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Precise Synthesis and Study on the Structure and the Biocompatibility of PEG Based Triblock Copolymers

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1. Introduction

Polymer materials have been applied to living body for various clinical purposes. They usually invoke foreign body reactions or impede the replacement by regenerated tissue during normal healing process when they are implanted in the human body during a long period of time. Biodegradable polymer, such as poly lactide or poly glycoride has also been used clinically. Their crystallinity is so high that it is unsuitable to apply them to the soft tissues because of their difference in compliance. It would be clinically significant if copolymerization with poly(ethylene glycol) (PEG) and polypeptide can solve these problems.

2. Results and Discussions

ABA triblock copolymers bearing poly(β-benzyl L-aspartate) PBLA segments adjacent to the both terminus of middle PEG segment were precisely synthesized by ring-opening polymerization of β-benzyl L-aspartate N-caroboxy anhydride. They presented mono-disperse molecular weight distribution, and self-assembled by casting from dichloromethane solution to make a flexible and elastic films in spite of their low molecular weight. It was revealed that these copolymers bearing α-helix- 7/2- helix- α- helix conformation were microphase separated to form a hierarchical structure that helped strength and flexibility. Formation of β-sheet was observed in PBLA segment worked a physical cross-link after thermal treatment. These observations seemed to be due to decreasing crystallinity and increasing interchain interactions.

These ABA copolymers rapidly swelled to yield soft and robust hydrogel. Swelling ratio and contents of water was capable to be manipulated by controlling PBLA content. It was observed that β-sheet appeared within PBLA chain region in hydrogels, which may enhance intermolecular interaction with PBLA block segments. Interchain β-sheet hydrogen bonding within the framework supports mechanical toughness in hydrogel. Structural model of these hydrogel was proposed. In comparison with conventional hydrogels, their surfaces were hydrophobic; it may be because nano meter level of PBLA rich layer exists beneath the surface.

Cellular adhesion and morphology of the cells were observed in order to preestimate interactions between polymer and macrophage, which is generally accepted to take participate in foreign body reaction against implants. Cell anchoring and spreading were controlled by polymerization degree of PBLA segment that provide flame-work in hydrogels. By monitoring of several gene expressions, signaling related to inflammation and cell motility were also affected by the composition of PBLA segments.

It also became clear that these polymers exhibited good compliance to the adjacent tissues and the foreign body reaction was also reduced from implantation into living animals. It was also observed that these polymers were resorbable to be excreted from peritonea to urine through glomerular filtrate. From the uterine horn adhesion model experiment, these copolymer hydrogels reduced the severity of adhesion so that these are expected to be barriers for post-operational adhesion.

3. Conclusions

This thesis deals with the synthesis, formation, and biological properties of copolymer hydrogels from PBLA and PEG. 1) Precisely synthesized polymers self-organized to be stable hydrogels in water. 2) Structural stability of hydrogels were attributed to β-sheet formation depending on thermal treatment and hydration in water 3) Biocompatible hydrogels were attained by *in vitro* assay with macrophages. 4) These hydrogels indicated good biocompatibility and restorability in animal tissues, which prevented post-operational adhesion *in vivo*.

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