Degradation of polyester-based hydrogels prepared by click chemistry:
The role of residual Cu(II) catalyzed hydrolysis

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The hydrolytic degradation of polyesters gels in aqueous media, for example polylactide and lactide copolymers, is known to be affected by two main parameters; namely the kinetics of hydrolysis of the ester bonds within the hydrogel network, and the physical structure of the gel. Both parameters control the process of network degradation.

The rate of ester hydrolysis may also be accelerated by increasing the hydrophilicity of the polymer network through the incorporation of a hydrophilic polymer, such as poly(ethylene glycol), in the back bone. Another factor that can moderate the rate of ester hydrolysis is activation of the reaction via coordination of a metal ion to the ester carbonyl group. Since the mid-1980s, hydrolysis of carboxylic and phosphoric esters has been extensively studied in the presence of metalloenzymes designed to mimic the macrocyclic metalloenzyme complexes found in biological systems.2 The function of the transition metal ions in these metalloenzymes is to serve as a template between the substrate and the nucleophile, as well as to activate the chemically-labile bonds of the substrate and the nucleophile. The metal ions that have been investigated as biomimetic models include3, Cu2+, Co2+, Ni2+ and Zn2+

In this study, a Cu(I)-catalyzed click reaction was chosen to prepare hyperbranched copolymers based on the commercially-available Boltorn™ H20 (BH20) (Fig.1). The chain ends of the copolymer were acrylated followed by crosslinking via free radical polymerization to fabricate biodegradable, ester-containing hydrogels.

For the first time since the discovery of the Cu(I)-catalyzed click reaction, we have been able to show the presence of complexed Cu(II) residues in polymerized gels and that Cu(II) can play an important role in the hydrolytic degradation of polyester-based gels. The change in morphology of the hydrogel due to degradation catalyzed by the coordinated Cu(II) is a critical piece of information elucidated by the cryoSEM and EPR spectroscopic studies. Furthermore, comparative cryoSEM studies of the hydrolysis of the gels either undoped or doped with additional copper revealed that the presence of complexed Cu(II) species contributed to the formation of pits in the pore walls of the hydrogel network (see Fig.2 B), which leads to acceleration of the degradation. The observation of metal-catalyzed hydrolysis of the gel esters has profound implications for the polymer stability. For example, the presence of complexed Cu(II) ions in the surrounding environment, intrinsically or extrinsically, can potentially cause rapid degradation of ester-based polymers. Further to that, this work provides a new insight into the utility of the Cu(I)-catalyzed click reaction in the preparation of hydrolyzable biomaterials.


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