Invest Ophthalmol Vis Sci. 2012 Apr 30;53(4):2292-9. doi: 10.1167/iovs.11-8829.

A novel cyclosporin a aqueous formulation for dry eye treatment: in vitro and in vivo evaluation.

Di Tommaso C[1], Valamanesh F, Miller F, Furrer P, Rodriguez-Aller M, Behar-Cohen F, Gurny R, Möller M.

Abstract

PURPOSE:

The aim of the present study was the in vitro and in vivo evaluation of a novel aqueous formulation based on polymeric micelles for the topical delivery of cyclosporine A for dry eye treatment.

METHODS:

In vitro experiments were carried out on primary rabbit corneal cells, which were characterized by immunocytochemistry using fluorescein-labeled lectin I/isolectin B4 for the endothelial cells and mouse monoclonal antibody to cytokeratin 3+12 for the epithelial ones. Living cells were incubated for 1 hour or 24 hours with a fluorescently labeled micelle formulation and analyzed by fluorescence microscopy. In vivo evaluations were done by Schirmer test, osmolarity measurement, CyA kinetics in tears, and CyA ocular distribution after topical instillation. A 0.05% CyA micelle formulation was compared to a marketed emulsion (Restasis).

RESULTS:

The in vitro experiments showed the internalization of micelles in the living cells. The Schirmer test and osmolarity measurements demonstrated that micelles did not alter the ocular surface properties. The evaluation of the tear fluid gave similar CyA kinetics values: AUC = 2339 ± 1032 min*μg/mL and 2321 ± 881.63; Cmax = 478 ± 111 μg/mL and 451 ± 74; half-life = 36 ± 9 min and 28 ± 9 for the micelle formulation and Restasis, respectively. The ocular distribution investigation revealed that the novel formulation delivered 1540 ± 400 ng CyA/g tissue to the cornea.

CONCLUSIONS:

The micelle formulation delivered active CyA into the cornea without evident negative influence on the ocular surface properties. This formulation could be applied for immune-related ocular surface diseases.