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A comparative study of preventing postoperative tendon adhesion using electrospun polyester membranes with different degradation kinetics

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Complications arising from tendon injury include tendon sheath infection and peritendinous adhesion, in which tendon adhesion often leads to serious motor dysfunction. In this work, the electrospun membranes of poly(*L*-lactide) (PLA) and poly(ε-caprolactone) (PCL) with different degradation kinetics were used to investigate their efficacy for anti-adhesion toward Achilles tendon repair. Compared with the PCL membrane, the PLA sample showed a faster rate of degradation in 42 d, and all the degradation media (i.e., phosphate-buffered saline) maintained at a constant pH of around 7.4. Meanwhile, the superior biocompatibility of both the PLA and PCL membranes were proved by the *in vitro* cellular adhesion tests and *in vivo* histopathological assays. Simultaneously, the PLA membrane was more effective than the PCL sample in decreasing adhesion and promoting functional recovery. Furthermore, the experiment result was further confirmed by hematoxylin-eosin and Masson's trichrome staining, and type I collagen immunohistochemical analysis. All results revealed that the model treated with the electrospun PLA membrane was obviously better with regard to both anti-adhesion and tendon repair than that in the PCL membrane group. Considering the results of degradation and adhesion prevention efficacy, the electrospun polyester membranes, especially the PLA one, would be applied with fascinating potential in clinical prevention of postoperative tendon adhesion.

anti-adhesion, Achilles tendon repair, biodegradability, electrospun membrane, poly(*L*-lactide), poly(ε-caprolactone)

1 Introduction

Tendon adhesion is one of the most serious complications after tendon trauma and tendon repair surgery that affects motor function seriously [1,2]. In order to prevent the tendon adhesion effectively after the operation of tendon repair, a variety of methods have been applied, such as drug implant, modification of suture, and biomaterial barrier [3–5]. Among them, the placement of physical barrier between the injured site and surrounding tissue, which is a very promising technology, has attracted widespread interest [6]. To date, lots of materials are used for the prevention of adhesion, such as hyaluronic acid, hydroxyapatite, and carboxymethyl chitosan [7–9]. Nevertheless, it is found that these materials do not achieve a perfect efficacy from clinical perspective [10]. For instance, the biodegradation rate of hyaluronic acid is too fast in the damage location, which will greatly influence the result of anti-adhesion [11]. Since hydroxyapatite cannot be absorbed by the body, it will exist

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for a long time in the body and may cause some mechanical irritation [9]. On the other hand, carboxymethyl chitosan shows no significant difference of anti-adhesion between the treatment and control groups in clinical trials [12].

Electrospinning, a promising technique, is applied to fabricate scaffolds in tissue engineering with unique advantages, such as high surface area and porosity, tunable aperture, and excellent anti-adhesion efficiency [13,14]. It has been proved that the microstructures of electrospinning scaffolds are similar to those of fibrous extracellular matrices [15], which can be conducive to the nutritional metabolism between scaffold-supported tissues or cells and surrounding microenvironment. The further researches reveal that the electrospinning fibrous membranes of biodegradable polyesters can not only provide the necessary texture and elasticity on preparation with optimized parameters, but also be discharged through the physiological metabolism of human body [16,17]. In the traditional understanding, the designed and prepared anti-adhesion membranes should possess appropriate mechanical property, stability, and degradation rate after implantation *in vivo* [18]. The electrospinning membranes can not only meet the above requirements, but also effectively reduce the inflammation and adhesion of postoperative lesions [19,20].

The polyester-based films that are biocompatible and biodegradable have generally been applied to the field of anti-adhesion [21]. For example, the films of poly(*L*-lactide) (PLA) and poly(ethylene glycol) (PEG) multiblock copolymers are prepared by both spin coating and electrospinning, and exhibit excellent performance in the rat cecum and heart adhesion models [22]. Poly(lactide-*co*-glycolide) (PLGA) mats formed via electrospinning cause an obvious reduction in postoperative adhesion bands and low inflammatory response [19]. The studies about electrospinning fibrous scaffolds of poly(α-hydroxy ester)s (PHEs) suggest that their properties, such as, good biocompatibility, biodegradability, and anti-adhesiveness, are appropriate for the applications in the field of biomedicine [18,23,24]. Although most of the electrospinning PHE membranes are proved to have good anti-adhesion effects, the efficacies among them are rarely compared.

Based on the above backgrounds, the PLA and poly (ε-caprolactone) (PCL) membranes were prepared by electrospinning for the prevention of postoperative adhesion in the Achilles tendon of rats in this study (Figure 1). The morphology, degradation rate, cell adhesion effect, biocompatibility, and anti-adhesion effect *in vitro* and *in vivo* were systematically compared between the PLA and PCL membranes. The experimental results revealed that the electrospun PLA membrane was a more promising candidate for effectively preventing tendon adhesion and reducing inflammation compared to that of PCL.

2 Experimental

2.1 Materials

PLA (M_η=~88 kD) and PCL (M_η=~80 kD) were taken from Changchun SinoBiomaterials Co., Ltd. (China). α-Chymotrypsin and elastase were purchased from Aladdin Industrial Inc. (Shanghai, China). Acetoxymethyl ester (calcein AM) and propidium iodider (PI) were supplied by Sigma-Aldrich (Shanghai, China).

