Electronic Supplementary Material (ESI) for Polymer Chemistry.

Electronic Supplementary Information

Self-assembled micelles prepared from amphiphilic copolymers bearing cell outer membrane phosphorylcholine zwitterions for potential anti-phagocytic clearance carrier

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1. Gel Permeation Chromatography (GPC) characterization.

GPC of poly(ε-caprolactone) macromonomer and all P(MPC-*co*-PCL) samples were measured on a Dionex Ultimate 3000 series GPC instrument with a Sheodex RI-101 refractive index detector and a Sheodex OHpak SB-803 column. THF was employed as the eluent at a flow rate of 1.0 mL/min and a temperature of 40 °C. Polystyrene standards (Showa Denko Ltd, Japan) with narrow molecular weight distributions were employed to make a calibration curve. The GPC traces of poly(ε-caprolactone) macromonomer and all P(MPC-*co*-PCL) samples were shown in Fig.S1.

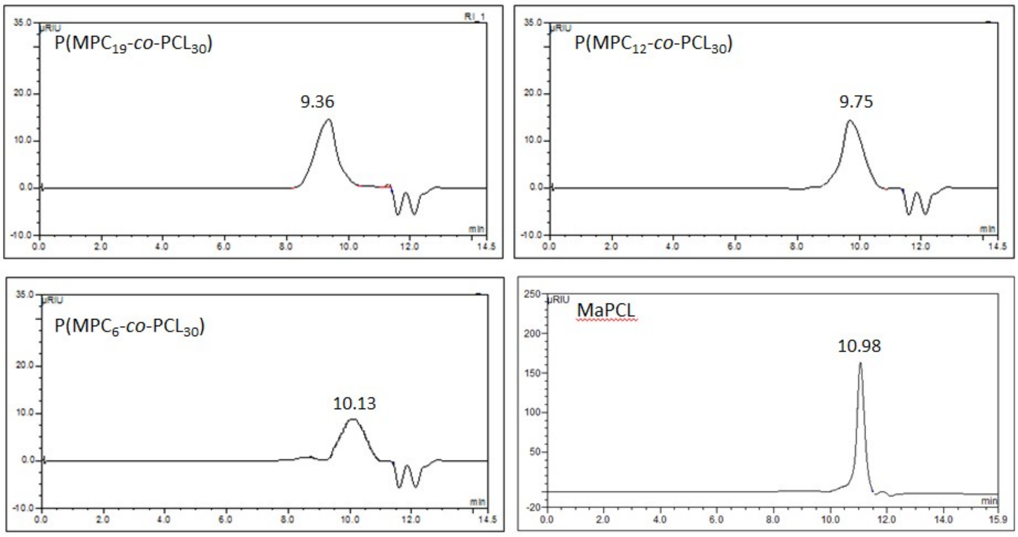

Fig. S1 GPC traces of poly(ε-caprolactone) macromonomer and all P(MPC-*co*-PCL) samples

2. Degradation of P(MPC-*co*-PCL) micelles

P(MPC-*co*-PCL) micelles were degraded in water (pH 7.4) and hydrochloric acid solution (pH 5.5) at 37 °C, respectively. In a typical procedure [1], 30 mg P(MPC-*co*-PCL) freeze-dried micelles power was scattered in 5 mL water or hydrochloric acid solution. Periodically, the undissociated micelles were separated from the aqueous phase by centrifugation at 16000 rpm for 1 h. Then, the supernatant was discarded and about 1.0 mL sediment was washed with distilled water three times and then frozen and lyophilized to obtain the dried residue micelles products for weight and ^{1}H NMR measurements.

The degradability of biodegradable amphiphilic copolymer micelles in aqueous solution is very important, because it will affect the drug encapsulation and release characteristics of micelles. Poly(ε-caprolactone) (PCL) is a kind of aliphatic polyester, and the PCL based polymer will be hydrolyzed in aqueous solution due to the ester bond breakage, which will lead to the decrease of molecular weight and the change of chemical composition of polymers. To micelles, it causes the size change or even disassembly of micelles during the degradation process. So, DLS was used to investigate the hydrolytic degradation behaviors of P(MPC-*co*-PCL) micelles at different pH media. Fig. S2 shows the sizes of P(MPC-*co*-PCL) micelles recorded in situ by DLS during the degradation procedure. It was found that the size of P(MPC-*co*-PCL) micelles was constant during the degradation procedure at pH 7.4. However, the size of the micelles decreases continuously during the degradation procedure at pH 5.5. The decrease in the size of micelles during the degradation procedure at pH 5.5 should be related to the degradation of P(MPC-*co*-PCL) micelles.

