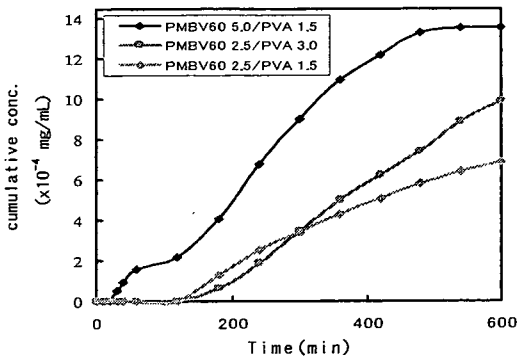

Fig. 6. Release profiles of PTX at the same location (middle in multilayer) from different polymer concentrations in PBS+0.1 % Tween 20

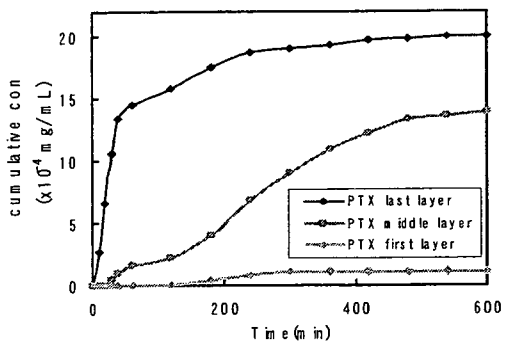

Fig. 7. Release profiles of PTX at different location from polymeric hydrogel multilayer of PMBV60(5.0 wt%) and PVA(1.5 wt%) in PBS+0.1 % Tween 20. Number of multilayer is the same as 6.

In device PMBV60(2.5 wt%)/PVA(3.0 wt%), the profile of releasing is linear, that is, the concentration of releasing PTX is constant. According to the polymer concentration, the release profile indicated various features.

To determine when the releasing time of PTX starts from the different location, three samples having different location of PTX in the PMBV60 layer were built up and the releasing experiments were performed. The 6 layered multilayer having PTX at difference location is indicated in Fig. 7. The PTX in the last layer (upper side) started releasing from 10 min. However, in case of middle layer, it was released from 30 min, whereas the PTX of the bottom of the multilayer started releasing from 180 min. It was confirmed that the location of layer with PTX allowed the difference of releasing timing. Through the observations made in this study, the thickness of layer is supposed to play an important role to control of the releasing timing of PTX.

4. CONCLUSION

The synthesis of water-soluble biocompatible phospholipid polymer(PMBV60) comprising MPC, BMA, and phenylboronic acid was achieved through a conventional radical polymerization. Moreover, the silanization allowed titanium surface to bond AWP containing azide group. The PMBV60 and PVA enabled to construct multilayer hydrogel system through boronate complex on the silanized titanium surface. Polymer hydrogel multilayer on the titanium was constructed conveniently and could load hydrophobic anticancer drug, PTX, in the hydrogel. As the locations of PTX layer in the polymer hydrogel multilayer changed, the releasing profile toward the time of PTX could be controlled. More detail works about the polymer multilayer hydrogel and the release of PTX are underway.

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BIODISSOCIATABLE PHOSPHOLIPID POLYMER HYDROGEL PREVENTS TENDON ADHESION WITHOUT IMPAIRING HEALING

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HYPOTHESIS: MPC-hydrogel, biodissociatable material that contains biocompatible 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer, can prevent peritendinous adhesion after tendon injury.

METHODS: Chicken FDP tendons were cut and repaired. Repaired site was covered by MPC-hydrogel. After 3 weeks of immobilization, tendon adhesion and healing were evaluated by macroscopic, histological and mechanical testings. Work of flexion, a method to measure tendon gliding, and tensile strength were measured by the mechanical test. The significant differences were determined by the Mann-Whitney U test.

RESULTS/STATISTICS: Macroscopic findings of the repaired tendons showed severe adhesion in the control group, while little or no adhesion was observed in the MPC group. The gel had been dissociated partially in the operative site (Fig.1). HE staining of the repaired tendons showed that gaps of the injured tendon in both groups were similarly filled with granulation and bridged by collagen fibers (Fig.2). In addition, the work of flexion of the MPC group was significantly less than that of the control group (Fig.3), and there was no significant difference on tensile strength between two groups (Fig.4).

SUMMARY POINTS:

1. The lines of results obtained in this study clearly demonstrate that MPC-hydrogel application after tendon suture efficiently prevents adhesion without impairing healing.
2. MPC-hydrogel can be prepared from a mixture of two MPC solutions immediately on an injured tendon, and dissociated to return the two solutions those are confirmed to be excellent at biocompatibility, respectively. In addition, the dissociation speed is controllable with ferric iron ions. As MPC-hydrogel has nano-scaled pores in a honeycomb structure, it may prevent invasion of inflammatory cells but allow transmission of cytokines and growth factors for tendon healing.
3. Since MPC provides a biomembrane-like surface, its application suppresses biological reactions. Some medical devices with MPC polymer, such as catheters and artificial lungs, have been authorized by the Food and Drug Administration.
4. Further studies on its clinical application are now underway.

