An antioxidant-releasing hydrogel vitreous substitute

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Statement of Propose

The vitreous humor is a fragile, transparent tissue between the lens and the retina, occupying 80% of the eye's volume. The vitreous serves as a mechanical cushion for the eye, absorbing impacts and protecting the lens and retina.[1] However, the vitreous degrades with age, which compromises its function as a shock absorber and causes complications such as retinal tear or detachment.[2] Aside from its mechanical function, the natural vitreous also has other chemical functionalities, notably its role in oxygen homeostasis. The vitrectomy operation and replacement with silicone oil disrupts this oxygen homeostasis, causing oxidative damage to the lens that results in cataract formation - up to 95% of patients require cataract extraction within 24 months after vitrectomy.[3] Neither the current gold standard, silicone oil, nor other experimental vitreous substitutes address this problem. The objective of this research is to create a novel hydrogel vitreous substitute that can replace not only the physical roles but also the chemical functions of the natural human vitreous.

Methods:

Hydrogels were prepared by free radical polymerization of 2-hydroxyethyl methacrylate (HEMA), poly(ethylene glycol) methacrylate (PEGMA), and poly(ethylene glycol) diacrylate (PEGDA) based on modifications of published protocols.[4] Briefly, HEMA:PEGMA:PEGDA copolymer hydrogels were polymerized in water. Ammonium persulfate and N,N,N',N'-Tetramethylethylenediamine were used to initiate and catalyze the reaction. Ascorbic acid, an antioxidant with concentration 50 times higher in the eye than in blood[5], was encapsulated in gelatin-alginate particles as previously described.[6] Briefly, Span 80 was added to an ascorbic acid solution to create an emulsion with corn oil. Gelatin and alginate were dissolved in water and slowly added to the water:oil emulsion with stirring for 30 min. The mixture was adjusted to pH 4.4 and stored at 4 ºC for 12 h. The viscosity of the hydrogel was measured at different shear rates to determine its shear thinning capability using a Kinexus ultra+ rheometer (Malvern Instruments Ltd, Worcestershire, UK). Ascorbic acid released from the encapsulating particles was determined using a Synergy HT multi-mode microplate reader (BioTek, Winooski, VT) at wavelength 265 nm.

Results:

Preliminary formulations of HEMA:PEGMA:PEGDA were synthesized and produced clear, soft gels that shear thin and were easily injectable through a small gauge needle without compromising viscoelasticity, as evidenced by the storage (G') and loss moduli (G") before and after injection (Figure 1, A, B). The hydrogel had >90% transparency in visible light spectrum and UV blocking ability. The encapsulation of ascorbic acid successfully prolonged its stability and release profile. The particles released ascorbic acid at 2 mM (normal concentration in the eye[5]) for more than 30 days (Figure 1, C) and could be incorporated with the hydrogel during injection.

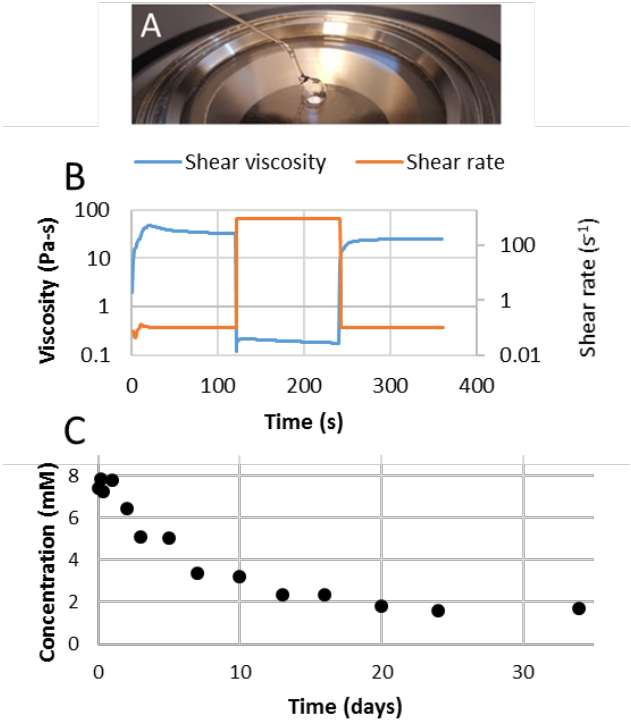

Figure 1. (A) Injection of shear thinning gel through needle and instant gel reformation. (B) Rheology demonstrating retained viscoelasticity. (C) Ascorbic acid release from gelatin-alginate particles demonstrating sustained release with concentration maintained around 2 mM for >30 days.

Conclusion:

A shear-thinning hydrogel embedded with antioxidant releasing particles was created as a novel vitreous substitute that can replace both the physical and chemical functions of the natural vitreous humor. The maintenance of the natural oxygen gradient by this vitreous substitute has the potential to prevent post-vitrectomy cataract formation, significantly reducing the cost of additional treatments for patients and health care providers.

References:

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