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# Poly(ethylene glycol)-grafted cyclic acetals based polymer networks with non-water-swellable, biodegradable and surface hydrophilic properties

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ABSTRACT

Cyclic acetals based biomaterial without acidic products during hydrolytic degradation is a promising candidate for tissue engineering applications; however, low hydrophilicity is still one limitation for its biomedical application. In this work, we aim to achieve non-water-swellable cyclic acetal networks with improved hydrophilicity and surface wettability by copolymerization of cyclic acetal units based monomer, 5-ethyl-5-(hydroxymethyl)-β,β-dimethyl-1, 3-dioxane-2-ethanol diacrylate (EHD) and methoxy poly(ethylene glycol) monoacrylate (mPEGA) under UV irradiation, to avoid swelling of conventional hydrogels which could limit their applicability in particular of the mechanical properties and geometry integrity. Various EHD/mPEGA networks were fabricated with different concentrations of mPEGA from 0 to 30%, and the results showed photopolymerization behavior, mechanical property and thermal stability could not be significantly affected by addition of mPEGA, while the surface hydrophilicity was dramatically improved with the increase of mPEGA and could achieve a water contact angle of 37° with 30% mPEGA concentration. The obtained EHD/mPEGA network had comparative degradation rate to the PECA hydrogels reported previously, and MTT assay indicated it was biocompatible to L929 cells.


## 1. Introduction

Synthetic hydrolytically degradable polymers have been remarkable developed in the application of biomedical and tissue engineering applications [1–2]. Among these polymers, cyclic acetals based polymer network is a promising candidate for tissue engineering applications because it has good biocompatibility, reproducibility, control over physical properties and hydrolytic degradability [3–8]. The most advantage of cyclic acetals based biomaterials compared with other wildly used synthetic biopolymer polyesters is in terms of the hydrolytically degradation products. Polyesters including poly(lactic acid) (PLA), poly(glycolic acid) (PGA), poly(lactic-co-glycolic acid) (PLGA), poly(propylene fumarate) (PPF), and poly(caprolactone) (PCL) always give rise to largely acidic products during hydrolytic degradation [9–13], while cyclic acetals based polymers can be hydrolytically degraded with products terminated with diol and carbonyl end groups containing 2-ethyl-2-(hydroxymethyl)-propane-1,3-diol and 2,2-dimethyl-3-hydroxypropanal [7], thus reducing the inflammatory response of tissues and avoiding self-accelerated degradation of the material.

In order to adjust cyclic acetals based biomaterials to achieve a wide range of tunable bulk and surface properties, many researchers have done efforts through copolymerization or blending cyclic acetal monomers with other oligomers or small molecules. In our previous study, we have developed cyclic acetals/hydroxyapatite composites through in-situ dispersed photopolymerization to improve the bioactivity and mechanical property of cyclic acetals based biomaterials [14]. However, low hydrophilicity is still one limitation for cyclic acetals based polymer network in its application owing to the wettability of medical devices is critical for allowing surrounding body fluids to penetrate and supply nutrients to cells and tissue that grow inside. Copolymerization of cyclic acetal monomer and poly(ethylene glycol) diacrylate (PEGDA) or combination of cyclic acetal unit and poly(ethylene glycol) (PEG) unit into one oligomer has been investigated with some success on forming cyclic acetals based hydrogels with improved hydrophilicity [15,16].

Instead of creating traditional hydrogels, we presently aim to achieve non-water-swellable cyclic acetal networks with improved hydrophilicity and surface wettability. Non-water-swellable gel networks with good hydrophilicity are a newly emerged concept and have not been widely developed [17,18]. Swelling of conventional hydrogels as a result of the difference in osmotic pressure may limit their applicability in particular of the mechanical properties and geometry integrity [19,20]. However, when non-water-swellable gel networks are used

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for surgical implantation, there will be no distortion of the implant shape or change in its designed dimensions which results from swelling.

Hence, in order to achieve non-water-swellable cyclic acetal networks with improved hydrophilicity and surface wettability, PEG chains with a double bond at one end were tethered both on surface and inside of cyclic acetal networks as pendent chains by photopolymerization of cyclic acetal monomer 5-ethyl-5-(hydroxymethyl)-β,β-dimethyl-1, 3-dioxane-2-ethanol diacrylate (EHD) and methoxy PEG monoacrylate (mPEGA) (see Scheme 1). Various EHD/mPEGA networks were fabricated with different concentrations of mPEGA, and the photopolymerization behavior, mechanical property, thermal stability, surface hydrophilicity, swelling ability, hydrolytic degradation and biocompatibility of the obtained networks were investigated.

## 2. Experiment

### 2.1. Materials

Methoxy poly(ethylene glycol) monoacrylate (mPEGA) (Mn = 375 Da) was purchased from Aladdin Industrial Inc. (Shanghai, China). 2-Hydroxy-[4-(2-hydroxyethoxy) phenyl]-2-hydroxy-2-methyl-propan-1-one (Irgacure 2959) was offered by Ciba-Geigy Chemical Co. (Switzerland). MTT (3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide) was supplied by Sigma-Aldrich (USA). Other reagents were all obtained from Shanghai Runjie Chemical Agent Co. (Shanghai, China) and used as received.

