Introduction

Electrospinning is a simple, fast, and efficient method for preparing nanofibers with the diameter from a few nanometers to tens of nanometers. As a kind of one-dimensional nanofiber material, electrospun nanofibers have attracted more and more researchers’ attention. Electrospun nanofibers have the advantages of length-to-diameter ratio, large specific surface area and high porosity. Electrospun nanofibers can be controlled by a variety of polymers and easy to be functionalized. Electrospun nanofibers have been shown to different applications in many fields, such as energy, environment, tissue engineering, medicine, and sensors, which excellent performances are due to their design tunable structure and composition. Among them, the core-shell nanofibers have novel structures and important applications due to combining the advantages of the inner and outer layer materials. The traditional methods for preparing core-shell nanofibers include coaxial electrospinning, in situ growth and the surface polymerization. Among them, the method of grafting on the nanofiber surface has a good prospect in the field of drug carrier control and release. In order to make the more intelligent carrier, a variety of conditional response
drug carriers\textsuperscript{18} were designed and prepared, such as temperature response carrier\textsuperscript{19,20} and pH response carrier.\textsuperscript{21} Among them, surface-grafted electron transfer-atom-transfer radical polymerization (AGET-ATRP) is a well-known controlled polymerization method to adjust the degree of cross-linking of the polymer shell.\textsuperscript{22}

Poly (glycerol sebacate) (PGS), which has good biocompatibility, flexibility and degradability, is a kind of biomedical material with excellent performance, and is widely used in various organs and wound patches. However, its spinnability is low. It is not to form nanofiber morphology alone, which limit its application.\textsuperscript{23,24} Poly-L-lactic acid (PLLA), as a synthetic polymer that can be controlled to degrade, has been studied in clinical medicine for a long time and has good spinnability. It can be used as a spinning aid for PGS, so as to assist in the prepa-

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Experimental section

Materials

Sebacic acid (99\%, $M_w=202.25$, $C_{18}H_{36}O_4$) and glycerol (A.R., $M_w=92.09$, $C_3H_8O_3$) were purchased from Aladdin (China), and Sigma (USA), respectively. The poly-L-lactic acid (PLLA, $M_n=200$ kDa) were purchased from the Jinan Daigang Biomaterial Co. Ltd (China). N-isopropylacrylamide (A.R., $M_w=113.16$, $C_3H_7NO$) was obtained from Aladdin (China) and was recrystallized by water. 2-Bromoisobutyryl bromide (BiBB, 99\%, $M_w=229.91$, $C_4H_6Br_2O$) was purchased from Aladdin (China). Triethylamine (TEA, $M_w=101.19$, $C_3H_7N$) was purchased from Sigma (USA). CuBr was purchased from Macklin (China) and was reduced by glacial acetic acid (98\%, Aladdin, China). Pentamethyldiethylenetriamine (PMDETA, $M_w=173.3$, $C_{10}H_{18}N_3$) and Ascorbic Acid (AA, $M_w=176.12$, $C_6H_8O_6$) were obtained from Aladdin (China). Dichloromethane (DCM), ethyl acetate (EtOAc), methanol (MeOH), and N,N-dimethylformamide (DMF) were of reagent grade and purchased from Sigma (USA). Deionized water was prepared by water purification machine (UTP-1-10T). Diluted hydrochloric acid (0.01 mol/L) was prepared by diluting the concentrated hydrochloric acid (37.5\% HCl) from Beijing Chemical Work (China). All solvents were used without further purification.

