

A soft anti-virulence liposome realizing antibiotics explosively release at infectious site to improve antimicrobial therapy

^a School of Pharmaceutical Sciences, Zhengzhou University, Zhengzhou, China

^b Key Laboratory of Targeting Therapy and Diagnosis for Critical Diseases, Henan Province, China

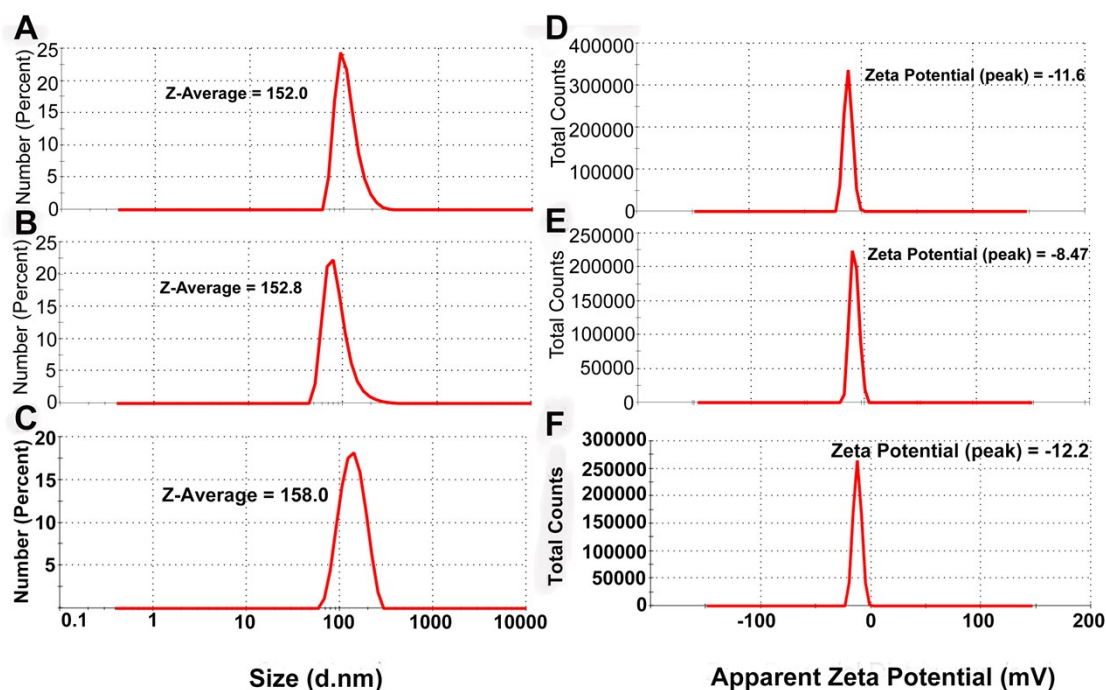
^c Collaborative Innovation Center of New Drug Research and Safety Evaluation, Henan Province, Zhengzhou, China

^d School of Materials Science and Engineering, Zhengzhou University, Zhengzhou, China

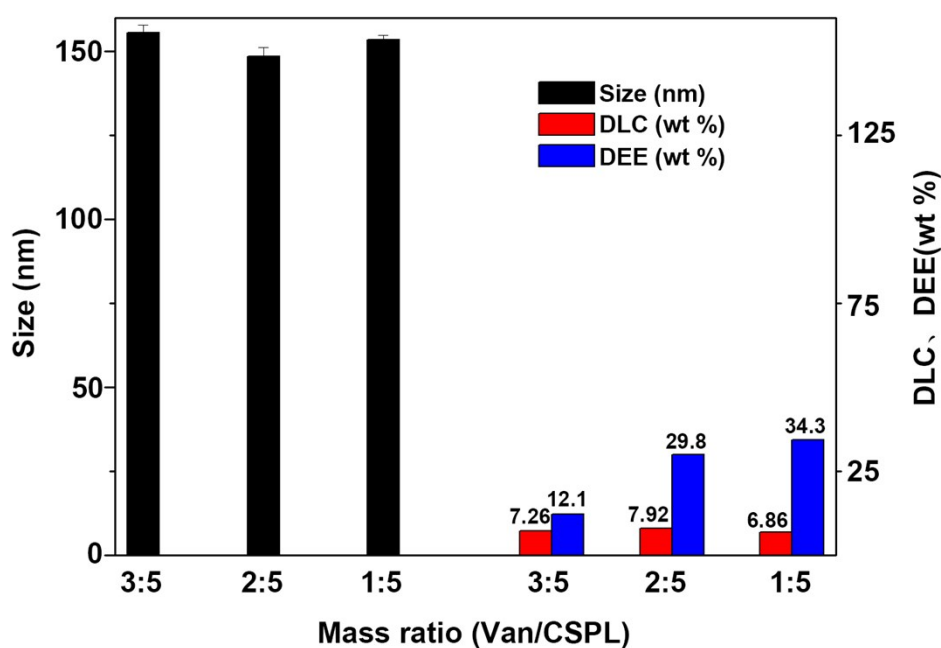
Shudong Zhang and Xiang Lu contribute equally.