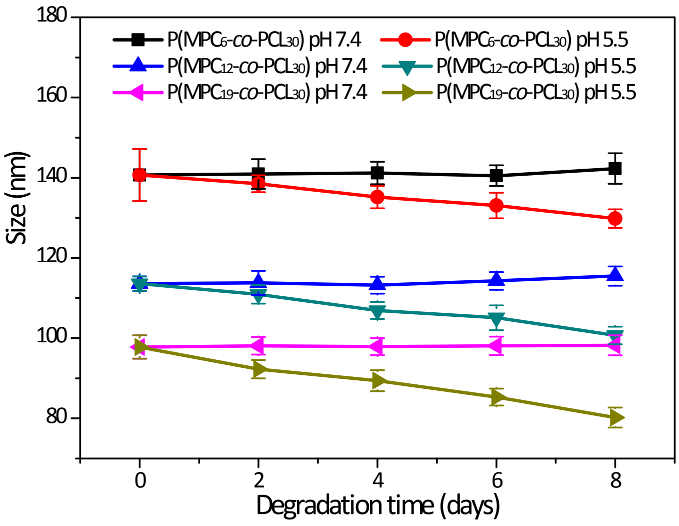

Fig. S2 Variation of size of P(MPC-*co*-PCL) micelles with the extending storing time in the medium with pH 7.4 and 5.5

On the other hand, ^{1}H NMR and weight loss are also used to characterize the degradation behavior of P(MPC-*co*-PCL) micelles. Fig. S3A shows the ^{1}H NMR spectrum of P(MPC$_{12}$-*co*-PCL$_{30}$) copolymer micelles after 8 days degradation in hydrochloric acid solution (pH 5.5) at 37 °C. The ^{1}H NMR signals were reasonably assigned to the P(MPC$_{12}$-*co*-PCL$_{30}$) copolymer (See Fig. 2 in manuscript) except the stronger ^1H NMR resonance signal appearing at 3.68 (peak f) which assigned to the methylene protons (-C$\boldsymbol{H}_2$OH) connected to the terminal hydroxyl group, this confirmed the degradation of PCL chain in P(MPC-*co*-PCL). Fig. S3B depicts the weight loss results of P(MPC-*co*-PCL) copolymer micelles. As for P(MPC_{12}-*co*-PCL_{30}) copolymer micelles, only 3.2±1.6% weight loss was detected after 8 days degradation in water (pH 7.4), and similar results could also be seen for P(MPC_6-*co*-PCL_{30}) and P(MPC_{19}-*co*-PCL_{30}) copolymer micelles (the data not shown). In contrast, significant weight loss was detected when the degradation medium changed to hydrochloric acid solution (pH 5.5). For example, the 10.3±1.4% weight loss of P(MPC_{12}-*co*-PCL_{30}) copolymer micelles was detected after 8 days degradation. The reason for significant weight loss was the faster ester bond breakage of PCL in acidic medium. As seen in Fig. S3B, increasing the PMPC content of a synthesized P(MPC-*co*-PCL) finally led to an obvious increase in the degradation rate in acidic medium, and an order of degradation rate was P(MPC_{19}-*co*-PCL_{30}) > P(MPC_{12}-*co*-PCL_{30}) > P(MPC_6-*co*-PCL_{30}). This result can be readily interpreted for their increasing hydrophilicity, the more PMPC content in copolymer would result in significant changes hydrophilicity.

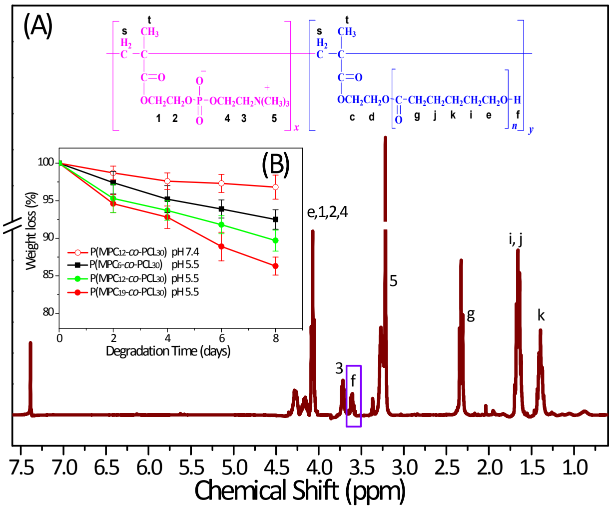

Fig. S3(A) The ^1H NMR of P(MPC_{12}-*co*-PCL_{30}) copolymer micelles after 8 days degradation in hydrochloric acid solution (pH 5.5) at 37°C; (B) The weight loss (%) of P(MPC-*co*-PCL) copolymer in water (pH 7.4) and hydrochloric acid solution (pH 5.5) at 37 °C.

References

(1) Y. Hu, Z. P. Jiang, R. Chen, W. Wu, and X. Q. Jiang, *Biomacromolecules*, 2010,**11**, 481-488.