pH-Responsive Self-Healing Hydrogels Formed by Boronate-Catechol Complexation

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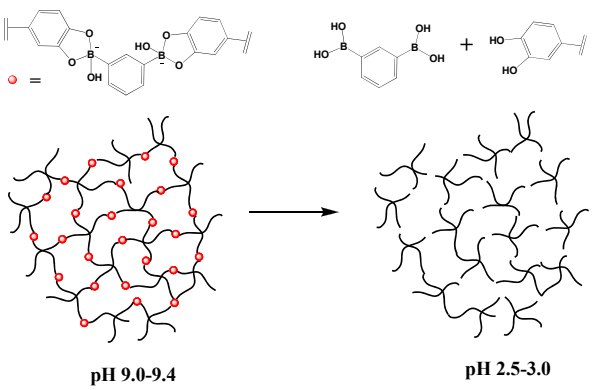
Introduction. Hydrogels are three dimensional networks of hydrophilic polymers, cross-linked via covalent or noncovalent interactions[1]. Recently, efforts have focused on stimuli-responsive hydrogels capable of pH and temperature or light induced modulation of properties[2].

Complexes of certain diols with boronic acid exhibit reversible pH-dependent behavior in aqueous solution. Inspired by mussel adhesive proteins with high catechol content, we have prepared a crosslinked polymeric hydrogel through complexation of 4-arm PEG catechol with 1,3-benzenediboronic acid (Scheme 1). The resulting polymer hydrogel exhibits pH responsive behavior.

Materials and Methods. 4-arm PEG amine (10kDa) and monofunctional PEG amine (MeO-PEG amine, 5kDa) were purchased from Laysan Bio Inc. 3-(3,4-dihydroxyphenyl) propionic acid (DHPA; Alfa Aesar, 98%) and other chemicals were used as received. 4-arm PEG catechol and MeO-PEG catechol were synthesized by a protocol similar to a previous report[3]. Hydrogels were prepared by mixing a PBS buffer solution of 4-arm PEG catechol and 1,3-benzenediboronic acid at different catechol to boronic acid molar ratios. Solutions were vigorously stirred at 20 ^{o}C, resulting in red viscous hydrogels within 30 min.

Results. As shown in Scheme 1, under basic aqueous conditions 1,3-benzenediboronic acid forms a tetrahedral borate ester with catechol endgroups of 4-arm PEG catechol, giving rise to a three dimensional polymeric network and gel formation. Model uv-vis studies using linear PEG-catechol with 1,3-benzenediboronic acid revealed a large absorption peak at 490 nm resulting from covalent borate ester formation (Figure 1A), which was distinct from absorption correlated to catechol oxidation (330 nm peak). The 490 nm peak disappeared upon reduction of the solution pH to 3.0, indicating dissociation of the borate ester bond. Figure 1B and 1C show the hydrogel formed in this way and its transition to a liquid solution after adjusting the pH to 3.0 using HCl. A more gradual gel-sol transition was observed at neutral pH. The gel to sol transition is accompanied by a color change from red to yellow, corresponding to a change in chemical state of the catechol in the system attributed to dissociation of the borate-catechol complex. Using similar stoichiometry of borate and catechol, hydrogels were observed to form at polymer concentration between 5-15wt%. Polymer hydrogels formed in this way are sticky to the touch, which is likely due to the viscoelastic nature of the gels and to the adhesive nature of the catechol.

It is interesting that polymer gels aring from borate-catechol complexation possess self-healing ability. Two pieces of fractured gel fragments can merge autonomously into a single piece instantly by simply bring them into contact. This self-healing property is repeatable and likely attributed to the dynamic nature of the reversible complexation between 1,3-benzenediboronic acid and catechol.



Scheme 1: Schematic illustration of pH-responsive hydrogel based on 4-arm PEG-catechol and 1, 3-benzenediboronic acid in aqueous solution at 20 ^{o}C

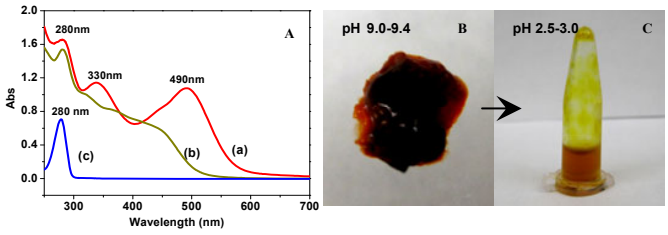


Figure 1. (A) Uv-vis spectra of MeO-PEG catechol/1, 3-benzenediboronic acid at (a) pH 9.0, (b) 3.0 and (c) MeO-PEG catechol at pH of 7.4. (B) Hydrogel formed from 4-arm PEG catechol and 1, 3-benzenediboronic acid at pH 9.0-9.4 and with molar ratio of 1:8, and (C) sols produced after hydrogel pH lowered (2.5-3.0). Polymer concentration in figure is 7.5wt%.

Conclusions: Novel pH-responsive and self-healing hydrogels were produced by complexation of 4-arm PEG catechol and 1, 3-diboronic acid in water at alkaline pH. These covalently cross-linked hydrogels were mechanically robust, but disassociate at neutral or acidic pH due to dissociation of the borate-catechol complex. These hydrogels exhibited self-healing properties which may be useful property for tissue repair and reconstruction.

References:

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