

Original Article

Development and performance test of biodegradable polymer porous composite membrane micro-coil skeleton system

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Abstract: Objective: To make biodegradable porous composite membrane micro-coil (MC) skeleton system with phosphorylcholine-grafted chitosan (PC-Chi) and to analyze its mechanical properties. Methods: Based on the restriction of the thickness and pore size of porous membrane, the interfacial bonding tightness of biodegradable polymer materials (chitosan, poly-ε-caprolactone and its phosphorylcholine grafted polymer) and tungsten, platinum, stainless steel materials was studied by using scratch tester and X-ray diffraction technique. Step-by-step casting, dipping and phase separation were adopted to combine the biodegradable polymer material on MC so as to prepare porous composite membrane MC skeleton system. Scanning electron microscopy was used to observe the adhesion morphology of porous composite membrane on MC. The biosensor was used to measure the tensile strength and elastic modulus of porous composite membrane MC skeleton system. Results: In comparison, the compressive stress of PC-Chi film was the largest; the minimum tensile stress was -243.1 MPa; the peel adhesion-critical load L_c was 5.9N. In this experiment, the binding ability of tungsten was the best. PC-Chi could well cover the surface of tungsten MC, but its elastic stress-strain had no significant difference comparing with common MC. Conclusion: PC-Chi can adhere well to metal surfaces. Within the elastic range, the porous composite membrane MC skeleton system with PC-Chi as coating material has favorable elastic stress and is suitable for practical application.

Keywords: Phosphorylcholine-grafted chitosan, X-ray diffraction, thin film, bond stress, scratch method, elastic stress-strain, micro-coil

Introduction

Micro-coil (MC) skeleton system is a kind of embolic material widely used in interventional therapy [1]. It mainly occludes lesion vessels and interrupts their blood supply to effectively control hemorrhage or treat diseases such as vascular lesions and tumors [2]. However, at present, many MC materials cannot meet clinical application standards [3, 4]. Relevant scholars have shown that rapid coagulation near the MC and good biological properties require MC materials with better structural performance and surface design [5]. With the rise of surface modification technology as well as the application and promotion of coagulation-degradable polymer materials, the coils with metal materi-

als containing biodegradable macromolecule will replace the bare coils to become a new direction in intervention field [6, 7].

Biodegradable macromolecule material is a polymer that can be degradable into micromolecule after a certain period of time and under certain conditions; the biodegradable polymer materials used for human body implantation can be divided into natural polymers (chitosan and collagen, etc.) and synthetic polymers (polylactic acid, poly-ε-caprolactone (PCL)) [8]. Chitosan (Chi) is a very abundant natural polysaccharide made from the shell of some shellfish and chitin deacetylation of some fungi's cell wall; it is important in agriculture, textile, printing and dyeing, medical and other indus-

tries [9-11]. By graft modification and other chemical methods, the advantages of chitosan and other substances can be effectively combined to obtain excellent properties of polymers [12-14]. PCL has favorable biocompatibility, and its degradation products are harmless to the human body. Related studies have shown that phosphorylcholine (PC) grafted polymer has good blood compatibility [15, 16]. Coating the graft-modified polymer can achieve the required properties of the material, but sufficient adhesive strength is the precondition for any coating to perform its functions [17-19]. Moreover, the coating film has an influence on the original mechanical properties of practical materials [20-22]. So, it is necessary to analyze the mechanical properties of the modified materials. In this paper, we used biodegradable polymer material (modifier of natural macromolecule degradable material chitosan: phosphorylcholine-grafted chitosan (PC-Chi)), which was suitable for autologous vascular endothelial cells culture, to coating (with solution) different metal surfaces, to prepare metal-based coated test specimens and porous composite membrane MC skeleton system test samples. Its structural properties were analyzed to obtain an ideal porous composite membrane MC.

Materials and methods

Equipment

Parameters of X350A X-ray stress meter: tube voltage 30 kV, tube current 10 mA, focal size $0.5 \times 0.5 \text{ mm}^2$, integrated stability $\pm 0.1\%$, scanning angle range $120^\circ \leq 2\theta \leq 170^\circ$ and angular accuracy 0.002° .

