Evaluating Mechanical performance of Hydrogel Based Adhesives for Soft Tissue Applications

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Statement of Purpose: Accidental laceration of the bladder is the most frequent complication during hysterectomy and is generally repaired by suturing[1]. Drainage via a catheter is required during recovery because inelastic sutures prevent normal distension of the bladder during filling. The long-term goal of our study is to develop a strong, yet highly compliant adhesive that will replace sutures and eliminate the need for catheters. Working toward this goal, we are currently exploring Tetronics, 4-arm amphiphilic AB block copolymers of polypropylene oxide (PPO) and polyethylene oxide (PEO) as an adhesive that exhibits rapid gelation at physiological temperatures. In the present study, three testing methods where developed to evaluate the performance of various compositions of Tetronic adhesive, along with cyanoacrylate and polyethylene glycol adhesives.

Methods: Tetronic adhesives were prepared from blends of acrylate terminated T904 and T1107. Acrylation was performed in dicholormethane using established methods[2]. Briefly, Tetronics where reacted with Triethlyamine (TEA) and acryloyl chloride was added dropwise. After stirring overnight the triethlyammonium precipitate was filtered out and the product was neutralized to pH 7.0. Crosslinking was achieved by the addition of dithiothreitol (DTT).

To quantify the adhesive strength tensile testing on both collagen sheets (sausage casing) and fresh bladder was performed. Briefly, specimens were sectioned into ½ inch strips and placed in a fixture that maintained end to end contact of two tissue pieces. Approximately 100 µl of each test adhesive (Tetronic, cyanoacrylate (CA) or PEG) was applied to the joint. For shear adherence tests collagen sheets were cut into ½ and ¾ inch wide strips; a 0.2 in diameter circular defect was created at one end of the ¾ inch strips and then placed over the ½ inch strip. Approximately 50 µl of adhesive was applied into the circular defect for shear adherence tests. This ensured that the adhesive was bonded to both the upper and lower substrates through the defect, isolating shear adherence to a known area. Only specimens that exhibited shear adhesive failure to the lower substrate where included in shear adherence results. In all experiments adhesives were cured for 30 min at 37° C before mechanical testing and hydration was maintained using 37° C PBS. The bonded specimens were subjected to uniaxial tensile loading and force of failure was measured using a MTS machine. Data were reported as either force of failure (lbf) or shear adherence stress (psi). Statistical analysis of the data was performed using the ANOVA and appropriate post-hoc tests with p-values less than 0.05 were considered statistically significant.

Results: Three blend ratios (1:1, 3:1, 1:3) of low and high molecular weight Tetronic components, T904 and T1107 respectively, were prepared. Since the 1:3 Tetronic blend displayed premature thermo-gelation at room temperature it was omitted from further mechanical testing.

End-to-end tensile testing of collagen sheets reveled that compared to CA (0.47 (+/-0.02) lbf) the forces to failure for all hydrogel adhesives were significantly ($P < 0.01$) lower (Figure 1). Among the hydrogels, the 1:1 blend Tetronic (50 %wt), exhibited the highest average force of failure (0.12 (+/-0.05) lbf). Comparison of failure modes revealed that PEG failed primarily cohesively, with residual material remaining on both sheets. The other groups exhibited primarily adhesive failure, where the bulk of the adhesive remained intact and attached to one sheet with no evidence of adhesive on the other.

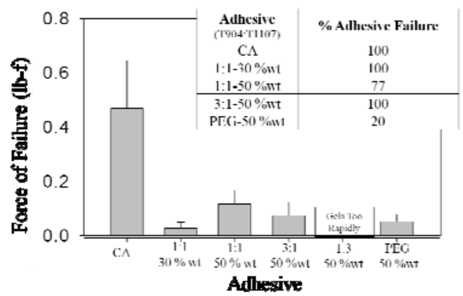

Figure 1: Force of failure and percent adhesive failure of end to end tensile testing with collagen sheets.

Shear adherence testing with collagen sheets demonstrated that shear adherence stress (shear force divided by the adhesion area) was significantly ($P < 0.05$) greater for 1:1 50 wt% Tetronic, 0.068 (+/- 0.01) psi, when compared to 50 %wt PEG and 0.053 (+/- 0.01) psi.

In fresh bladder end-to-end tests, the average force of failure was 0.81 (+/-0.03) lbf for CA-bonded bladder tissue, and 0.08 (+/-0.02) lbf for 50 wt% 1:1 Tetronic adhesive.

Conclusions: The results of the present study indicate that reversible thermo-gelaton of Tetronic blends provides an ideal characteristic for a surgical tissue adhesive, reducing flow from the application site as the hydrogel crosslinks. However, excessive T1107 content would lead to extremely rapid gelation and not allow application of the adhesive, as exhibited by the 1:3 blend in the present study. While the overall adhesive strength needs further improvement, the predominantly adhesive failure pattern in the end-to-end tests indicate that cohesive performance of the Tetronic was adequate for the current failure strength. This is in contrast to PEG, where the bulk material strength was inferior to adhesive strength, resulting in primarily cohesive failure. Thus, to improve the overall performance of the tissue adhesive, both of these parameters must be carefully tailored; it is necessary to increase not only the bulk strength of the hydrogel but also the bonding strength with soft tissues.

References: (1) Cogan, S., Int Urogynecol J, 2007.
(2) Cellesi, F., BioMat, 2004. 24: p. 5115-5124.