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Supplementary Information

Morphology tailoring and temperature sensitivity control of waist cross-linked micelles and their application evaluating as intelligent drug carriers

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Synthesis

2-butenedioic acid (Z)-, monooctadecyl ester (O-Be) 13.5 g of Maleic anhydride (0.05 mol) and 4.9 g of octadecyl alcohol (0.05 mol) were dissolved in methylbenzene (0.5 mol, 53 ml). The reaction mixture was refluxed 4 h, the disappearance of peaks at 1850 and 1780 cm^{-1} (C=O stretch vibration of Maleic anhydride) in IR spectrum indicated that the reaction was carried out completely. After evaporating methylbenzene by rotary evaporator, O-Be was obtained (18.1 g , 98%).

O-B-EG800 14.6 g of PEG800 (0.0125 mol) and *p*-toluene sulphonic acid (0.172g, 1 mmol) was dissolved in methylbenzene (0.3 mol, 31.8 ml), and 4.6 g of O-Be (0.0125 mol) was dissolved in 21.2 ml of methylbenzene (0.2 mol). O-Be solution was dropwised into PEG-800 solution under a stirring condition, the reaction mixture was refluxed 6 h, and a water segregator was used to remove the generated water. Then methylbenzene was evaporated by rotary evaporator. The product was dialyzed in water using a dialytic-bag (molecular weight cutoff 3500) to remove unreacted materials (O-B-EG can form micelles in water and can not pass though the dialytic-bag). Final product (O-B-EG) was obtained after drying at a temperature of 60 ^{O}C for several days (9.6 g, 79%). O-B-EG1000 and O-B-EG1500 were synthesized via the same route using PEG-1000 and PEG-1500 as materials, respectively.

O-B-EG800 micelles O-B-EG800 was dispersed in water. After stirring for 4 h, the O-B-EG800 micelles were obtained. O-B-EG1000 micelles and O-B-EG1500 micelles were also obtained using the same way.

WCMs800 O-B-EG800 was dispersed in water. After 4 h stirring, $K_2S_2O_8$ and MBA were added simultaneously in N_2 atmosphere. The reaction mixture was stirried for 6 h at a temperature of 68 ^{O}C, the disappearance of the peak at 1640 cm^{-1} in IR spectrum indicated that O-B-EG800 was polymerized completely, and the WCMs800 was obtained. We also synthesized WCMs1000 and WCMs1500 via the same route using O-B-EG1000 and O-B-EG1500 as materials, respectively. In order to obtain different morphology of WCMs, 0.5 mg ml^{-1}, 2.0 mg ml^{-1}, 3 mg ml^{-1} and 4 mg ml^{-1} of O-B-EGs were used.

Characterization

The ^{1}H NMR spectra of O-B-EG and WCMs were measured on a Bruker ARX 800MHz spectrometer with 1500 scans at a relaxation time of 2 s. Fourier-transform infrared (FT-IR) spectroscopy (Nicolet Avatar 360) was also used to confirm the chemical structures of the obtained products.

To obtain microscope images of WCMs, samples were dispersed in deionized water. Then the mixture was dropwised onto aluminium sheets. After air-drying for 24h at room temperature, the samples were gold sputtering treated, and field emission scanning electron microscope (FE-SEM, LEO-1530) was used to observe the surface morphology of micelles.

The shrinking speed of WCMs was also measured by DLS on a ZetaPALS with temperature controlled system. Firstly, the diameters of WCMs in aqueous solutions were measured at low temperatures (for example: WCMs800 was placed at 38 ^{O}C; WCMs1000 was placed at 40 ^{O}C; WCMs1500 was placed at 42 ^{O}C). Then the system temperature was rapidly increased to a high level (for WCMs8000, WCMs1000 and WCMs1500, the temperature was increased to 42 ^{O}C, 44 ^{O}C and 46 ^{O}C, respectively), and the diameters of WCMs were measured at regular time interval.