Parameters of STRA-1 surface profiler: probe radius $2 \mu\text{m}$, sampling interval $2.5 \mu\text{m}$. During the experiment, the scanning length was 17.5 mm, so that each contour had a total of 7,000 data, which were stored in the computer for morphology analysis.

Parameters of WS-2000 film adhesion scratch tester: radius of diamond indenter tip 0.2 mm, scratch speed 2 mm/min, loading speed 2 N/min, scratch range 20-30 mm and ending load 100 N.

Parameters of AGS2500ND strong tensile machine (from Shimadzu, Japan): clip distance 80 mm, pretension 0.05 N.

Automatic displacement booster: self-developed.

Sample preparation

Metal substrate and coating test samples: Tungsten, platinum and stainless steel were processed to sheet samples with thickness of 3 mm and diameter of 20 mm. After polishing and cleaning samples' surface, 1%-3% aqueous solutions containing Chi, PC-Chi, PCL, phosphorylcholine grafted poly- ϵ -caprolactone (PC-PCL) polymers were spin-coated on the surface of materials respectively, after natural airing for 12 hours then drying in a vacuum oven at 60°C .

Porous composite membrane MC skeleton system test samples: The Chi, PC-Chi polymers were configured as aqueous solutions and dipping on the surface of the tungsten MC by controlling the treated time, temperature and concentration, after natural airing for 12 hours then drying in a vacuum oven at 60°C . The surface of MC substrate formed relatively complete porous polymer membrane with pore size $1\text{-}50 \mu\text{m}$ (standby application).

Analysis of structural performance

Adhesion analysis of metal substrate and coating: Internal stress was a common problem in thin film materials. The causes of internal stress in thin film were complicated. Its measurement methods were divided into measuring the lattice distortion and the substrate deformation, while X-ray diffraction was a general method to measure lattice distortion.

The X350A X-ray stress meter was used to measure the phase structure of coating and the internal stress in the film. The instrument was using roll-fixed Ψ scan mode, and cross-correlation function was used to determine the peak.

The atoms in metal materials were usually regularly arranged to form lattices and a series of crystal planes. When there was tensile stress in the material, the spacing of the crystal planes paralleling to the stress direction was narrowed; meanwhile, the spacing of the crystal planes in other directions was widened. See **Figure 1**. When there was compressive stress in the material, the variation of interplanar spacing was opposite to the tensile stress. Therefore, the stress value in material could be

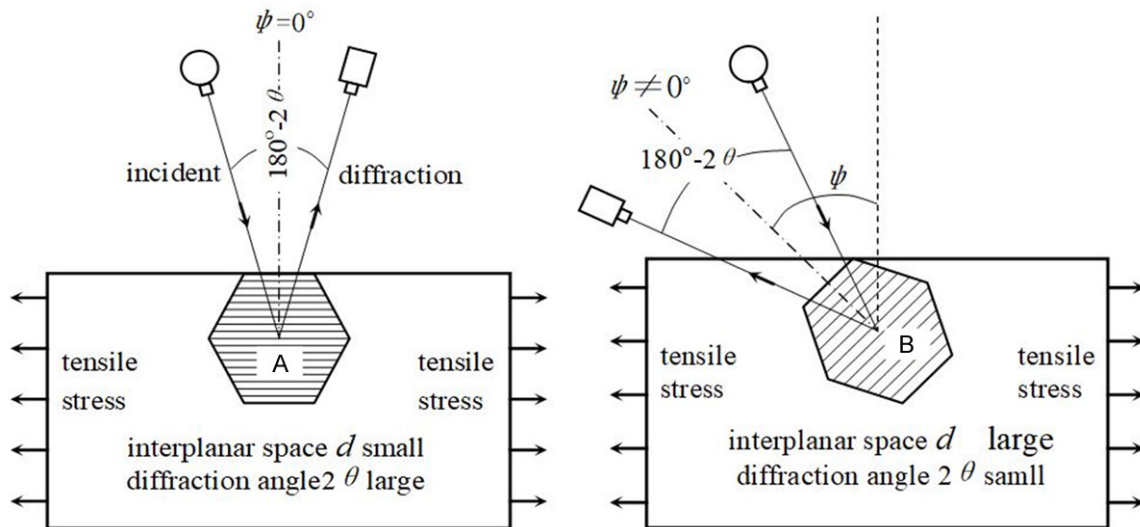


Figure 1. Interplanar spacing in different azimuths.