* Corresponding Author: Email address: zhanghongling729@zzu.edu.cn (Hongling Zhang); Tel.: +86 371 6778 1911. Fax: +86 371 6778 1908.

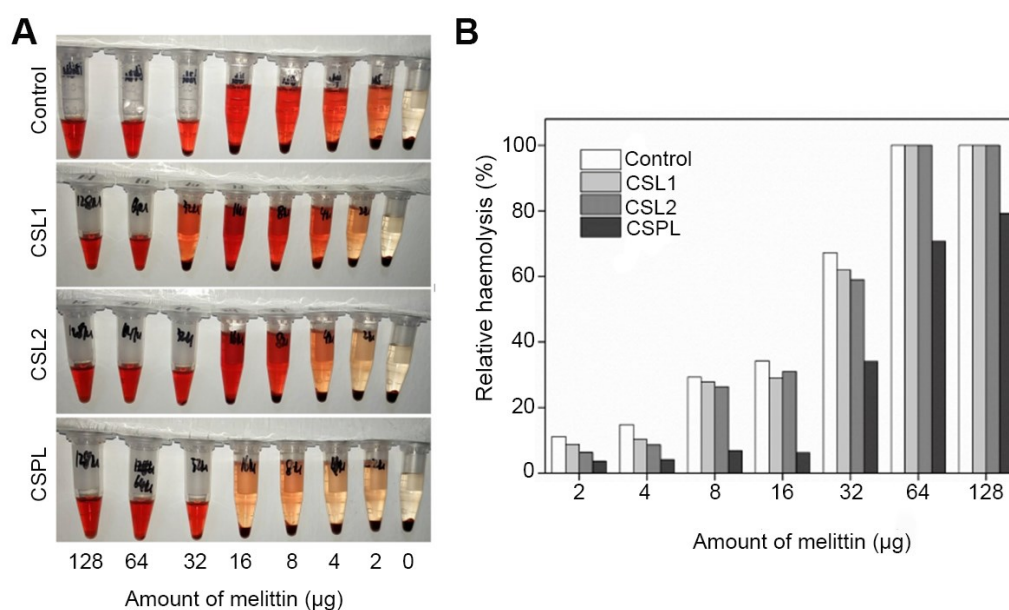
Mailing address: No.100, Kexue Avenue, Zhengzhou 450001, China



Supplementary Figure 1. DLS analysis of CL, CSL1 and CSL2. (A) Size distribution of CL; (B) Size distribution of CSL1; (C) Size distribution of CSL2; (D) Zeta potential of CL; (E) Zeta potential of CSL1; (F) Zeta potential of CSL2.

