OPTIMIZATION AND EVALUATION OF POLYETHYLENE GLYCOL DIACRYLATE AS A NONADSORPTIVE POLYMERIC MATERIAL FOR MICROFLUIDICS
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ABSTRACT
Polydimethylsiloxane (PDMS), commonly used in microfluidics, is susceptible to nonspecific adsorption of molecules and biological analytes, such as proteins. PDMS requires coating or chemical modification to overcome this problem. We optimized a single-monomer formulation of polyethylene glycol diacrylate (PEGDA), which upon polymerization to form poly-PEGDA, provides reduced susceptibility to nonspecific protein adsorption, as well as better resistance to permeation of small molecules than PDMS. Furthermore, poly-PEGDA can be utilized as a substrate for microchip electrophoresis, demonstrating symmetrical peaks with good theoretical plate counts.

KEYWORDS: Microchip Electrophoresis, Microfabrication, Polydimethylsiloxane

INTRODUCTION
Polydimethylsiloxane, although prevalent in microfluidics, is prone to nonspecific adsorption and requires complex surface modification processes to address this issue. Previously, Kim et al. demonstrated that PEGDA and polyethylene glycol dimethacrylate (PEGDMA), combined with photoinitiator, could be polymerized through UV exposure to make features as small as 50 nm. Polymerized PEGDMA had lower nonspecific protein and cell adhesion than either PDMS or polyethylene glycol (PEG) silanized PDMS, but poly-PEGDA was not studied in great detail. Liu et al. polymerized acrylate monomers, some containing PEG groups, and demonstrated the resulting material’s use in microchip electrophoresis. These and other alternatives to PDMS have been researched extensively, but still have failed to gain a significant foothold in microfluidics. Any replacement material for PDMS must be simple to fabricate, compatible with soft lithography techniques, and superior in properties to PDMS to gain broad use in microfluidics. Here, we demonstrate that optimized poly-PEGDA formulations provide inherent resistance to nonspecific adsorption, comparable optical quality to PDMS, and excellent electrophoretic separations for amino acids and proteins, while utilizing the same methods for fabrication as PDMS.

EXPERIMENTAL
Several poly-PEGDA formula variations were tested to optimize for optical clarity, polymerization, and aqueous stability. The formula variations included the PEG subchain length in PEGDA (258 vs. 575 Da), levels of photoinitiator (0.05% vs. 3% 2,2’-dimethoxy-2-phenylacetophenone, DMPA), and additives such as PEGMEMA and methyl methacrylate in comparison with a single-monomer PEGDA formulation. Comparisons of each formula were made for 10 s and 25 s polymerization times using a 0-2 scale for optical clarity and a 0-5 scale for polymerization. Water stability was tested by submerging polymerized samples for 16 hrs.

Burst pressure was used to evaluate bond stability between poly-PEGDA layers by pressurizing a channel at the interface with water using a syringe pump and an in-line pressure sensor according to the setup from Satyanarayana et al. Nonspecific adsorption of small molecules in PDMS and poly-PEGDA was compared by flowing 10 µM rhodamine B at 0.2 µL/min through a 50 µm wide and 20 µm tall channel embedded into each material. Fluorescence signal was probed over several hours, taking care to block the laser between measurements to reduce the effect of photobleaching. Nonspecific protein adsorption in PDMS and poly-PEGDA was evaluated over time during exposure to a model adsorptive protein. Microchip electrophoresis was conducted using an offset-T design molded in poly-PEGDA. An injection voltage of -500 V, a separation voltage of -1400 V, and pH 9.3 carbonate buffer were utilized to separate FITC-labeled amino acids. Separation of FITC-β-lactoglobulin A and FITC-thyroglobulin used -900 V for injection, -2000 V for separation, and pH 10.0 carbonate buffer.

RESULTS AND DISCUSSION
We optimized a single-monomer formulation of PEGDA, photopolymerized with DMPA to provide an adsorption-resistant polymer with water stability, bonding robustness, and optical clarity. Poly-PEGDA formulations with 258 Da PEGDA and ≤0.1% DMPA were the most stable in water while still having good optical properties.

