**Hydrolysable Linkers and Crosslinkers for Absorbable Polymers**

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The process of chemically joining two or more molecules via a covalent bond is referred to as linking. The reagents that are used to carry out linking are referred to as linkers. Linkers contain reactive end groups specific to functional groups on various molecules, including proteins. In addition to covalently linking two molecules, these linkers are commonly used to modify nucleic acid, drugs and surfaces. Furthermore, they are used in preparation of protein drug conjugates, antibody-enzyme conjugates, immunoproteins and labeled reagents. Moreover, they are also used in studies directed at determining the three dimensional structures of proteins, solid phase immobilization and molecular associations in cell membranes.

In this paper, we report the development of hydrolysable linkers and crosslinkers. The key attributes of these hydrolysable linkers and crosslinkers that distinguishes them from those available commercially, or those reported in the literature are (a) presence of a hydrolytically degradable linkage, either along the main chain or along the arms of the linker or crosslinker (b) hydrolytic degradation rates that can be controlled by varying the chain length of the degradable linkage and by varying the safe and biocompatible molecule, i.e., replacing glycolide with lactide or p-dioxanone and (c) upon hydrolysis under physiological conditions, these degradable linkers and crosslinkers are expected to yield safe and biocompatible products.

These linkers and crosslinkers can be used to synthesize a variety of end-functionalized as well as reactive absorbable macromers and oligomers, such as UV curable ester-urethane-acrylates or in-situ gelling oligomers. Furthermore, they can also be used to prepare linear or crosslinked absorbable polymers including poly(ester-urethanes), poly(ester-amide-urethanes) and poly(ester-amides). These linear or crosslinked polymers, derived using these linkers and crosslinkers, will find use in a number of potential applications, including controlled release applications, tissue adhesive and sealants, and adhesion prevention barriers.

Synthesis and characterization of these linkers and cross-linkers will be presented. Applications of these linkers and cross-linkers will be discussed.

**Results and Discussion:**

Hydrolysable amine linkers: Figure 1 displays the structures of hydrolysable diamine linkers derived from p-aminophenol and p-aminobenzoic acid, respectively. These diamine linkers have varying hydrolytic degradation rates. Similarly, figure 2 displays the structure of absorbable acrylate end-functionalized cross linker.

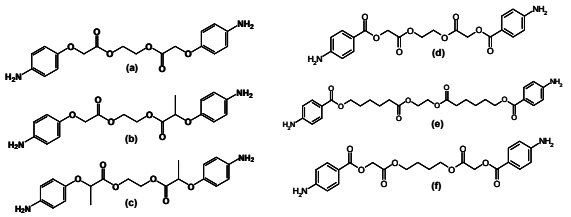

**Figure 1.** Absorbable aromatic diamine linkers with varying hydrolytic degradation rates

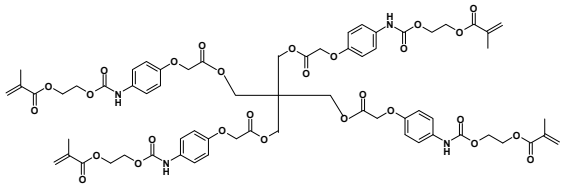

**Figure 2.** Absorbable acrylate end-functionalized crosslinker

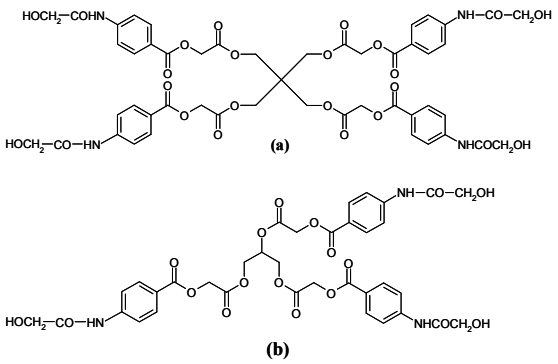


**Figure 3.** Hydrolysable Amide-diol Crosslinkers with Varying Hydrolytic Degradation Rates

These hydrolysable linkers and crosslinkers can also be conjugated to drug molecules or biologically active compounds containing carboxylic acid groups such as aspirin and naproxen, thereby enabling controlled release of such compounds. Moreover, these linkers can be conjugated to the triclosan molecule and can be used as anti-microbial macromers or oligomers.

**References:**

1. Bezwada, Rao S. U.S. Pat. Publication 20090082540