Cytocompatibility of Dextran-Based Tissue Sealants for Surgical Wound Closure

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We have developed the ActaMax™ sealant family of hydrogel tissue adhesives, formed by reacting an oxidized polysaccharide with a water-dispersable multi-arm polyether amine. Specifically, we have developed tissue adhesives composed of two components: dextran aldehyde and multi-arm PEG amine, which undergo a Schiff base reaction to form a crosslinked hydrogel (Figure 1). This two-component tissue adhesive system crosslinks in water, cures rapidly (<1 min) at room temperature, adheres to moist tissue, and degrades hydrolytically.

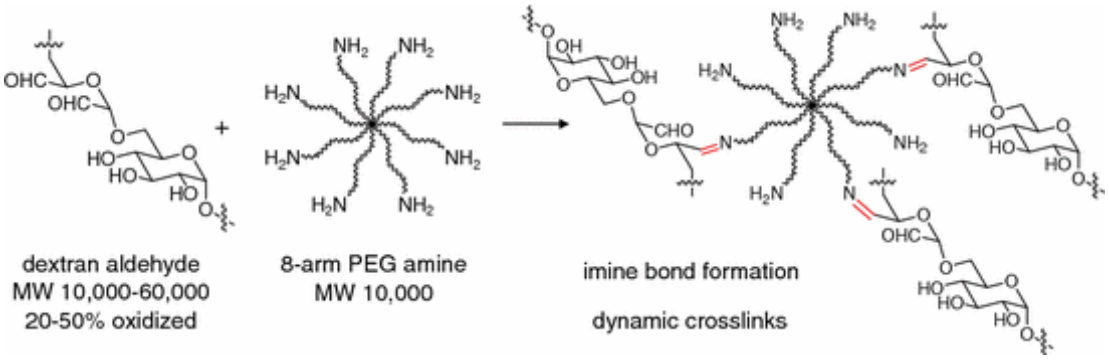

Figure 1. Foundation chemistry for polysaccharide-based tissue adhesives. The oxidized polysaccharide dextran aldehyde reacts with an 8-arm star PEG amine to form a crosslinked hydrogel network.

The effects of dextran-based tissue adhesives on cell survival and inflammatory cell activation were determined using in vitro mouse cell cultures. Cytotoxicity of tissue adhesives was evaluated by placing adhesives in direct contact with 3T3 fibroblast cells. Polysaccharide-based tissue adhesives composed of dextran aldehyde and star PEG amine were non-cytotoxic to fibroblasts; in contrast, a commercial adhesive composed of 2-octyl cyanoacrylate was highly cytotoxic to fibroblasts (Figure 2). The inflammatory potential of tissue adhesives was evaluated by exposing J774 macrophage cells to adhesives, and measuring TNF-alpha release from macrophages. Polysaccharide-based tissue adhesives did not elicit inflammatory TNF-alpha release from macrophages (Figure 3). These results suggest that dextran-based tissue adhesives are non-cytotoxic and non-inflammatory; the results are therefore significant in the design of novel tissue sealants, as well as cell culture systems to study biomaterials.