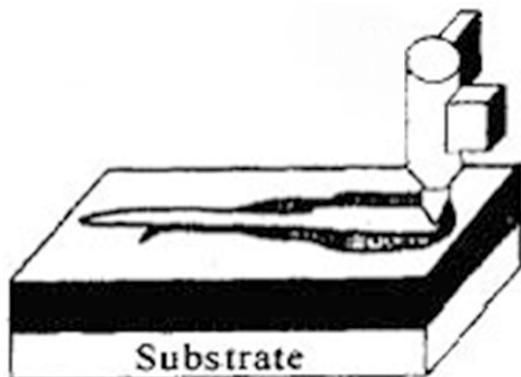


Figure 2. Sketch of scratch measurement.

Table 1. Scratch test of metal substrate and coating film (critical load, N)

Metal substrate	Coating material			
	Chi	PC-Chi	PCL	PC-PCL
Tungsten	29.1	27.6	28.8	26.6
Platinum	28.5	26.8	27.4	27.2
Stainless steel	4.4	2.6	3.3	2.5

Note: Chi for chitosan, PC-Chi for phosphorylcholine-grafted chitosan, PCL for Poly-ε-caprolactone, PC-PCL for phosphorylcholine grafted poly-ε-caprolactone.

determined by measuring the interplanar spacing corresponding to different azimuth angles (ψ).

When X-ray was incident on the material, the diffraction phenomenon occurred inevitably. The interplanar spacing of the material (d), the X-ray diffraction angle θ and wavelength λ follows the Bragg equation: $2d \sin \theta = \lambda$.

According to the theory of elastic mechanics and the Bragg equation, the residual stress σ could be deduced as follows: (K as the X-ray stress constant of the material, 2θ as the diffraction angle and ρ as crystalline density of the sample): $\sigma = K (\rho (2\theta) / \rho (\sin^2 \psi))$.

The film adhesion was measured by a scratch tester, and the film thickness of each sample was measured by a surface profilometer with computer data acquisition system.

WS-2002 coating adhesion scratch tester was used in this experiment (Figure 2). Acoustic emission detection technology, tangential force detection technology and microcomputer-controlled technology were used. Load was continuously added to the stylus (diamond indenter) through the automatic loading mechanism while moving the samples, so the stylus could contact the coating (0.5-20 μm) surface. Acoustic emission signals, load variations, and tangential force variations were obtained by each sensor while scratching. After amplification, they were input into a computer, and the measurement results were drawn into graphs through A/D conversion. Thereout, bonding strength (critical load) L_c of the substrate and the film (with a thickness of 3-5 microns) could be obtained.

Tensile strength and elastic modulus test of porous composite membrane MC skeleton system: There were 6 groups of samples, including $\phi 6$ mm MC, Chi-MC and PC-Chi-MC, as well as $\phi 10$ mm MC, Chi-MC and PC-Chi-MC respec-

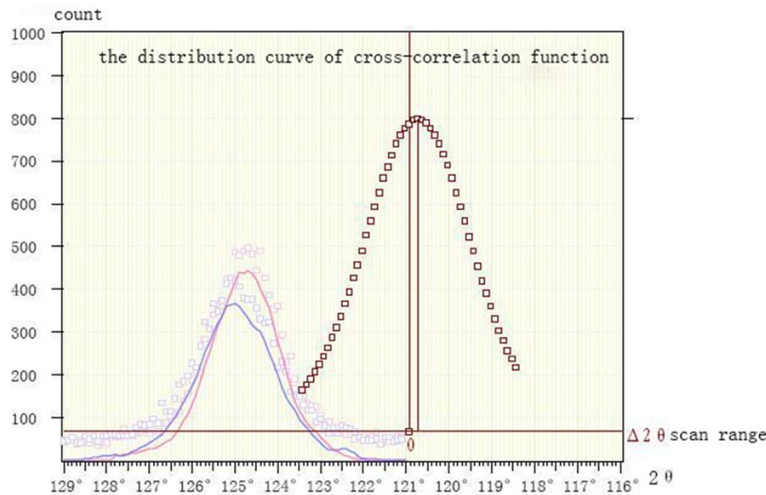


Figure 3. Binding force of phosphorylcholine-grafted chitosan coating and tungsten.