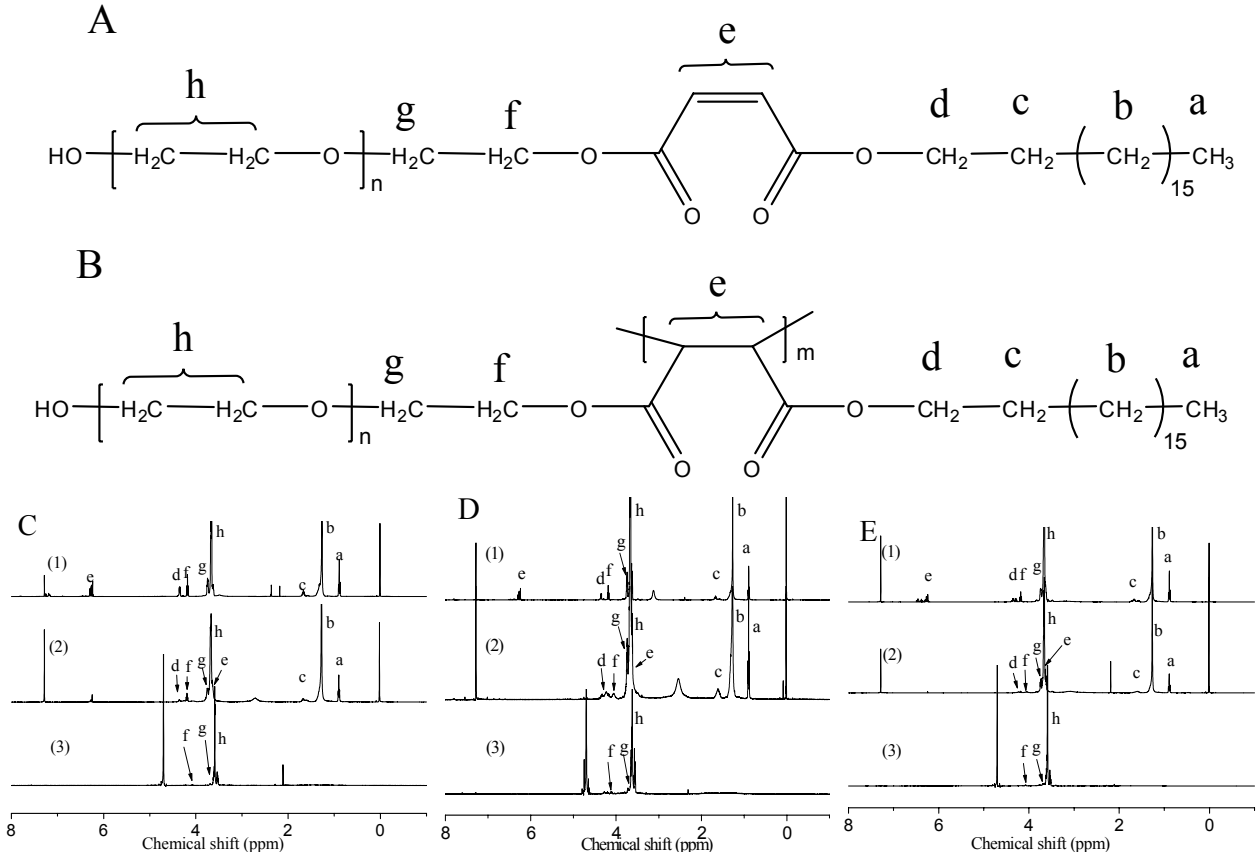

Fig. 1S. Chemical structure O-B-EG (A) and WCMs (B); ^{1}H NMR spectra of O-B-EG and WCMs with different molecular weight of PEG chains (C-1) O-B-EG800 in $CDCl_3$, (C-2) WCMs800 in $CDCl_3$, (C-3) WCMs800 in D_2O, (D-1) O-B-EG1000 in $CDCl_3$, (D-2) WCMs1000 in $CDCl_3$, (D-3) WCMs1000 in D_2O, (E-1) O-B-EG1500 in $CDCl_3$, (E-2) WCMs1500 in $CDCl_3$, and (E-3) WCMs1500 in D_2O.