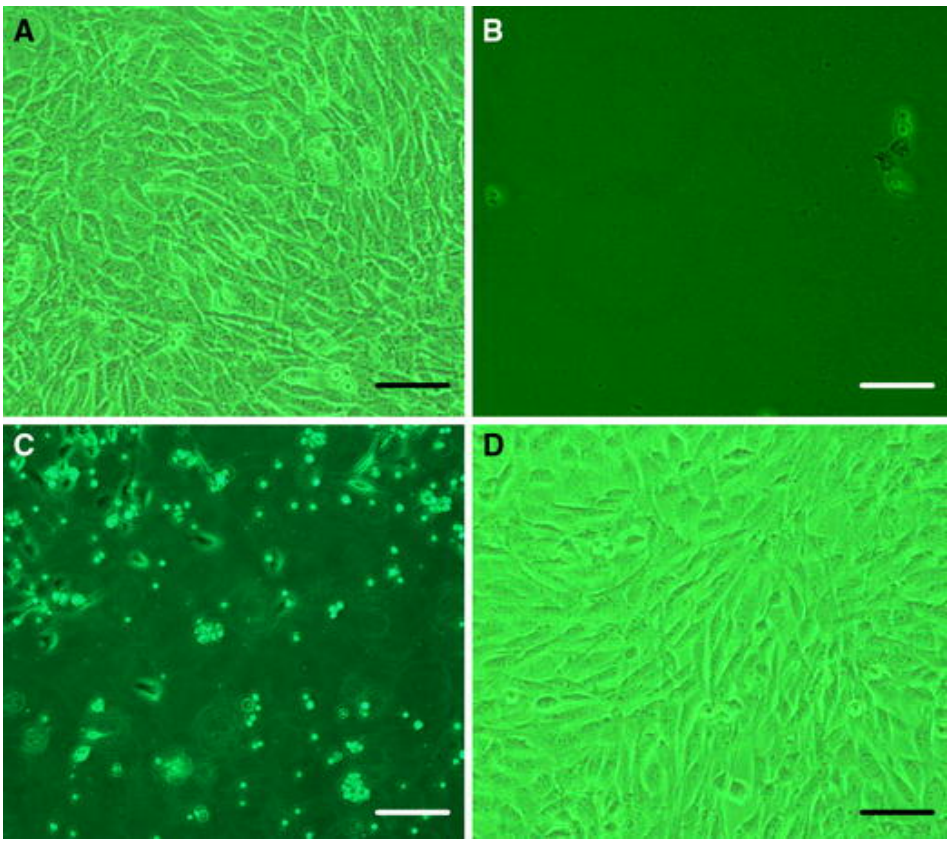

Figure 2. Responses of mouse 3T3 fibroblasts to tissue adhesives. Fibroblast cells were incubated in direct contact with material samples for 24 h at 37°C. Scale bars = 100 μm
(A) Ultra-high molecular weight polyethylene; non-cytotoxic negative control.
(B) Organo-tin PVC; cytotoxic positive control.
(C) Cyanoacrylate-based Dermabond tissue adhesive.
(D) Polysaccharide-based tissue adhesive composed of dextran aldehyde (60,000 MW, 20% aldehyde conversion, 17% solids) + 8-arm PEG amine (10,000 MW, 50% solids).

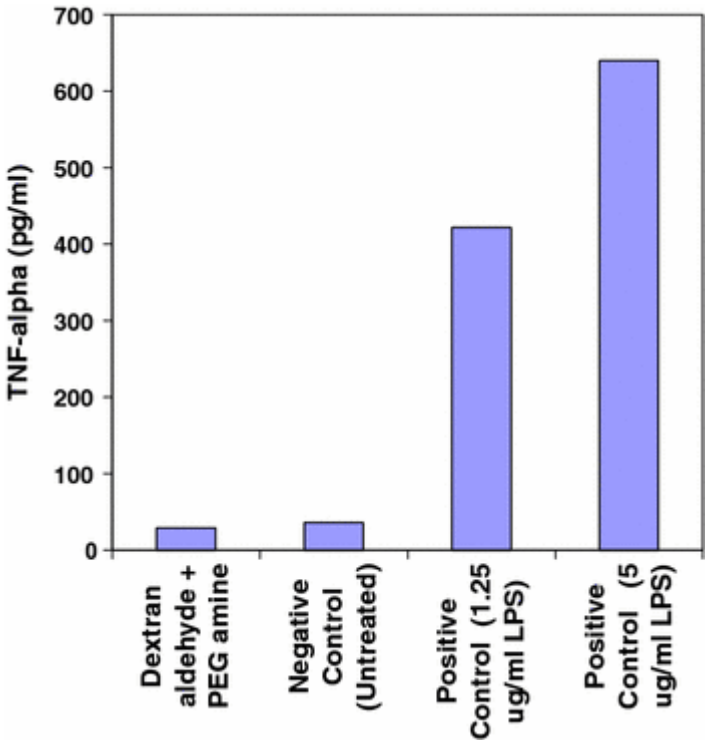

Figure 3. Response of mouse J774 peritoneal macrophages to polysaccharide-based tissue adhesive. Macrophage cells were incubated in direct contact with material samples for 48 h at 37°C. Following incubation, TNF-α release from macrophages was measured by ELISA.

References:

S. K. Bhatia, S. D. Arthur, H. K. Chenault, G. K. Kodokian, “Interactions of Polysaccharide-Based Tissue Adhesives with Clinically Relevant Macrophage and Fibroblast Cell Lines,” *Biotechnology Letters* (2007), 29:1645-1649.

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