BIOCOMPATIBLE PHOSPHOLIPID POLYMER HYDROGEL PREVENTS TENDON ADHESION WITHOUT IMPAIRING THE HEALING

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INTRODUCTION

Adhesion is an unavoidable problem in the treatment of tendon injury of the hand. Despite many studies for its prevention, there is yet no definite solution. Considering that synovial membrane is known to prevent tendon adhesion, we hypothesized that a biocompatible and biodissociatable material could be a substitute for the membrane. 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer is an original biocompatible polymer whose side chain is composed of phosphorylcholine that resembles phospholipids of biomembrane [1]. The MPC hydrogel can be generated by mixing aqueous solutions of poly (MPC-*co*-methacrylic acid) (PMA) and poly (MPC-*co*-*n*-butyl methacrylate) (PMB) [2] (Fig.1). The present study investigated the effects of the MPC-hydrogel application on tendon adhesion and healing. We also sought to learn whether the dissociation speed of MPC hydrogel is controllable by changing the concentration of ferric iron ions (Fe^{3+}).

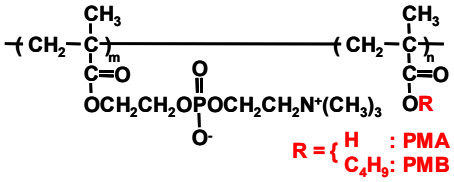

Fig. 1: Chemical structure of PMA and PMB.

METHODS

(1) The ability of MPC hydrogel to prevent cell adhesion was investigated using cultured mouse fibroblastic cell line NIH3T3. The cells were cultured for 6-36 h on dishes with or without the MPC-hydrogel coating, and cell adhesion was evaluated microscopically.
(2) To evaluate the dissociation of MPC hydrogel *in vivo*, chambers containing the MPC hydrogel with Fe^{3+} (0, 0.07, or 0.14 M) were subcutaneously implanted in rats. Macroscopic and scanning electron microscopic (SEM) observations were performed after one and three weeks.
(3) The ability of MPC hydrogel to prevent tendon adhesion was determined using the rabbit tendon injury model. After the FDP tendon was cut at Zone 2 and repaired by a cruciate suture, the hydrogel was applied to cover the injury site and the wound was closed. After three weeks of external fixation by casting, tendon healing and adhesion were evaluated by microscopic and histological observations. This study was approved by our institutional review board.

RESULTS

(1) The NIH3T3 cells adhered to a non-coated plastic dish after the seeding and proliferated during the culture up to confluence; however, the MPC hydrogel markedly inhibited the adhesion so that no cell remained after 36 h.
(2) The MPC hydrogel without Fe^{3+} dissociated to PMA and PMB within one week, while that with Fe^{3+} remained undissociated in a dose-dependent manner for three weeks, indicating that the dissociation speed of the hydrogel was controllable by changing the concentration of Fe^{3+}. The SEM image showed that MPC hydrogel with 0.14 M Fe^{3+} maintained a honeycomb structure even after three weeks (Fig.2).
(3) In the rabbit tendon injury model, the microscopic finding of the repaired tendon after three weeks showed severe adhesion in the control group, while little or no adhesion was observed in the MPC group (Fig.3). The histological findings by HE staining of the repaired tendon showed that the gap of the injured tendon in both groups was similarly filled with granulation and bridged by collagen fibers. These results indicate that MPC-hydrogel application immediately after the tendon suture efficiently prevents the adhesion without impairing the healing.

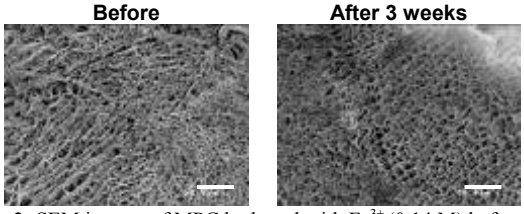

Fig. 2: SEM images of MPC hydrogel with Fe^{3+} (0.14 M) before and after 3 weeks of implantation (scale bars 20 μm).

Fig. 3: Microscopic findings of the repaired tendon after 3 weeks. Arrows indicate the adherent area.

DISCUSSION

Since MPC polymer provides a biomembrane-like surface, its application suppresses biological reactions such as foreign body reaction, cell adhesion, and protein adsorption. Some medical devices with MPC polymer have already been authorized by the Food and Drug Administration (FDA). In the orthopaedic field, we have reported that the surface grafting of the MPC on the polyethylene liner extended longevity of artificial hip joints by preventing aseptic loosening [3].

The dissociation speed of the MPC hydrogel was controllable by changing the concentration of Fe^{3+}. Because Fe^{3+} can interact with carboxylate anions in the PMA, the hydrogel is crosslinked via hydrogen bonding and electrostatic interaction. This result suggests that the local survival of the hydrogel can be controlled in clinical settings. MPC hydrogel has nano-scaled pores in a honeycomb structure, which may prevent the invasion of inflammatory cells but allow the access of cytokines and growth factors for tendon healing.

In conclusion, MPC hydrogel offers a safe and effective material to prevent adhesion during tendon repair without impairing the healing. Further studies on its clinical application are now underway.

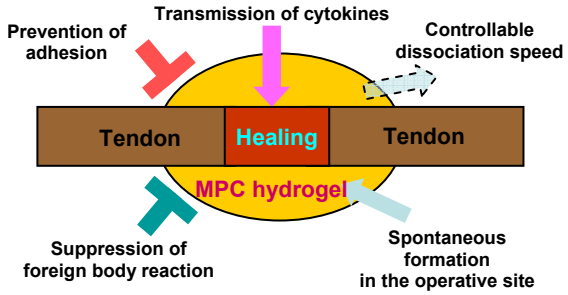

Fig. 4: Expected mechanisms of MPC hydrogel to prevent tendon adhesion.

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