1. Experimental

1.1. Materials

Polyvinylpyrrolidone K60 (PVP K60, $M_w = 360,000$) was purchased from BASF Corp. (Shanghai, China); acyclovir (ACY) was obtained from Zhejiang Charioteer Pharmaceutical Company (Hangzhou, China); tristearin (GTS) was purchased from Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan); N, N-dimethylacetamide (DMAc), anhydrous ethanol and chloroform were provided by Shanghai Shiyi Chemicals Reagent Co., Ltd. (Shanghai, China). All chemicals used were analytical grade. Water was double distilled just before use.

1.2. Co-axial electrospinning process

A co-dissolving solution of 10% (w/v) PVP and 2% (w/v) ACY in a mixed solvent of DMAc : ethanol (4:6, v:v) was used as core fluid. The electrospinnable sheath liquid consisted of 10% (w/v) PVP and 2% (w/v) GTS in chloroform.

A concentric spinneret and the corresponding co-axial electrospinning apparatus are shown in Fig. S1. The inner and the outer capillary are co-planar. Two syringe pumps (KDS100 and KDS 200, Cole-Parmer®, Vernon Hills, IL, USA) were employed to drive the sheath and core fluids at a flow rate of 2.0 ml h$^{-1}$ and 0.3 ml h$^{-1}$, respectively. An alligator clip was used to connect the spinneret with the high voltage supply (Shanghai Sute Electrical Co., Ltd) and the applied voltage was fixed at 12 kV. The fibers were received on a metal collector wrapped with aluminum foil kept a
fixed distance of 15 cm away from the needle tip of the spinneret. The co-axial electrospinning processes were recorded using a digital video recorder (PowerShot A640, Canon, Japan) under different magnifications. The generated core-sheath nanofibers were stored in a desiccator before characterization or molecular self-assembly process were undertaken.

1.3. Characterization

*Field emission scanning electron microscope (FESEM)*

The morphology of the surface and the cross-sections of the nanofiber mats were assessed using a S-4800 field emission scanning electron microscope (Hitachi, Tokyo, Japan). The average fiber diameter was determined by measuring diameters of composite nanofibers at over 100 places from FESEM images, using Image J software (National Institutes of Health, Bethesda, MD, USA). Before carbon-coating, the cross-sections of the nanofiber mats were prepared by placing them into liquid nitrogen for over 15 minutes, and then they were broken manually.

*Transmission electron microscopy (TEM)*

TEM images of the samples were taken on a JEM 2100F field-emission transmission electron microscope (JEOL, Tokyo, Japan).

TEM samples of core-sheath nanofibers were prepared by fixing a lacey carbon coated copper grid on the metal collector. Fibers were spun directly onto the grid for several minutes.

Core-sheath fiber mats (0.1 g) were placed in 100 ml water for self-assembly. One drop of the self-assembled systems was spread onto a carbon coated thin film on 200 mesh copper grids.

*Physical status characterization*

Differential scanning calorimetry (DSC) analyses were carried out using an MDSC 2910 differential scanning calorimeter (TA Instruments Co., USA). Sealed samples were heated at 10 °C min⁻¹ from 20 to 300 °C under a flow of nitrogen gas (40 ml min⁻¹), the results are shown in Fig. S2. X-ray diffraction patterns (XRD) were obtained on a D/Max-BR diffractometer (RigaKu, Tokyo, Japan) with Cu Kα radiation over the 2θ range 5-60° at 40 mV and 30 mA. Attenuated total reflectance
Fourier transform infrared (ATR-FTIR) analysis was carried out on a Nicolet-Nexus 670 FTIR spectrometer (Nicolet Instrument Corporation, Madison, USA) over the range 500-4000 cm$^{-1}$ and at a resolution of 2 cm$^{-1}$, the results are shown in Fig. S3.

**Static and dynamic laser scanning (SDLC)**

Average hydrodynamic diameter and size distribution of the self-assembled particles were determined using BI-200SM Static and dynamic light scattering (SDLC) instruments (Brookhaven Instruments Corporation, Austin, Texas USA).

**Polarization microscope**

Self-assembly processes were observed under polarized light using an XP-700 polarized optical microscope (Shanghai Changfang Optical Instrument Co., Ltd). The microscope was connected to a digital video recorder (PowerShot A640, Canon, Japan). The magnification was 7 × 40.

A drop of water from a micro-injector was placed on some fibers collected on a glass slide to observe the self-assembly process using an XP-700 polarized optical microscope (Shanghai Changfang Optical Instrument Co., Ltd, Shanghai, China). The microscope was connected to a digital video recorder (PowerShot A640, Canon, Tokyo, Japan). The self-assembled and naturally dried sample was also observed using FESEM.

**Drug entrapment efficiency**

The drug content in the core-shell nanoparticles was determined by calculating the difference between the total drug concentrations in the self-assembled suspension and the amount of free drug in its supernatant. The supernatant was separated from the nanoparticles by ultra-centrifugation. The amount of free drug present in the supernatant ($w_f$) was determined using a UV–vis spectrophotometer (Unico Instrument Co. Ltd., Shanghai, China) at $\lambda_{max} = 252$ nm. A standard calibration curve of concentration versus absorbance was plotted for this purpose. The amount of drug in the supernatant was subtracted from the total amount of drug in the electrosprayed microparticles ($W_t$) to calculate the amount of drug entrapped in the self-assembled nanoparticles. Percentage drug entrapment was calculated using the formula:

$$\text{Entrapment} = \frac{(W_t - w_f)}{W_t} \times 100\%$$
In vitro drug release tests One milliliter of the self-assembled core-shell nanoparticles was placed in a dialysis tube (MWCO = 3500 Da). The dialysis sacs were then dialyzed in 10 ml of normal saline as dissolution medium at 37 °C, with a stirring rate of 100 rpm. At predetermined times, the PBS was removed and replaced with the same volume of fresh solution. The amount of drug released was determined by UV–vis spectrometry as described above. Release studies were conducted six times, and mean values plotted against time.

Figures

![Digital picture of the co-axial electrospinning process. The inset in the upper-right corner was taken under a magnification of 11.](image)

**Fig. S1** Digital picture of the co-axial electrospinning process. The inset in the upper-right corner was taken under a magnification of 11.

![Differential scanning calorimetry thermograms (DSC).](image)

**Fig. S2** Differential scanning calorimetry thermograms (DSC).
Fig. S3 Attenuated total reflectance-Fourier transform infrared (ATR-FTIR) spectra.