Surfactant-inspired photopolymerized liposomes reduce corticosteroid dose requirements in preclinical asthma models

Morales, Estefania[1]; Guerrieri, Constanza[1]; Arregui , Gonzalo[2]; Maruri, Alejandro[1]; Sánchez, Vanesa[1]; Goldman, Alejandra[1]; Chiaramoni, Nadia[2]; Fenoy, Ignacio[1]

[1] Instituto de Tecnologías Emergentes y Ciencias Aplicadas, ECyT-UNSAM, CONICET, Gral. San Martín, Buenos Aires, Argentina
[2] Grupo de Biología Estructural y Biotecnología GBEyB IMBICE-CONICET-CIC PBA. Buenos Aires, Argentina.

emorales@unsam.edu.ar

Área temática: F. Nanotecnología y salud

Asthma is a chronic inflammatory disease affecting over 300 million people worldwide. Current treatments rely on long-term corticosteroid use, often associated with significant adverse effects. Here, we developed photopolymerized liposomes based on pulmonary surfactant phospholipids as a delivery system for dexamethasone (DEX) to the lung. Multilamellar vesicles were prepared by dehydration–rehydration using a lipid mixture of DC8,9PC (50%), DMPC (25%), DPPC (20%), and PMPC (5%). Small unilamellar vesicles (~100 nm) were obtained by extrusion and subsequently photopolymerized by UV irradiation (254 nm) through repeated cycles under controlled low-temperature conditions, inducing covalent crosslinking of diacetylenic chains. Formulations were lyophilized in sucrose/PBS for storage. Structural characterization by SAXS and SEM confirmed spherical morphology, with mean diameters of 94±2 nm for empty liposomes and 85±2 nm for DEX-loaded formulations. No cytotoxicity was observed in A549 cells treated with the liposomal formulations, as determined by an MTT cell viability assay. Anti-inflammatory activity was evaluated in vitro using A549 cells, which naturally secrete high levels of the inflammatory chemokine CXCL-8. Its secretion was significantly reduced by both free dexamethasone (DEX) and DEX-loaded liposomes ($p<0.05$), whereas empty liposomes showed no effect. In vivo efficacy was assessed in a papain-induced BALB/c asthma model. Treatment with a suboptimal dose of DEX-loaded liposomes significantly reduced lung inflammation. Histological analysis revealed decreased peribronchial inflammatory infiltrate, mucus-producing goblet cells, and mast cell infiltration in lung tissue ($p<0.05$). Moreover, DEX-loaded liposomes reduced serum IgE levels and decreased IL-5 production in ex vivo splenocyte cultures. These results suggest that photopolymerized, surfactant-inspired liposomes effectively modulate airway inflammation both in vitro and in vivo, enabling significant therapeutic effects at reduced corticosteroid doses. This platform represents a promising strategy to improve the efficacy and safety of asthma treatments through targeted pulmonary drug delivery.