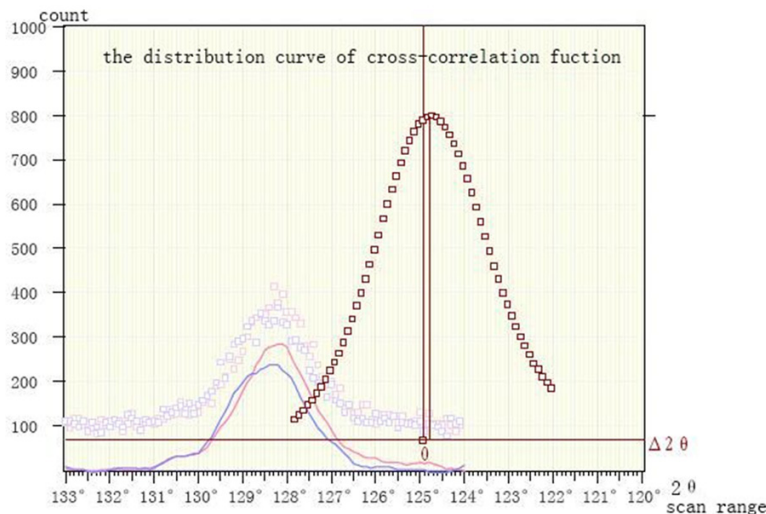


Figure 4. Binding force of chitosan coating and platinum.

tively. The mechanical properties were measured by a Shimadzu AGS2500ND strong tensile machine [23]. Scanning electron microscopy was used to determine the structure of PC-Chi film and MC multiple layers.

Test methods of mechanical properties: automatic displacement booster was used for sample gripping; the center of the straightened coil was the base point; displacement of 10 mm, 15 mm, 20 mm and 25 mm was another point of action; the lifting speed of the fixture was 250 mm/min. After completion, the change of level two spiral was observed; meanwhile, electron microscopy was used for the observation of porous composite membrane MC system after stretching.

Statistical method

SPSS19.0 statistical software was used for statistical analysis. Enumeration data were expressed as rate and tested by chi-square test. $P < 0.05$ for the difference was statistically significant.

Results

Binding ability of film

While coating the stainless steel surface, coating materials were clustered as ball shapes and not easy to form a film. Measurement showed that the thickness of the film was uneven, and scratch test showed that its load was extremely low, which proved that the adhesion was not good, so, we did not use stainless steel for further phase structure and internal stress tests. Coating on the surface of tungsten and platinum had good adhesion. See **Table 1**.

Phase structure of coating and internal stress in film measured by X-ray stress meter

The stress of the film system was indirectly characterized by measuring the stress of under-film base metal with the use of under-film substrate diffraction method. Corresponding measurements are shown in **Figures 3, 4, Tables 2 and 3**.

Different substrate materials resulted in different positions of diffraction peaks; different coatings on the surface caused to different changes of diffraction peak's position while the diffraction angle was changing, so that the corresponding bonding stress between the substrate and the material could be calculated. The measurement results of each sample are shown in **Table 4**.

The surface of the metal substrate had compressive stress (negative stress) itself. It was more meaningful to compare the adhesion of

Table 2. Binding force of pc-chi and tungsten

Measurement results		
ψ	0.0°	45.0°
2 θ p	124.766°	124.969°
Peak count	442	364
Width of half peak	1.87°	2.07°
Integral intensity	885	816
Integral width	2.00°	2.24°
Stress σ	-243.1 Mpa	

Note: ψ as azimuth angle, 2θ as diffraction angle, p as crystalline density of the sample, stress σ as residual stress.

Table 3. Binding force of Chi and platinum

Measurement results		
ψ	0.0°	45.0°
2 θ p	128.258°	128.448°
Peak count	286	236
Width of half peak	1.88°	2.06°
Integral intensity	596	505
Integral width	2.08°	2.14°
Stress σ	-227.4 Mpa	

Note: ψ as azimuth angle, 2θ as diffraction angle, p as crystalline density of the sample, stress σ as residual stress.