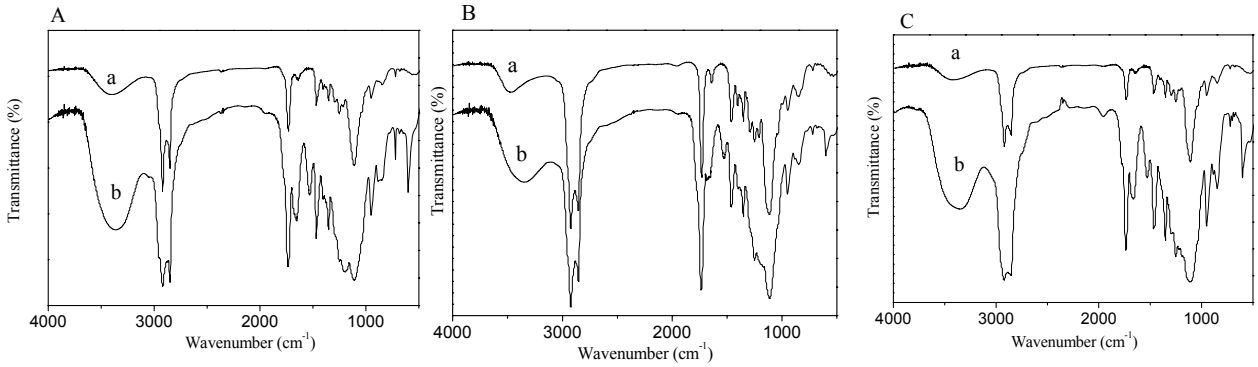

Fig. 2S. IR spectra of O-B-EG800 (A-a), WCMs800 (A-b), O-B-EG1000 (B-a), WCMs1000 (B-b), O-B-EG1500 (C-a) and WCMs1500 (C-b).

