Absorbable Tissue Adhesives

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Introduction:

The past few years have witnessed an increasing interest towards replacing and augmenting sutures with tissue adhesives. The advantage of using tissue adhesive is increased rate of wound healing without excessive tissue deformation. This requires tissue adhesive to have high initial tack and ability to bond rapidly to living tissue. Furthermore, the strength of the flexible bond should be sufficiently high to adhere tissues together. Moreover, the degradation products of the tissue adhesives should be safe and biocompatible. Although a number of tissue adhesives based on different chemistries including the polyurethanes[1a-c] have been investigated but none of them have gained wide acceptance as they failed to meet one or other of the aforementioned requirements. In this study, we present for the first time our efforts towards developing novel absorbable tissue adhesives that meet all the requirements of tissue adhesives.

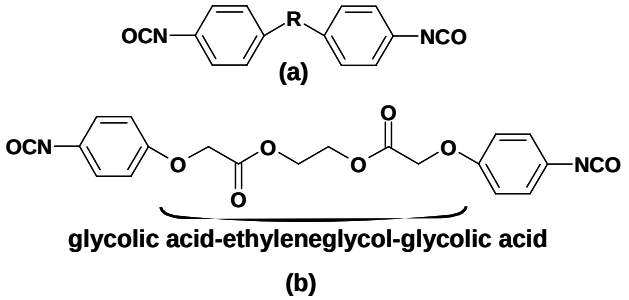

Figure 1. (a) Novel absorbable aromatic isocyanate (b) Absorbable aromatic diisocyanate derived from safe and bicompatible glycolic acid and ethylene glycol monomers and paracetamol precursor

Results/Discussion:

In this study we have developed novel degradable aromatic isocyanates derived from paracetamol precursor and safe and biocompatible monomers as shown in Figure 1(a) where R represents a segment containing degradable linkages derived from glycolic acid, lactic acid, caprolactone, p-dioxanone and diols, an example of which is shown in Figure 1(b). These monomers are the building blocks of majority of biodegradable polymers used to make commercial medical devices. The resulting novel absorbable isocyanates were then chain extended with polyethylene glycols and reacted with multiarmed absorbable isocyanates in presence of moisture from tissue as shown in figure 2 to form crosslinked tissue adhesive. The aromatic isocyanates developed by our company can cure within one minute.

Furthermore, the polyurethanes derived from these aromatic diisocyanates and polyol and amine chain extenders have hydrolyzable urethane and urea hard segments. Moreover, changing the absorbable monomer component in the isocyanates can control the hydrolytic degradation rate of these polyurethane tissue adhesives. The synthesis and characterization of these tissue adhesives will be presented in detail in the meeting.

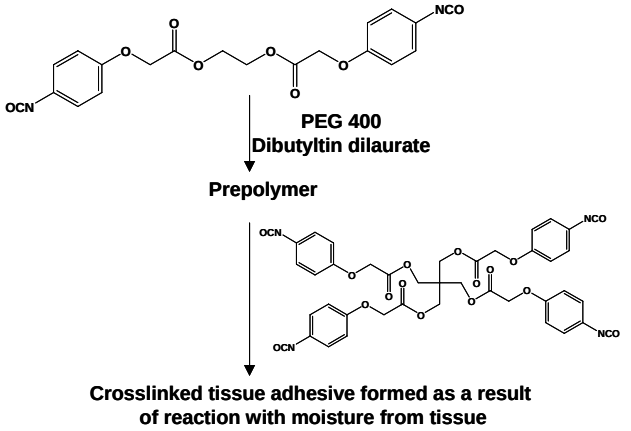

Figure 2 Absorbable crosslinked polyurethane based tissue adhesive

Conclusions: In this paper we report for the first time the development of absorbable polyurethane based tissue adhesives from novel aromatic isocyanates containing degradable hard segment derived from safe and biocompatible glycolic acid and lactic acid monomers. Furthermore, the hydrolytic degradation rate of these tissue adhesives can be controlled by changing the lactic acid instead of glycolic acid and vice versa in the novel isocyanates. Moreover, the polymers derived from the novel absorbable linear diisocyanates can be used in various other biomedical applications such as polymer therapeutics and tissue engineering.

References:

(1) (a) Roby et al. US Patent No. 6894140 (b) Matsuda et al. US Patent No. 4994542 (c) Fuller et al. US Patent No. 4829099 (d) Bezwada, R.S. US Patent Publication No. 2006/0188547.
(2) Bezwada, R.S. PMSE Preprints 2006; 95:1054.