Table 4. Measurement results of stress (base stress, MPa)

Metal substrate	Coating material			
	Chi	PC-Chi	PCL	PC-PCL
Tungsten	-291.0	-243.1	-332.4	-289.7
Platinum	-227.4	-285.0	-267.0	-277.6
Stainless steel	-241.3	-239.6	-251.3	-190.9

Note: Chi for chitosan, PC-Chi for phosphorylcholine-grafted chitosan, PCL for Poly- ϵ -caprolactone, PC-PCL for phosphorylcholine grafted poly- ϵ -caprolactone.

the films on the same metal substrate material surface. For example, the tungsten samples had a gradually decreased order of PCL > Chi > PC-PCL > PC-Chi about substrate compressive stress (negative stress). Moreover, taking into account that the change trend of substrate stress was the opposite of the film, the above gradual decrease order of substrate compressive stress reflected the gradual increase of film compressive stress or the gradual decrease of film tensile stress, which was helpful for improving the bonding force between the film and the substrate. Therefore, in comparison, PC-Chi film had the largest compressive stress,

the least tensile stress and the best binding ability with tungsten.

Film adhesion determined by scratch test

The bonding strength tests of the metal substrate and coating film were shown in **Figures 5** and **6**.

The experiment showed that both PC-Chi and Chi materials were able to adhere well to metal surfaces compared with other materials.

Detection of porous composite membrane MC skeleton system

After Chi and PC-Chi were coated on the surface of the tungsten MC, there was no obvious change in the appearance of the coil. Scanning electron microscopy showed that the membranous material uniformly covered on the surface of the MC with a thickness of 10 μ m or less. Where there was a film shedding, white tungsten MC body could be seen (indicated by arrow in **Figure 7**).

Tensile strength and elastic modulus test of porous composite membrane MC skeleton system

As can be seen from the stress-strain curve shown in **Figure 8**, the shapes of the various MC tensile curves on the basis of the original metallic material were similar and naturally retracted to near the original baseline after stretching, indicating that the materials were good elastomers. However, after several long-distance stretching, their self-contrast showed a decrease in baseline and kurtosis, indicating a decrease of elasticity.

The values recorded in **Table 5** were statistically analyzed. Comparing the stress and strain of the MC with different diameters (ϕ 6 mm and ϕ 10 mm) but with the same composite membrane, it was found that the strain of ϕ 6 mm coil had greater response to stress (better elasticity), while the diameter of ϕ 10 mm coil showed poor elasticity. The difference between the two was statistically significant ($P < 0.01$). Within the tested elongation range, the changes of level two spiral were not significant in both diameter ϕ 6 mm and ϕ 10 mm MC, and were considered to be within their elastic limits.

Comparing MC with the same diameter (ϕ 6 mm) but with different materials, it was found

