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Sporopollenin microcapsules as ocular drug delivery platforms

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1. Introduction

In the present work we developed an ocular drug delivery platform based on natural pollen grains. The hollow microcapsules obtained upon the treatment of pollen present a highly porous structure with a 3D microneedle-like surface and are expected to enhance mucoadhesion and residence time of drugs administered to the ocular surface.

2. Methods

Purification of natural pollen grains from Helianthus and Matricaria sp. was performed by sequential washing steps to remove the external pollenkitt and the intracellular components. [1] Morphology and chemical composition were analyzed by FT-IR, elemental analysis, thermogravimetry and SEM.

Evaluation of the immune response to potential allergens was performed in vitro, using human monocyte-derived dendritic cells. Biocompatibility and physical irritation were evaluated upon ocular administration to rat eye in vivo.

Immunostaining of the different sections of the rat eye was accomplished with ocular lymphocyte and dendritic cells markers to evaluate activation after pollen exposition. Additional analysis of epithelial damage was carried out in vitro by means of measuring the transepithelial resistance (TEER) on an artificial 3D cornea model of human sclerocorneal limbus epithelium (HCLEC).

3. Results and discussion

Purified pollen microcapsules preserved the characteristic external 3D structure of intact, natural pollen grains but were free of external contaminants and intracellular compounds.

The immune cell recognition assay showed that the instillation of different pollen grains did not cause higher cell activation than that observed in non-treated eyes, which is an indicator of an optimal purification procedure able to avoid allergenicity when used via ocular route.

Moreover, regarding ocular biocompatibility and tolerability, no signs of hyperemia, anormal mucus/tear secretion or animal discomfort were detected in vivo by in-situ macroscopic observation even 6 hours after pollen administration. Finally, the 3D corneal HCLEC tissue model showed that no epithelial rupture took place, showing preserved integrity over 3 h of exposure.

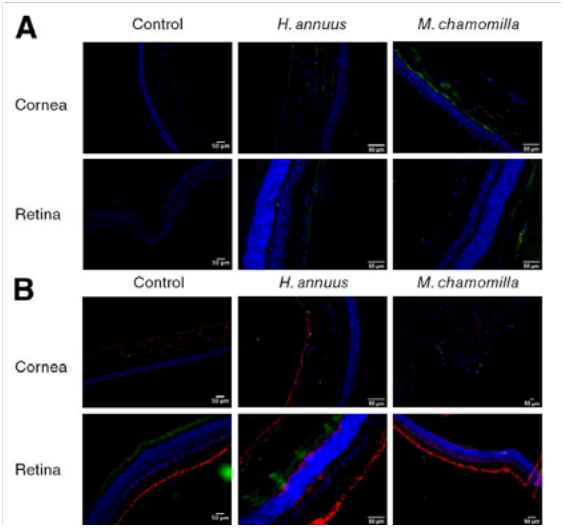

Fig 1. - Fluorescence images of rat cornea and retina upon the administration of different pollen grains. A. Immunostaining with TNF α (green) y CamKII (red). B. Immunostaining of CD4 lymphocytes and the S100 protein (red). Cell nuclei were stained with DAPI (blue)

4. Conclusions

The biocompatibility of the developed 3D mironeedle-like platforms, as well as their mucoadhesion properties make them a promising strategy to overcome the biological and mechanical barriers of ocular drug delivery.

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