RESEARCH ARTICLE

Application of antibacterial biomaterials based on improved traditional Chinese medicine *Polygonatum sibiricum* polysaccharide in wound repair

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Wound infection and poor healing are major challenges facing clinical practice. This study aimed to develop and evaluate the application of a novel antibacterial biomaterial based on the improved traditional Chinese medicine *Polygonatum sibiricum* polysaccharide (PSP) in wound repair. The study extracted and purified PSP from *Polygonatum sibiricum* medicinal materials through water extraction, alcohol precipitation, protein removal, and decolorization, and then subjected it to quaternization chemical modification to enhance its antibacterial activity. Polycaprolactone-modified PSP surgical suture was prepared using electrospinning technology, and PSP hemostatic sponge was prepared using sodium periodate crosslinking combined with the freeze-drying method. *In vitro* experimental results showed that the modified PSP solution had significant antibacterial effects on both *Staphylococcus aureus* and *Pseudomonas aeruginosa* with the diameters of the inhibition zone against *Staphylococcus aureus* and *Pseudomonas aeruginosa* as 15.67 mm and 13.54 mm, the minimum inhibitory concentrations (MIC) of 125.00 μg/mL and 175.00 μg/mL, respectively. The diameters of the inhibition zone against *Staphylococcus aureus* for polycaprolactone-PSP suture and PSP sponge were 12.89 mm and 14.32 mm, respectively. Cytotoxicity tests showed that the above materials had no significant toxicity to mouse fibroblasts, and the relative cell survival rate was higher than 98%. The scratch test showed that the modified PSP solution achieved a scratch healing rate of 78.13% within 24 h, significantly promoting cell migration. In the mouse model of full-thickness skin defect infection, the PSP sponge achieved a wound healing rate of 92.11% on day 12, significantly better than the control group's 75.39%. This study successfully developed an antibacterial biomaterial based on improved traditional Chinese medicine PSP, which provided a safe and effective strategy for the treatment of infected wounds and had broad clinical application prospects.

Keywords: *Polygonatum sibiricum* polysaccharide; antibacterial biomaterials; quaternization modification; wound healing; electrostatic spinning.

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Introduction

Wound infection and healing have always been a major challenge in surgical treatment, especially in the context of chronic wounds, diabetic feet, and postoperative infection. Traditional treatment methods often have unsatisfactory efficacy due to insufficient antibacterial ability, slow healing speed, or frequent dressing changes [1, 2]. Therefore, the development of new wound dressing materials that combine antibacterial properties, biocompatibility, and tissue regeneration capabilities has become one of the hot research directions in biomedical materials [3].

Polygonatum sibiricum as a traditional Chinese medicine (TCM) plant with both medicinal and edible properties has received widespread attention in recent years due to its rich bioactive components and diverse pharmacological effects. *Polygonatum sibiricum* is rich in active ingredients such as polysaccharides, saponins, flavonoids, *etc*. It has various biological activities such as anti-inflammatory, anti-aging, and immune regulation and is considered a potential functional nutritional resource [4]. Li *et al*. suggested that *Polygonatum sibiricum* was transitioning from traditional medicinal use to functional food, and developing varieties that had not been fully researched could help expand its applications in the food and health industry [5]. Yang *et al*. found that *Polygonatum sibiricum* polysaccharide (PSP) was mainly composed of Glc, Man, and Gal in its structure. Different extraction methods significantly affected its biological activity, among which PSP-5 had a good inhibitory effect on acetylcholinesterase [6]. Yuan *et al*. confirmed that PSP could improve liver fibrosis by regulating the TGF-β/Smad pathway and had anti-inflammatory, antioxidant, and anti-fibrotic potential [7]. However, traditional polysaccharide antibacterial materials often rely on physical adsorption or simple drug encapsulation to achieve antibacterial functions, which have problems such as unstable release of active ingredients, limited antibacterial effects, and weak binding with substrate materials. These materials are difficult to meet the clinical needs of sustained antibacterial and efficient healing [8, 9]. In addition, some studies have tried to apply PSP to biomedical materials, but most of them focus on a single dosage form such as hydrogel or coating, lacking systematic material engineering design and *in vivo* verification [10]. There are still significant gaps in antibacterial mechanisms, material mechanics matching, and synergistic regulation of biological activity [11].