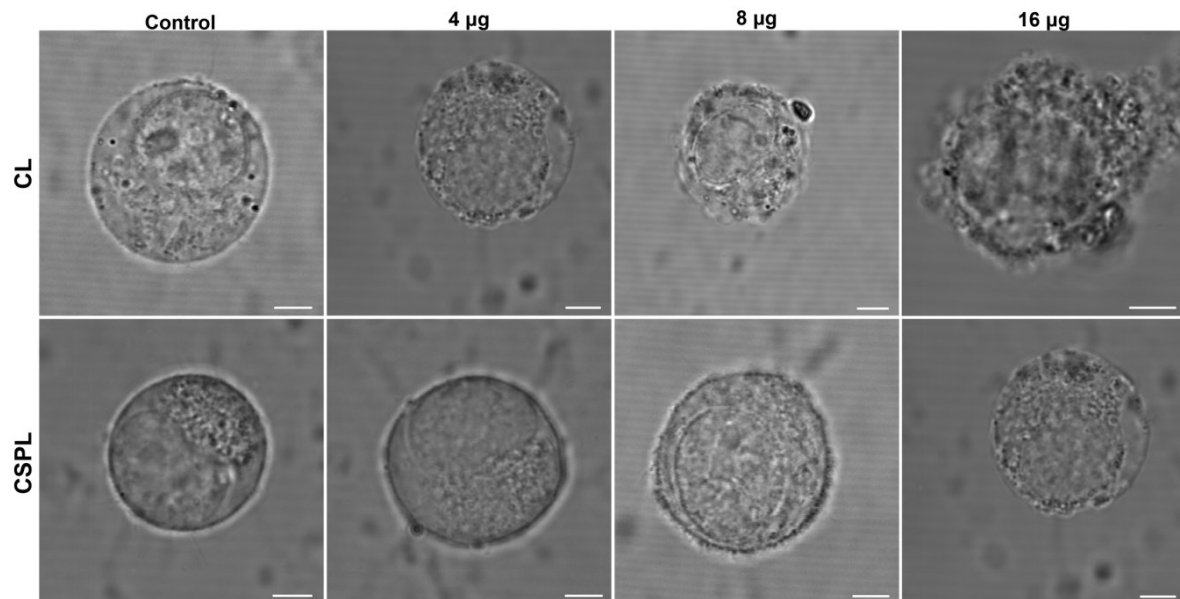


Supplementary Figure 2. Characterization of Van@CSPL. Black histogram indicates the average size of Van@CSPL with different mass ratio of Van and CSPL. Red histogram indicates the drug-loading content (DLC) of Van@CSPL with different mass ratio of Van and CSPL. Blue histogram indicates the drug encapsulation efficiency (DEE) of Van@CSPL with different mass ratio of Van and CSPL.

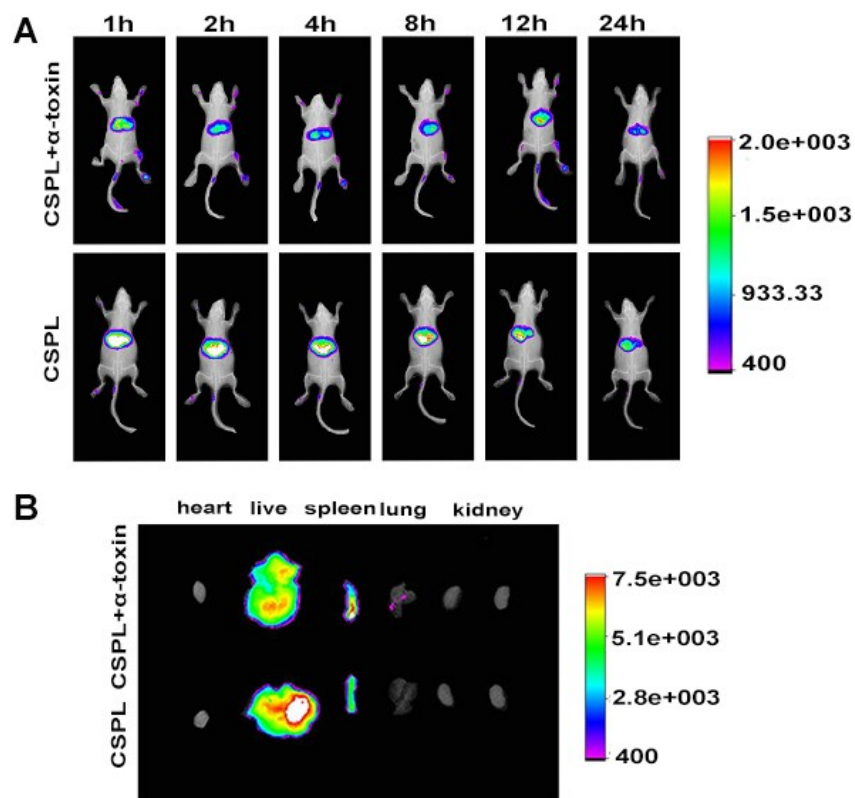


Supplementary Figure 3. In vitro anti-hemolysis assay of CSPL. (A) Centrifuged RBCs after incubating with the mixture of CSL1, CSL2, or CSPL and melittin, PBS was used as control. (B) The relative

