Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.
This journal is © The Royal Society of Chemistry 2023

Supporting Information for

Hybrid Hydrogel Constructed by Drug Loaded Mesoporous Silica and Multiple Response Copolymer as an Intelligent Dressing for Wound Healing of Diabetic Foot Ulcers

Wenrui Zhang[a], Zun Yang[a], Mingzu Zhang[a], Jinlin He[a], Shenzhi Li[b], Xingwei Sun[b,*], and Peihong Ni[a,*]

[a] College of Chemistry, Chemical Engineering and Materials Science, State and Local Joint Engineering Laboratory for Novel Functional Polymeric Materials, Jiangsu Key Laboratory of Advanced Functional Polymer Design and Application, Suzhou Key Laboratory of Macromolecular Design and Precision Synthesis, Soochow University, Suzhou 215123, P. R. China

[b] Intervention Department, The Second Affiliated Hospital of Soochow University, Suzhou 215004, P. R. China

* To whom correspondence should be addressed. Peihong Ni (E-mail: phni@suda.edu.cn) and Xingwei Sun (E-mail: sdfeysxw@163.com).

Experimental

Synthesis of 3-Methacrylamidophenylboronic Acid (AAPBA)

First, 3-methacrylamidophenylboronic acid (AAPBA) was prepared by substitution reaction. 20 mL of 2 M prepared sodium hydroxide solution was added to a 100 mL round bottom flask, and then the round bottom flask was placed in a low-temperature reactor (0 °C) for cooling. After that, 3-aminophenylboronic acid (1.37 g, 10 mmol) was added and stirred to completely dissolve. Subsequently, acryloyl chloride (1.81 g, 20 mmol) was added dropwise and the reaction mixture was stirred at 25 °C for 5 h. Five hours passed, the pH of the reaction solution was adjusted to about 1 with 1 M HCl, and a large amount of white precipitates appeared. The precipitate was filtered and washed three times with cold deionized water. Finally, the solid precipitate was recrystallized three times to obtain pure pale yellow solid AAPBA. (1.17 g, yield: 36.80%).

Synthesis of Copolymer PB

Before the start of the reaction, the polymerization inhibitor in dimethyl aminopropyl methacrylamide (DMAPMA) was removed using a short column of neutral alumina. The copolymer, PB with 5.00 mol% AAPBA, was synthesized by radical copolymerization. Briefly, to a Schlenk tube, a mixture of AM (0.60 g, 8.5 mmol), AAPBA (0.01 g, 0.50 mmol) and DMAPMA (0.16 g, 1 mmol) was dissolved in 12 mL DMSO, and the mixture freezing vacuum for 10 min. After the mixture thawed, AIBN (0.01 g, 0.06 mmol) was also added to the Schlenk tube. The reaction mixture was

stirred magnetically at 70 °C under nitrogen for 24 h. Then the mixture was dialyzed (MWCO 5000 Da) against deionized water for 3 d to remove impurities. The solution was collected and then freeze-dried under vacuum to obtain the white product PB (0.67 g, yield: 78%).

Synthesis of Mesoporous Silica Nanoparticles (MSNs)

MSNs were synthesized using a sol-gel method.[1] Briefly, 0.90 g CTAB and 5 mL TMB were dissolved in a mixed solution of 90 mL deionized water and 30 mL ethanol. The pH of the reaction solution was adjusted to about 11 with ammonium hydroxide solution, then heated up to 60 °C. Subsequently, 3.60 mL TEOS was added dropwise and the reaction mixture was stirred at 60 °C for 2 h. After the reaction solution was cooled to room temperature, the reaction solution was centrifuged (9000 rpm, 10 min), and the white precipitate was washed with excess deionized water and ethanol. The precipitate was dried in a vacuum drying oven for 24 h to obtain white solid. Finally, 0.39 g of the above product was dispersed in a mixed solution of 144 mL absolute ethanol and 12 mL hydrochloric acid and refluxed for 24 h to remove the template CTAB. Then the reaction solution was centrifuged (8000 rpm, 5 min), and the white precipitate was washed with excess deionized water and ethanol, and then the precipitate was dried in a vacuum drying oven for 24 h to obtain white solid MSN.

Synthesis of PDA-Modified MSNs (MSN@PDA)

50 mg of MSNs were dispersed ultrasonically in 50 mL of Tris-HCl solution (10 mM, pH 8.5).[2] Then, hydrochloride dopamine (50 mg) was added and the mixture was

continuously stirred for 24 h in the dark at room temperature. Finally, the black particles (MSN@PDA) were collected by centrifugation (9000 rpm, 10 min), and the washed three times with water, and then the precipitate was dried in a vacuum drying oven for 24 h to obtain black solid MSN@PDA.