### 2.2. Synthesis and characterization of EHD

Cyclic acetal monomer 5-ethyl-5-(hydroxymethyl)-β, β-dimethyl-1, 3-dioxane-2-ethanol diacrylate (EHD) was synthesized according to the previous literatures [14,16]. Briefly, 5-ethyl-5-(hydroxymethyl)-β, β-dimethyl-1, 3-dioxane-2-ethanol (EHE) was first synthesized by aldolization reaction, and then EHD was obtained by the reaction of EHE with acryloyl chloride. Detailed synthesis procedures and structure characterization of EHE and EHD could be found in our previous work [14].

### 2.3. EHD/mPEGA network fabrication by photopolymerization

A monomer mixture of EHD/mPEGA with different contents (by mass) of mPEGA (5%, 10%, 20% and 30%) were prepared before polymerization, followed by dissolving photoinitiator 2959 (1% by mass) in all samples. Photopolymerization of samples occurred under UV irradiation of 365 nm (Omni-cure Series 1000, EFOS company, Canada) with an irradiation intensity of 50 mW/cm$^2$ for 15 min in a mold made from glass slides and spacers with 15 ± 1 mm in diameter and 1.2 ± 0.1 mm in thickness. After curing, the obtained crosslinked samples were soaked in acetone for three days with at least three times of changing the medium to remove the unreacted monomers and completely dried in vacuum for further characterizations.

### 2.4. Characterization of EHD/mPEGA networks

#### 2.4.1. FTIR

To investigate the chemical composition, FTIR spectra of the EHD/mPEGA networks and EHD, mPEGA monomers were obtained using a Nicolet iS 5 Fourier transform infrared spectrometer (Thermo Fisher Scientific Inc.). Sample was prepared as KBr pellet and scanned against a blank KBr pellet background at wavenumber ranging from 4000 to 650 cm$^{-1}$ with resolution of 4.0 cm$^{-1}$.

The double bond conversion of samples was monitored by real-time FTIR to test the photopolymerization behavior of EHD/mPEGA networks. The samples in a mold made from glass slides and spacers with 15 ± 1 mm in diameter and 1.2 ± 0.1 mm in thickness were placed in the compartment of an IR spectrometer (7000–4000 cm$^{-1}$) and were simultaneously exposed to a UV-light source and an IR analyzing light beam. The absorbance change of the ═C—H peak area from 6094.90 to 6174.50 cm$^{-1}$ was correlated to the extent of polymerization. The degree of conversion, DC, can be expressed by the following relation [21,22]:

$$DC\% = (A_0 - A_t) \times 100/A_0 \quad (1)$$

where $A_0$ is the initial peak area before irradiation, and $A_t$ is the peak area of the double bonds at t time. All of the peak areas are measured by the peak area tool from the software OMNIC.

#### 2.4.2. NMR

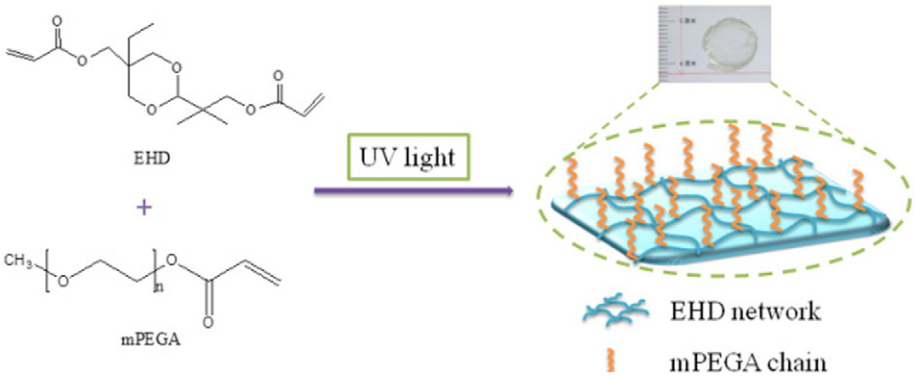
The chemical structure of EHD/mPEGA networks with different mPEGA content was confirmed by solid state $^{13}$C nuclear magnetic resonance (NMR) with a BrukerAV600 unity spectrometer operated at 600 MHz. The structure of monomer EHD and mPEGA was also evaluated by $^{13}$C NMR with $CDCl_3$ as solvent and tetramethysilane (TMS) as the internal standard.

#### 2.4.3. DMA

The tensile storage modulus of dry samples (n = 3) were determined on a V DMTA (Rheometyic of Scientific Inc.). Specimens (2 mm × 7 mm × 30 mm) were cut with a parallel blade cutter and loaded onto a film tension fixture with a grip separation of 10 mm, with a heating rate of 5 °C/min from room temperature to 300 °C. The number of crosslink moles per volume unit (n) can also be determined from DMA experiments in the rubbery zone using the following equation [23,24]:

$$n = E\prime/(3RT) \quad (2)$$

where R, T and E represent the perfect gas constant (8.314 J mol$^{-1}$ K$^{-1}$), the temperature (Tg + 50 K) and elastic modulus (Pa), respectively.




**Scheme 1.** Schematic route for preparation of EHD/mPEGA networks.