

Electronic Supplementary Information (ESI)

A Synergy Effect Between the Hydrophilic PEG and Rapid Solvent Evaporation Induced Formation of Tunable Porous Microspheres from Triblock Copolymer

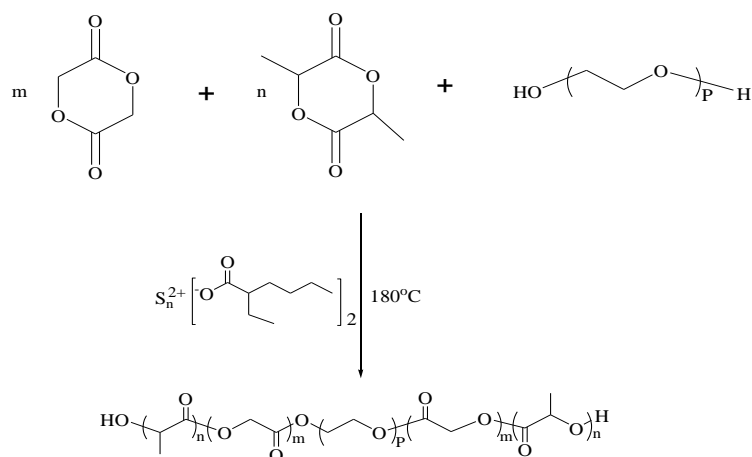
Jun-Bing Fan,^a Yongyang Song,^a Shutao Wang,^a Lei Jiang,^a Ming-Qiang Zhu^{*b} and Xinglin Guo^{*a}

^a Beijing National Laboratory for Molecular Sciences (BNLMS), Key Laboratory of Organic Solids, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, P. R. China; ^b Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan, Hubei, China

Materials

L-Lactide (L-LA) and glycolide (GA) were purchased from PURAC(Holland) and recrystallized twice from ethyl acetate. Polyethylene glycol (PEG) with molecular weight (Mw) of 1000, 2000 and 4000 were purchased from Alfa. Stannous octoate (from Sigma) was used as received without further purification. Ethyl acetate (from Beijing Beihua Fine Chemicals Company, China) was dried with P₂O₅ overnight and distilled before use. Dichloromethane (DCM) (from Beijing Chemical Factory, Ahina) and other reagents were of analytical grade and used without further purification.

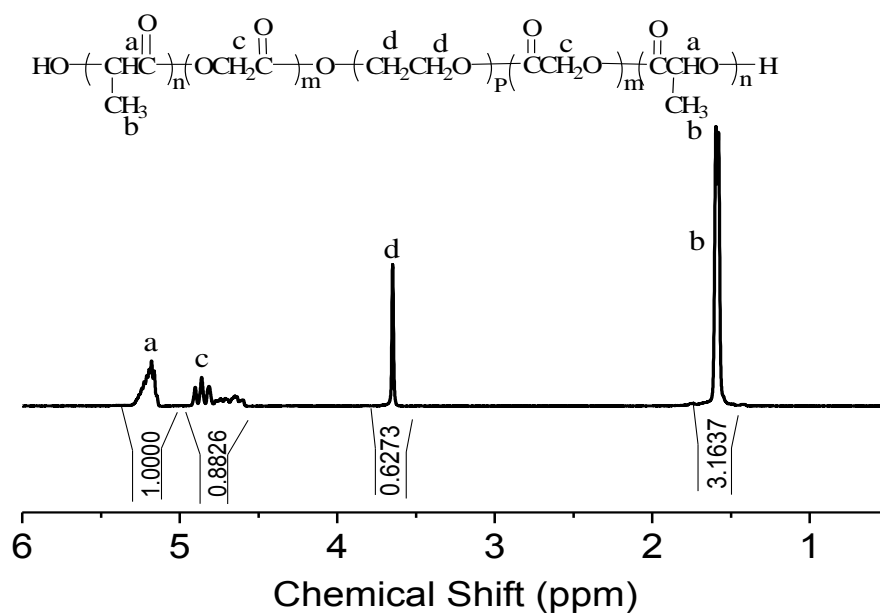
Synthesis and characterization of PLGE tri-block copolymers



- Fig. S1. The synthetic route of amphiphilic PLGE porous microspheres.

