Supporting Information

Adaptive Chitosan Hollow Microspheres as Efficient Drug Carrier

Ya-nan Fu,[†] Yongsan Li,^{†,‡} Guofeng Li,[†] Lei Yang,[§] Qipeng Yuan,[†] Lei Tao,[‡] and Xing Wang^{*,†}

[†]Beijing Laboratory of Biomedical Materials, Beijing University of Chemical Technology, Beijing 100029, People's Republic of China

^{*}The Key Laboratory of Bioorganic Phosphorus Chemistry and Chemical Biology (Ministry of Education), Department of Chemistry, Tsinghua University, Beijing 100084, People's Republic of China China

[§]CancerCancer Institute and Hospital, Peking Union Medical College and Chinese Academy of Medical Science, Beijing 100021, People's Republic of China

*E-mail address: wangxing@mail.buct.edu.cn

1. Synthesis and Characterization of BF



Figure S1. Synthesis of borneol 4-formylbenzoate (BF) via a one-step esterification method.



Figure S2. FT-IR spectra of BF (top) and borneol (bottom).



Figure S3. ¹H NMR spectra of BF.



Figure S4. GC-MS spectra of BF.

2. Analysis of Morphology

2.1. Drug-loading capability of the CHM



Figure S5. Characterization of the coumarin-6-loaded microspheres. (A) the optical image; (B) the fluorescent image; (C) the overlying image of A and B; insert is a result of DLS analysis. The scale bar is 25 µm.

Table S1. Characterization of the coumarin-6-loaded microspheres (A) with or (B) without passing through 0.22 μ m microporous membrane. The particle Size, Zeta Potential, and PDI were listed.

Sample	size	zeta potential	PDI
А	396 nm – 1000 nm	$18.6 \pm 2.7 \text{ mV}$	0.319
В	122 nm – 2670 nm	$13.1 \pm 2.9 \text{ mV}$	0.556



Figure S6. The standard curve of PTX in methanol for quantification.



Figure S7. SEM (A, B, C) images of the shape-adaptive transformation of the CHM after passing through the microporous membrane (0.22 μ m). The scale bar is 200 nm.



2.3. The pH Responsive Behavior of the CHM

Figure S8. Optical microphotographs of the CHM in various pH mediums before (A, B, and C) and after 10 min treatments (A', B', and C'): A, A': pH 7.06; B, B': pH 6.03; C, C': pH 5.01. The scale bar is 10 μm.



Figure S9. MTT assays of (A) BF, (B) GC, and (C) the CHM blank on L929 cells at denoted times. The control (no treated cells) was taken as 100%. The data are presented as the mean plus or minus the standard deviation (n = 6 for each group).



Figure S10. MTT assays of (A) BF, PTX combined with BF, and (B) GC, PTX combined with GC on HepG2 and A549 cells at denoted times. The control (no treated cells) was taken as 100%. The data are presented as the mean plus or minus the standard deviation (n = 6 for each group).

		Cell Viabilities (%) ^b				
Sample	Concentration	HepG2		A549		
		24 h	48 h	24 h	48 h	
Free PTX (PTX: μg/mL)	5	93.4 ± 2.3	78.2 ± 1.7	92.5 ± 3.5	74.6 ± 3.3	
	10	82.7 ± 2.9	70.3 ± 4.2	91.9 ± 0.8	64.5 ± 2.0	
Blank CHM (CHM: mg/mL)	0.86	105.5 ± 2.2	102.0 ± 4.6	101.6 ± 3.8	111.7 ± 5.0	
	1.72	97.4 ± 2.3	95.6 ± 2.2	102.1 ± 6.8	81.0 ± 6.3	
PTX-loaded CHM ^a (PTX: µg/mL)	5	81.7 ± 2.4	49.4 ± 0.7	83.9 ± 1.9	64.3 ± 3.8	
	10	32.5 ± 1.8	9.4 ± 5.0	26.4 ± 4.7	10.3 ± 7.1	

Table S2. MTT assays of free PTX, the CHM blank and PTX-loaded CHM on HepG2 and A549

 cells.

^a $\overline{\text{CHM}: 0.86 \text{ mg/mL};}$ ^b The data are presented as the mean plus or minus the standard deviation (n = 6 for each group). The control (no treated cells) was taken as 100%.