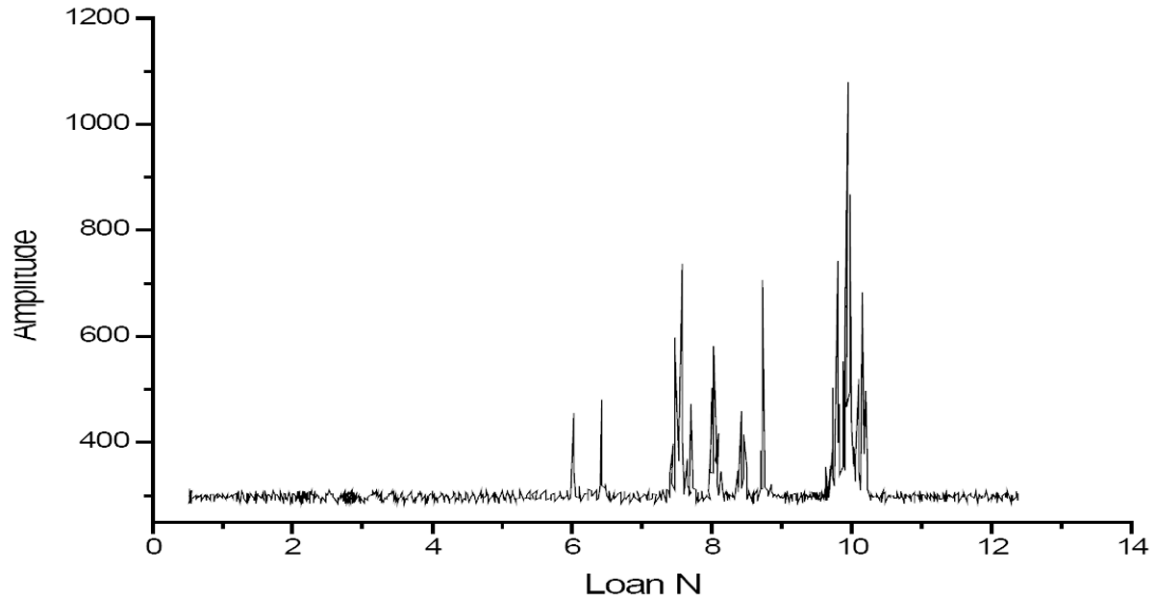


Figure 5. Bonding strength of film and substrate. Changes of phosphorylcholine-grafted chitosan and tungsten film-substrate binding force, the critical load L_c was 5.9 N.

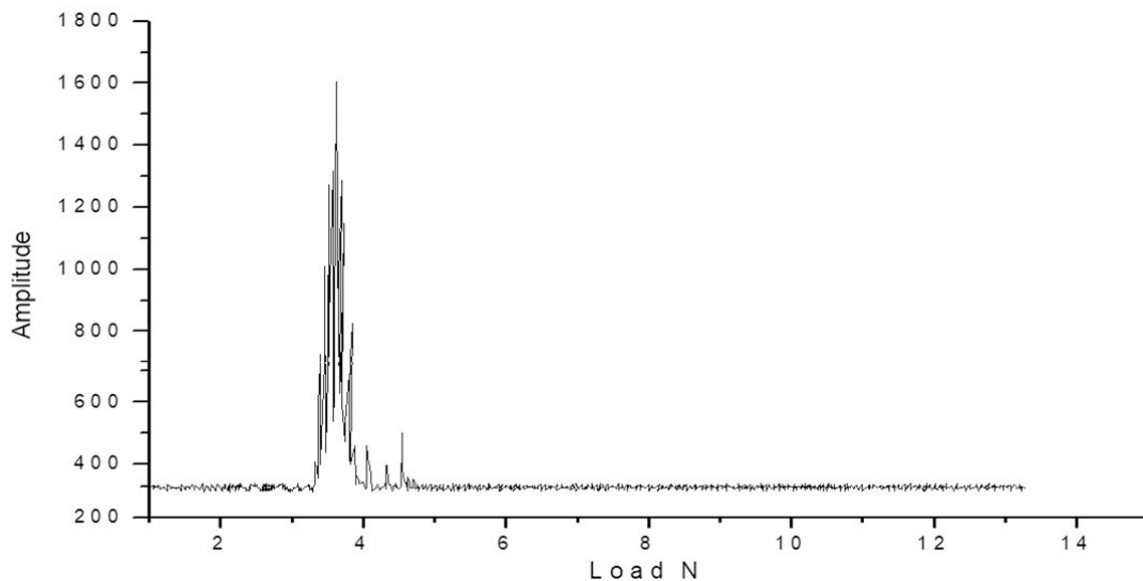


Figure 6. Bonding strength of film and substrate. Change of chitosan and platinum film-substrate binding force, the critical load L_c was 3.4 N.

that there was a significant difference ($P < 0.01$) between Chi-MC and MC; the comparison between PC-Chi-MC and Chi-MC was also with significant difference ($P < 0.01$). However, stress change showed no significant difference among three materials MC with larger diameter of $\phi 10$ mm when the tensile length was less than 20 mm. When the tensile length was longer than

20 mm, there was significant difference ($P < 0.01$).

