Electronic Supplementary Information

PEG/lecithin-liquid-crystalline composite hydrogels for quasi-zero-order combined release of hydrophilic and lipophilic drugs

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1. Materials

Lecithin (from soybean) was produced by SERVA Electrophoresis GmbH, PEGDA1000 (molecular weight is about 1000) was from Shin-Nakamura Chemical CO., LTO (Japan), ammonium persulfate (APS), tetramethylethylenediamine (TEMED) were offered by Sinopharm Chemical Reagent Beijing Co., Ltd. Doxorubicin hydrochloride (Dox) and aspirin (Asp) were purchased from Aladdin reagent Co., Ltd. All chemicals were used without further purification.

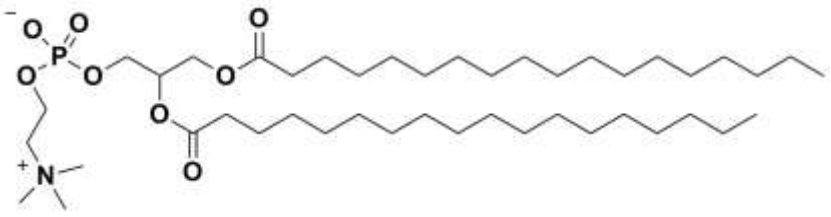

Figure S1. Chemical structure of distearoylphosphatidylcholine (DSPC) which is the main component of lecithin.

2. Preparation of PEG/lecithin composite hydrogels

Lecithin was mixed with deionization water by stirring to get lecithin solutions of four concentrations (6 wt%, 12 wt%, 18 wt% and 24 wt%). These solutions were stored at room temperature over night to stable state, then 15 wt% PEGDA1000 based on the lecithin solution was added and stirred slowly to obtain the hydrogel precursor solutions. Redox initiator APS/TEMED (0.04 wt%, 0.04 wt%) was mixed with the hydrogel precursor solution and then let PEGDA1000 polymerized slowly at 37 ℃

to form the composite hydrogels. It could take 3-5 min to complete the hydrogel transforming. Each hydrogel sample was about 0.5 g.

3. Characterization

3.1 Microscopic analysis

Birefringence of the composite hydrogel samples before and after polymerization was observed by Olympus BX-51 polarizing optical microscope (POM). The measurements were carried out at 37 °C with a magnification of 400.

3.2 Rheology study

Rheological measurements were performed for hydrogel precursor solutions using a rheometer (MCR 301, Anton Paar) of cone-plate geometry with a diameter of 35 mm, cone angle of 1°. The linear viscoelastic range (LVR) of a material was determined before carrying out the oscillatory measurements. Frequency-dependent rheological measurements were conducted in the range of 0.01-100 rad/s at 37 °C. Figure S2 is the rheological curve of 15 wt% PEGDA1000 solution without lecithin. It was almost like newtonian fluid as its low concentration and low molecular weight of PEGDA1000.

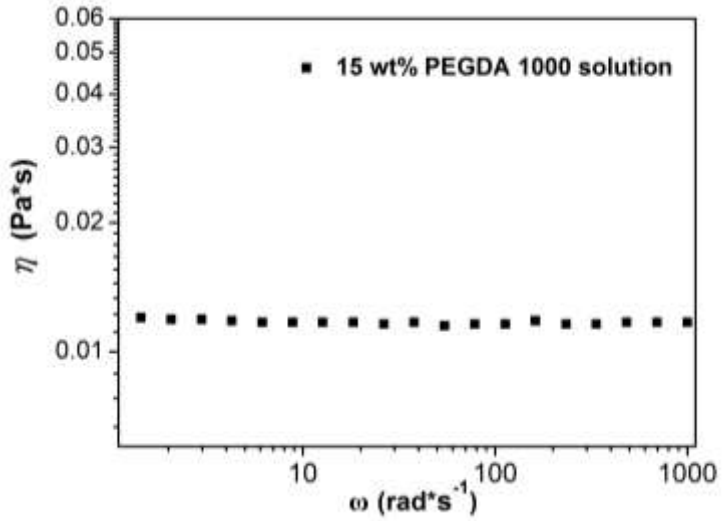

Figure S2. Complex viscosity η as a function of applied frequency ω for 15 wt% PEGDA1000 without lecithin.

3.3 Small-Angle X-ray Diffraction (SAXS)

SAXS (SAXSess, Anton Paar) measurements were used to identify the ordered structures formed from lecithin molecules in hydrogel. Hydrogels after polymerization (without drying) were directly used to test.

4. Drug loading and release in vitro

Analgesic drug Asp and anticancer drug Dox were used as hydrophilic and lipophilic model agents respectively. Asp was directly dissolved in PEGDA1000 water solution then mixed with lecithin thoroughly. The mixture was stored over night at room temperature before crosslinking. For Dox, lecithin was mixed with PEGDA1000 water solution first then 5 μL of Dox dispersed ethanol solution (50 mg of Dox in 1 mL ethanol) was added and mixed. The mixture was also stored over night at room temperature before crosslinking. Redox initiator APS/TEMED (0.04 wt%, 0.04 wt%) was then employed for polymerization [s1, s2].