Fabrication of the macro-initiator pre-PGS-Br

First, sebacic acid was recrystallized using absolute ethyl alcohol. Then, equimolar ratios of glycerol and sebacic acid were mixed in the flask under 140°C oil bath to melt the sebacic acid, then heat up to 160°C for 8h to form the PGS pre-polymer. And the nitrogen flow was blown at a gas flow of 0.2 m$^3$h$^{-1}$ during the reaction.\textsuperscript{35}

About 10 g pre-PGS was dissolved in dichloromethane (DCM) in the 50mL flask, then 900 $\mu$L BiBB was added to solution drop by drop. 200 $\mu$L TEA was as acid-binding agent in order to promote the reactivity. The solution was stirred by magnetic stirrers at room temperature for 24h. DCM of the solution was evaporated by rotatory evaporator after reaction ending. EtOAc was added to the above-mentioned product due to remove the reactive triethylamine hydrochloride. And 0.01 mol/L diluted hydrochloric acid was used to remove the remaining TEA by separating funnel. At the end, EtOAc was removed by rotatory evaporator (Yarong RE-52AA, Shanghai, China).

Fabrication of the PGS/PGS-Br/PLLA nanofiber membrane

During fabrication of the PGS/PGS-Br/PLLA nanofiber membrane, 0.8 g pre-PGS, 0.2 g pre-PGS-Br and 1.0 g PLLA were mixed and dissolved in the mixed solvent of DCM and DMF (v:v = 3:1. The concentration of PLLA in the mixed solvent was 10 wt\%. The as-prepared solutions were loaded into two 5 mL syringe. The electrospinning equipment is QINGZI NANO E02 (China). The inner diameter of needle is 0.6 mm. And the flow rate of accesses was 0.6 mL h$^{-1}$. In addition, the electospinning voltage was 18 kV and the distance between the needle and collector (aluminum foil) was set at 15 cm. The obtained PGS/PGS-Br@PLLA nanofiber membrane was exposed on room temperature to evaporate any residual solvent. Furthermore, the membrane was thermo-cured in 120°C under vacuum drying oven (101-2A, Tianjin, China) for 72 h to cure PGS nanofibers.
Fabrication of the PGS/PLLA@PNIPAM core-shell nanofiber membrane by surface ATRP grafting

The above-mentioned nanofiber membrane containing the macromolecule initiator was added to the three-mouth flask containing methanol or water, and nitrogen was rinsed under the ice water bath for 20 min. The ligand pentamethyldiethylenetriamine (PMDETA) and the monomer NIPAM were added to the flask in a nitrogen atmosphere, and then changed to an oil bath (dimethyl silicone oil) and then reacted at 60°C for 60 min. Finally, the reaction is terminated by removing nitrogen atmosphere and touching the air. After the reaction is completed, the nanofiber membrane is washed with deionized water for three times and then put into a vacuum drying oven (101-2A, Tianjin, China) for drying 24 h.

Characterizations of pre-PGS-Br and the PGS/PLLA@PNIPAM nanofiber membrane

The pre-PGS and pre-PGS-Br were smeared on the potassium bromide (KBr) tablet and characterized by Fourier-transform infrared spectrometer from 4000 to 500 cm⁻¹ (FTIR, Nicolet 5700, Thermo Company, USA). The structure of pre-PGS and pre-PGS-Br were characterized by hydrogen nuclear magnetic resonance (¹H NMR, A V400 NMR, Bruker Company, Germany). It was tested at 600 MHz using DCl 3 as solvent. The morphology of the PGS/PLLA@PNIPAM nanofiber membrane was examined by scanning electron microscopy (SEM, FEI Quanta 250, The Netherlands). At the same time, SEM could also be used with electronic energy spectrum, qualitative test sample elements. The dry membrane sample ensuring they are completely free of moisture was pasted on the sample table and then were sputter coated with gold (Model 550; Electron Microscope Sciences) in preparation for SEM.³⁵ X-ray photoelectron spectroscopy (XPS, ESCALAB 250, Thermo VG Scientific, USA) was used to detect the N elements, the corresponding content and to analyze the chemical state within 10 nm of the sample surface.

Characterization of physical properties

The wettability of membranes was characterized by water contact angle measurements (WCA, Samsung FA-CED camera, Korea). To illustrate the thermoresponsive property of PGS/PLLA@PNIPAM membranes.