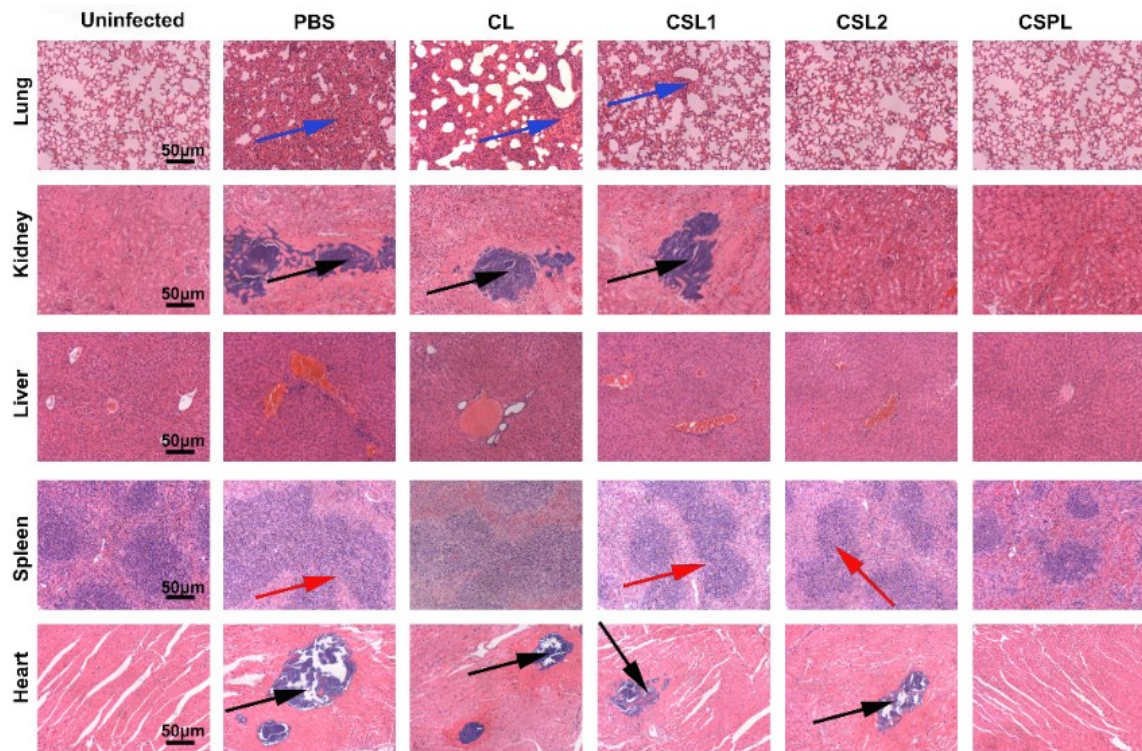
hemolysis of samples in A.



Supplementary Figure 4. The cell uptake of HUVECs after adding the mixture of CL or CSPL with varying amounts of α -toxin (4, 8, and 16 μg) for 4 h; HUVECs mixed with CL or CSPL alone as controls. And the light field was imaged by Laser Scanning Confocal Microscope. (scale bars, 7.5 μm).



Supplementary Figure 5. Biodistribution of CSPL (8 mg/mL, 200 μ L) in mice. (A) 2D fluorescence reflectance imaging of mice with or without α -toxin (a bolus lethal dose of 75 μ g/kg). Dir-labeled CSPL were intravenously administrated into mice 2 min after the injection of α -toxin. (B) The distribution of fluorescence in the main organs 24 h after the injection.



Supplementary Figure 6. Septic mice, infected intravenously with *S. aureus* ATCC29213, were given an intravenous administration of 50 mg/kg CL, CSL1, CSL2 or CSPL 4 h and 10 h after infection and evaluated for H&E staining of major organs (including heart, liver, spleen, lung, and kidney). Blue arrow indicates inflammatory infiltration in lungs. Black arrow indicates calcifications in kidney and heart. Red arrow indicates the combination of white-pulp. Scale bar, 50 μ m.