Synopsis of Original Research Paper

Preparation of Collagen-Mimic Compounds Capable of Controlled Release

Chie Kojima

Nanoscience and Nanotechnology Research Center, Research Organization for the 21st Century, Osaka Prefecture University

Collagen is the most abundant protein in mammals, and it is composed of glycine-proline-(hydroxy)proline (Gly-Pro-Pro(Hyp)) repeats to form a triple helix. It has been used as a biomaterial. For example, collagen gels are useful for long-term slow release in drug delivery applications. However, the release from collagen gels is generally uncontrollable. Therefore, functional collagen materials capable of controlled release are desired. Artificial collagen materials have been studied as an alternative to natural collagens extracted from animals, because natural collagens can be contaminated with infectious pathogens and allergens. However, short collagen peptides cannot form a triple helix, which limits the preparation. Dendrimers have highly controllable sizes, topologies and surface properties, quite different from linear polymers. We have reported that polyethylene glycol (PEG)-attached dendrimers are a potential drug carrier. In addition, dendrimers were used as a knot, whose terminal groups were modified with collagen model peptides to induce the triple helical structures.

In this study, a collagen model peptide ((Pro-Pro-Gly)$_5$)-attached dendrimer was synthesized as a potential functional collagen material. The peptides which clustered at the surface of the dendrimer formed a collagen-like triple helix. Interestingly, the helical structures were thermally reversible, different from a natural collagen. For the biomedical applications, the thermal stability of the triple helical structure in the collagen-mimic dendrimer remains to be improved. Various collagen-mimic dendrimers were prepared by using different generation dendrimers and a longer collagen model peptide, (Pro-Pro-Gly)$_{10}$. The peptide length much affected the triple helical structures, but the dendrimer generation did not. The peptide binding ratio slightly affected it. These results suggest that the peptide length and the peptide density were influenced on the triple helix formation. Interestingly, the (Pro-Pro-Gly)$_{10}$-modified dendrimer assembled below 40°C and the assembly was dissolved by heating. On the other hand, the (Pro-Pro-Gly)$_5$-modified dendrimer did not. The hydrogels using these collagen-mimic dendrimers were prepared. Even though the (Pro-Pro-Gly)$_5$-modified dendrimers formed the hydrogels by cooling only in the presence of ethanol and sodium sulfate, the (Pro-Pro-Gly)$_{10}$-modified dendrimer could in the absence of any additives. In addition, the hydrogel was dissolved at 45°C. Therefore, this kind of collagen-mimic material is useful for drug delivery system and regenerative medicine.