Formulation and Evaluation of HPMC and Xanthan Gum Ophthalmic Inserts for Delivery of Cyclosporine A
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Purpose
The aim of this study was to develop and characterize a novel sustained-release drug delivery system of cyclosporine A (CsA) using hydroxypropyl methylcellulose (HPMC) and xanthan gum (XG) for treating dry eye syndrome. Both HPMC and CsA are widely used in treating dry eye disease. CsA acts as an immunosuppressant, while HPMC provides lubrication. We hypothesized that combination treatment with HPMC and CsA would be beneficial in treating dry eye. XG was added as a release retarding agent.

Methods
Polymeric inserts of CsA were prepared using the solvent casting technique with a 2x3 full factorial design to evaluate the effect of HPMC and XG ratios on drug content, uniformity of weight, thickness, surface pH, moisture absorption and loss, folding endurance, morphology, thermal analysis, wettability and in vitro drug release. Inserts with an optimized ratio of HPMC and XG were sterilized with UV light and evaluated for stability at 40°C, 25°C, and 4°C, and cytotoxicity in cultured bovine corneal endothelial cells.

Results
The addition of XG increased the release time of CsA and enhanced the folding endurance of films. All the films showed uniformity in drug content, weight, and thickness. Formulation F2 composed of 1% HPMC and 0.25% XG exhibited good folding endurance and sustained the release of CsA for up to 24h. F2 was further sterilized with UV light and tested for sterility, stability and cytotoxicity. Sterility testing of F2 using plate and direct inoculation confirmed the formulation sterility and validated the sterilization method. The formulation was stable for at least 6 months. No cytotoxicity was observed in cultured bovine corneal endothelial cells for up to 24 h.

Conclusion
In conclusion, combination therapy with HPMC and CsA can be a potential once-a-day formulation for treating dry eye disease.

![Sterility validation test](image)

**Figure 1:** Stereo-microscopy images of films after 24h storage, showing absence of microbial growth in formulation F2.

**Figure 2:** Scanning electron microscopy images of cyclosporine A, blank insert, and drug-loaded insert.

**Figure 3:** Cell viability of the optimized formulation after incubation with bovine corneal endothelial cells for 24 h (n=3). No significant difference was observed between the insert and the control.