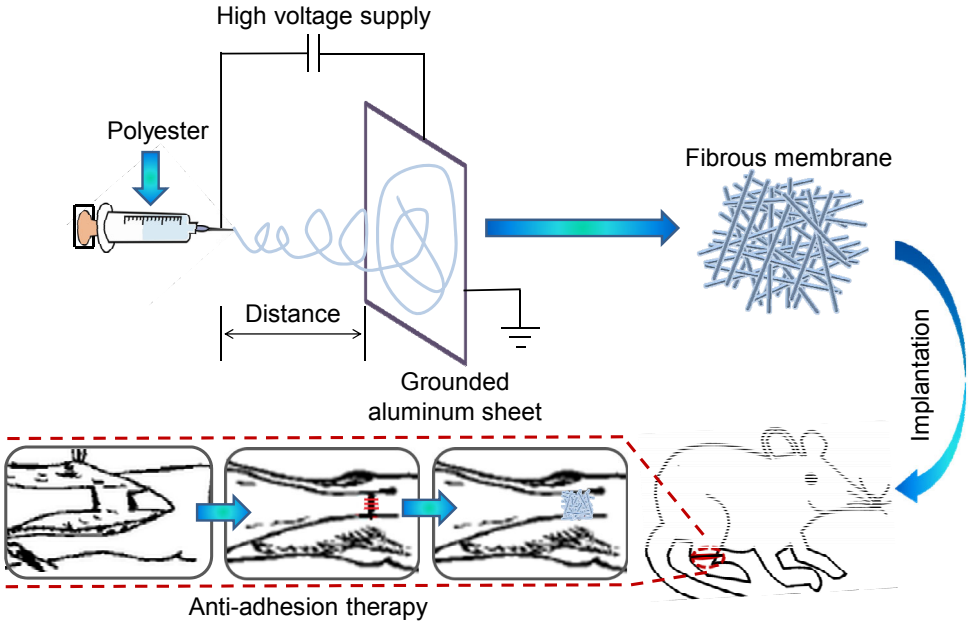

Figure 1 Sketch map of electrospinning process and application of electrospun polyester membrane in prevention of adhesion after Achilles tendon repair surgery.

2.2 Fabrications of electrospun PLA and PCL membranes

As shown in Figure 1, two kinds of electrospun membranes were fabricated by the following steps. First, PLA and PCL were dissolved in chloroform at a concentration of 6.0 wt%. Second, the PLA or PCL solution was loaded in a 10 mL syringe, which was fixed at approximately 10° from horizontal in order to minimize the falling drop at the end of capillary tip. An electrical field of 20 kV was applied by a high voltage power supply, and the injection rate of solution was set as 0.1 mm/min. Both the electrospun membranes with a thickness of 0.1 mm were collected on a grounded aluminum sheet kept at a distance of 15 cm from the needle tip.

2.3 Characterizations of electrospun membranes

2.3.1 Morphology observations

To test the surface morphology of electrospun membrane, a field emission scanning electron microscopy (SEM; Inspect-F, FEI, Finland) was used under high vacuum and with an acceleration voltage of 20 kV. The average diameters of electrospun fibers were calculated on the basis of SEM micrographs, using the image analysis software, Nano Measurer 1.2.5 (Fudan University, China).

2.3.2 *In vitro* degradation evaluations

The degradation rates of PLA and PCL membranes were an important feature, which changed in different hydrolysis solutions. 3.0 mg of electrospun PLA or PCL membrane was placed in the pre-weighted vial, and then 2.0 mL of phosphate-buffered saline (PBS) with α-chymotrypsin or elastase (1.0 IU/mL, 0.1 mol/L, pH 7.4), or PBS (0.1 mol/L, pH 7.4) were added separately. The vial was incubated with continuous reciprocal oscillation of 75 r/min at 37 °C. The whole degradation process was lasted for a cycle of 3 weeks in PBS with α-chymotrypsin or elastase, or 6 weeks in PBS. In order to maintain the activity of enzyme, the incubation medium was replaced every day. The medium was carefully removed, when the predetermined degradation time reached. Later, the samples in vials were rinsed with distilled water and freeze-dried. Subsequently, the gross weight of sample and vial was tested, and the weight of sample was calculated. In order to clarify the weight loss of experimental sample during the degradation process, the real-time weight (W_r) was normalized in contrast to the initial one (W_0), that is, Normalized Weight (%)=$W_r/W_0\times100\%$. Meanwhile, the pH of residual medium after degradation that was replaced daily was also detected carefully to assess the impact of degradation on the body fluids. The degradation experiments were conducted in triplicate.

2.3.3 Biocompatibility of electrospun membranes

The biocompatibility of two kinds of electrospun membranes was characterized *in vitro* and *in vivo*. The cytocompatibility of both electrospun membranes were tested through a live/dead and Cell Counting Kit-8 (CCK-8, Dojindo, Japan) tests. The sample was sterilized by UV-irradiation on each side for 0.5 h before use, and then both electrospun membranes were smoothly placed on the bottom of 48-well tissue culture plate (TCP). Subsequently, the L929 cells cultured in Dulbecco's modified Eagle's medium (DMEM; Invitrogen corporation, Gibco, USA) were seeded at 1.0×10^4 cells per well. After incubation for 1, 6, 12, or 24 h, the medium was removed, and cells were rinsed thrice with PBS. Subsequently, 10.0 μL of PBS containing calcein AM (2.0 g/mL) and PI (3.0 g/mL) was added to each well, and incubated for another 30 min at 37 °C. Finally, the stained cells were detected by a Nikon fluorescence microscope (TE 2000, Nikon Co., Japan).