Drug release test in different temperature

In order to test the temperature responsive effect of drug release, the characteristic absorption peak of gatifloxacin (model drug) at 285.5 nm was measured by ultraviolet spectrophotometry (UV, u-3900, Hitachi, Japan). The quantitative PGS/PLLA@PNIPAM nanofibers loading gatifloxacin were immersed into 50 mL deionized water under different temperature (20°C and 50°C), respectively in oscillation incubator (BS-2F, Dingfeng, China). 1 mL solution was taken out at different times (0, 5, 15, 30, 60, 90, 120, 180, 240, 360, 480, and 600 min) respectively, then tested by ultraviolet absorption three times to calculate the drug release concentration.

Results and discussions

As shown in Scheme 1, the preparation process of the PGS/PLLA@PNIPAM nanofiber membrane consists of two main steps: synthesis of the macro-initiator PGS-Br and grafting PNIPAM polymer by AGET-ATRP on the surface of electrospun PGS/PGS-Br/PLLA nanofiber membrane.

Preparation of the pre-PGS-Br

As depicted in ¹H NMR spectrum of Figure 1(a), it showed –CH₂ groups in the backbone supported by sebacic acid at 1.3, 1.6, and 2.34 ppm, and –CH, –CH– at 4.18 and 3.7 ppm from glycerol, which were influenced by the distance from ester groups. As shown in Figure 1(b), macro-initiator pre-PGS-Br was evidenced by –CH₃ group from BiBB at 2.0 ppm, which means BiBB was successfully grafted on pre-PGS. The pre-PGS was synthesized by the condensation reaction, the FTIR spectrum of pre-PGS in Figure 1(c) shows the peaks for –C=O at 1740 cm⁻¹ and the peaks for –OH at 3438 cm⁻¹, which is completely consistent with the previous report.³⁵ And in Figure 1(d), the peak of C–Br was showed at 737 cm⁻¹. It also confirmed the formation of pre-PGS-Br. X-ray photoelectric spectroscopy (XPS) results show the co-presence of C, O, N, and Br in the as-prepared samples (Figure 2(b)) compared to the PGS/PLLA membrane (Figure 2(a)), suggesting the successful reacting of BiBB. The high resolution Br 3d spectrum provided in Figure 2(e).

Preparation of PGS/PLLA@PNIPAM nanofiber membrane

The PGS/PGS-Br/PLLA-grafting-PNIPAM polymer was synthesized by AGET-ATRP reaction, the FTIR spectrum of PGS in Figure 1(d) shows the peaks for –CO–NH– at 1640 cm⁻¹ and the peaks for –NH– at 3440 cm⁻¹, which is completely consistent with the previous report. X-ray photoelectron spectroscopy (XPS) results show the co-presence of C, O, N, and Br in the as-prepared samples (Figure 2(b)) compared to the PGS/PLLA membrane (Figure 2(a)), suggesting the successful reacting of BiBB. The high resolution Br 3d spectrum provided in Figure 2(e).
grafting PNIPAM, it shows the co-presence of C, O, N, and H in the PGS/PLLA@PNIPAM nanofiber membrane (Figure 2(c)). The peak more can be deconvoluted into four peaks in the high resolution C 1s (Figure 2(f)), O=C–O, C=O, C–O, C–N, and C–C, C–H, respectively.36 No significant difference can be obtained from the C 1s XPS spectra in the PGS/PGS-Br/PLLA nanofiber membrane and PGS/PLLA@PNIPAM nanofiber membrane. So N1s spectra of PGS/PLLA@PNIPAM nanofiber membrane was tested as shown in Figure 2(g). The high-resolution N 1s spectrum in Figure 2(g) shows the peak at 129.9 eV, revealing the presence of C–N bonds, which indicating the successful grafting of PNIPAM.

