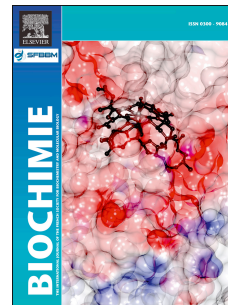


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Corticoids modulate liposome membrane fluidity and permeability depending on membrane composition and experimental protocol design

Samar Kaddah, Nathalie Khreich, Fouad Kaddah, Lhoussain Khrouz, Catherine Charcosset, H el ene Greige-Gerges



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ABSTRACT

Given that literature data may give inconsistent results on the effect of a drug on lipid membrane properties, this work aims to investigate the impact of the liposome composition and experimental protocol design on glucocorticoids (GRs: cortisol, cortisone, fludrocortisone acetate, methylprednisolone, prednisolone and prednisone)-modulating membrane fluidity and permeability. GRs-loaded liposomes consisting of dipalmitoylphosphatidylcholine (DPPC) and cholesterol (CHOL) were prepared by reverse phase evaporation technique (REV) at DPPC:CHOL:GR molar ratios of 100:100:2.5, and 100:100:10. The formulations were characterized for their size and homogeneity, encapsulation efficiency and loading rates of GRs, incorporation rates and loading rates of DPPC and CHOL. Changes in DPPC membrane fluidity (CHOL% 0, 10, 20, 30 and 100) after exposure to methylprednisolone were monitored by using 5- and 16-doxyl stearic acids (DSA) as spin probes. For permeability studies, the above-mentioned GRs-loaded liposomes and the preformed liposomes exposed to GRs (2.5 mol%) were compared for the leakage of an encapsulated fluorescent dye, sulforhodamine B (SRB), at 37°C in buffer (pH 7.5) containing NaCl. The SRB release kinetics were analyzed by the Higuchi model for two release phases (from 0 to 10h, and from 10 to 48 h). All formulations exhibited a monodispersed size distribution of liposomes with a mean particle value close to 0.4 μm , also the DPPC and CHOL were highly incorporated (> 95%). High loading rate values of DPPC (> 78%) and CHOL (> 95%) were also obtained. Except for fludrocortisone acetate (51%) and prednisolone (77%), high loading rate values of GRs were obtained (> 81%). Fluidity and permeability studies showed that the GR concentration, CHOL content, experimental protocol design including the period of incubation represent critical parameters to be considered in analyzing the effect of drugs on the membrane properties.

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