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Ion-Assisted Fabrication of Neutral Protein Crosslinked Sodium Alginate Nanogels

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Highlights

- Oxidized sodium alginate could reversibly form nanogels *via* ion-crosslinking.
- Neutral protein crosslinked alginate nanogels were obtained in ion-assisted method.
- The nanogels displayed good biocompatibility and maintained their bioactivities.

ABSTRACT: Protein crosslinked nanogels which combine the merits of nanogels and the specific biological activity from protein have emerged as fascinating protein delivery systems. However, the fragility and low density of reactive group in proteins, especially low electric density of neutral proteins seriously limited the fabrication of protein crosslinked nanogels without affecting their bioactivities. Here, we demonstrated a facile ion-assisted method to fabricate neutral protein crosslinked nanogels. Oxidized sodium alginate (OSA) with aldehyde groups and low viscosity was successfully synthesized, which could reversibly form nanogels *via* addition and removal of divalent cation. Subsequently, hemoglobin and myoglobin were used as representative neutral proteins to fabricate stable protein crosslinked OSA nanogels under the assist of divalent cation followed by *in situ* Schiff base formation between OSA and proteins. The mild fabrication condition guaranteed the structural integrity and bioactivity of proteins in the obtained protein crosslinked nanogels. This ion-assisted method was expected to bring a new opportunity for fabricating versatile functional biohybrid nanogels systems.

KEYWORDS: Neutral protein; Nanogels; Sodium alginate; Ion-assisted method; Bioactivity

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