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## Cysteamine polysaccharide hydrogels: Study of extended ocular delivery and biopermanence time by PET imaging.

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### Abstract

Cystinosis is a rare autosomal recessive disorder in which cystine crystals accumulate within the lysosomes of various organs, including the cornea. Ocular treatment is based on the administration of cysteamine eye drops, requiring its instillation several times per day. We have introduced the cysteamine in two types of previously developed ocular hydrogels (ion sensitive hydrogel with the polymers gellan gum and kappa-carrageenan and another one composed of hyaluronic acid), aiming at increasing the ocular retention in order to extend the dosing interval. The biopermanence studies (direct measurements and PET/CT) show that these formulations present a high retention time on the ocular surface of rats. From the in vitro release study we determined that both hydrogels can control the release of cysteamine over time, showing a zero order kinetics during four hours. At the same time, these hydrogels could act as corneal absorption promoters, as they allow a higher permeation of cysteamine through bovine cornea compared to a solution. HET-CAM test and cytotoxicity assays show no irritation on the ocular surface. These results demonstrate that the developed formulations present a high potential as vehicles for the topical ocular administration of cysteamine.

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**KEYWORDS:** Corneal permeation; Cysteamine; Cysteamine (CID: 9082); Dithionitrobenzoic acid (CID: 6254); Drug delivery; Gellan gum (CAS Number 71010-52-1); Hyaluronic acid (CID: 3084050); Hydrogel; Kappa carrageenan (CID: 11966249); Ocular retention time; Safety; Small-animal PET/CT

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