Biomolecular hydrogels for biocompatible contact lens materials

A collaborative project of Prof. Carolyn Bertozzi, Department of Chemistry, UC Berkeley, and Materials Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, and Sunsoft Corp., Albuquerque, NM

ABSTRACT

Nature has evolved complex and elegant materials well suited to fulfill a myriad of functions. Lubricants, structural scaffolds and protective sheaths can all be found in nature, and these provide a rich source of inspiration for the rational design of materials for biomedical applications. Many biological materials are based in some fashion on hydrogels, the crosslinked polymers that absorb and hold water. Biological hydrogels contribute to processes as diverse as mineral nucleation during bone growth and protection and hydration of the cell surface. The carbohydrate layer that coats all living cells, often referred to as the glycocalyx, has hydrogel-like properties that keep cell surfaces well hydrated, segregated from neighboring cells, and resistant to non-specific protein deposition. With the molecular details of cell surface carbohydrates now in hand, adaptation of these structural motifs to synthetic materials is an appealing strategy for improving biocompatibility.

The goal of this collaborative project between Prof. Bertozzi's research group the Center for Advanced Materials at Lawrence Berkeley National Laboratory and Sunsoft Corporation was the design, synthesis and characterization of novel hydrogel polymers for improved soft contact lens materials. Our efforts were motivated by the urgent need for improved materials that allow extended wear, and essential feature for those whose occupation requires the use of contact lenses rather than traditional spectacles. Our strategy was to transplant the chemical features of cell surface molecules into contact lens materials so that they more closely resemble the tissue in which they reside. Specifically, we integrated carbohydrate molecules similar to those found on cell surfaces, and sulfoxide materials inspired by the properties of the carbohydrates, into hydrogels composed of biocompatible and manufacturable substrates. The new materials were characterized with respect to surface and bulk hydrophilicity, and non-specific protein adsorption, properties which are thought to correlate with comfort in the eye. The outcome of these studies was the discovery of a new material that is superior to present commercial materials. Contact lenses composed of a sulfoxide acrylate and 2-(hydroxyethyl)methacrylate are presently undergoing clinical evaluation at Sunsoft and, if successful, these novel lenses should be commercially available within the next two years.

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Project description and goals

Nature has evolved complex and elegant materials well suited to fulfill a myriad of functions. Lubricants, structural scaffolds and protective sheaths can all be found in nature, and these provide a rich source of inspiration for the rational design of materials for biomedical applications. Many biological materials are based in some fashion on hydrogels, the crosslinked polymers that absorb and hold water. Biological hydrogels contribute to processes as diverse as mineral nucleation during bone growth and protection and hydration of the cell surface. The carbohydrate layer that coats all living cells, often referred to as the glycocalyx, has hydrogel-like properties that keep cell surfaces well hydrated, segregated from neighboring cells, and resistant to non-specific protein deposition. With the molecular details of cell surface carbohydrates now in hand, adaptation of these structural motifs to synthetic materials is an appealing strategy for improving biocompatibility.

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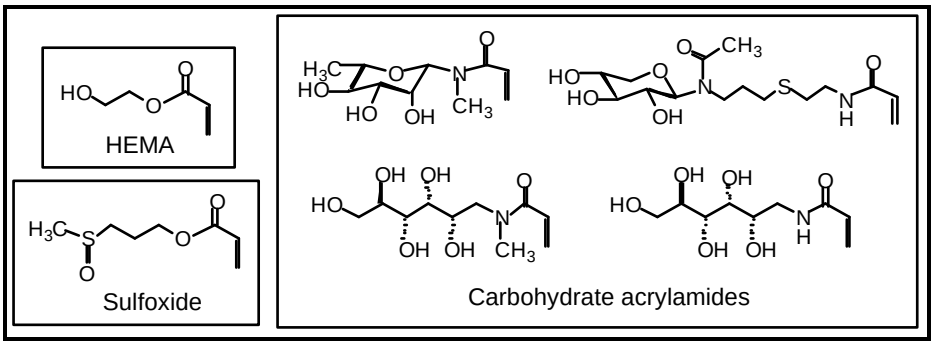
Accomplishments

Our initial studies focused on two classes of hydrogels: cross-linked copolymers of (2-hydroxyethyl)methacrylate (HEMA), widely used in biomedical implants, and synthetic carbohydrate acrylamides (Figure 1). The carbohydrate monomers were constructed using new methods developed in our lab, and then co-polymerized with HEMA to form, after hydration, cross-linked hydrogels. The materials were analyzed for surface hydrophilicity using contact angle measurements, and for bulk hydrophilicity using equilibrium water content and water retention measurements. Finally, the adsorption of proteins from an artificial tear fluid was evaluated. We discovered that incorporation of carbohydrate moieties into hydrogel copolymers had the dual effect of increasing the equilibrium water content dramatically while reducing non-specific protein binding. Collectively, these properties are ideal for soft contact lens applications. Moreover, this combination of effects is quite difficult to achieve and, to our knowledge, has been documented in only one other HEMA-based copolymer.