Discussion

At present, MC for embolization therapy is the main method of vascular intervention therapy. MC mainly includes bare coil and biologically-

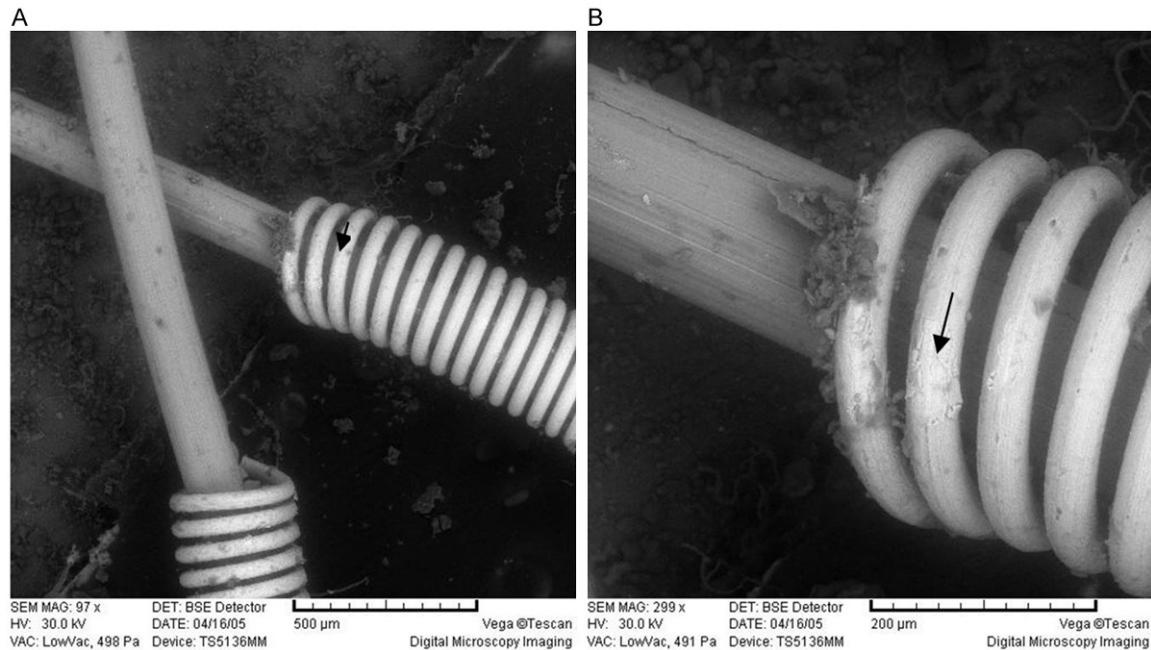


Figure 7. Scanning electron microscopy graphs of porous composite membrane MC skeleton system. A: X97, B: X293.

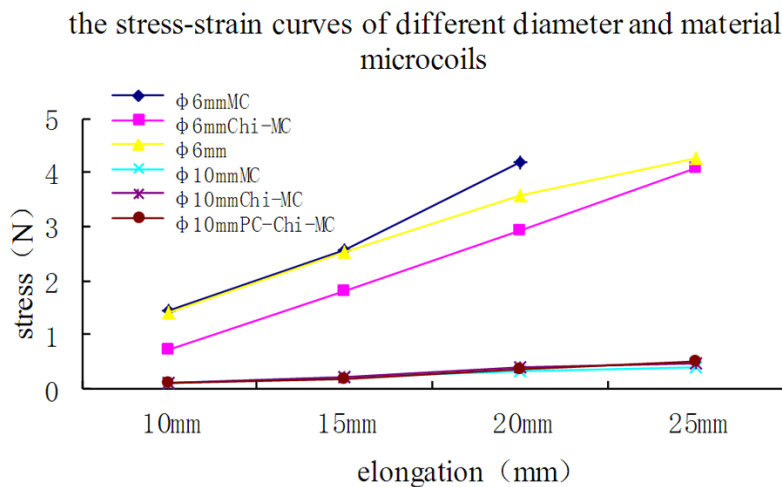


Figure 8. Stress-strain curve of micro-coils with different diameters and materials.

modified coil. Due to the bio-inertness of bare coil, inflammation occurs easily with slow scar formation, which leads to recanalization of aneurysm. However, the biologically-modified coil, with good biocompatibility, can accelerate the organization of tissues in aneurysm, and it is the future direction of development. Its surface is modified with extracellular matrix proteins, biodegradable polymers, cationic implants and fiber forming cells that can secrete

growth factors. For example, lactic-co-glycolic acid-modified platinum coils are used to increase the postoperative recanalization rate [24]; hydrolysable and water-expansion MC is used to increase the filling rate of embolized vessels [25]; vascular endothelial growth factor-modified MC has better occlusion for aneurysm [26].