For CCK-8 assay, the quantitative numbers of L929 cells were evaluated by adding CCK-8 solution to each well. At predetermined time intervals, 0.4 mL of CCK-8 solution in DMEM (10%, *V*/*V*) was added to each well. After incubation for 4 h, the absorbance of the above medium at 450 nm was measured using a microplate reader of Bio-Rad Company (Model 550, Hercules, USA). Furthermore, the absorbance at 630 nm was measured for baseline correction. The relative cellular adhesion was calculated with respect to the result on Day 1.

To evaluate the inflammatory response of electrospun membranes *in vivo*, both the membranes (3.0 mg) were subcutaneously implanted to 6 healthy male Sprague-Dawley rats weighing 250–300 g, which were randomly divided into two groups. All animals were handled under the protocol approved by the Institutional Animal Care and Use Committee of Jilin University, and all efforts were made to minimize suffering. One of three rats was randomly sacrificed by cervical amputation in every group at the time points of 3, 6, and 9 weeks. Subsequently, the skin tissues close to the materials were isolated, sliced, and stained by hematoxylin-eosin (H&E), and observed by an optical microscope (Nikon Eclipse *Ti*, Optical Apparatus Co., Japan).

2.4 *In vivo* evaluations of electrospun PLA and PCL membranes

For this assay, a total of 30 male SD rats weighing 250–300 g were randomly divided into three groups: Group I and II were wrapped with 1 cm×2 cm PLA or PCL membrane for anti-adhesion in the suture site of Achilles tendon, and Group III was control group without any treatment. All the rats underwent the standard operation as follow. After intramuscular injection of chloral hydrate with a dosage of 30.0 mg/kg, the rat fur was shaved, and the skin was disinfected with alcohol. A 5 cm median skin incision from calcaneal bone was made in the middle position of right Achilles tendon skin. After isolating the tissues, the tenotomy was performed and sutured with 4–0 silk suture (PGA Resorba®, Resorba, Germany). The wound was sutured

directly in Group III after completing the above steps. In Group I and II, the tendon was surrounded with the PLA or PCL membrane before the wound closure, respectively.

2.4.1 Macroscopic evaluations

The apparent inflammation and ulcer of the surgical sites were recorded before the animals were sacrificed at 3 weeks after surgery. The breadth and severity of Achilles tendon adhesion were scored. The degree of tendon adhesion based on surgical findings was graded on 1 to 5 scale based on the adhesion scoring system of previous studies: score 1 meant no adhesion; score 2 referred to mild adhesion, which could be separated by blunt dissection; score 3 meant that less than or equal to 50% of the adhesion scopes need to be separated by sharp dissection; score 4 showed that 51%–97.5% of the adhesion area need to be separated by sharp dissection; and score 5 meant more than 97.5% of the adhesion scopes need to be separated by sharp dissection [25]. According to the rate of adhesion, the degree of tendon adhesion was carefully quantified. The entire region of tendon adhesion that must be separated by sharp dissection was detected by caliper. These two parameters were determined by two observers under double-blind conditions to assess each experimental group.

2.4.2 Histological analyses

After the animals were sacrificed, the tissue separated from the animals was carefully rinsed with PBS, and then fixed in 4% (*W*/*V*) PBS-buffered paraformaldehyde and embedded in paraffin. 5.0 μm thick longitudinal slices were observed following the H&E or Masson's trichrome staining. In Masson's trichrome staining, the collagen was stained green, nucleus was stained blue or brown, and cytoplasm, blood cells and muscle fibers were stained red [26].

The expression and localization of type I collagen were analyzed in Achilles tendon tissue by immunohistochemistry. Typically, the slice was dewaxed in xylene and hydrated in a graded array of alcohol. For the recovery of antigen, the section was placed in 10.0 mL of citrate buffer (pH 6.0) and then heated in microwave twice. The goat serum diluted by 1:100 and 0.3% (*V*/*V*) hydrogen peroxide were used to block the nonspecific binding and the activity of endogenous peroxidase, respectively. Subsequently, the antibody of type I collagen (Abcam Company, USA) was used to incubate overnight at 4 °C. The section was washed for three times with PBS and nurtured with anti-mouse rabbit secondary antibody at 37 °C for 1 h. Finally, it was stained in DAB solution (Dako primary antibody incubation developed, Hamburg, Germany) and contrastly stained by hematoxylin.

2.5 Statistical analyses

All experiments were performed for at least three times, and the results were represented as means±standard deviation (SD). Statistical significances were analyzed using SPSS (Version 13.0, USA). $p<0.01$ and $p<0.001$ were considered highly statistically significant.

3 Results and discussion

3.1 Characterizations of electrospun PLA and PCL membranes

The performances of electrospinning fibrous membranes can be principally affected by their diameters and distributions that are the key parameters of electrospun fibers. According to the SEM micrographs, the microstructures of electrospun PLA (Figure 2(a)) and PCL (Figure 2(c)) membranes were shown to have a three-dimensional network, and the diameters of PLA and PCL fibers were measured to be between about 3 and 10 μm with a smooth surface. Figure 2(b, d) clearly revealed the charts of semiquantitative data, which included fiber diameters and normal distributions. It revealed that, in fact, the average diameters of electrospun PLA and PCL fibers were 4.3 and 8.2 μm, respectively, under the same fabrication conditions.

