

**Covalent self-assembled nanoparticles with pH-dependent enhanced tumor  
retention and drug release for improving tumor therapeutic efficiency**

Yongwei Hao <sup>1, 2</sup>, Cuixia Zheng <sup>1</sup>, Lei Wang <sup>1, 2, 3</sup>, Yujie Hu, Haochen Guo, Qingling Song<sup>1</sup>, Hongling Zhang <sup>1</sup>, Zhenzhong Zhang <sup>1, 2,\*</sup> and Yun Zhang <sup>1, 2,\*</sup>

1. School of Pharmaceutical Sciences, Zhengzhou University, 100 Kexue Avenue, Zhengzhou 450001, P. R. China.

2. Key Laboratory of Targeting Therapy and Diagnosis for Critical Diseases, Henan Province, Zhengzhou 450001, P. R. China.

3. School of Chemistry and Molecular Engineering, 100 Kexue Avenue, Zhengzhou 450001, P. R. China.

\*Correspondent: Prof. Zhenzhong Zhang and Prof. Yun Zhang, School of Pharmaceutical Sciences, Zhengzhou University, 100 Kexue Avenue, Zhengzhou, Henan Province 450001, P.R. China. Tel: 86-371-67781910; Fax: 86-371-67781908; Email: zhangzz08@126.com; [zhang\\_yun@ymail.com](mailto:zhang_yun@ymail.com);

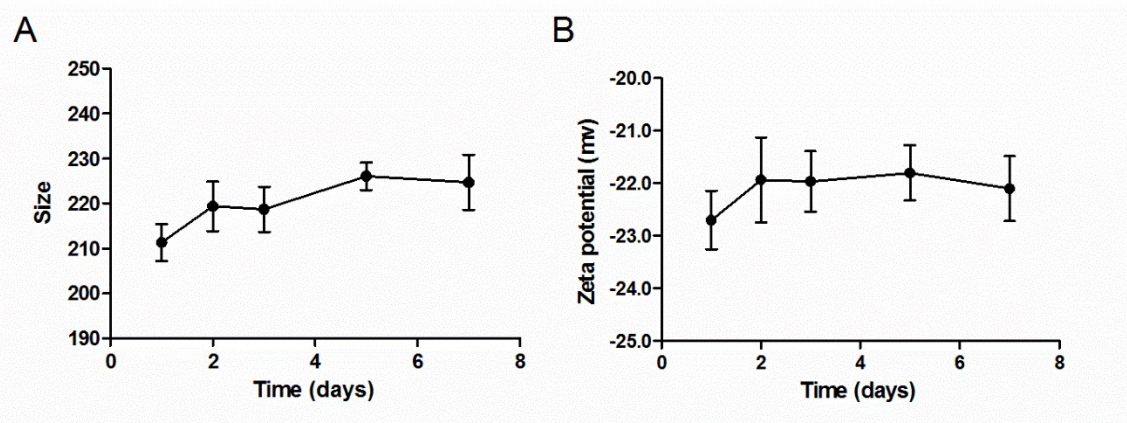


Figure S1 Size and zeta potential of DOX/BNPs in one week after preparation. (A) Mean size of DOX/BNPs at different times; (B) Mean zeta potential of DOX/BNPs at different times.