In a typical synthesis, a total of 10 g of L-LA, GA and PEG (the molar ratio of LA/GA/PEG=63/27/10) were added into a vigorously polymerization tube followed by the addition of 0.05 wt% stannous octoate as catalyst. After de-oxygenating with argon three times, the tube was sealed under vacuum and polymerized at 160°C for 24 h. Finally, the crude product was purified with 300 mL chloroform and precipitated in 800mL ethanol, and then dried under vacuum at room temperature until constant weight.

The molecule of weights of PLGE copolymers were determined by ¹H NMR (Bruker DMX400 spectrometer) with CDCl₃ as solvent, and Gel Permeation Chromatography (GPC) (Waters 510 apparatus equipped with Shodex GPC KF-800 columns) at 35°C. Chloroform was served as eluent at flow rate of 1.0mL/min. Polystyrene standard was used for calibration.



• Fig. S2 ¹H NMR characterization of amphiphilic copolymer PLGE.

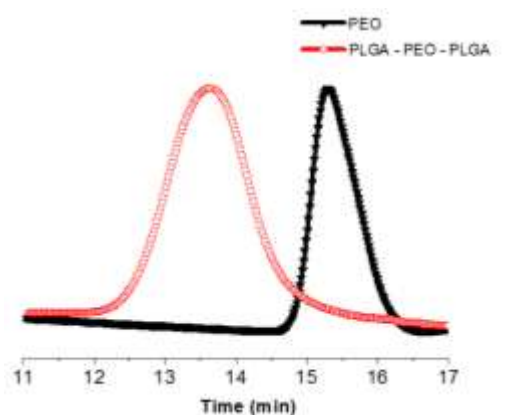


Fig. S3 Gel permeation chromatography (GPC) characterization of amphiphilic copolymer PLGE.

Preparation of Evansblue-loaded PLGA microspheres

Hydrophobic PLGA porous microspheres were prepared by a modified double emulsion (W/O/W)-solvent evaporation technique. In typical, 0.2 g PLGA was dissolved in 6 mL dichloromethane (DCM), 0.02 g Evansblue were dissolved in 1mL deionized water. The two solutions were mixed and emulsified for 60s using an ultrasonic cell disruptor to form W1/O emulsion. Subsequently, the W1/O emulsion was slowly injected into 200 mL of 1% polyvinyl alcohol (PVA) aqueous solution and homogenized at 15000rpm for 1 h, and then 500rpm for 2 h at 40 °C to allow the solvent evaporation and solidification of microspheres. The obtained microspheres were washed three times with distilled water and freeze-dried for 48 h.

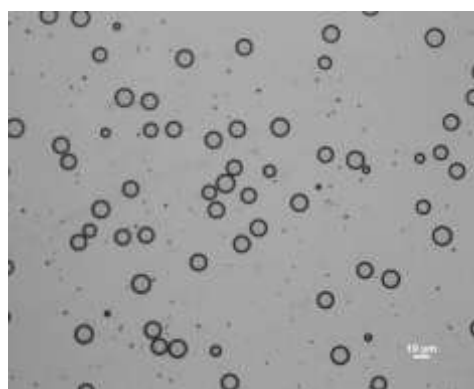


Fig. S4. Optical microscope images of the prepared $W_1/O/W_2$ double emulsion.