The degradation plots of biodegradable polyesters are decided jointly by the inherent properties of polymers and the external environments [26–28]. The inherent properties of polymer include internal structure and molecular weight of monomer, crystallinity, and surface area, simultaneously, the external environment contains enzymes, temperature, pH, etc. [29–32]. In this work, the *in vitro* degradation of two kinds of electrospun membranes with respect to mass loss was monitored in three kinds of media (i.e., PBS with α-chymotrypsin or elastase, or PBS) for 3 weeks or even longer. As depicted in Figure 3, the degradation of electrospun PLA and PCL membranes was impacted evidently by different types of media. Figure 3(a) showed the mass loss process of PLA membrane in the test duration, and the presence of elastase could accelerate the degradation rate more efficiently compared with that of α-chymotrypsin. It followed that the residual mass of electrospun PLA membrane was 80.8 wt%. By contrast, the degradation of PLA membrane in PBS was significantly slower than that in the presence of enzymes. Concretely, the mass loss of PLA membrane in the PBS group was lower than that of elastase group for over 15 wt% of initial weight under similar conditions. Directly shown in Figure 3(c), the degradation rates of PCL film in all the three degradation media were slow. Nearly for 3 weeks, the PCL sample exhibited no more than 5 wt% mass loss with or without enzymes. In detail, the degradation rates of PCL membrane in two kinds of media with both α-chymotrypsin and elastase had no obvious difference. At the same time, the degradation rate of PCL sample in PBS was the slowest, and the mass loss was not more than 3 wt% by 42 d. It could be explained that the electrospun PLA membrane was more sensitive to elastase

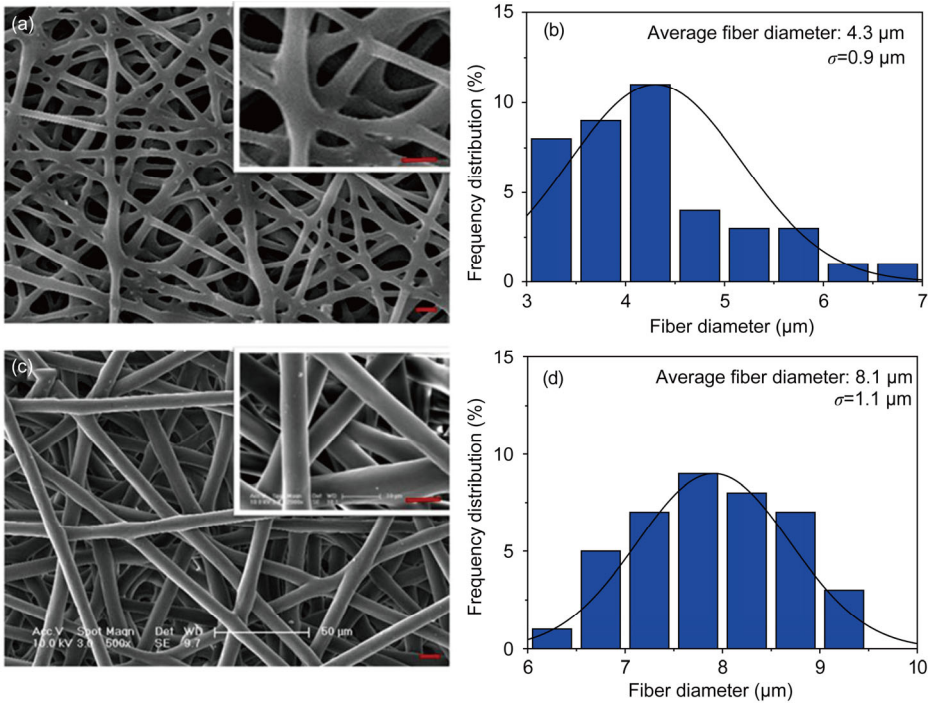

Figure 2 Typical SEM micrographs (a, c), and statistical diameters and frequency distributions (b, d) of electrospun PLA (a, b) and PCL membranes (c, d). Scale bar represented 10 μm (color online).

