Evaluating Performance of Hydrogel-Based Adhesives for Soft Tissue Applications

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Statement of Purpose: One of the most common complications during hysterectomy surgeries is accidental laceration to the bladder[1]. Current treatments for the bladder injuries are limited to sutures, which prevents proper distention of the bladder wall during filling and necessitates use of a catheter during recovery. Although a number of tissue adhesives and sealants approved by the FDA for surgical use are currently available, none of them are suitable for application to the bladder because of their inadequate strength, compliance, or biocompatibility. Therefore, the goal of the present study is to develop a novel, hydrogel-based tissue adhesive that provides proper mechanical properties for bladder application. More specifically, we are currently exploring the synthesis process for bi-functionalization of Tetronic(BASF), a 4-arm, PEO-PPO block co-polymer with 3,4-dihydroxyphenylalanine (DOPA) and acryloyl chloride to achieve a balance between bulk and adhesive strengths of the hydrogel suitable for bladder application.

Methods:

Preparation of tissue adhesive: Bi-functional Tetronic adhesive was prepared through multi-step process. Acrylation was first performed in dicholormethane using published methods[2]. Briefly, Tetronic T1107 (MW: 15,000) with Triethlyamine (TEA) and acryloyl chloride was stirred for 24 hours. Triethlyammonium precipitate was filtered out and the product was neutralized to pH 7.0, then washed with ethyl either. The partially acrylated T1107 was then, modified with DOPA through reactions with 4-Dimethylaminopyridine (DMAP), Succinic Anhyride and TEA in Tetrahydrofuran (THF) for 12 hours, N-Hydroxysuccinminide (NHS) and Dicyclohexylcarbodimide (DCC) in THF for 4 hours, and DOPA in Dimethylformamide (DMF) for 6 hours. Chemical crosslinking of acrylate-ends was achieved by addition reaction with appropriate amount of thiol-group donor, dithiothreitol (DTT) as previously described[2].

Mechanical testing of tissue adhesive: Four blend ratios (100:0, 75:25, 50:50, 25:75) of T1107-acrylate (DOPA-) and T1107-acrylate-DOPA (DOPA+) were prepared, and shear adherence testing on collagen sheets was performed to quantify bonding strength of the adhesive. Briefly, collagen sheets were cut into 4cm x 1cm strips with 60 µl of adhesive applied to a 1cm x 1cm area of one strip and another strip was placed over it. Adhesives were cured under hydrated conditions in PBS at 37° C for one hour before mechanical testing. The bonded specimens were subjected to uniaxial tensile loading and force of failure was measured using a MTS machine. Data were plotted as bond strengths (kPa) and statistically analyzed using ANOVA and Tukey's HSD post-hoc testing for comparison of different blend ratios.

Results: Acrylation percent and product yield for T1107-acrylate (DOPA-) were 93% and 63%, respectively. Acrylation percent and DOPA conversion rate for DOPA+ were 65% and 31%, respectively with 64% product yield. Shear adherence testing with collagen sheets demonstrated that all Tetronic blends containing DOPA+ show higher strengths than 100% DOPA-adhesive. The bond strength was greatest for the 75:25 blend (DOPA-:DOPA+), 27 kPa, when compared to the other blends tested (Figure 1), which is approximately a two-fold increase in bond strength compared to the previously published data on Tetronic-based tissue adhesives[2].

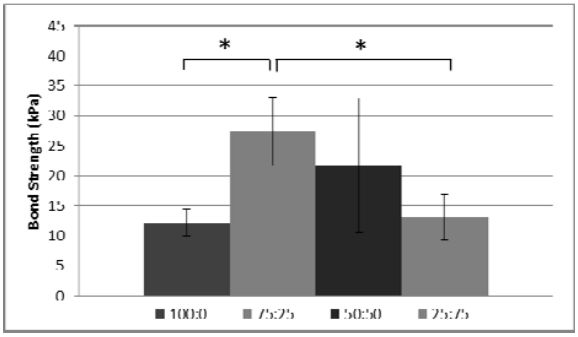

Figure 1. Adhesive bond strength for various Tetronic hydrogel blends (DOPA-:DOPA+) on collagen sheets. Data are mean +/- standard deviation, *p<0.05, n=4.

In several instances, the DOPA containing adhesive's bond strength exceeded the strength of the testing material, collagen sheets (253 N/m), resulting in material failure rather than adhesive failure (data not shown).

Conclusions: The results of the present study suggest that DOPA can significantly improve Tetronic-based adhesive's bond strength to biological materials. Although the contribution of DOPA is clearly demonstrated, the adhesive strength was shown to depend on the acrylate ends for crosslinking with the thiol group. Further testing, however, is needed to demonstrate the actual utility of our bi-functional Tetronic tissue adhesive for bladder applications in vivo.

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References: [1]Ostrzenski, et al., Obs & Gyn Survey, 1998.53:p.175-180. [2]Cho, et al., Acta, 2012.8:p.2223-2232.