Given the biological potential and the application bottlenecks of PSP, this study aimed to optimize its polysaccharide structure through chemical modification to improve its antibacterial activity and material properties. The quaternization modification was applied to the purified PSP to improve its antimicrobial efficacy. The modified-PSP was then utilized as the core functional component to construct two distinct forms of antibacterial biomaterials including a nanofiber suture fabricated *via* electrospinning technology and a porous hemostatic sponge prepared using freeze-drying methods. The results of this research established a comprehensive approach for natural medicinal polysaccharides from component extraction, structural modification, to the application of functional materials and provided a theoretical basis and a technical platform for the development of novel antibacterial wound dressings for infected wound management.

Materials and methods

Extraction, purification, and modification of PSP

Polygonatum sibiricum medicinal herb was purchased from Bozhou Chinese Herbal Medicine Market (Bozhou, Anhui, China) and authenticated by the College of Pharmaceutical Sciences, Wenzhou University (Wenzhou, Zhejiang, China). 100 g of sample was sieved and dissolved in 10 times volume of distilled water (v/w). The extraction was performed at 90°C water bath for 3 hours before filtering through gauze. The residue was extracted with the same procedure one more time. The two extracts were then combined and concentrated under reduced pressure at 55°C to 1/4 of its original volume followed by the addition of 4 times the volume of anhydrous ethanol. After standing at 4°C overnight, the sample was centrifuged at 8,000 rpm for 20 min. The precipitate was washed sequentially with anhydrous ethanol and acetone followed by vacuum drying at 45°C for 24 hours to obtain crude polysaccharides of *Polygonatum sibiricum*. The crude polysaccharide was dissolved in distilled water to make the concentration of 20 mg/mL. 1/4 volume of Sevage reagent (chloroform:n-butanol = 4:1) was then added, vigorously shaken for 30 min, and centrifuged at 5,000 rpm for 15 min to remove the protein layer. The procedure was repeated

until no white interface was observed. The supernatant was then decolorized using an AB-8 macroporous adsorption resin column (Sigma Aldrich, St. Louis, Missouri, USA) with the column volume of 200 mL and flow rate of 2 BV/h. The effluent was placed in a dialysis bag with a cut-off molecular weight of 3,500 Da (Sigma Aldrich, St. Louis, Missouri, USA) and dialyzed in distilled water for 72 hours, during which the dialysate was replaced every 8 hours. The purified PSP was obtained by freeze-drying the solution after dialysis using FreeZone 4.5 freeze dryer (Labconco, Kansas City, Missouri, USA). The structure of the modified product was characterized by using Nicolet iS10 Fourier transform infrared spectroscopy (FTIR) (Thermo Fisher Scientific, Waltham, MA, USA), while Avance III 400 MHz Nuclear Magnetic Resonance (NMR) (Bruker, Billerica, MA, USA) and Waters e2695 Gel Permeation Chromatography (GPC) (Waters, Milford, MA, USA) were employed to determine the functional group, preliminary structural composition, molecular weight, and distribution of PSP. By introducing positively charged groups through quaternization, the temperature, time, and material ratio were optimized to ensure structural stability and enhance antibacterial activity. Meanwhile, the physicochemical properties such as solubility and thermal stability of modified polysaccharides were evaluated, providing basic data for the preparation of subsequent biomaterials.

