Bacteria-Responsive Shape Memory Polymer Wound Dressing

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Statement of Purpose:

Chronic wounds, including diabetic ulcers, affect more than 5 million patients per year, and their treatment costs over $25 billion each year [1]. Several factors delay healing in these wounds, but bacterial infection and subsequent biofilm formation have been implicated as major contributors [2]. Biofilms are complex communities of microbes with a protective layer [3]. More than 80% of all bacterial infections results in biofilm formation, which interferes with wound healing processes [3]. Biofilms are difficult to dislodge, and their mechanical barrier makes them less susceptible to antimicrobial treatment and to phagocytic cells penetration from the host immune system [4]. Clinical treatments for chronic wound healing include bandages, pads and gauze; swabbing for biofilms, infection cleaning/wound debridement, and wound dressings [2, 5]. In severe situations, amputations are required. Current dressing options require daily changes, which cause pain and discomfort and increase infection susceptibility [6]. These dressings do not eradicate biofilms [5], and continuous, non-specific release of antibiotics can contribute to antibiotic resistance. Solving these issues requires development of new approaches that can sense chronic wound infections and eradicate biofilms. A bacteria-responsive dressing could restore potency of antibiotics, reduce tissue damage, and aid in wound healing processes. To meet this clinical need, we designed a shape memory polymer (SMP) containing a bacteria-responsive peptide sequence. The SMP is synthesized in a primary shape, heated above a transition temperature and deformed into a stable, temporary shape that would be maintained after implantation. If bacteria are present on the SMP wound dressing, the peptides are cleaved by bacterial enzyme release and the SMP recovers to its original shape. This shape change can release antimicrobials and dislodge adhered biofilms, making bacteria more susceptible to treatment.

Methods: Segmented polyurethanes (SPUs) were synthesized using hexamethylene diamine (HDI), polypropylene glycol (PPG), and triethylene glycol (TEG) through a two-step process. First, a prepolymer was synthesized using HDI and PPG (soft segment). Then, a chain extender (TEG) was added at varied ratios relative to HDI. The structure of the polymers was characterized by Fourier transform infrared (FTIR) and nuclear magnetic resonance (^{1}H-NMR) spectroscopy. Glass transition (Tg) and melting (Tm) temperatures of the SPUs were measured by differential scanning calorimetry (DSC). Tensile testing was employed to measure the mechanical properties. Oxidative and hydrolytic degradation profiles in accelerated media (20% H_2O_2 and 0.1M NaOH, respectively) are being obtained.

Results: FTIR and NMR spectra confirmed that SPUs were successfully synthesized with varied hard segment ratios. Tensile properties (Table 1) revealed that an increase in the HDI to PPG ratio increases tensile strength, Young's modulus, and elongation at break. This result indicates that desirable mechanical properties for flexible wound dressings can be achieved using synthesis variables. Tg and Tm of the three SPU's are above body temperature, providing SMPs that could be stable in their secondary shape after implantation. Minimal mass loss in accelerated degradation media (Fig. 1) and maintained thermal transition temperatures throughout degradation indicates high potential of wound dressings to remain stable after implantation unless bacteria are present.

Table 1. NMR results, tensile and thermal properties of the polymer.

Theoretical Ratios	Actual Ratios from NMR Test	Mechanical Properties			Thermal Properties	
		Tensile Strength (KPa)	Elongation at Break (%)	Modulus (KPa)	Tg (ºC)	Tm (ºC)
3 HDI: 1 PPG: 2 TEG	3.75 HDI: 1PPG: 2.75 TEG	680 ± 10	13.35 ± 4.1	39 ± 1	56.13	81.18
4 HDI: 1 PPG: 3 TEG	4.87 HDI: 1PPG: 3.79 TEG	2190 ± 20	56.50 ± 15.36	54 ± 1	57.95	86.10
5 HDI: 1 PPG: 4 TEG	5.75 HDI: 1PPG: 4.91 TEG	2400 ± 40	34.64 ± 1.4	80 ± 8	55.32	83.26

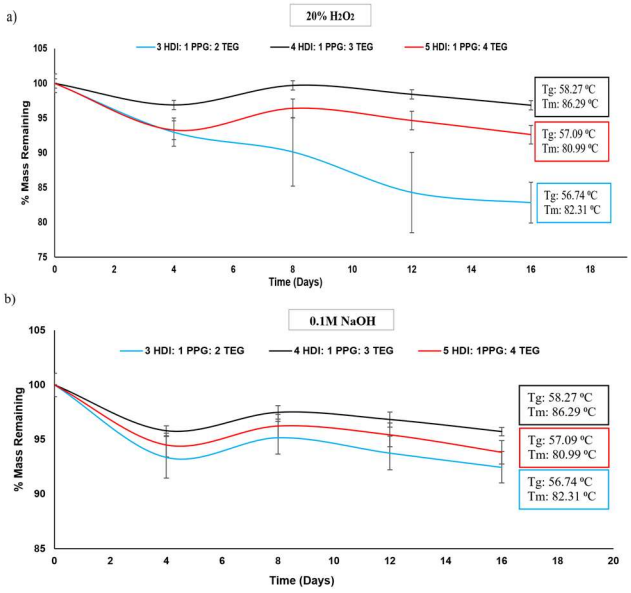

Fig 1. Mass loss and thermal transitions of SPUs during degradation in a) 20% H_2O_2 and b) 0.1M NaOH

Conclusions: The SPUs showed desirable chemical, thermal, and mechanical properties for use in a bacteria-responsive wound dressing. Current work is focused on synthesizing SPUs with bacterial enzyme-labile peptide sequences and characterizing their activity in the presence of bacteria.

References:

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