Supplementary Material (ESI) for *Soft Matter*

Thermoreversible gelation of poly(ethylene glycol)/poly(ester anhydride) triblock copolymer nanoparticles for injectable drug delivery systems

Yanqin Liang,[a] Yong Qiao,[b] Shutao Guo,[a] Lei Wang,[c] Chaopeng Xie,[a] Yinglei Zhai,[a] Liandong Deng*[a], Anjie Dong[a]

[a] *School of Chemical Engineering and Technology, and* [b] *School of Material Science and Engineering, Tianjin University, Tianjin 300072, China*

[c] *Tianjin Institute of Medical and Pharmaceutical Science, Tianjin 300020, China*

Synthesis of mPEG-*b*-P(OA-DLLA)-*b*-mPEG

PPOA was prepared from the purified OA (10 g) by refluxing in the presence of excess acetic anhydride (100 mL) at 150°C for 40 min under nitrogen protection. Acetic acid and excess acetic anhydride were removed under vacuum at 50°C~60°C. The hot clear viscous residue was dissolved in 40 mL toluene, then cooled to 0°C overnight and precipitated with 400 mL of a 1:1 mixture (v/v) of ethyl ether and petroleum ether. The white precipitate was collected by a LD5-2A centrifuge (Beijing Medical Centrifuge Factory, Beijing, China), dried in vacuo at room temperature for 48 h, and stored at -20°C until used.

D,L-lactic acid oligomers (ODLLA) were prepared by the melt polycondensation at 120°C under vacuum of 0.1MPa for 2 h. The molecular weight measured by titration

was 400±20.

PPOA (7.8 g) and ODLLA (2.2 g) was heated to 140ºC (and allowed to melt) under 0.1 mmHg for 1 h, and then refluxed in the presence of acetic anhydride (1:10, m/v) at 150 ºC for 30 min under nitrogen protection. Acetic acid and excess acetic anhydride were removed by distillation under vacuum. The hot clear viscous residue was dissolved in 40 mL toluene, and subsequently precipitated with 300 mL cooled ethyl ether. The obtained white precipitate was collected by LD5-2A centrifuge (Beijing Medical Centrifuge Factory, Beijing, China), and dried under vacuum at room temperature to obtain poly(octadecanedioic anhydride-*D,L*-lactic acid) prepolymer (PP(OA-DLLA)).

mPEG (10 g) and PP(OA-DLLA) (10 g) were placed into the reactor in an oil bath at 180°C, under vacuum for 90 min, to perform melt polycondensation.[33,41,44] The final product was dissolved into chloroform, and precipitated in cooled and anhydrous ethyl ether. The precipitate was separated by filtration and washed with anhydrous ethyl ether for three times. Finally, copolymers were dried in vacuo at room temperature for 48 h.

Characterization of mPEG-*b*-P(OA-DLLA)-*b*-mPEG

The FTIR spectra of mPEG-*b*-P(OA-DLLA)-*b*-mPEG are illustrated in Fig. S1. The spectrum of mPEG-*b*-P(OA-DLLA)-*b*-mPEG presents the characteristic peaks of mPEG and POA. The peaks at 2935-2915 cm^{-1} and 2854-2840 cm^{-1} correspond to the methyl and methylene vibrations. The peaks at 1818 cm^{-1} and 1740 cm^{-1} are the

characteristic peaks of anhydride bonds. The C-O-C stretching band appears at 1110 cm $^{-1}$. Compared with the peak intensity at 1818 cm^{-1}, the relative intensities of characteristic peak of C=O of ester group (1740 cm^{-1}) and C-O-C of ether group (1110 cm^{-1}) are enhanced with introduction of ODLLA and mPEG, respectively. ODLLA and mPEG, which have many ester groups and ether groups, can make the new ester group be formed by the reaction of the end hydroxy groups with anhydride groups. Therefore, the enhancement of the relative intensities at 1740 cm^{-1} and 1110 cm^{-1} indicates that the composition of copolymers is consistent with that of the designed polymer.

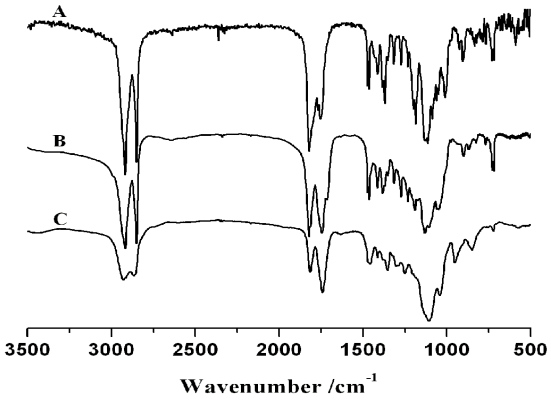

Fig. S1. FTIR spectra of POA (A), P(OA-DLLA) (B) and mPEG-*b*-P(OA-DLLA)-*b*-mPEG (C).