Preparation and characterization of modified PSP-based antibacterial biomaterials

Two types of materials including surgical suture and hemostatic sponge were prepared and systematically characterized in this research. Surgical sutures were prepared by using YFSP-GIII Electrospinning Machine (Yufan Technology Co., Ltd., Tianjin, China). Polycaprolactone (PCL) (Sigma-Aldrich, St. Louis, MO, USA) was used as the matrix material, and different concentrations of modified PSP were added to prepare the spinning solution. By controlling parameters of flow rate, voltage, and distance between the needle tip and collector, the structure and properties of the nanofibers were optimized. The effective drug loading and sustained drug release were achieved through adjusting the ratio of PCL to PSP. The surface morphology and fiber arrangement of obtained PCL-PSP suture were observed by using Nova NanoSEM 450 Scanning Electron Microscope (SEM) (FEI, Hillsboro, OR, USA). The encapsulation of polysaccharides was confirmed by FTIR. The hydrophilicity of the suture was evaluated by using a DSA30 contact angle measuring instrument (KRÜSS GmbH, Hamburg, Germany). The mechanical properties including tensile strength and maximum tensile stress of the suture were evaluated using a Instron 5967 Universal testing machine (Instron, Norwood, MA, USA) to verify its feasibility in clinical suturing. The adhesion was tested to evaluate its adhesion ability to the tissue surface. Furthermore, the PSP hemostatic sponge was prepared using sodium periodate crosslinking combined with a freeze-drying method utilizing FreeZone 4.5 freeze dryer (Labconco, Kansas City, MO, USA).

***In vitro* biological performance evaluation of modified PSP-based antibacterial biomaterials**

The *in vitro* antibacterial performance was evaluated against *Staphylococcus aureus* (ATCC 25923) and *Pseudomonas aeruginosa* (ATCC 27853) (ATCC, Manassas, VA, USA). Bacteria were cultured in LB broth (Sigma-Aldrich, St. Louis, MO, USA). The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were determined using the microbroth dilution method. Serial dilutions of the modified PSP solution and material extracts were incubated with 1×10^5 CFU/mL bacterial suspension at 37°C for 24 hours. MIC was defined as the lowest concentration with no visible turbidity, while MBC was determined by plating the clear wells onto nutrient agar plates. For the inhibition zone test, 1×10^8 CFU/mL bacterial suspensions were spread on nutrient agar plates. Sterilized circular samples with 6 mm diameter of the PCL-PSP suture and PSP sponge were placed on the agar and incubated at 37°C for 24 hours. Bacterial growth kinetics were tracked by co-culturing *S. aureus* with material extracts in LB broth. The optical density (OD) at 600 nm was

measured at intervals using a SpectraMax M3 microplate reader (Molecular Devices, San Jose, CA, USA). Biofilm inhibition was assessed by staining *S. aureus* biofilms with 0.1% crystal violet solution after culturing for 48 hours in 96-well plates and quantifying the absorbance at 570 nm. Biofilm clearance was visualized using LSM 880 Confocal Laser Scanning Microscopy (Zeiss, Oberkochen, Germany) after staining with a live/dead bacterial viability kit (Thermo Fisher Scientific, Waltham, MA, USA). Four *in vitro* experiments for evaluating the antibacterial activity of materials were conducted. Cytotoxicity and biocompatibility evaluation were performed using NIH 3T3 mouse fibroblast cells (ATCC® CRL-1658™) (ATCC, Manassas, VA, USA) in a Heracell 150i constant temperature incubator (Thermo Fisher Scientific, Waltham, MA, USA). The CCK-8 method was used to detect cell viability using Leica DMI8 Inverted Fluorescence Microscope (Leica Microsystems, Wetzlar, Germany). Meanwhile, cell adhesion and spreading tests were conducted to assess the material's ability to support the cell growth environment, thereby verifying its biocompatibility. To test the promotion of wound healing, the material's promoting effect on cell migration was evaluated through cell scratch assay and Transwell migration assay. Expression levels of extracellular matrix related molecules such as collagen and fibronectin were detected to reveal the potential mechanisms of the materials in tissue repair.

