Characterization of Poly(2-Hydroxyethyl Methacrylate) Hydrogels for Corneal Grafts

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Statement of Purpose: It is estimated that nearly 10 million people in the world suffer blindness or reduced vision due to damage of the cornea[1]. Current treatment for corneal damage involves a full or partial-thickness corneal transplant (keratoplasty) from a cadaver donor. Drawbacks of this technique include rejection of the donor tissue (22% after 10 years) and development of glaucoma.[2] Biomaterials currently under investigation for use as implants in place of corneal grafts have been constructed from polymers, hydrogels, and collagen sponges. These implants are not yet ideal due to problems with mechanical integrity and optical clarity.

The challenge for creation of a successful corneal implant is to match the mechanical and optical properties of the natural cornea. We are investigating poly(2-hydroxyethyl methacrylate) (pHEMA) hydrogels as an implant material. PHEMA hydrogels are widely used for ophthalmic applications such as contact lenses because of their transparency and high refractive index. The pHEMA hydrogel formulation can also be tuned in order to match the mechanical properties of the native cornea.

Methods: All materials used in the synthesis of pHEMA hydrogels were purchased from Sigma Aldrich and used as received, except where otherwise noted.

PHEMA hydrogels were produced based on a formulation described previously.[3] Briefly, inhibitors in (2-hydroxyethyl) methacrylate (HEMA) monomer and ethyleneglycol dimethacrylate (EGDMA) crosslinker were removed by adding molecular sieves (4 Å pore size) and incubating for 24 hours at 4 °C. Hydrogels of various weight percent (wt%) of monomer were produced by mixing the desired amount of HEMA with 0.5 wt% ammonium persulfate (APS), 0.4 wt% tetraethylene diamine (TEMED), and 0.1 wt% EGDMA. The remaining hydrogel solution was made up of 90 wt% phosphate-buffered saline (PBS, 100 mM, pH 7.4) and 10 wt% ethylene glycol. The hydrogels were stored at room temperature for 24 hours to allow for equilibration, and then swelled in PBS for 48 hours with frequent buffer changes to remove unreacted monomer.

The refractive index and percent transmission of pHEMA hydrogels were measured with a refractometer (Rudolph J257) and UV-vis spectrophotometer (HP 8453), respectively. Mechanical testing was conducted on swelled hydrogels with a TA Instruments rheometer (AR1000). The hydrogels were tested at 37 °C in a moist environment. Both creep and oscillation tests were conducted. Shear modulus values were reported from data at 1 Hz.

Results/Discussion: The refractive index and percent transmission values for the hydrogels as a function of monomer weight percent are shown in Table 1. The refractive index does not appear to change with monomer weight percent, but does closely match the refractive index of the human cornea[4], 1.41. As expected, the percent transmission decreases with increasing weight percent monomer. The percent transmission[5] of the human cornea is approximately 93% at 488 nm. The mechanical properties of the hydrogels (Figure 1) exhibit the expected result of increased compressive and shear moduli with increasing monomer weight percent. The compressive modulus[6] of the human cornea is about 500 kPa. The 70 weight percent PHEMA hydrogel has a compressive modulus of 522 ± 103 kPa, closely matching that of the human cornea.

Table 1. Refractive index (n) and percent transmission (%T) at 488 nm for hydrogels of varying monomer weight percent.

Wt%	n	% T
60	1.4229 ± 0.0014	88 ± 5
70	1.4208 ± 0.0003	85 ± 4
80	1.4187 ± 0.0027	74 ± 1

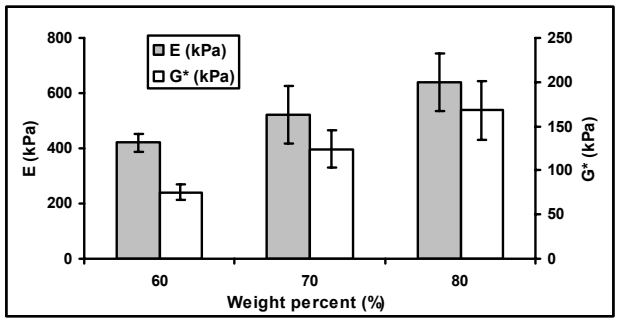

Figure 1. Compressive (E) and shear (G*) moduli of hydrogels with varying monomer weight percent.

Conclusions: We have successfully produced and characterized pHEMA hydrogels for use as corneal implants. As demonstrated above, the range of monomer weight percent studied produced pHEMA hydrogels with properties that encompass the mechanical and optical properties of the native cornea. Ongoing research will elucidate the diffusion, cell adhesion, and cell proliferation properties of the PHEMA hydrogels as well as effects of their subsequent surface modification with cell-adhesion molecules. We would like to thank the National Institutes of Health for funding.

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