

Facile preparation of photodegradable hydrogel by photo-mediated crosslinking

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Statement of Purpose: Photodegradable hydrogels have received significant attention in recent years and have been used to control matrix stiffness and availability of matrix-tethered biomolecules in a spatial-temporally controlled manner.^[1,2] Current methods for fabricating photodegradable hydrogels are restricted to non-photochemistries, including redox reactions, emulsion polymerizations, Michael-type addition reactions, or orthogonal click chemistry.^[1,2] Here, we present a visible light-mediated thiol-ene photopolymerization scheme to synthesize UV light-sensitive photodegradable hydrogels (Figure 1A). Multi-arm poly(ethylene glycol)-norbornene (PEG-NB) and *bis*-cysteine peptide containing a nitrophenylalanine (NPA) moiety were crosslinked by visible light ($\lambda > 400$ nm) exposure using eosin-Y as the only photoinitiator.^[3] Photodegradation of these photopolymerized hydrogels was achieved via flood UV irradiation.

Methods: A *bis*-cysteine peptide (Ac-CGOGC-NH₂) containing 2-nitrophenylalanine (2-NPA: O) was synthesized by microwave-assisted solid phase peptide synthesis. Photolysis of the peptide under UV light (365 nm) exposure was characterized by analytical RP-HPLC. For hydrogel fabrication, multi-arm (4 or 8 arms) PEG-NB and Ac-CGOGC-NH₂ were dissolved in PBS with photoinitiator (eosin-Y or lithium arylphosphanate (LAP)) and the solution was exposed to visible light (400-700 nm) for 4 minutes. Visible light-mediated gelation was monitored by *in situ* photo-rheometry while photodegradation was evaluated by mass loss of the photodegradable hydrogels under UV light (302 or 365 nm) exposure.

Results: UV/Vis spectrum of photolabile Ac-CGOGC-NH₂ peptide showed that this peptide has strong absorbance in the UV range ($\lambda < 400$ nm) but not visible light region (400-700 nm). Specifically, the molar absorptivity of this photolabile peptide at 365 nm was approx. $950 \text{ M}^{-1}\text{cm}^{-1}$. Upon UV light irradiation, the peptide was photolyzed in a light dosage-dependent manner. Visible light-mediated gelation was achieved with multi-arm PEG-NB and photoinitiator (0.1 mM eosin-Y or 1 mM LAP). When eosin-Y was used as the photoinitiator, the gelation was much faster compared to using LAP (Figure 1B). To evaluate the photodegradability of these photopolymerized hydrogels, disc-shaped gels (1 mm thickness) were exposed to UV light at different wavelengths and intensities. The color of gel changed from transparent to yellowish after UV light exposure (Figure 2A), likely due to the newly formed aromatic cinnoline group in the degradation products. Gel mass decreased monotonically as a function of light exposure time, indicating a surface erosion mechanism in these step-growth hydrogels (Figure 2B). Further, the photodegradation rates were faster under higher UV light intensity or lower wavelength (Figure 2B).

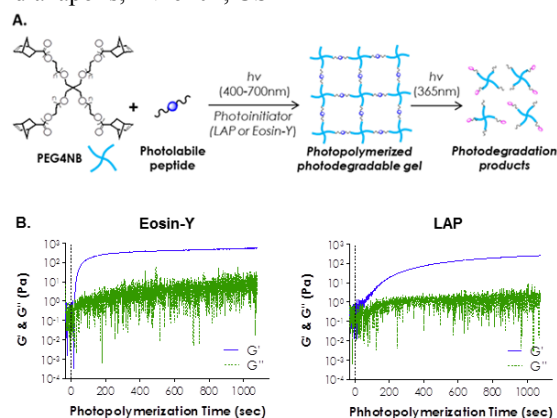


Figure 1. (A) Schematic of photocrosslinking and photodegradation of step-growth thiol-ene hydrogels. (B) Evolution of shear (G') and loss (G'') moduli during visible light-mediated photopolymerization of photodegradable PEG4NB (5 wt%) hydrogels crosslinked by CGOGC using 0.1 mM eosin-Y or 1 mM LAP as the photoinitiator.

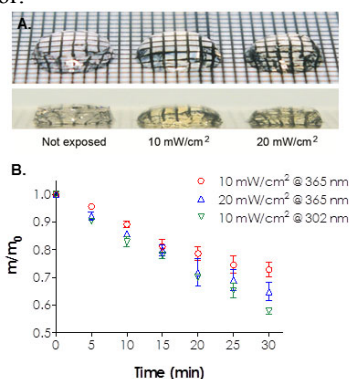


Figure 2. (A) Photographs of photodegraded hydrogels (8 wt% of 4 arm-PEG-NB crosslinked by CGOGC). The hydrogels were exposed to UV light (365 nm) of different intensities for 30 min. Grid length is 1 mm. (B) Effect of UV lights wavelength and intensity on mass loss of photodegradable hydrogels.

Conclusions: We have shown that photodegradable hydrogels could be prepared through highly efficient visible light-mediated thiol-ene photopolymerization. This system provides a convenient way to fabricate photodegradable hydrogels without using cytotoxic compounds or tedious chemical process. These photopolymerized and photodegradable hydrogels are promising materials for dynamically controlling matrix properties in drug delivery and tissue engineering applications.

References: [1] Kloxin AM, Kasko AM, Salinas CN, Anseth KS. *Science*. 2009;324:59-63. [2] Deforest CA, Anseth KS. *Nat Chem*. 2011;3:925-31. [3] Shih H, Lin CC. *Macromol Rapid Comm*. 2012;DOI: 10.1002/marc.20120 0605.