Animal wound repair experiment

A total of 27 male, 6 - 8 weeks old, 19 - 22 g weight C57BL/6 mice (Shanghai Laboratory Animal Center, Shanghai, China) were involved in this study as *in vivo* wound model. The mice were kept in a constant temperature and humidity with a light-dark cycle of 12 h/12 h [12]. All procedures of animal experiments were approved by the Animal Care and Use Committee (Zibo Polytechnic University, Zibo, Shandong, China). After anesthesia, two 6 mm full-thickness skin defects were created on the back of each mouse using a biopsy punch (Acuderm Inc., Ft. Lauderdale, FL, USA). A 10 µL solution containing 1×10^7 CFU/mL of *S. aureus* was added to each wound. The wounds were incubated for 15 min, then covered with a 3M Tegaderm film (3M, St. Paul, MN, USA) and secured with an elastic bandage. After two days of post-infection (Day 0), the mice were randomly divided into control group treated with normal saline, commercial medical gelatin sponge positive group, and modified PSP hemostatic sponge group with 9 mice in each group. The respective treatments were applied to the wounds and re-bandaged. On days 2, 4, and 6, wound exudate was collected for bacterial colony counting. Wound healing was photographically documented on days 0, 2, 4, 6, and 12 to calculate the healing rate. On days 6 and 12, mice from each group were euthanized, and wound tissues were harvested. The tissues were fixed, embedded in paraffin, and sectioned using a Leica RM2235 paraffin slicer (Leica Biosystems, Wetzlar, Germany). HE staining, Masson, and Sirius red staining were used for histological analysis to evaluate inflammation, epithelial regeneration, and collagen remodeling. Immunohistochemistry (Keratin) was used to confirm epithelial regeneration, and slides were observed using Leica DMI8 inverted fluorescence microscope.

Statistical analysis

All quantitative data were expressed as the mean ± standard deviation (SD). Statistical analysis was performed using GraphPad Prism 9 (GraphPad Software, San Diego, CA, USA). Comparisons between multiple groups were conducted using a one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test. *P* value less than 0.05 was considered statistically significant.

Results

Extraction, purification, and characterization of PSP

The results showed that the yield of crude PSP was 18.35% with significantly low purity of 65.21%. After purification, purity increased to 93.76% with the molecular weight of 32,589.67 Da and the PDI was 1.345, indicating a relatively uniform distribution of the polymer. Further

Table 1. *In vitro* antibacterial effects of different materials on *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Bacteria	Sample group	Inhibition zone diameter (mm±SD)	MIC (μg/mL)	MBC (μg/mL)
Staphylococcus aureus	Control (PBS)	0.00 ± 0.00	> 1,000.00	> 1,000.00
	PCL suture	0.00 ± 0.00	> 1,000.00	> 1,000.00
	Modified PSP solution	15.67 ± 1.23	125.00	250.00
	PCL-PSP suture	12.89 ± 0.98	250.00	500.00
	PSP sponge	14.32 ± 1.15	150.00	300.00
Pseudomonas aeruginosa	Control (PBS)	0.00 ± 0.00	> 1,000.00	> 1,000.00
	PCL suture	0.00 ± 0.00	> 1,000.00	> 1,000.00
	Modified PSP solution	13.54 ± 1.05	175.00	350.00
	PCL-PSP suture	10.78 ± 0.87	300.00	600.00
	PSP sponge	12.19 ± 0.93	200.00	400.00

chemical modification was carried out through quaternization to enhance its antibacterial activity, resulting in a slight decrease in yield of 11.52% with the purity of 92.11% and an increase in molecular weight of 33,125.43 Da. The quaternization degree of PSP reached 23.87%, confirming the successful introduction of functional groups.

Characterization of modified PSP-based antibacterial biomaterials

Through SEM observation, PCL-PSP suture presented a uniform and smooth nanofiber structure with a narrow fiber diameter distribution and regular pore structure formed between fibers, which was conducive to drug loading and sustained release. PSP hemostatic sponge exhibited a highly porous 3D network structure with uniform pore size distribution. The results showed that, with the PSP loading increased from 0 to 0.86 mg/m, the fiber diameter gradually decreased from 345.12 nm to 312.05 nm, indicating that the introduction of PSP had a certain impact on fiber forming. The tensile strength of the material showed a decreasing trend from 125.68 MPa to 92.67 MPa, while the elongation at break increased from 189.73% to 221.39%, indicating that a high content of PSP could enhance the ductility of fibers, but sacrifices some mechanical strength.