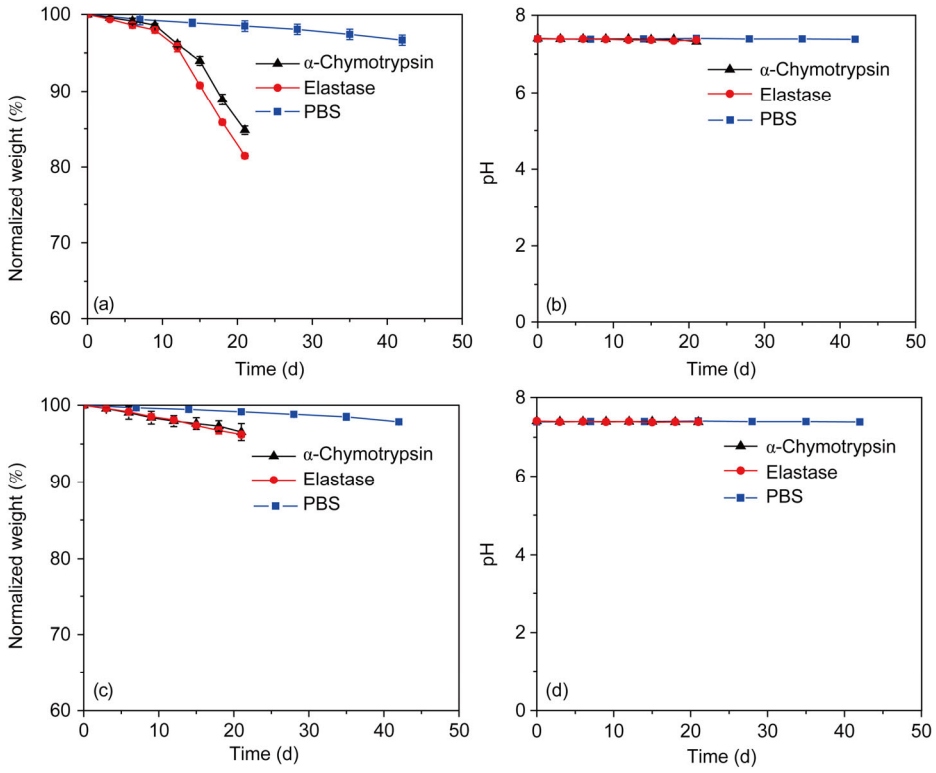

Figure 3 Degradation profiles (a, c) and pH values of degradation media at different degradation times (b, d) of electrospun PLA (a, b) and PCL membranes (c, d) in PBS with α-chymotrypsin or elastase, or PBS. Data were presented as mean±SD (n=3).

than any others, which may be due to the different enzymatic hydrolysis characteristics of PLA. Throughout the degradation of electrospun PLA membrane, less pre-mass loss of specimen was observed. Compared with the PCL

membrane group, when the degradation of PLA membrane reached a certain stage (i.e., Day 8 in this work), the degradation accelerated. It might be attributed to the internal structure change of PLA membrane caused by immersion and hydrolysis. The degradation trends of electrospun PLA and PCL membranes could be observed in the aforesaid profiles, and their degradation rates *in vitro* can be regulated by different chemical structures and hydrolysis solutions.

Simultaneously, the pH values of all degradation media for both the PLA and PCL membranes were monitored during the whole degradation cycle. The pH values were kept constant in all experimental groups (Figure 3(b, d)). It demonstrated that the degradation showed negligible impact of the surrounding media. Correspondingly, the current study suggested that the pH of surrounding environment was less affected by the degradation of sample. The degradation characteristics of two electrospinning membranes could provide great help for the prevention of postoperative adhesion, because it could meet the special bioprocessing applications and the body required balance. Through the comparison of two kinds of materials, PLA was more in line with the demand of anti-adhesion materials. Because of a reasonable time of rehabilitation, the electrospun PLA membrane with more appropriate degradation rate was more conducive to early recovery.

The biocompatibility of two kinds of electrospun membranes both *in vitro* and *in vivo* were analyzed by cellular live/dead staining and CCK-8 test, and histopathological evaluation, respectively. First, the cytocompatibility of two kinds of electrospun membranes was observed by the adhesion behaviors of L929 cells (mouse fibroblast cells) by live/dead and CCK-8 assays. According to Figure 4, L929 cells were cultured on two kinds of electrospun membranes for 1, 6, 12, or 24 h, at which the live and dead cells were fluorescently marked to green and red, respectively [33]. Blank TCP was used as the control group. The fluorescence micrographs suggested that the cellular adhesion on PLA sample was similar to that of PCL sample. The number of cells was slightly smaller than those in the control group. In addition, in all the three experimental groups, almost all L929 cells were active, and no dead cells were observed. It meant that both the electrospun membranes exhibited insignificant toxicity to fibroblasts, demonstrating their excellent cytocompatibility.

Moreover, CCK-8 is a colorimetric reagent, and it can convert the mitochondrial dehydrogenase of living cells into highly water-soluble yellow crystals, that are detected by the direct colorimetric assay without cell lysis. Therefore, CCK-8 can be employed for evaluating the activity of cells through measuring the absorbance value of culture medium after coincubation with cells. This approach is simple, convenient, and highly accurate. In this work, L929 cells were seeded on both the electrospun PLA and PCL membranes. After the predetermined durations, the relative adhesion of cells on the two kinds of membranes was detected with

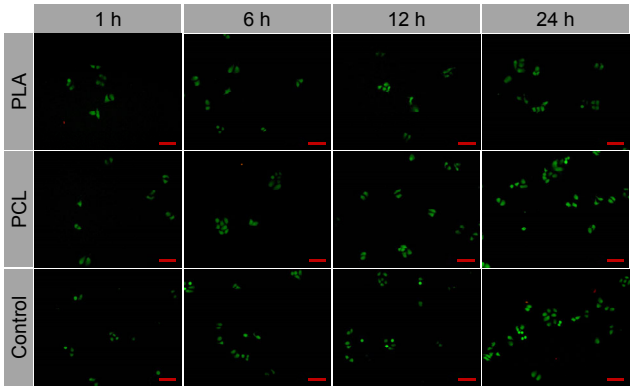

Figure 4 Typical fluorescence micrographs of L929 cells on electrospun PLA or PCL membrane, or TCP after *in vitro* culture for 1, 6, 12, or 24 h. Live cells were stained green by calcein AM, and dead cells were stained red with PI. Scale bar represented 10 μm (color online).