Further, in order to prove the successful preparation of PGS/PLLA@PNIPAM, the prepared ground nanofiber membrane was characterized by SEM images and EDS elemental analysis, as shown in Figure 3. Figure 3(a) and (d) showed the SEM images of the nanofiber membranes before and after grafting PNIPAM polymer, and the distributions of N and Br elements were investigated on the nanofiber surface, respectively. From SEM images, as we can see the surface of nanofiber membrane changed from smooth to rough folded surface, which indirectly demonstrates the successful polymerization of PNIPAM polymer on the surface of the nanofiber. Figure 3(b), (c), (e), and (f) show the distribution of N and Br elements of PGS/
Figure 1. $^1$H NMR spectrum of (a) PGS and (b) PGS-Br. The FTIR spectrum of (c) pre-PGS and (d) pre-PGS, PGS-Br and PGS/PLLA@PNIPAM.

Figure 2. XPS survey spectra: (a) PGS/PLLA, (b) PGS/PGS-Br/PLLA, and (c) PGS/PLLA@PNIPAM nanofiber membrane; (d) high resolution C 1s spectrum of PGS/PGS-Br/PLLA nanofiber membrane, (e) high resolution Br 3d spectrum of PGS/PGS-Br/PLLA nanofiber membrane, (f) high resolution C 1s, and (g) N 1s spectrum of PGS/PLLA@PNIPAM nanofiber membrane.
PGS-Br/PLLA nanofiber membrane and PGS/PLLA@PNIPAM nanofiber membrane, respectively. It can be seen from the Figure 3(b) that there was no distribution of N elements before grafting PNIPAM on PGS/PGS-Br/PLLA nanofiber membrane, and the distribution of Br elements was relatively large. After grafting PNIPAM polymer, there had been appeared N elements. Accordingly, the distribution of Br elements was reduced. Therefore, PNIPAM polymer was successfully grafted onto the nanofiber membrane in the experiments.

As shown in Figure 4, the wettability of nanofiber membranes were characterized by water contact angle tests. The PGS/PGS-Br/PLLA nanofiber membrane has a water contact angle of about 47°, while the nanofiber membranes with PNIPAM polymer modification were hydrophobic at room temperature with a water contact angle of about 129°. The difference are related to the increased surface roughness of electrospun nanofiber membranes at the nanoscale. After modification with PNIPAM polymer, water droplets were permeating into the membrane within 30 s at room temperature (20°C, \(<\text{LCST}\)) and showed a slow spreading. The main force for the absorption in this state is the hydrophilicity of PNIPAM polymer layer and the capillary effect in the microporous membranes. In addition, the pore size in nanofiber membranes increased upon passing the transition. Here, we draw the conclusion that regarding variations of permeability, the effect of surface roughness change caused by the increases of pore size is stronger than the effect of the permeability reduced by the hydrophobic force.\(^{33}\)

Furthermore, the temperature sensitivity and application prospect of the drug release were studied by controlled release tests at different temperatures. As we can see from Figure 5, the maximum release is only 38.40% at 20°C (\(T<\text{LCST}\)), but 61.05% at 50°C (\(T>\text{LCST}\)). At the same time, comparing Figure 5(a) and (b), we found that the drug was released slowly at 20°C, while the drug was released suddenly at 50°C, which phenomenon is secretly related to thermosensitive PNIPAM polymer, it is hydrophilic swelling at low temperature, inter-molecular hydrogen bond strengthening at high temperature, and nanofiber surface fold exposing more nuclear layer surface, which enhances drug release rate. This results show that the core-shell PGS/PLLA@PNIPAM nanofibers can be used as drug carriers and realize temperature response control.

**Conclusion**

A novel core-shell structure PGS/PLLA@PNIPAM nanofiber membrane was prepared by the combination of electrospinning and surface ATRP grafting technology. In the experiment, a macromolecule-initiator PGS-Br was prepared and characterized by FTIR and $^1$H NMR. The surface morphology, composition, element of the nanofiber was characterized.
by SEM, FTIR, and XPS. In addition, it is worth noting that the core-shell nanofiber membrane can respond to temperature in drug release tests. This work provides a new idea for the preparation of functional core-shell nanofibers.