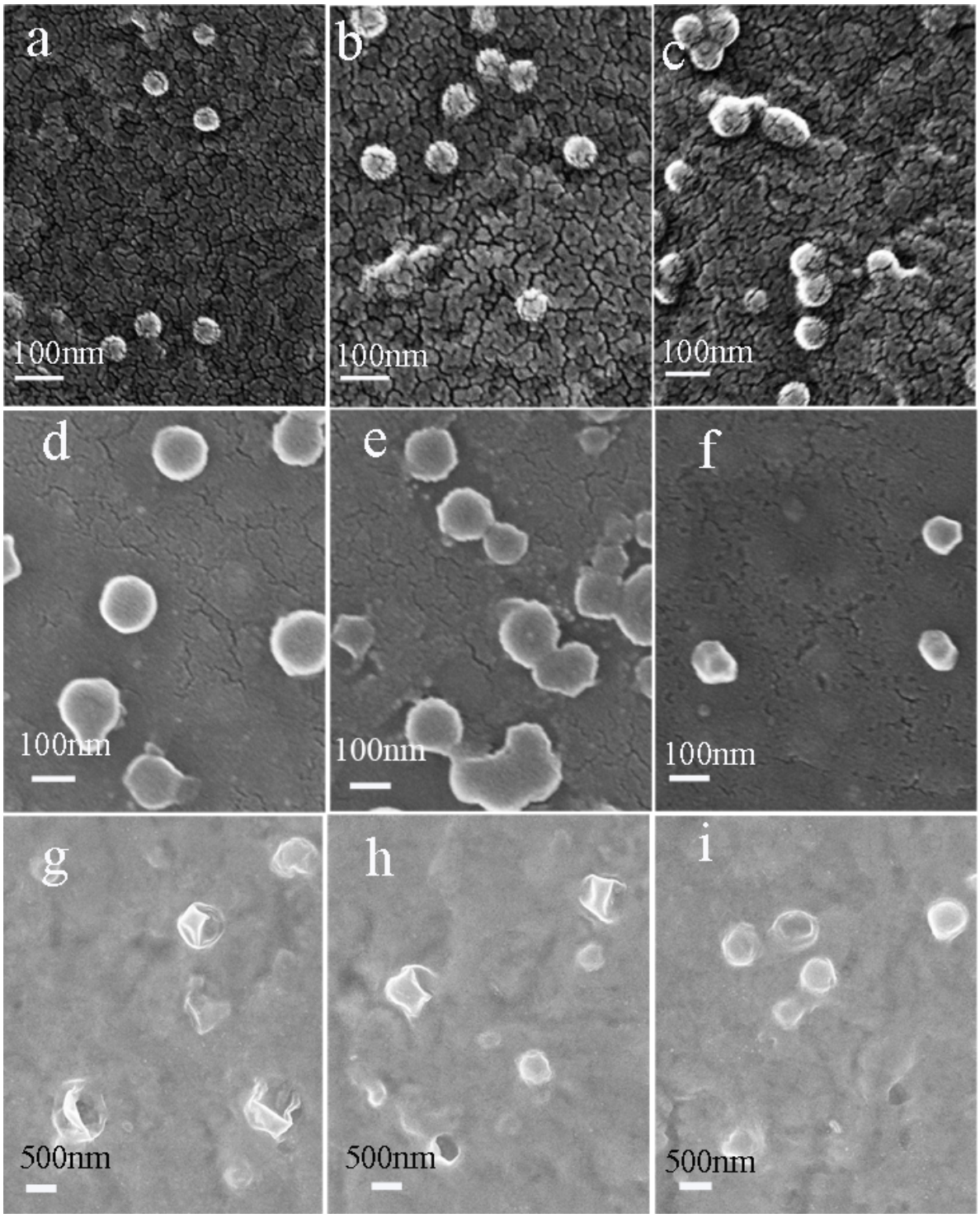

Fig. 3S. SEM images of (a) monolayer WCMs800, (b) monolayer WCMs1000, (c) monolayer WCMs1500, (d) compound WCMs800, (e) compound WCMs1000, (f) compound WCMs1500, (g) vesicle-like WCMs800, (h) vesicle-like WCMs1000 and (i) vesicle-like WCMs1500.

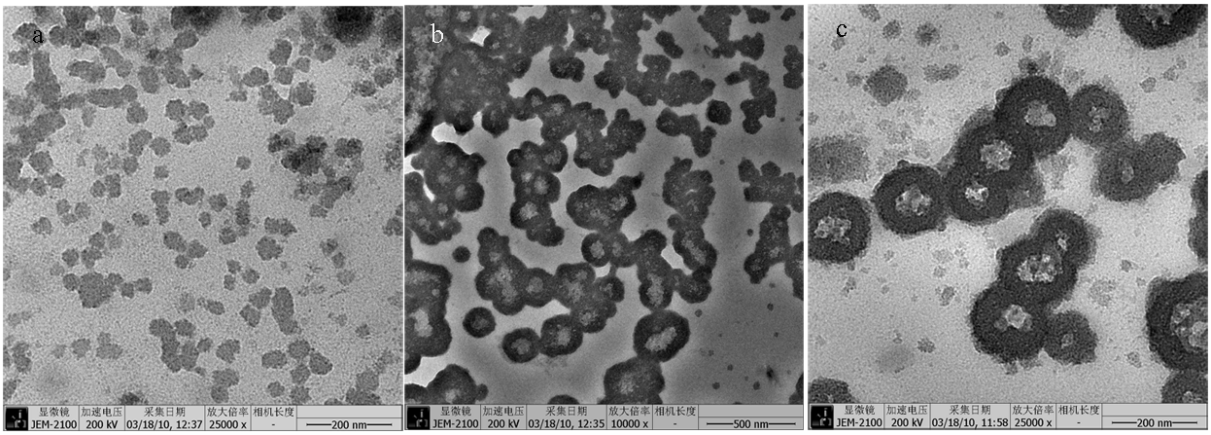

Fig. 4S. TEM images of O-B-EG1000 micelles obtained from 4.0 mg ml^{-1} of O-B-EG1000 aqueous solution (a), WCMs1000 prepared from 3.0 mg ml^{-1} of O-B-EG aqueous solution and WCMs1000 synthesized from 4.0 mg ml^{-1} of O-B-EG aqueous solution (c).

O-B-EG1000 micelles obtained from 4.0 mg ml^{-1} of O-B-EG1000 aqueous solution show compound structure; WCMs1000 prepared from 3.0 mg ml^{-1} of O-B-EG1000 aqueous solution exhibit both compound structure and vesicle-like structure; while WCMs1000 synthesized from 4.0 mg ml^{-1} of O-B-EG1000 aqueous solution show vesicle-like structure.