CCK-8 reagent, which could quantitatively reflect the situation of cellular adhesion on the membranes. The results have been displayed in Figure 5. In practice, L929 cells can be efficiently adhered on the surface of both the electrospun PLA and PCL membranes. In addition, the cells adhered on the surface of PLA film were 34% lower than that of control group, and almost 13% lower than that of the PCL membrane group. The results further revealed the good cytocompatibility of both the PLA and PCL membranes, and demonstrated the greater potential of PLA film for anti-adhesion application benefited from the lower cellular adhesion compared with the PCL membrane.

The electrospun PLA and PCL membranes, which were implanted subcutaneously in rats, were intuitively observed after implantation for 3, 6, or 9 weeks. The results showed that the residue of PCL film was more than that of PLA one, and both materials were surrounded by fibrous connective tissue; while the surrounding tissue showed negligible hyperemia, metatropy or thanatosis. Additionally, as shown in Figure 6, H&E staining revealed that the sections of two

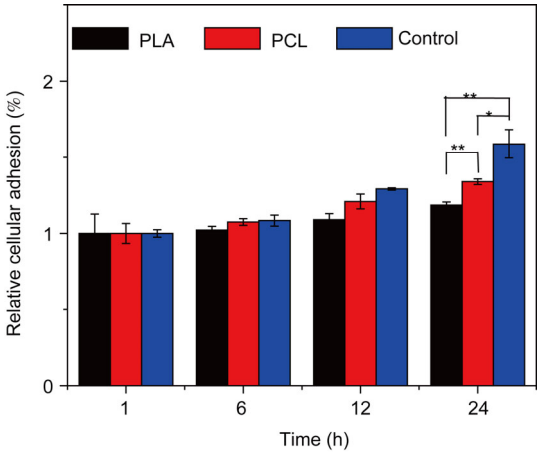

Figure 5 Relative cellular adhesion of L929 cells cultured on electrospun PLA or PCL membrane, or TCP for 1, 6, 12 or 24 h *in vitro*. Data were presented as mean±SD (n=3; * p<0.01, ** p<0.001).

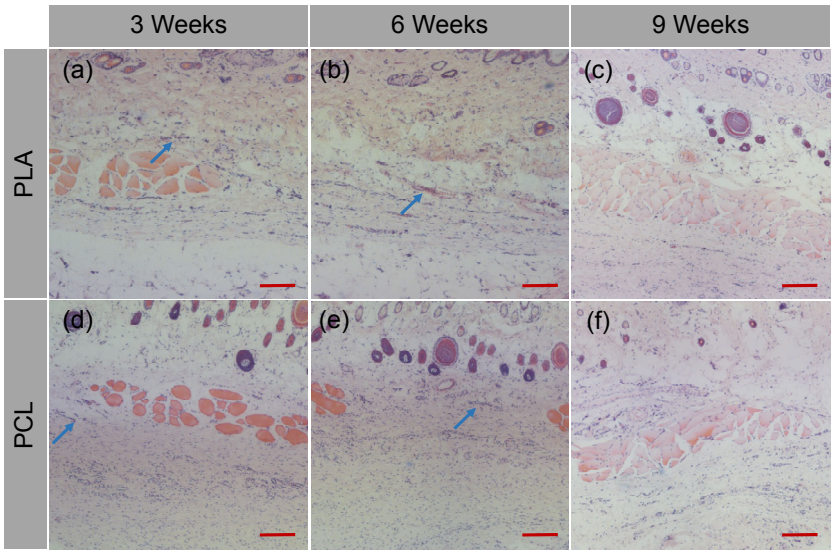

Figure 6 H&E staining of skin tissue sections after 3 (a, d), 6 (b, e), or 9 weeks (c, f) of subcutaneous implantation of electrospun PLA (a–c) and PCL membranes (d–f). Blue arrows indicated the inflammatory cells. Scale bar represented 200 μm.

groups with both the PLA and PCL membranes did not cause large numbers of neutrophile granulocytes, macrophages, and other inflammatory cells after surgery for 3, 6, or 9 weeks similar to the morphology of normal skin tissue (Figure S1, Supporting Information online). The number and morphology of inflammatory cells were different for both the PLA and PCL membranes-pretreated tissues at all tested three time points. It was found that the biodegradable polyester membranes had no serious inflammatory response (Figure 6), which once again demonstrated that the PLA and PCL films exhibited good biocompatibility.

3.2 *In vivo* anti-adhesion assessment after Achilles tendon repair surgery

Animal experiments were performed for comparing the roles of PLA and PCL membranes in anti-adhesion treatment and the repair of Achilles tendon. During the whole experiment, all experimental animals were ensured to be healthy without any infection of wound. Figure 7 showed the photographs of Achilles tendon, when the rats were sacrificed before surgery and at 3 weeks post-operation. Compared with normal group without injury, just a small area of tissue adhesion could be observed in both the PLA and PCL membrane groups, and the synechia regions could be easily separated by blunt dissection (Figure 7(b, c)). In addition, the adhesion of PLA membrane was smaller and could be more easily separated compared to that of PCL membrane group. However, a wide range of fibrous tissue adhesion between Achilles tendon and surrounding tissue was displayed in the untreated control group (Figure 7(d)). Furthermore, compared to the PLA and PCL membrane groups, a significant thickness of Achilles tendon was observed for the control group. It was because that the boundary between tendon and surrounding tissue was not obvious, which made it difficult to be completely separated in the control group.