In this paper, MC modified by biodegradable polymer (Chi and PC-Chi) porous composite membranes were used as the research objects. By means of X-ray stress

meter, scratch tester, tensile strength and elastic modulus, system performance of different MC was tested to provide some reference for MC study. Experimental study on metal-based coatings revealed that the biodegradable polymers including Chi, PC-Chi, PCL and PC-PCL had poor adhesion and film-forming ability on stainless steel surface, but their binding force with tungsten and platinum was good [27]. The results of under-film substrate diffraction test

Table 5. Elastic stress changes and baseline shift of different materials MC with different elongation

Diameter	Coating	Stress change (N)				Baseline shift (N)			
		10 mm	15 mm	20 mm	25 mm	10 mm	15 mm	20 mm	25 mm
6 mm	MC	1.50	2.60	4.30			0.05	0.25	
		1.43	2.55	4.20			0.05	0.32	
		1.45	2.55	4.00		0.02	0.05	0.35	
	Chi-MC	0.70	1.75	2.95	4.18		0.05	0.20	0.58
		0.73	1.85	3.00	4.13		0.07	0.25	0.63
		0.70	1.85	2.85	3.95		0.08	0.28	0.65
	PC-Chi-MC	1.40	2.55	3.65	> 4.25	0.06	0.20	0.45	0.80
		1.45	2.56	3.58	> 4.25	0.06	0.20	0.48	0.80
		1.40	2.45	3.50	4.15	0.08	0.20	0.50	0.80
	10 mm	MC	0.10	0.20	0.30	0.41			0.04
0.10			0.21	0.32	0.39			0.06	0.09
0.10			0.20	0.33	0.39			0.06	0.10
Chi-MC		0.13	0.20	0.40	0.50		0.03	0.05	0.08
		0.12	0.23	0.39	0.45	0.02	0.03	0.06	0.08
		0.12	0.23	0.38	0.48	0.03	0.03	0.08	0.08
PC-Chi-MC		0.10	0.18	0.40	0.50		0.05	0.05	0.07
		0.10	0.17	0.40	0.48	0.02	0.07	0.07	0.08
		0.11	0.14	0.35	0.48	0.03	0.08	0.08	0.10

Note: MC for micro-coil, Chi-MC for chitosan coated micro-coil, PC-Chi-MC for phosphorylcholine-grafted chitosan coated micro-coil.

showed that the PC-Chi combined with tungsten had the highest under-film compressive stress, the highest critical load L_c and better binding force, while Chi combined with platinum had the highest under-film compressive stress, better critical load L_c and better binding force.

Tensile strength and elastic modulus test of porous composite membrane MC skeleton system showed that PC-Chi could adhere well to tungsten surface compared with other materials. This may be related to the presence of a large number of free amino groups in chitosan, for they increased the adhesion to the metal surface. Within the elastic range, the porous composite membrane MC skeleton system with PC-Chi as coating material had favorable elastic stress. Different diameters of MC varied widely in their stress. The smaller the diameter, the larger their tensile stress. Coils with the same diameter, but with different materials had different stress, with the increase of tensile length, the difference of stress between different materials also increased.

In summary, PC-Chi can be well attached to the tungsten coil surface. Within the elastic range,

the porous composite membrane MC skeleton system with PC-Chi as coating material has favorable elastic stress and is suitable for practical application. However, there are some shortcomings in this study. For example, based on the binding force between the biodegradable polymer film and the metal substrate, we only chose tungsten (with better binding force) as coil skeleton system for performance study. We did not carry out research about porous composite membrane platinum coil skeleton system, neither did we compare that with PC-Chi composite membrane tungsten coil skeleton system. The shortcomings will be supplemented in subsequent studies.

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Disclosure of conflict of interest

None.

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