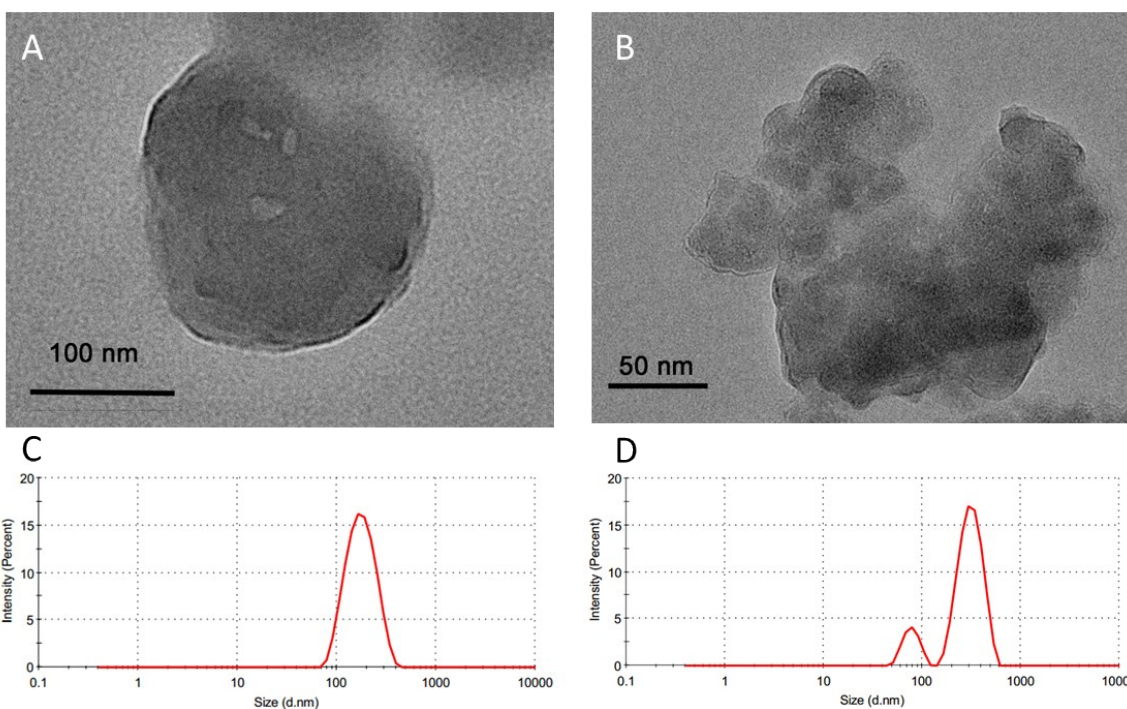


Figure S2 The morphology of DOX/BNPs determined by TEM; (A) The TEM image of DOX/BNPs treated with an acid medium with a pH of 6.5 for 0.5 h; (B) The TEM image of DOX/BNPs treated with an acid medium with a pH of 4.0 for 0.5 h; (C) Size distribution of DOX/BNPs treated with an acid medium with a pH of 4.0 for 0.5 h; (D) Size distribution of DOX/BNPs treated with an acid medium with a pH of 6.5 for 0.5 h

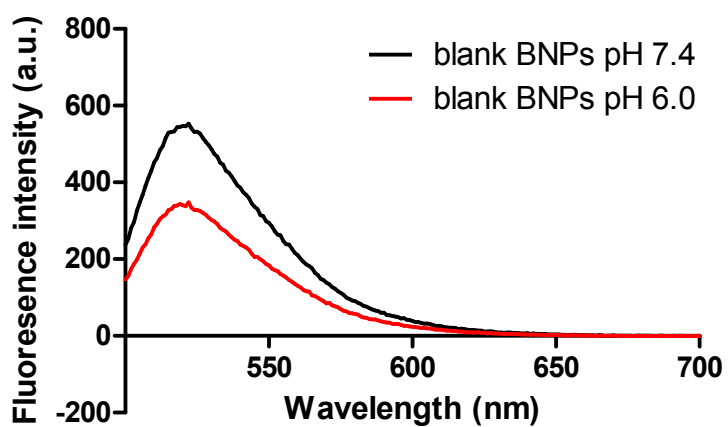


Figure S3 The fluorescence emission spectra of the FITC-labelled PSA in the supernatant of two groups;

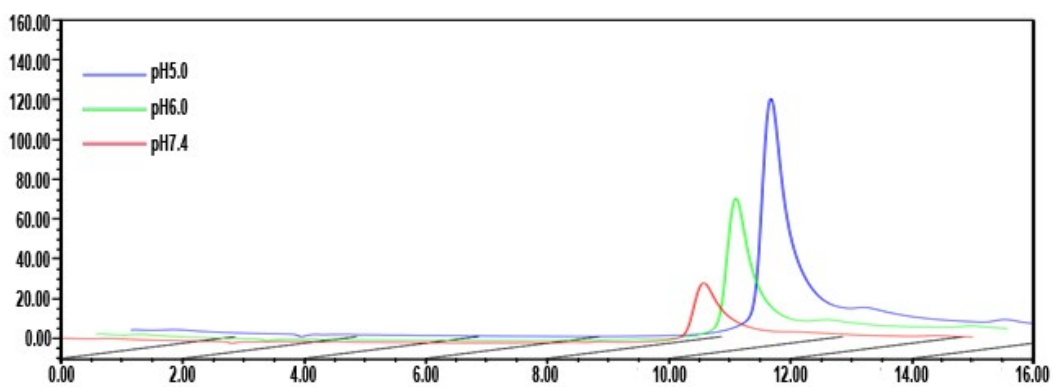


Figure S4 Representative HPLC chromatograms of released DOX in the different media at 24 h;