

Novel Degradable Polyurethane 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 application of tissue adhesive results in increased rate of wound healing without excessive tissue deformation. This requires tissue adhesive to have high initial tack and the ability to bond rapidly to living tissue forming a permeable flexible bond. Furthermore, the strength of the bond should be sufficiently high to cause tissue failure before bond failure. Moreover, the degradation products of the adhesive should be safe and biocompatible. Although a number of tissue adhesives based on different chemistries^{1a-c} including polyurethanes 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 biodegradable polyurethane tissue adhesives that incorporate all the properties inherent to a tissue adhesive.

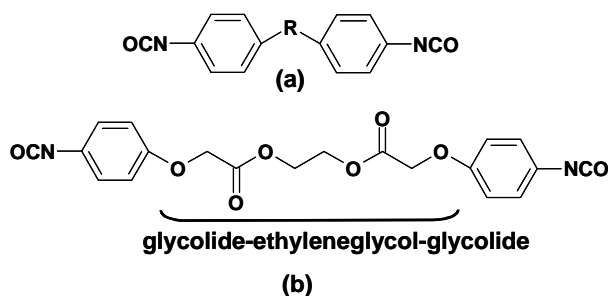
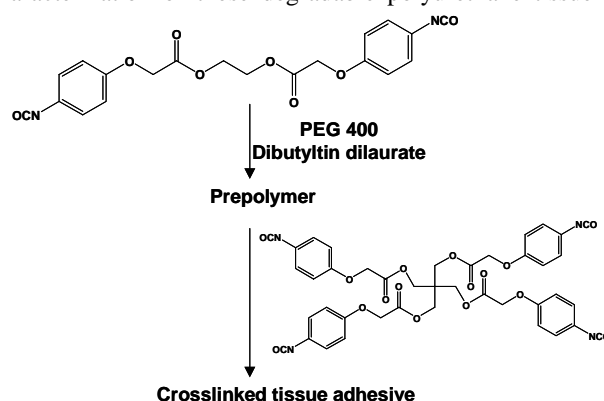


Figure 1. (a) MDI, Methylene diphenyl isocyanate (b) Biodegradable aromatic diisocyanate derived from safe and biocompatible glycolic acid and ethylene glycol monomers.

Results/Discussion: In this study we present biodegradable polyurethane tissue adhesives formed as a result of the reaction between novel degradable linear and multiarmed aromatic isocyanates with polyethylene glycols. The biodegradable aromatic isocyanates in the present study were derived from paracetamol precursor and safe and biocompatible monomers such as glycolic and lactic acid as shown in figure 1(b). R in figure 1(b) represents a segment containing degradable linkages derived from glycolic acid, lactic acid, caprolactone, p-dioxanone and diols. These monomers are the key components of majority of biodegradable polymers used to make commercial medical devices. The resulting novel biodegradable isocyanates were then chain extended with polyethylene glycols and reacted with multiarmed degradable isocyanates as shown in Figure 2 to form cross-linked

polyurethane tissue adhesives. The biodegradable aromatic isocyanates developed by our company can cure within one minute. Furthermore, the polyurethanes derived from the reaction of these aromatic diisocyanates with polyol and amine chain extenders have hydrolyzable urethane and urea hard segments. Moreover, changing the biodegradable monomer component in the isocyanates can control the hydrolytic degradation rate of these polyurethane tissue adhesives. The synthesis and characterization of these degradable polyurethane tissue



adhesives will be presented in detail in the meeting.

Figure 2 Biodegradable polyurethane tissue adhesive

Conclusions: In this paper, we report for the first time the development of biodegradable polyurethane 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 deriving the degradable hard segment from lactic acid instead of glycolic acid and vice versa. Moreover, the biodegradable polyurethanes of the present study 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) (a) Bezwada, R, S. PMSE Preprints 2006; 95:1054.