In order to quantitatively measure the degree of adhesion, as shown in Figure 8, all the distributions of adhesion fractions and areas of Achilles tendon in rats were carefully assessed. Tendon injury repair group without treatment showed a high degree of adhesion with 4 or 5 points, and the average area was 1.90 cm^2. In comparison, the electrospun PCL membrane group showed slighter adhesion with 1, 2 or 3 points, and the proportion of adhesion was at only 0.61 cm^2 that was less than 40% with an average adhesion area. More encouragingly, the electrospun PLA membrane group exhibited the slightest adhesion with 1 or 2 points, the proportion of adhesion was less than 20%, and the average adhesion area was only 0.25 cm^2. The excellent anti-adhesion efficacy endowed the electrospun polyester membranes, especially the PLA membrane, with great prospect in clinical application.

The scar of exogenous healing causes the formation of adhesion and affects the tendon gliding [34]. For further investigation into the degree of adhesion, H&E, Masson's trichrome staining, and type I collagen immunohistochemistry were performed to detect the distribution and density of collagen regeneration after the repair surgery. The results showed that less collagen was discovered between tendon and surrounding tissue indicating almost absence of adhesion in the groups of electrospun PLA (Figure 9(a, b)) and PCL membranes (Figure 9(d, f)). In stark contrast, in the untreated control group, a large amount of collagen fibers were generated and connected with each other between tendon and surrounding tissue (Figure 9(g, h)). It demonstrated that the electrospun polyester films, especially the PLA one, had significant anti-adhesion ability. In addition, the white cavities appeared in the site of materials due to the

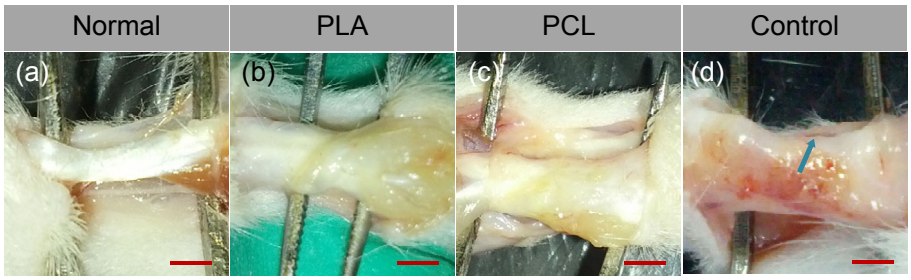

Figure 7 Contrast images of Achilles tendon adhesion in experimental animals at different situations. (a) Gross appearance of preoperative Achilles tendon tissue; (b–d) Achilles tendon injury treatment by electrospun PLA (b) or PCL membrane (c), or without treatment (d). Blue arrows indicated the Achilles tendon adhesion at 3 weeks after repair surgery. Scale bar represented 0.5 cm.

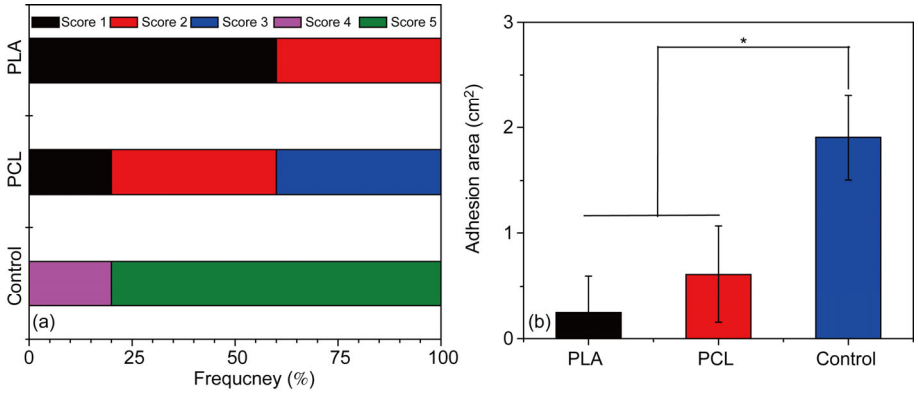

Figure 8 Distribution of adhesion scores (a) and statistical adhesion areas (b) of Achilles tendons treatment with electrospun PLA or PCL membrane, or without treatment for 3 weeks after Achilles tendon repair surgery. Data were presented as mean±SD (n=10; * p<0.01).

