Poly(Ethylene Glycol)-Hyaluronic Acid Antioxidant Hydrogels for Prevention of Iatrogenic Cataracts

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Statement of Purpose: Cataract formation is characterized by a cloudiness of the lens that typically progresses slowly with age or pathological conditions (e.g. diabetes). Although there are various types of cataracts, nearly all are associated with oxidative stress within the eye and subsequent damage to the lens. Certain procedures, e.g. vitrectomy (removal of the vitreous humor behind the lens) result in an efflux of oxygen inside the eye through diffusion from the retina-choroid complex and/or ion-assisted transport of oxygen through the vitreous humor. Vitrectomy, an essential step of many vitreoretinal surgical procedures, is performed on 500,000 patients per year. Nearly half of these patients develop secondary cataracts due to iatrogenic or natural elevation of intraocular oxygen levels during the procedure. There is currently no medicinal or surgical method that has been shown through clinical trials to effectively prevent the onset of vitrectomy related cataracts. The goal of this work is to develop an injectable oxygen barrier that can be molded to the lens and photo-polymerized *in situ* prior to vitrectomy procedures to seal and protect the lens from formation of vitrectomy-related cataracts while allowing the patient to maintain normal eye function.

Methods: Hydrogel solutions were formed by mixing 100 mg/mL poly(ethylene glycol) diacrylate (PEG-DA) with 10 mg/mL hyaluronic acid (HA, viscosity 5200 mP·sec), and trehalose (various amounts in powder or particulate form) in HEPES buffer solution followed by either acetophenone, Irgacure 2959, or Eosin Y/triethanolamine/N-vinylpyrrolidone as photoinitiator. Trehalose particles were prepared via spray-drying. The refractive index of the unpolymerized solutions was measured from 25-37 °C using an Abbe refractometer. Polymerizability was determined by radiating the solutions with ultraviolet (for Acetophenone and Irgacure 2969) or green (for Eosin Y) light and recording polymerization time. Gels produced with the Eosin Y photoinitiator system were polymerized using a custom built LED light source. Refractive indices of the polymerized gels were measured using a prism coupler. Optical transparency was assessed through UV-visible transmittance measurements. Suitability for surgical application was assessed through a qualitative rating of injectability, spreadability, cohesiveness, leveling, and coverage when applied to the bottom of a suspended culture dish using a 26 gauge syringe needle. Elasticity was determined using an extensional rheometer. The oxygen permeability of the gels was determined by coating the probe of a dissolved oxygen meter with the gel and measuring the time required for oxygen to migrate through the gel to the sensor.

Results: Gelation using acetophenone as photoinitiator resulted in cloudy gels, whereas gels made with Irgacure 2959 or Eosin Y/triethanolamine/N-vinylpyrrolidone produced clear gels. The custom LED light source for gelation using the Eosin Y photoinitiator system was fabricated and characterized. The gelation parameters were optimized to minimize heat- and photo-induced damage of the gel material while also minimizing gelation time. The refractive indices of the PEG-DA/HA mixtures both pre- and post-gelation measured between 1.33-1.34 in the range of 22-37°C. The gels were found to be optically transparent over the range of 265-800 nm. Elasticity measurements of the gel gave a value of 41.5 Pa. The gel was adhesive enough to apply to inverted surfaces while retaining the ability to be molded in place, Figure 1. The gel provided a 34-fold decrease in oxygen permeability, which was further increased upon addition of antioxidant trehalose particles to the gel.

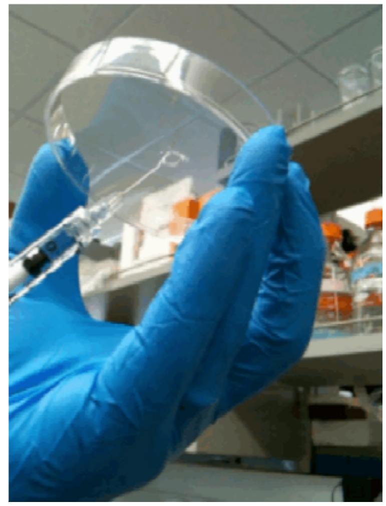

Figure 1. Application of the PEG-DA/HA gel to an inverted surface.

Conclusions: Antioxidant-loaded PEG-DA/HA hydrogels were formulated as oxygen barriers to protect the lens from oxygen-exposure during vitrectomy procedures. The material proved to meet the major design requirements for the project including: optical transparency, high elasticity, a refractive index similar to that of the lens, is polymerizable *in situ*, is injectable and moldable, and has low permeability to oxygen. Studies in animal models for cataract formation are currently ongoing.