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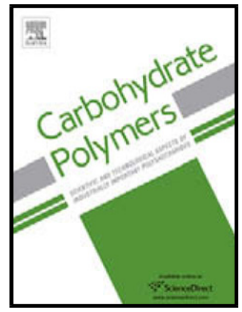

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Strengthening injectable thermo-sensitive NIPAAm-*g*-chitosan hydrogels using chemical cross-linking of disulfide bonds as scaffolds for tissue engineering

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Research highlights:

- N-acetyl cysteine covalently conjugated with NIPAAm-g-chitosan hydrogel for thiols modification successfully.
- With disulfide bonds cross-linking strategies, rheological and mechanical properties of synthesized hydrogels were significantly improved.
- The physical characteristics of thermo-sensitive hydrogels such as swelling equilibrium, micro-appearance and LCST were tunable with thiol modification.
- Thiol-modified NIPAAm-g-chitosan hydrogels maintained their biocompatibility without cytotoxicity in mesenchymal stem cells, fibroblasts, and osteoblasts.

Abstract

In the present study, we fabricated non-toxic, injectable, and thermo-sensitive NIPAAm-*g*-chitosan (NC) hydrogels with thiol modification for introduction of disulfide cross-linking strategy. Previously, NIPAAm and chitosan copolymer has been proven to have excellent biocompatibility, biodegradability and rapid phase transition after injection, suitable to serve as cell carriers or implanted scaffolds. However, weak mechanical properties significantly limit their potential for biomedical fields. In order to overcome this issue, we incorporated thiol side chains into chitosan by covalently conjugating N-acetyl-cysteine (NAC) with carbodiimide chemistry to strengthen mechanical properties. After oxidation of thiols into disulfide bonds, modified NC hydrogels did improve the compressive modulus over 9 folds (11.4kPa). Oscillatory frequency sweep showed the positive correlation between storage modulus and cross-liking density as well. Additionally, there was no cytotoxicity observed to mesenchymal stem cells, fibroblasts and osteoblasts. We suggested that the thiol-modified thermo-sensitive polysaccharide hydrogels are promising to be a cell-laden biomaterial for tissue regeneration.