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Biocompatible Anti-adhesion Effect of Biodissociated Phospholipid Polymer Hydrogel

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Introduction: Tissue adhesion is a severe complication in clinical treatments. It is hoped to create a novel biomaterial which does not impair tissue healing and effectively prevents tissue adhesion. Then we used 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer that is our original biocompatible polymer whose side chain is composed of phosphorylcholine that resembles phospholipids of biomembrane [1], and created an anti-adhesion material of spontaneous forming hydrogel from mixture of aqueous solutions of poly (MPC-*co*-*n*-butyl methacrylate-*co*-*p*-vinylphenylboronic acid) (PMBV) and poly (vinyl alcohol) (PVA) [2]. We designated the hydrogel "PMBV gel". The condition of PMBV gel is maintained by reversible covalent bonds between PMBV and PVA. The mechanical property and dissociation speed of the hydrogel are controllable by changing the concentration of the polymers. The present study investigated the effects of the PMBV-gel application on tendon healing and adhesion.

Materials and Methods: (1) The ability of PMBV gel 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 PMBV-gel coating, and cell adhesion was evaluated microscopically.

(2) To evaluate the dissociation of PMBV gel *in vivo*, chambers containing PMBV gel were subcutaneously implanted in rats. Macroscopic and scanning electron microscopy (SEM) observations were performed after one and three weeks.

(3) The ability of PMBV gel to prevent tendon adhesion was determined using a rabbit flexor tendon injury model. After a FDP tendon was cut at Zone 2 and repaired by a modified Kessler suture, the hydrogel was applied to cover the injury site and the wound was closed. After 3 weeks of external fixation by casting, tendon healing and adhesion were evaluated by microscopic, histological and mechanical observations. In the microscopic evaluation, we counted the number of fibrous adhesion tissue between the tendon and surround tissues, and observed the continuity between the tendon stumps. In addition, blood flow of the tendon injury site was observed by a laser blood flow meter. In the histological evaluation, we observed the tendon collagen fibers of the injury site and adhesion tissues. In the mechanical evaluation, we measured maximal tensile strength and work of flexion. 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, PMBV gel markedly inhibited the adhesion so that little no cell remained after 36 h (Fig. 1).

(2) PMBV gel partially remained undissociated for three weeks, partially dissociated to PMBV and PVA. The SEM image showed that PMBV gel maintained a honeycomb structure even after three weeks.

(3) In the rabbit flexor tendon injury model, the microscopic finding of the repaired tendons after 3 weeks showed the similar continuity of the tendons between the control group and the PMBV group. There was severe adhesion in the control group, while little or no adhesion was observed in the PMBV group (Fig.2 and 3). In addition, the blood flow at the tendon injury sites recovered similarly in both groups. The histological finding by HE staining of the repaired tendons showed that the gap of the tendon in both groups was similarly filled with granulation and bridged by collagen fibers. There was tenacious fibrous adhesion tissues in the control group, while little or no adhesion tissue in the PMBV group was observed. The mechanical findings presented no significant difference between the maximal tendon tensile strength (Fig.3) and significant difference between the work of flexion of both groups.

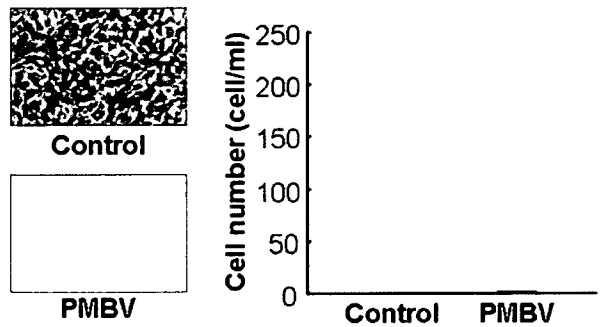

Fig. 1: Microscopic findings of the cell adhesion after 36 hours.

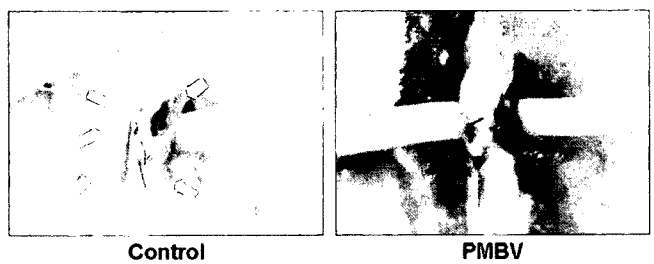

Fig. 2: Microscopic findings of the repaired tendon after 3 weeks.

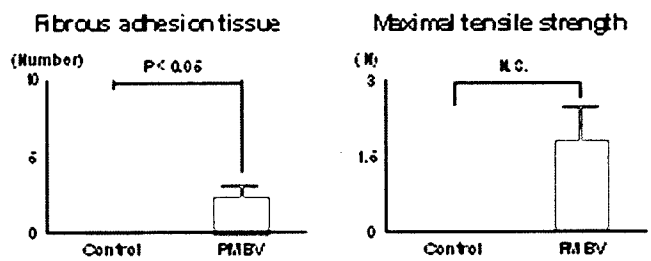

Fig. 3: Quantitative evaluations of the repaired tendon after 3 weeks.

Discussion: Despite many studies for prevention of tissue adhesion, there is yet no definite solution. The convensional anti-adhesion materials are not good at biocompatibility and handling especially in a small operative site. 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 addition, PMBV gel can easily be used to a operative site which has intricate shape because it can form spontaneously in not only dry but also wet condition.

The lines of results obtained in this study suggest PMBV gel 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, PMBV gel can be a safe and effective solution to prevent adhesion without impairing tissue healing. Further studies on its clinical application are now underway.

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