

## Supporting Information

### 1. Preparation of drug-loaded silk fibroin **nanospheres**

Briefly, a 0.5 mg/mL CUR ethanol solution was added by dropwise into 3 wt% RSF solution under gentle stirring (100 rpm) for 2 min with the volume ratio of  $V_{\text{ethanol}}/V_{\text{RSF}}=8:20$ . The mixture was incubated in a refrigerator at  $-20^{\circ}\text{C}$  for 24h, and then it was defrosted at room temperature yielding a yellow emulsion. After remove the non-encapsulated drug, the emulsion was ultracentrifugated, and CUR-loaded **nanospheres** could be obtained by lyophilizing.

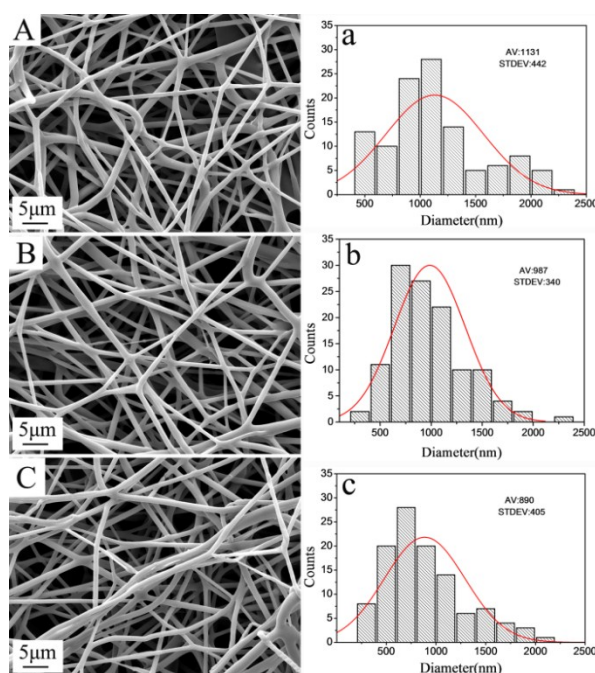
### 2. Encapsulation efficiency and drug loading of **nanospheres**

5 mL diluted emulsion was dialyzed against 2000 mL deionized water to remove most of curcumin that did not encapsulated in RSF **nanospheres**, the curcumin concentration in the dialysate was determined by measuring the absorbance of curcumin with the UV-8000S spectrophotometer at 425 nm. The encapsulation efficiency (E, %) and drug loading was were calculated as follows:

$$\text{Encapsulation efficiency \%} = \frac{\text{Amount of CUR in nanospheres}}{\text{Amount of CUR initially added}} \times 100\%$$

$$\text{Drug loading content \%} = \frac{\text{Amount of CUR in nanospheres}}{\text{Amount of the nanospheres}} \times 100\%$$

### 3. Effect of distance between the tip of needle and the collector on the morphology and the diameter of dual drug loaded nanofibers



**Fig.S1** SEM images and the diameter distribution diagrams of dual drug loaded RSF nanofibers embedded with 3 wt% CUR-loaded nanospheres at different distance from tip to collector. (A) and (a) 13cm, (B) and (b) 15cm, (C)and (c) 17cm.

Meanwhile, RSF solution was 33 % and applied voltage was 30 kV constantly.

There are many processing parameters that affect the morphology and diameter of RSF nanofibers, such as solution concentration, applied voltage, and the distance between the tip of needle and collector. In our previous study, we have obtained optimization parameters for electrospinning pure RSF aqueous solutions [1]. In the current study, the concentration of RSF aqueous solutions was selected 33 %, applied voltage was selected 30 KV and the distance between the tip of needle and collector was changed from 13 cm, 15 cm to 17 cm. and the results is presented in Fig.1. It is can be seen that the average diameter of dual drug loaded RSF nanofibers embedded with 3 wt% CUR-loaded nanospheres in core and 0.1% DOX-HCl in shell was 1131 nm, 987nm and 890 nm respectively, In addition, compared to Fig.1 a and c, the standard deviation of the fiber in Fig.1 b was smaller, i.e. 340 nm. Therefore, the suitable distance from tip to collector was 15 cm in this electrospinning process. The optimal parameters were the concentration of RSF aqueous solutions 33 %, applied voltage 30 KV and the distance from tip to collector 15 cm.

#### Reference

[1] J. Zhu, H. Shao and C.Hu, *Int. J. Biol. Macromol.* 2007, **41**, 469–74.