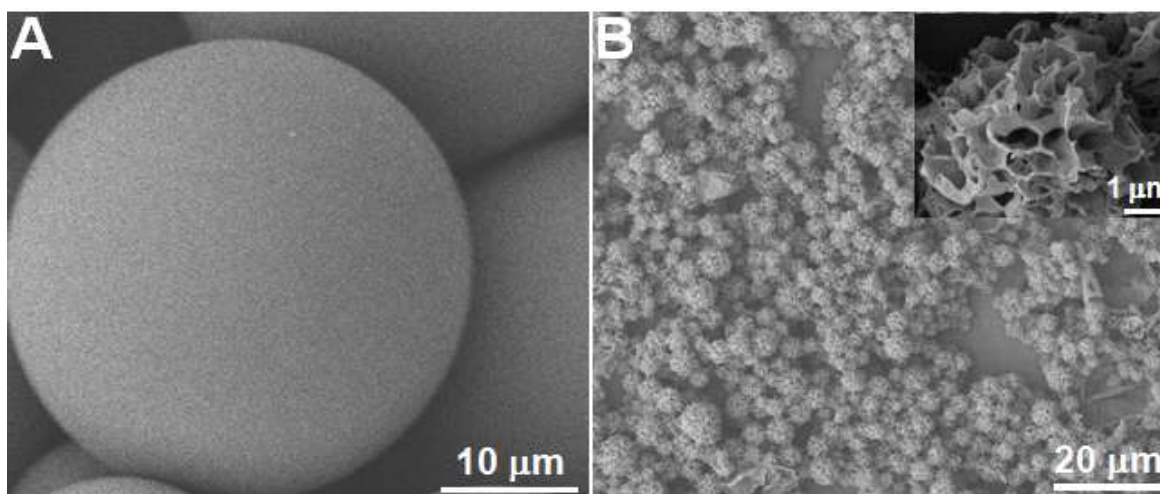


Fig. S5 (A) SEM images of PLGA microspheres prepared by a modified double emulsion (W/O/W)-solvent evaporation technique; (B) SEM images of PLGE porous microspheres prepared by increasing the volume of DCM to 1.5 times.

Preparation of Evansblue-loaded PLGE porous microspheres

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Determination of drug encapsulation efficiency

The Evansblue loading capacities in the PLGE porous microspheres were determined by an ultrasound-extraction strategy. Briefly, 10 mg of Evansblue-loaded PLGE porous microspheres were dissolved in a centrifuge tubes containing 3 mL of dichloromethane (DCM), which was placed on a shaker water bath with 100rpm at 37°C. After 30 min, 7 mL phosphate buffer saline

(PBS, PH 7.4) were added followed ultrasonic waves assisted to allow the PLGE dissolved completely. The Evansblue supernatant was extracted by centrifugation. The concentration of Evansblue was measured by ultraviolet spectrophotometer at 609 nm.

The drug encapsulation efficiency of Evansblue-loaded PLGE porous microspheres were defined as following equation:

Entrapment efficiency(%)= weight of Evansblue in PLGE porous microspheres / weight of Evansblue fed initially.

Drug release behavior of Evansblue-loaded PLGE porous microspheres in vitro

Evansblue-loaded PLGE porous microspheres were precise weighted and placed in a centrifuge tubes containing 60 mL PBS (PH 7.4). Subsequently, the tube was placed in a shaker water bath with 100rpm at 37°C. At 3 min intervals, 3mL of drug loaded microspheres were drew out quickly and centrifuged at 10000rpm. Finally, the supernatant was collected for UV spectrophotometer analyzed. These drug release assays were persisted for 15 min.

Characterization of Evansblue-loaded PLGE porous microspheres

The surface morphology of Evansblue-loaded PLGE porous microspheres were observed by scanning electron microscope (SEM) (6700, JEOL, Japan). All samples were coated with platinum using a vacuum evaporator before SEM. The size of Evansblue-loaded PLGE porous microspheres were analyzed by the Image-Pro Plus 6.0 software. At least 100 microspheres captured from SEM pictures were analyzed and averaged by Image-Pro Plus 6.0 software for the diameter of each sample.