In the ^{1}H NMR spectrum, the peaks assigned to protons of the POA, mPEG and DLLA units can be clearly observed. The characteristic peaks of methene protons (H_a) of mPEG segments appear at 3.49 ppm and the peaks of methyl protons (H_b) of mPEG segments appear at 3.38 ppm, while the peaks of POA at 2.17 ppm(H_c), 1.47

(H_d) ppm and 1.22 (H_e) ppm were seen, respectively. The peaks of DLLA appear at 1.36 ppm(H_g) and 5.18 ppm(H_f). The ^{1}H NMR results further indicate that mPEG-*b*-P(OA-DLLA)-*b*-mPEG were successfully synthesized.

According to the ratio of peak area of H_a, H_e and H_g, the molecular weights of mPEG-*b*-P(OA-DLLA)-*b*-mPEG were calculated.

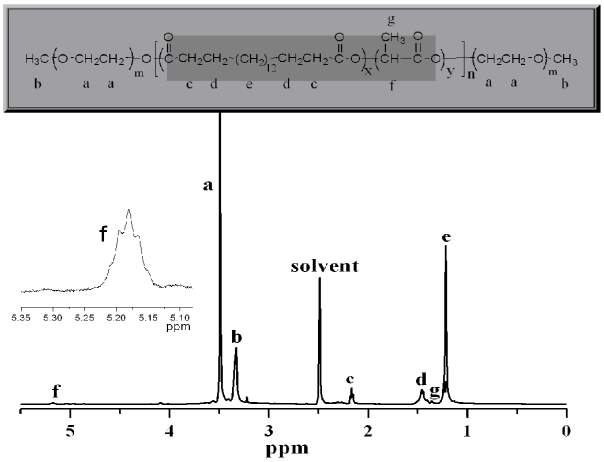

Fig. S2. ^{1}H NMR of mPEG-*b*-P(OA-LA)-*b*-mPEG -11

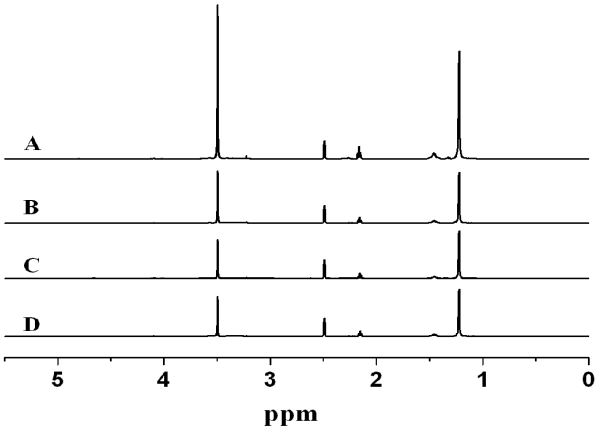

Fig. S3. ^{1}H NMR spectra of the freeze-dried hydrogels after degradation for 1 (A), 3 (B), 10 (C) and 15 (D) days.

***In vivo* gel formation**

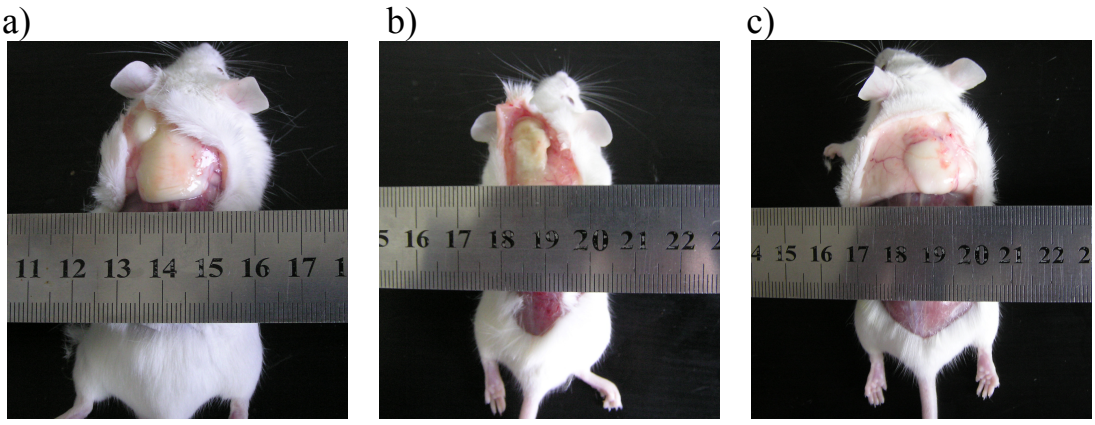

Fig. S4. *In vivo* gel formation of aqueous dispersion (25 wt%, 0.4 mL) of mPEG-*b*-P(OA-DLLA)-*b*-mPEG-12 NP-FDP by subcutaneous injection. a): day 1; b): day 5; c): day 15.