Drug-loaded hydrogel samples were fabricated in a test tube (10 mm in diameter) by polymerization of the drug containing precursor solutions (0.5 g) under the conditions as described before. 1h after the drug-loaded composite hydrogels formation, 3 ml of PBS solution was added into the tube and the release was carried out the 37 °C. At different time intervals, 1.5 ml of medium was pipetted out and 1.5 ml of fresh PBS was replenished. The medium was first ultrasonicated then centrifuged. Then upper medium was taken out for test. The concentrations of released drugs were quantified using a UV-visible spectrophotometer (V-570, JASCO, Japan) and their established standard curves obtained in PBS solution.

5. Weight loss and swelling of PEG/lecithin composite hydrogels

Weight loss of the composite hydrogels with time in PBS was measured by recording the weight changes of dry gels after a specified time of incubation. Briefly, polymerized hydrogels were vacuum dried to constant weight (Wd_0), then the dried gels were immersed in different PBS solutions (10 mL) and incubated at 37 °C. At

regular time intervals samples were taken out, washed with deionized water and dried in reduced pressure until constant weight (Wd_t) was reached. The weight loss was finally determined by $(Wd_0 - Wd_t)/Wd_0 \times 100\%$. All experiments were performed in triplicate.

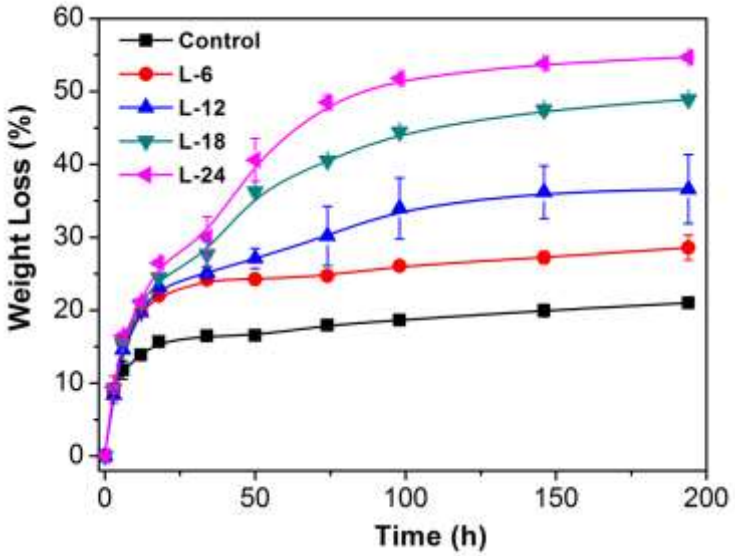

Figure S3. Weight loss of PEG/lecithin composite hydrogels with time.
(Control: 15 wt% PEG1000 hydrogel)

Dynamic swelling behaviors of the composite hydrogels were also investigated by their swelling ratios (SRs) in PBS solutions at 37 °C. Briefly, hydrogel samples were weighed (W_0) first after the polymerization, followed by swelling in different PBS solutions. At a predetermined time point, the swollen samples were taken out, removed excess water carefully and weighed (W_t). After each weighing, the samples were returned to the containers with refreshed buffer solution. The SR of hydrogel was calculated by $W_t/W_0 \times 100\%$. All experiments were performed in triplicate.

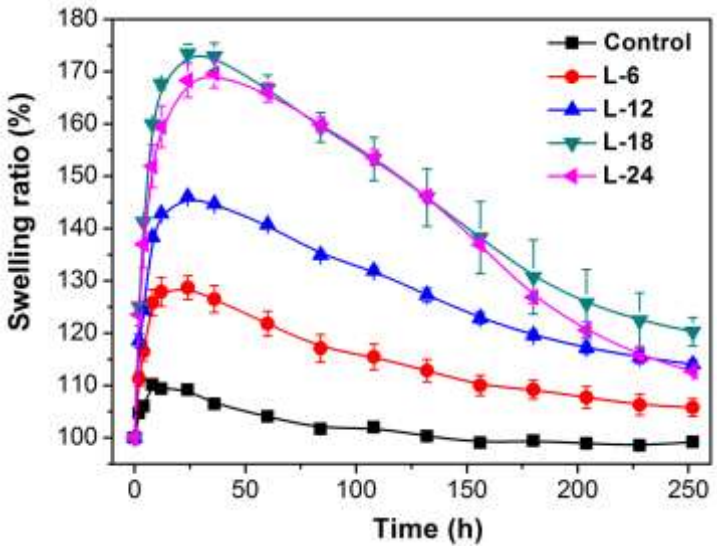

Figure S4. Swelling behaviors of PEG/lecithin composite hydrogels with time. (Control: 15 wt% PEG1000 hydrogel)

Reference

[s1] Y. Hwang, C. Zhang and S. Varghese. J. Mater. Chem. 2010, 20, 345-351.

[s2] X. Zhang, M. R. Battig and Y. Wang. Chem. Commun. DOI: 10.1039/c3cc45594g. (Preview paper)