***In vitro* evaluation of antibacterial performance**

The modified PSP-based antibacterial biomaterial exhibited significant *in vitro* antibacterial activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa* compared to the control and PCL groups. MIC and MBC further confirmed the effective antibacterial ability of the improved material. The results demonstrated that neither the control group nor the simple PCL suture showed antibacterial activity with an inhibition zone of 0 and MIC and MBC greater than 1,000 μg/mL. The antibacterial zone of the modified PSP reached 15.67 mm and 13.54 mm with MIC of 125 μg/mL and 175 μg/mL and MBC of 250 μg/mL and 350 μg/mL for *Staphylococcus aureus* and *Pseudomonas aeruginosa*, respectively, demonstrating the strongest antibacterial effect. PCL-PSP suture and PSP sponge also showed significant antibacterial activities, producing inhibition zones of 12.89 mm and 14.32 mm for *Staphylococcus aureus* and 10.78 mm and 12.19 mm for *Pseudomonas aeruginosa*, respectively, with MIC and MBC values significantly lower than the control group (Table 1), which indicated that the introduction of modified PSP in the material effectively endowed it with antibacterial function. The analysis of the bacterial growth curve showed that the growth of bacteria was significantly inhibited in the presence of materials. More importantly, biofilm inhibition and clearance experiments showed that the modified PSP-based material could effectively inhibit the formation of bacterial biofilms and had a certain clearance effect on the already formed biofilms.

Cell toxicity and biocompatibility evaluation

Table 2. Effects of different materials on the relative survival rate of NIH 3T3 cells.

Sample group	Time	Absorbance (OD_{450}) ± SD	Relative cell viability (%) ± SD	*P* value (vs. control)
Control	24 h	0.85 ± 0.02	100.00 ± 2.56	-
	48 h	1.21 ± 0.04	100.00 ± 3.31	-
	72 h	1.63 ± 0.06	100.00 ± 3.68	-
PCL Suture	24 h	0.84 ± 0.03	98.75 ± 3.12	> 0.05
	48 h	1.20 ± 0.05	99.17 ± 4.13	> 0.05
	72 h	1.61 ± 0.07	98.77 ± 4.30	> 0.05
Modified PSP Solution	24 h	0.90 ± 0.02	105.34 ± 2.87	> 0.05
	48 h	1.32 ± 0.05	109.09 ± 4.13	< 0.05
	72 h	1.83 ± 0.07	112.27 ± 4.29	< 0.01
PCL-PSP Suture	24 h	0.87 ± 0.03	102.91 ± 3.01	> 0.05
	48 h	1.26 ± 0.04	104.13 ± 3.31	> 0.05
	72 h	1.72 ± 0.06	105.52 ± 3.68	> 0.05
PSP Sponge	24 h	0.88 ± 0.03	103.68 ± 2.95	> 0.05
	48 h	1.28 ± 0.04	105.79 ± 3.31	> 0.05
	72 h	1.76 ± 0.05	107.98 ± 3.07	< 0.05

Table 3. Effects of different materials on scratch healing rate of NIH 3T3 cells.

Sample group	0 h (%)	12 h (%) ± SD	24 h (%) ± SD
Control Group (PBS)	0.00	28.15 ± 3.78	55.62 ± 4.19
PCL Suture	0.00	30.08 ± 3.91	58.07 ± 4.05
Modified PSP Solution	0.00	45.92 ± 4.56	78.13 ± 5.23
PCL-PSP Suture	0.00	41.67 ± 4.31	72.89 ± 4.97
PSP Sponge	0.00	43.55 ± 4.48	75.01 ± 5.11

The cytotoxicity of modified PSP-based biomaterials on NIH 3T3 fibroblasts demonstrated that none of the materials in each group showed significant cytotoxicity, and the cell survival rate was above 98%. The modified PSP solution had the highest relative survival rate of 105.34%, while the relative survival rates of PCL-PSP suture and PSP sponge were 102.91% and 103.68%, respectively, slightly higher than the control group (Table 2). The results indicated that the material not only had good biocompatibility but also might even have a certain promoting effect on cell growth.