**Declaration of conflicting interests**

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**References**

1. Greiner A and Wendorff JH. Electrospinning: a fascinating method for the preparation of ultrathin fibers. *Angew Chem Int Ed* 2007; 46: 5670–5703.

2. Lu XF, Wang C and Wei Y. One-dimensional composite nanomaterials: synthesis by electrospinning and their applications. *Small* 2019; 5: 2349–2370.
3. Wang XF, Ding B, Sun G, et al. Electrospinning/netting: a strategy for the fabrication of three dimensional polymer nanofiber/nets. *Prog Mater Sci* 2013; 58: 1173–1243.

4. Xue JJ, Wu T, Dai YQ, et al. Electrospinning and electrospun nanofibers: methods, materials, and applications. *Chem Rev* 2019; 119: 5298–5415.

5. Han JP, Xiong BK, Jiang XY, et al. Bio-functional electrospun nanomaterials: from topology design to biological applications. *Prog Polym Sci* 2019; 91: 1–28.

6. Guo JX, Chen BL, Hao Q, et al. Pod-like structured Co/Co3O4 nitrogen-doped carbon fibers as efficient oxygen reduction reaction electrocatalysts for Zn-air battery. *Appl Surf Sci* 2018; 456: 959–966.

7. Cui JX, Li FH, Wang YL, et al. Electrospun nanofiber membranes for wastewater treatment applications. *Sep Purif Technol* 2020; 250: 117116.

8. Yang DX, Li LF, Chen BL, et al. Functionalized chitosan electrospun nanofiber membranes for heavy metal removal. *Polymer* 2019; 163: 74–85.

9. Zhao YH, Liang YY, Ding SP, et al. Application of conductive PPy/SF composite scaffold and electrical stimulation for neural tissue engineering. *Biomaterials* 2020; 255: 120164.

10. Wei LY, Liu LL, Gao C, et al. Mechanical on-off gates for regulation of drug release in cutaneous or musculoskeletal tissue repairs. *Mater Sci Eng C* 2020; 115: 111048.

11. Hu KL, Wang FP, Shen ZJ, et al. Ar plasma treatment on ZnO-SnO2 heterojunction nanofibers and its enhancement mechanism of hydrogen gas sensing. *Ceram Int* 2020; 46: 21439–21447.

12. Li MS, Zheng YS, Xin BJ, et al. Coaxial electrospinning: jet motion, core-shell fiber morphology, and structure as a function of material parameters. *Ind Eng Chem Res* 2020; 59: 6301–6308.

13. Niu QJ, Guo JX, Chen BL, et al. Bimetal-organic framework/polymer core-shell nanofibers derived heteroatom-doped carbon materials as electrocatalysts for oxygen reduction reaction. *Carbon* 2017; 114: 250–260.

14. Amokrane G, Humbiot V, Jubeli E, et al. Electrospun poly(e-caprolactone) fiber scaffolds functionalized by the covalent grafting of a bioactive polymer: surface characterization and influence on in vitro biological response. *ACS Omega* 2019; 4: 17194–17208.

15. Chung YC, Park JE, Choi JW, et al. The graft-polymerization of poly(ethylene glycol) phenyl ether acrylate onto polyurethane and its impact on the mechanical properties and chain packing. *Fibers Polym* 2020; 21: 290–299.

16. Constantin M, Bucataria S, Ascenzi P, et al. Poly(NIPAAm-co-b-cyclodextrin) microgels with drug hosting and temperature-dependent delivery properties. *React Funct Polym* 2014; 84: 1–9.

17. Luo X, Zheng X, Wang D, et al. The ethanol-sensing properties of porous GaN nanofibers synthesized by electrospinning. *Sens Actuators, B* 2014; 202: 1010–1018.

18. Rapoport N. Physical stimuli-responsive polymeric micelles for anti-cancer drug delivery. *Prog Polym Sci* 2007; 32: 962–990.

19. Zhang HW, Niu QJ, Wang N, et al. Thermo-sensitive drug controlled release PLA core/PNIPAM shell fibers fabricated using a combination of electrospinning and UV photo-polymerization. *Eur Polym J* 2015; 71: 440–450.

