

Title	ドラッグデリバリー応用を目指したマイケル付加酸化デキストランハイドロゲルの分解性制御
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## *Abstract*

Previously the biomedical application of polysaccharide hydrogel that was derived from aldehyde-introduced dextran by periodate oxidation and polyamine was reported and the hydrogels showed rapid degradation through main chain scission in the oxidized dextran which was triggered by Schiff base formation with amine and subsequent Maillard reaction [1, 2]. However, the formation and degradation of this hydrogel was simultaneously occurred after multiple Schiff base formation reaction between aldehyde and amino groups, therefore the degradation timing control was difficult [1, 3]. To overcome this uncontrollable degradation of the hydrogel, the oxidized glycidyl methacrylate derivatized dextran (Dex-GMA)-based hydrogel formed via thiol-en cross-linking by Michael addition without using aldehyde group was prepared. The prepared hydrogel was stable in phosphate buffer solution (PBS) but degradation could be initiated by addition of amino compounds by causing Maillard reaction. These findings indicate that the degradation of hydrogel can be controlled by the amino group addition. In addition, the degradation speed of oxidized Dex-GMA-based hydrogel was also controlled independently of mechanical properties because the crosslinking points and degradation points are different. And by kinetic analysis with NMR measurement, molecular mechanism behind the crosslinking between thiol and aldehyde groups was observed to explain control of the degradation of dextran derivatives. To lead this hydrogel to a smart material, the release of amino source should be controlled for further controlling the degradation of hydrogel. In this part, amino compounds were functionalized on carrageenan chain (amino-CG) to act as dual-functioned material of being amino source and showing temperature-responsive behavior. The polydopamine microspheres (PDA), which is an NIR photothermal agent, were composited with carrageenan derivative (amino-CG@PDA micromposite). The role of PDA is to convert NIR light to energy and then to transform it to heat. The amino-CG@PDA beads are sensitive to the temperature change, finding that the amino compounds were released at 40 °C via gel-to-sol phase

transition but dissolution of beads were not observed at 37 °C. The release of amino groups from the phase transition of amino-CG@PDA microcomposites was enhanced by increasing temperature and more greatly under external NIR light. Thus, the release rate of amino compounds can be controlled by switching NIR-light irradiation. In addition, the degradation of oxidized Dex-GMA by amino groups release from amino-CG@PDA was investigated. The amino-CG provides the ability to be the amino source for the reaction with aldehyde groups from oxidized Dex-GMA to introduce the main chain degradation. The release of doxorubicin (DOX) from oxidized Dex-GMA-based hydrogel was controlled under NIR irradiation due to the Schiff base reaction of amino compound release from amino-CG and the preserved aldehyde on hydrogel, consequently, the degradation occurred and drug can be released. Thus, this work presents an alternative way for controlling the degradation of hydrogel to potentialize in clinical applications for cell scaffolds in regenerative medicine and drug delivery system carriers.

**Keywords:** hydrogel, biodegradation, aldehyde dextran, NIR irradiation, drug delivery

## References

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