Thermal Stability of MSNs and MSN@PDA

The thermal stability of MSNs and MSN@PDA were performed on an instrument (Discovery, TA) with about 5 mg of the sample in the platinum plate under a nitrogen atmosphere. The test temperature range is 35 °C to 700 °C, and the heating rate is 10 °C min^{-1}

Cytocompatibility Evaluation of PP/MSN@PDA Hydrogel

In the experiment, the cytotoxicity of PP/MSN@PDA hydrogel was tested by MTT method, and human umbilical vascular endothelial cells (HUVEC cells) and mouse fibroblast cells (L929 cells) were selected as experimental cells. The specific steps were as follows: 5 mg freeze-dried PP/MSN@PDA hydrogel sample was weighed and put into 5 mL PBS 7.4 solution, and then placed in a shaker incubator at 37 °C for 48 h. After that, 0.22 μm filter membrane was used to filter the hydrogel extraction solution, and the extraction solution was used to evaluate the biocompatibility of the hydrogels. 100 μL of cell in RPMI 1640 culture medium at a density of 4000 cells per well was added to each well in a 96-well plate, and then the well plate were incubated at 37 °C in a 5% CO_2 atmosphere for 12 h to enable cells to adhere to the wall. After that, a series of 25 μL hydrogel extraction solution with different concentrations were

added to the wells. The first row of cells in each plate was added with the same amount of PBS 7.4 as a control. Following another 48 h of incubation, 25 µL MTT stock solution (5 mg ml^{-1} in PBS) was added to each well. Following another 4 h of incubation, DMEM medium was carefully removed from each well plate and DMSO (150 µL) was added to dissolve the purple formazan. Finally, the absorbance of each well at 570 nm was measured by a microplate reader (Bio Rad 680). The cell viability (%) was calculated by the following formula:

$$\text{Cell viability (\%)} = \frac{OD_{sample}}{OD_{control}} \times 100 \qquad (1)$$

where OD_{sample} and $OD_{control}$ represent the OD values of the sample wells and the control wells treated with PBS.

RESULTS AND DISCUSSION

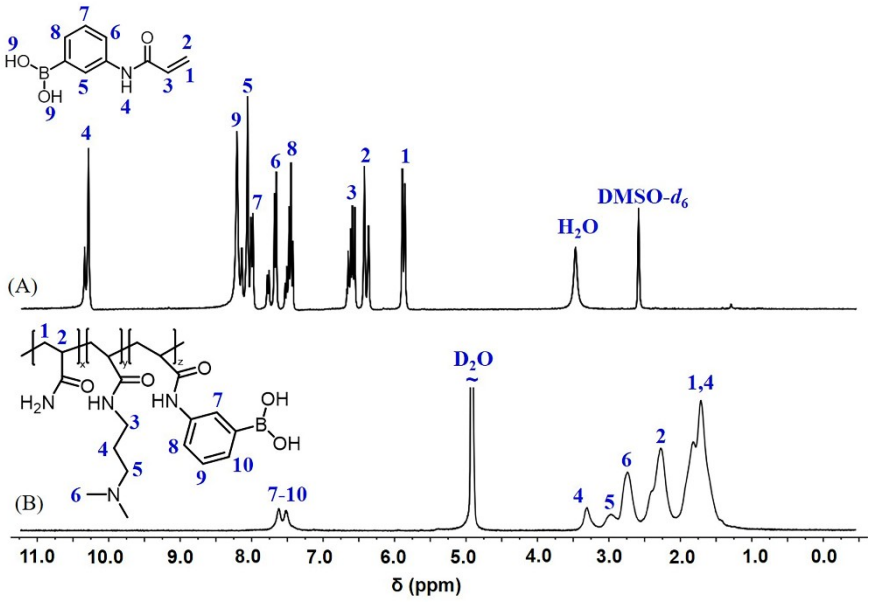

Figure S1. ^{1}H NMR spectra of (A) AAPBA, (B) PB.

REFERENCES

1. L. Hou, Y. Z. Zheng, Y. C. Wang, Y. R. Hu, J. J. Shi, Q. Liu, H. J. Zhang and Z. Z. Zhang, *ACS Appl. Mater. Interfaces,* 2018, **10**, 21927-21938.

2. W. Cheng, C. Y. Liang, L. Xu, G. Liu, N. S. Gao, W. Tao, L. Luo, Y. X. Zuo, X. S. Wang, X. D. Zhang, X. W. Zeng and L. Mei, *Small*, 2017, **13**, 1700623-1700635.