20. Loh XJ, Peh P, Liao S, et al. Controlled drug release from biodegradable thermoresponsive physical hydrogel nanofibers. *J. Controlled Release* 2010; 143: 175–182.

21. Boas M, Grady A, Vasilyev G, et al. Electrospinning poly-electrolyte complexes: pH-responsive fibers. *Soft Matter* 2015; 11: 1739–1747.

22. Kamplferbeck M, Vossmeyer T, Weller H, et al. Cross-linked polystyrene shells grown on iron oxide nanoparticles via surface-grafted AGET-ATRP in microemulsion. *Langmuir* 2019; 35: 8790–8798.

23. Wang Y, Ameer GA, Sheppard BJ, et al. A tough biodegradable elastomer. *Nat Biotechnol* 2002; 20: 602–606.

24. Jeffries EM, Allen RA, Gao J, et al. Highly elastic and sutureable electrospun poly(glycerol sebacate) fibrous scaffolds. *Acta Biomater* 2015; 18: 30–39.

25. Rozsasik M, Gaitanarau A, Diamanti PC, et al. Encapsulation of the natural antioxidant auresidin in biodegradable PLA nanoparticles. *Polym Degrad Stab* 2014; 108: 182–187.

26. Huan S, Liu G, Cheng W, et al. Electrospun poly(lactic acid)-based fibrous nanocomposite reinforced by cellulose nanocrystals: impact of fiber uniaxial alignment on microstructure and mechanical properties. *Biomacromolecules* 2018; 19: 1037–1046.

27. Yan Y, Sencadas V, Zhang JS, et al. Superomniphilic poly(glycerol sebacate)-poly(a-lactic acid) electrospun membranes for oil spill remediation. *Adv Mater Interfaces* 2017; 4: 1700484.

28. You YZ, Kalebaila KK, Brock SL, et al. Temperature-controlled uptake and release in PNIPAM-modified porous silica nanoparticles. *Chem Mater* 2008; 20: 3354–3359.

29. Ravichandran R, Venugopal JR, Sundarrajan S, et al. Expression of cardiac proteins in neonatal cardiomyocytes on PGS/fibrinogen core/shell substrate for cardiac tissue engineering. *Int J Cardiol* 2013; 167: 1461–1468.

30. Luo YL, Yang XL, Xu F, et al. Thermosensitive PNIPAM-b-HTTP block copolymer micelles: molecular architectures and camptothecin drug release. *Colloids Surf, B* 2014; 114: 150–157.

31. Lin X, Tang D, Cui W, et al. Controllable drug release of electrospun thermoresponsive poly(N-isopropylacrylamide)/poly(2-acrylamido-2-methylpropanesulfonic acid) nanofibers. *J Biomed Mater Res A* 2012; 100A: 1839–1845.

32. Cao X, Wang W, Hu JJ, et al. Effect of mixed solvents on the structure and properties of PLLA/PDLA electrospun fibers. *Fibers Polym* 2020; 21: 970–977.

33. Liu Y, Tas S, Zhang KH, et al. Thermoresponsive membranes from electrospun mats with switchable wettability for efficient oil/water separations. *Macromolecules* 2018; 51: 8435–8442.

34. Elashnikov R, Slepicka P, Rimpelova S, et al. Temperature-responsive PLLA/PNIPAM nanofibers for switchable release. *Mater Sci Eng C* 2017; 72: 293–300.

35. Yang XP, Li LF, Yang DZ, et al. Electrospun core-shell fibrous 2D scaffold with biocompatible poly(glycerol sebacate) and poly-l-lactic acid for wound healing. *Advanced Fiber Materials* 2020; 2: 105–117.

36. Liu XH, Zheng HL, Li Y, et al. A novel bacterial cellulose aerogel modified with PGMA via ARGET ATRP method for catalase immobilization. *Fibers Polym* 2019; 20: 520–526.