered statistically significant at $p<0.05$, $n=3$.

RESULTS AND DISCUSSION: The vesicle size varied from 1669.0±55.1 (1st day) to 1583.5±78.8 nm (60th day). Due to a relatively high absolute value of zeta potential at the beginning, the absence of a significant change in the size was expected. PDI value, as a measure of the particle size distribution, significantly increased during the 60-day study, from 0.231±0.043 to 0.497±0.079 indicating the existence of a non-uniform system [5]. A single phospholipid provides the liposomal population with significantly lower PDI (better uniformity) in comparison to the commercial phospholipid mixture employed in the present study [3]. The zeta potential and mobility significantly decreased (absolute value), from -29.43±0.55 to -14.43±1.00 mV, and from -2.307±0.043 to -1.127±0.086 μmcm/Vs, respectively. After 60 days of storage, the liposomes had significantly higher PDI, but lower zeta potential and mobility, indicating their instability. However, even though the zeta potential value was low on the 60th day, there was no occurrence of fusion and fission confirmed by the absence of statistically significant changes in the diameter of liposomes.

CONCLUSIONS: Coumarin derivate-loaded liposomes were unstable during 60-day storage at 4°C, resulting in changes in PDI value, zeta potential, and mobility, therefore additional experiments for improving their stability should be performed.

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