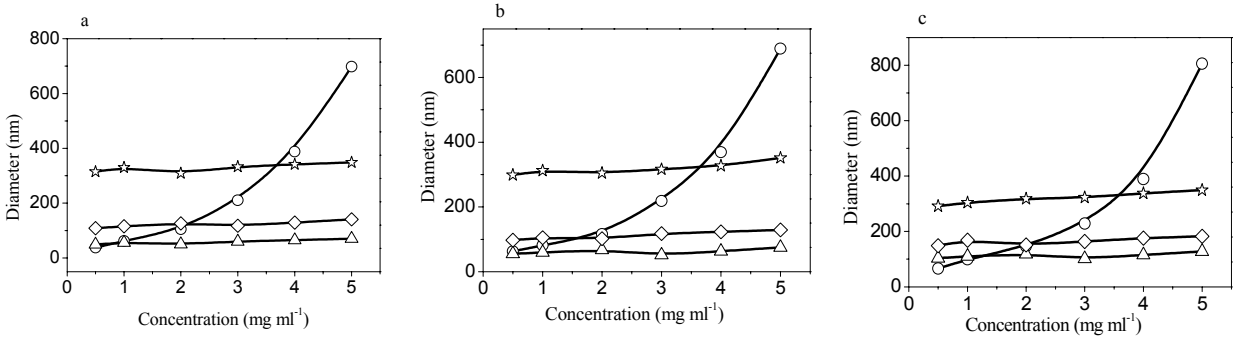

Fig. 5S. The particle size of O-B-EG micelles (○), monolayer WCMs (△), compound WCMs (◇) and vesicle-like WCMs(☆) with different molecular weight of PEG chains as an effect of micellar concentration, (a) PEG800, (b) PEG1000, (c) PEG 1500.

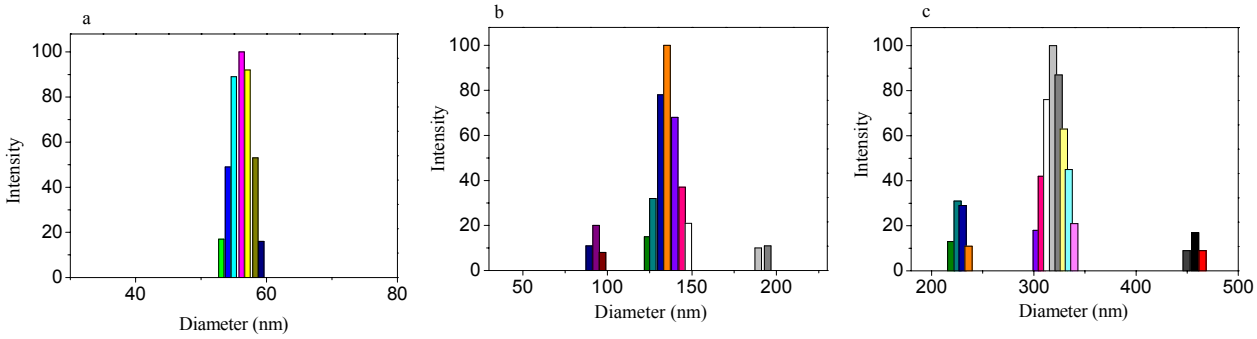

Fig. 6S. Particle size distributions of WCMs1000 with different morphologies, (a) monolayer WCMs1000, (b) compound WCMs1000 and (c) vesicle-like WCMs1000.

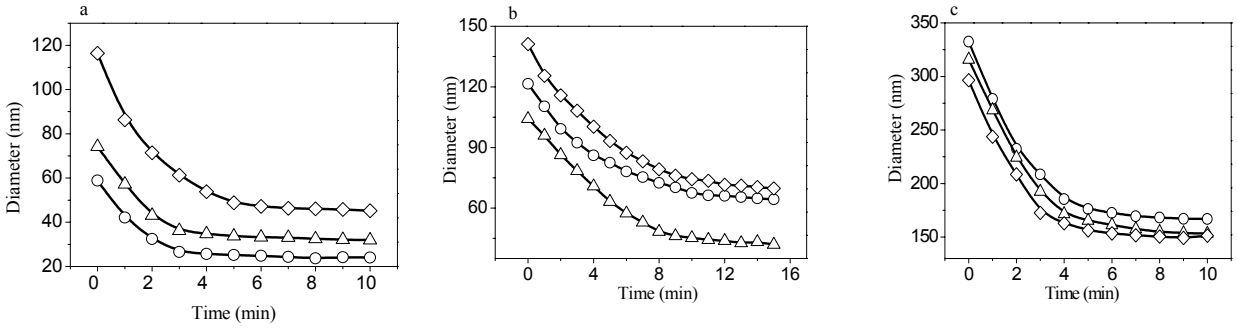

Fig. 7S. The shrinking speed of (a) monolayer WCMs, (b) compound WCMs and (c) vesicle-like WCMs with different molecular weight of PEG chains (○) PEG800, (△) PEG1000 (◇) PEG1500.