Evaluation of *in vitro* wound healing promotion

The results of *in vitro* cell scratch assay demonstrated that modified PSP-based biomaterials significantly promoted the migration of fibroblasts. The effect of different materials on the scratch healing rate of NIH 3T3 cells showed that, at 12 hours, the healing rate of the modified PSP solution group was the highest at 45.92%, while the control group was only 28.15%. By 24 hours, the healing rate of the modified PSP solution group further increased to 78.13%, significantly better than other groups. The PSP sponge group and PCL-PSP suture group also performed well, reaching 75.01% and 72.89%, respectively (Table 3), which indicated that modified PSP-related materials could significantly promote cell migration, thereby improving the efficiency of in vitro wound healing.

Animal wound repairing

In the mouse model of full-thickness skin defect infection wounds, modified PSP-based biomaterials showed excellent wound repair effects. Macroscopic observation showed that the wound healing speed of the PSP sponge

group was significantly faster than that of the control group and the medical gel sponge group. The wound area decreased rapidly, and granulation tissue formed well. The results showed that the wound healing rate of the PSP sponge group was 38.91% on the 4th day, which was significantly higher than that of the control group and the medical gel sponge group. The healing rate reached 92.11% on the 12th day, which was much higher than that of the control group of 75.39% (Figure 1). The results indicated that the PSP sponge had significant advantages in promoting rapid wound healing and was more effective than traditional medical sponges.

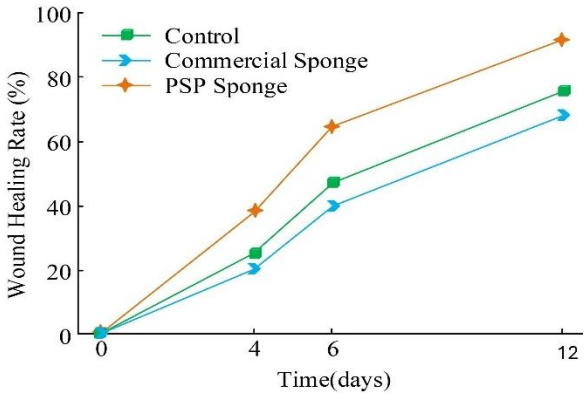

Figure 1. Changes in wound healing rate (%) of mice in different treatment groups over time.

The changes in inflammatory cell infiltration scores on the wound surface and the difference in the number of neovascularizations of different treatment groups on day 6 and day 12 demonstrated that the PSP sponge group had the lowest inflammation score of 0.67 on day 12 and the highest number of new blood vessels of 15.63 per field of view on day 12, indicating excellent performance of the material in promoting angiogenesis and reducing inflammatory response (Figure 2).

Discussion

This study developed and evaluated the potential application of antibacterial biomaterials based on improved TCM PSP in wound repair. *Polygonatum sibiricum* has been a medicinal and dietary homology for two thousand years, and fructooligosaccharides, saponins, and flavonoids have lipid-lowering and anti-inflammatory activities. Natural polysaccharides have limited physicochemical properties and require quaternization or microbial fermentation modification to enhance solubility, stability, and sustained release, thereby enhancing its performance in antibacterial, biocompatibility, and tissue repair promotion [13, 14]. Si *et al*. emphasized that their understory planting resources were abundant, but their basic research was weak [15]. Wound healing is a complex biological process. In the study, the significant healing effect of modified PSP biomaterials was consistent with previous research on *Polygonatum sibiricum* and its polysaccharide activity. Li *et al*. emphasized the diversity of various bioactive compounds in *Polygonatum sibiricum*, providing a material basis for the pleiotropy of PSP in wound healing. This study optimized the physicochemical properties of PSP through quaternization and other modifications, which was expected to more effectively release active ingredients or mediate biological effects in a specific way, thereby enhancing its role in wound repair [16]. Zhao *et al*. suggested that PSP's anti-inflammatory, antioxidant, and immunomodulatory effects could alleviate wound inflammation [17], while Li *et al*. investigated the effects of TCM processing on active ingredients and therapeutic efficacy and suggested that the modification method had a profound impact on the healing mechanism of PSP [18]. Quaternary ammonium modification may alter the charge distribution of polysaccharides, enhance antibacterial efficacy, and directly solve the obstacles of infection to healing. Meanwhile, this structural change may also optimize the interaction between polysaccharides and host cells, promote cell adhesion, proliferation, and migration, accelerate granulation tissue formation and the epithelialization process. Yuan *et al*. found that PSP inhibited scar collagen through the TGF-β/Smad pathway, providing a basis for improving