With these results in hand, we proceeded to generate a second generation material with chemical properties similar to the carbohydrate-HEMA hydrogels but with better manufacturing characteristics. Our criteria included moieties with hydrogen bond acceptor, but not donor, capability and high dipole moments, properties shareed by carbohydrate molecules. The sulfoxide acrylate in Figure 1 met these criteria and so we investigates hydrogels composed of this substrate and HEMA. Indeed, sulfoxide-HEMA hydrogels had high water content, high water retention and low protein adsorption. Contact lenses composed of sulfoxide and HEMA

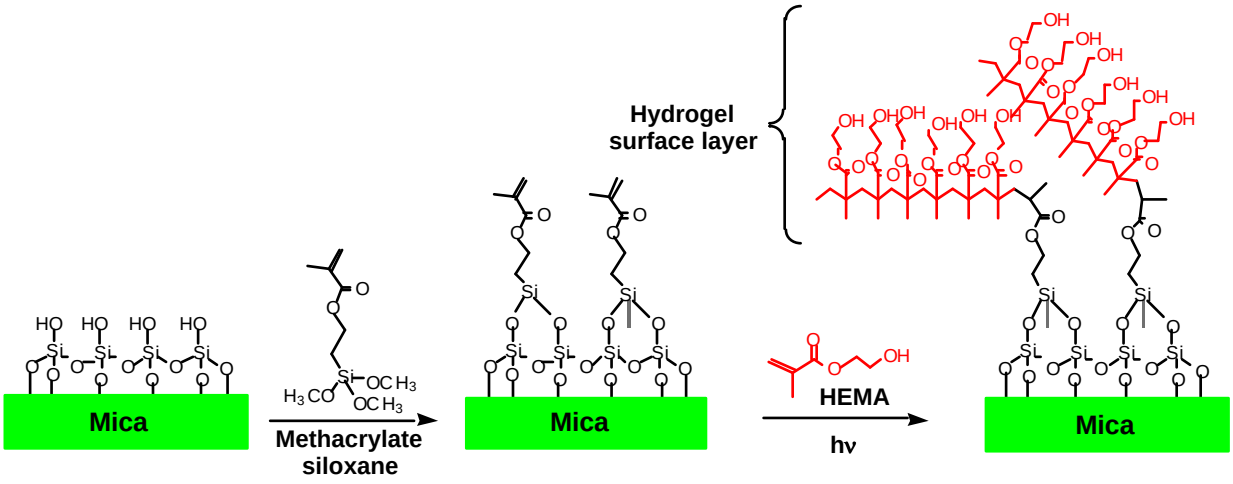
are presently undergoing clinical evaluation in human trials at Sunsoft and, if successful, the material should be on the market late in the year 2000.

Figure 1. Synthetic monomers incorporated into polyHEMA copolymers.



In parallel with our efforts in material design and synthesis, we have developed analytical tools to study the molecular details of protein adsorption to hydrogel copolymer surfaces. Toward this end, we established a method for the synthesis of polyHEMA films on mica surfaces which are of sufficient uniformity and flatness for analysis by atomic force microscopy (Figure 2). The hydration of these HEMA-coated surfaces has been studied in real time and our future plan is to

Figure 2. A method for the synthesis of polyHEMA films on mica.



visualize protein deposition as it occurs in real time as well. The results of this study will shed light on the molecular details of protein adsorption and facilitate the design of advanced materials resistant to protein deposition.

Publications

Chen, Q.; Mukkamala, R.; Bertozzi, C. R. Synthesis and Characterization of Carbohydrate Acrylamide/2-Hydroxyethylmethacrylate (HEMA) Copolymers: A New Class of Biomolecular Hydrogel Materials, submitted to *Macromolecules*.

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Chen, Q.; Zhang, D.; Somorjai, G.; Bertozzi, C. R. Probing the Surface Structural Rearrangement of Hydrogels by Sum-Frequency Generation Spectroscopy. *J. Am. Chem. Soc*. **1999**, *121*, 446-447.

Patent application

Bertozzi, C. R.; Mukkamala, R.; Chen, Q. Novel Biomimetic Hydrogel Materials. Application filed 9/2/98 (Lawrence Berkeley National Laboratory).

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