Poly-PEGDA was characterized by comparing (with PDMS) the optical transmission and nonspecific adsorption of small molecules and proteins. Transmission spectra for PDMS and poly-PEGDA indicate that poly-PEGDA has comparable transparency to PDMS over the 300-1000 nm wavelength range. Bonded poly-PEGDA microdevices withstand pressures to at least 420 kPa, the pressure at which the sensor detached in our measurement setup. Exposure to a flowing rhodamine B solution revealed significant differences between poly-PEGDA and PDMS devices, as illustrated in Figure 1. In PDMS the fluo-
rescence signal increased greatly in both intensity and spatial distribution as a function of time as rhodamine B diffused into the PDMS material. In contrast, the fluorescence signal in poly-PEGDA showed no appreciable increase in either intensity or spatial distribution over the same three-hour time period.

![Graph](image)

**Figure 1**: Fluorescence comparison of PDMS and poly-PEGDA as rhodamine B is flowed through a 50 µm wide channel. Initial fluorescence for PDMS and poly-PEGDA was comparable, so only the PDMS signal is shown. After three hours of exposure to rhodamine B the fluorescence signal for poly-PEGDA remained within the channel, while the fluorescence signal for PDMS demonstrated that rhodamine B diffused extensively into the bulk of the PDMS.

Poly-PEGDA also exhibited long-term resistance to nonspecific adsorption compared to PDMS when exposed to a low concentration of a model adsorptive protein. The initial fluorescence signal in PDMS remained lower than in poly-PEGDA for 20 min, but gradually increased to three times the signal in poly-PEGDA after 100 min. The lower initial signal in PDMS was most likely due to protein nonspecifically adsorbing to the channel surface before reaching the detection point. Once the upstream surface was saturated, the fluorescence signal began to increase at the detection point. The signal in poly-PEGDA, while initially higher than in PDMS, remained flat over the same (100 min) time scale with no appreciable increase.

![Graph](image)

**Figure 2**: Microchip electrophoresis of FITC-labeled amino acids.

Poly-PEGDA sustains electroosmotic flow and can be used to separate analytes via microchip electrophoresis, as shown in Figures 2 and 3. The amino acid separation shown in Figure 2 has well-resolved peaks with theoretical plate numbers of 3900 (1.6 x 10^5 N/m) for FITC-lysine and 2800 (1.1 x 10^5 N/m) for FITC-tryptophan. The separation of 10 µM FITC-lysine resulted in two peaks (mono- and di-FITC-lysine) with a resolution of 1.4 and a theoretical plate count of 3200.
(1.3 x 10^5 N/m) for the smaller di-FITC-lysine peak. Separation of FITC-β-lactoglobulin A and FITC-thyroglobulin in Figure 3 had a resolution of 1.2 with theoretical plate numbers of 6400 (2.6 x 10^5 N/m) for FITC-thyroglobulin and 5700 (2.3 x 10^5 N/m) for FITC-β-lactoglobulin A. Symmetrical peaks without tailing demonstrate the lack of analyte interactions with the surface, showing great promise to improve separations. The nonspecific adsorption characteristics, optical clarity, and compatibility with microchip separations of poly-PEGDA demonstrate its strong potential to replace PDMS as a microfluidic substrate.

CONCLUSION

Photopolymerized polyethylene glycol diacrylate can be made through similar fabrication processes to PDMS. Poly-PEGDA has excellent stability in water, high bond strength, and similar optical properties to PDMS. Poly-PEGDA demonstrates greater resistance than PDMS over time to surface fouling at low protein concentration, and resistance to permeation of small hydrophobic molecules. Symmetrical, resolved peaks with good theoretical plate counts in microchip electrophoresis further showcase the utility of poly-PEGDA in bioanalysis. These favorable performance characteristics of poly-PEGDA demonstrate its potential as a replacement for PDMS in microfluidics.

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REFERENCES


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