Novel Polyoxetane Hydrogel for Drug Delivery
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Statement of Purpose: Oxetanes have been recognized as an essential element in many drugs and play a pivotal role in facilitating desirable pharmacokinetic properties. Oxetanes can also be utilized as monomers to synthesize linear or branched polymers via ring-opening polymerization (ROP) (JA Burkhard et al., Angew. Chem. Int. Ed. 2010, 49, 9052). The purpose of the work presented herein is to synthesize novel cross-linked polyoxetane hydrogel and investigate its potential for drug delivery.

Methods: Synthesis. As illustrated in Scheme 1, 3-Ethyl 3-(hydroxymethyl) oxetane is modified with 1,4-dibromobutane and coupled with polyethylene glycol (Mn=1500 gmol⁻¹) via its terminal hydroxyl groups. Following acetylation, a cross-linked polyoxetane hydrogel network forms in the presence of boron trifluoride diethyl etherate. The obtained hydrogel was then washed and dried.

Characterization: ¹H NMR was used to characterize structure of intermediates and polyoxetane. SEM was applied to examine morphology of the network. TGA and DSC were applied to examine thermal properties of the hydrogel. Polyoxetane hydrogel swelling and degradation behaviors were examined in pH 7.4 PBS at 37ºC. FITC-dextran was used as a model compound, and its in vitro release from the hydrogel was studied.

Results: We had success synthesizing PEG bisoxetane macromonomer (Fig. 1). To avoid undesired reaction of free hydroxyl groups with Lewis acid during ring opening polymerization, unmodified hydroxyls were acetylated. PEG bisoxetane then undergoes ring-opening polymerization to form a hydrogel network. The TGA thermogram (not shown) shows that the hydrogel (dehydrated) begins to degrade at 233ºC. DSC data shows that melting temperature (Tm) of the cross-linked polymer is 5 ºC higher than that of the macromonomer. But its crystallization temperature is 1 ºC lower than that of the macromonomer (Fig. 2).

Fig. 1. ¹H-NMR spectrum of PEG bisoxetane.

FITC-dextran was slowly released over a period of 24 h (Fig. 3). Cross-linked polyoxetane has improved cytocompatibility at high concentrations (Fig. 4).

Fig. 3. FITC-dextran release.

Conclusions: We successfully synthesized and characterized novel polyoxetane hydrogel and assessed its potential for drug delivery. Our future work will be oriented toward wound dressing development based on this novel hydrogel.