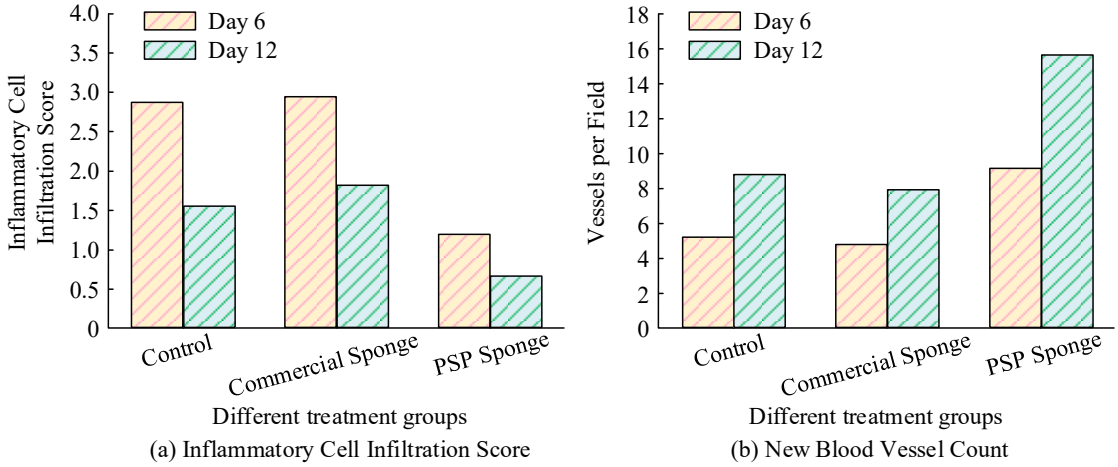

Figure 2. Inflammatory cell infiltration score and the numbers of neovascularization in wounds of mice in different treatment groups.

materials to promote remodeling and reduce scars [19]. This mechanism has important implications for tissue remodeling and scar formation in wound healing. If modified PSP can also regulate similar pathways locally in the wound, it will improve the appearance and function of the healed skin by promoting normal collagen deposition and inhibiting abnormal scar collagen production. Based on those previous reports, the developed antibacterial biomaterial based on modified PSP would have multiple benefits in wound repair due to the inherent pharmacological activity of PSP and the performance improvement brought by chemical modification. These improvements gave the material excellent antibacterial and anti-infective capabilities and comprehensively promoted the wound healing process by regulating inflammation, promoting cell proliferation and migration, and optimizing the collagen remodeling mechanism. The overall results indicated that modified PSP-based antibacterial materials had significant advantages in antibacterial properties, tissue compatibility, and healing-promoting effects, and had good clinical translation prospects. The results confirmed the effectiveness of the material and sparked in-depth thinking on the application mechanisms of PSP in the biomedical field. However, there is still room for further expansion in the analysis of material functional mechanisms such as further exploration of the molecular mechanisms regulating the immune microenvironment. Future work can further combine intelligent delivery systems or collaborate with other natural medicines to broaden the application scope in areas such as chronic wounds and postoperative infections.

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