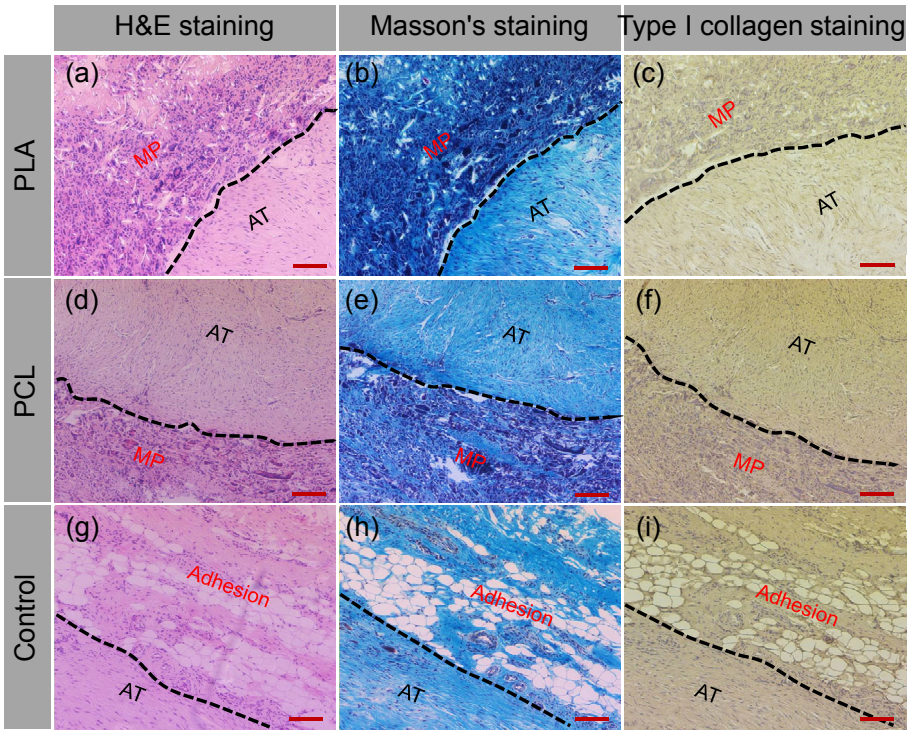

Figure 9 Typical micrographs of H&E staining (a, d, g), Masson's tritchrome staining (b, e, h), and type I collagen immunohistochemistry (c, f, i) for the injury site of Achilles tendon at 3 weeks after repair surgery, which treated with PLA (a–c) or PCL membrane (d–f), or without treatment (g–i). AT: Achilles tendon; MP: material position. Scale bar represented 100 μm.

biodegradation of electrospun membranes. The white cavities of PLA membrane group (Figure 9(a, b)) were more than those of PCL membrane group (Figure 9(d, e)), which should be attributed to a faster degradation of PLA membrane than that of the PCL sample. Moreover, the collagen fibers and tendon cells were densely arranged in order for both the PLA and PCL membrane groups, and the staining areas exhibited no visual difference in the repaired and normal positions. It revealed that the anti-adhesion electrospun PLA and PCL membranes seldom affected Achilles tendon repair. From what has been discussed above, the electrospun polyester membranes, especially the PLA one, could not only ensure the treatment effects, but also contribute to the patient's early recovery.

The previous literatures suggested that the extracellular matrix of tendon is predominantly composed of type I collagen, which is also involved in many of the metabolic and inflammatory peritendinous connective tissues [35,36]. In this work, the immunohistochemistry of type I collagen was used to further confirm the degree of adhesion and recovery of tendon. In this assay, type I collagen in all groups were rendered as brown (Figure 9(c, f, i)). The arrangement and direction of type I collagen fibers exhibited no visual difference in the PLA and PCL membrane groups, and the control group, while the positive staining area of two treated groups were slightly larger than that of control group. It was shown that the treatments with the PLA and PCL films had a positive role in repairing the Achilles tendon.

Achilles tendon could be effectively separated from the surrounding tissue without obvious damage after the treatments with two kinds of polyester samples, especially the PLA membranes, which simultaneously promoted the repair of Achilles tendon. The degradation rates of anti-adhesion materials are very important [37]. Too rapid degradation can lead to severe tissue adhesion, while too slow degradation may adversely affect the normal function of tissue and lead to foreign body reaction [38–40]. In order to overcome these situations, the PLA and PCL membranes were studied in this work for selection. The results of experiments showed that the degradation rate of PLA membrane was quicker than that of PCL membrane. Of course, the degradation rates of PLA and PCL membranes could be regulated through different approaches, such as changing the polymeric molecular weight and the diameter of electrospinning fiber. In order to regulate these parameters, more in-depth studies will be conducted in the near future. Based on the results, it can be said that the electrospun polyester membranes were promising for the reduction of postoperative adhesion mainly benefited from the porous structures and appropriate degradation rates. Especially, compared to the PCL material, the overall anti-adhesion effect of electrospun PLA membrane was more noteworthy.

4 Conclusions

Adhesion is one of the most common problems, which arises from post-trauma surgery. Herein, the PLA and PCL membranes prepared by electrospinning were used to prevent or relieve postoperative tendon adhesions. The morphology, degradation kinetic, compatibility, anti-adhesion efficacy, and histopathological and immunohistochemical analyses between the PLA and PCL samples were systemically compared. As a result, the electrospun PLA membrane was found to have excellent microstructure and appropriate degradation kinetic compared with the PCL sample. More importantly, a significant adhesion reduction between tendon and surrounding tissue, and an improved tendon healing were observed after the treatments with the electrospun polyester membranes, especially with the PLA membrane. It demonstrated that the electrospun polyester membranes with appropriate degradation kinetic and excellent efficacy are promising candidates for the prevention of postoperative adhesions after tendon repair surgery. Apparently, the electrospun polyester films could also be applied to other anti-adhesion therapeutics, such as anti-adhesion of flexor tendon, intestine, and pelvis.

Supporting information

The supporting information is available online at chem.scichina.com and link.springer.com/journal/11426. The supporting materials are published as submitted, without typesetting or editing. The responsibility for scientific accuracy and content remains entirely with the authors.

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