

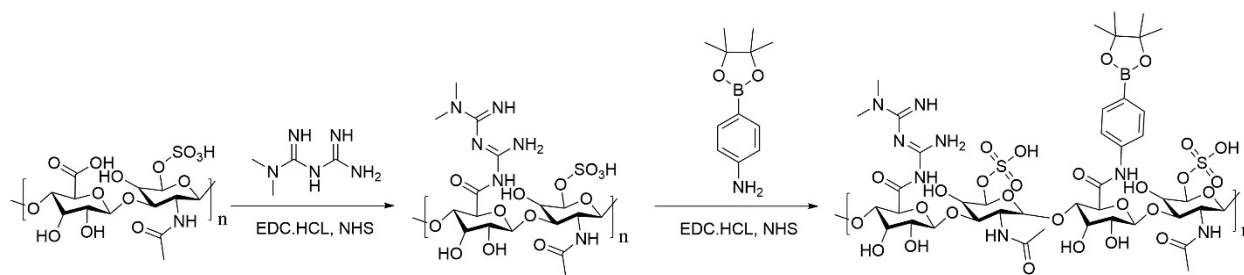
Supplementary Information

Adipocyte-targeted Celastrol Delivery via Biguanide-modified Micelles Improves Treatment of Obesity in DIO Mice

Hongling Ouyang,^a Yunxiao Zhang,^a Yueting Zhu,^a Tao Gong,^a Zhirong Zhang^a and Author Yao Fu ^{*a}

a Key Laboratory of Drug- Targeting and Drug Delivery System of the Education Ministry and Sichuan Province,
Sichuan Engineering Laboratory for Plant-Sourced Drug and Sichuan Research Center for Drug Precision Industrial
Technology, West China School of Pharmacy, Sichuan University, Chengdu, 610041, China.

*Address correspondence to yfu4@scu.edu.cn (Y. Fu).



Scheme 1. Scheme of synthesis routes of MET-CS-PBE.

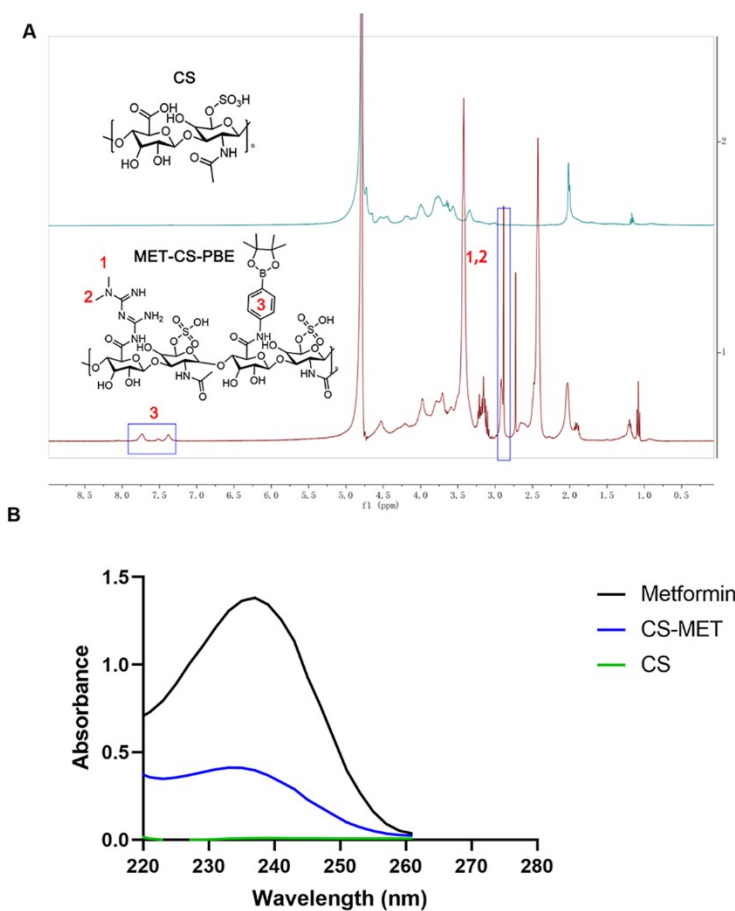


Fig. S1. Characterization of MET-CS-PBE materials. (A) Comparison of ^1H NMR (D_2O) spectrum of MET-CS-PBE and CS. (B) the maximum absorption wave of CS-MET measured by ultraviolet spectrophotometer.

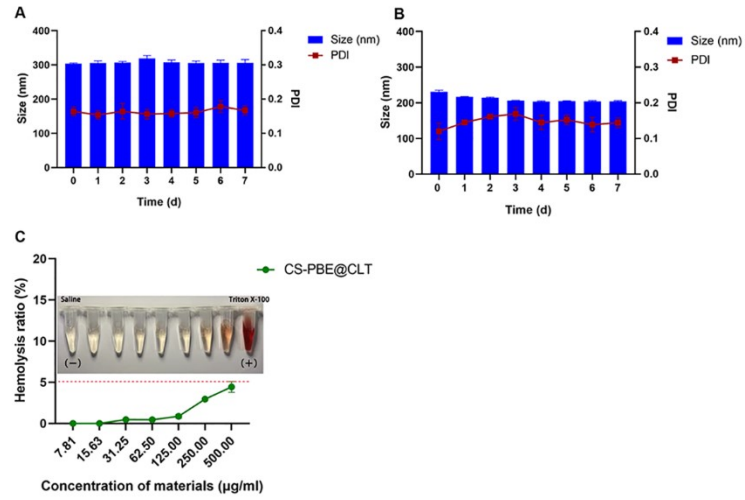


Fig. S2. Micellar stability and serum stability. (A-B) The stability of MET-CS-PBE (A) and MET-CS-PBE@CLT (B) micelles. (C) The hemolysis rate of CS-PBE@CLT.

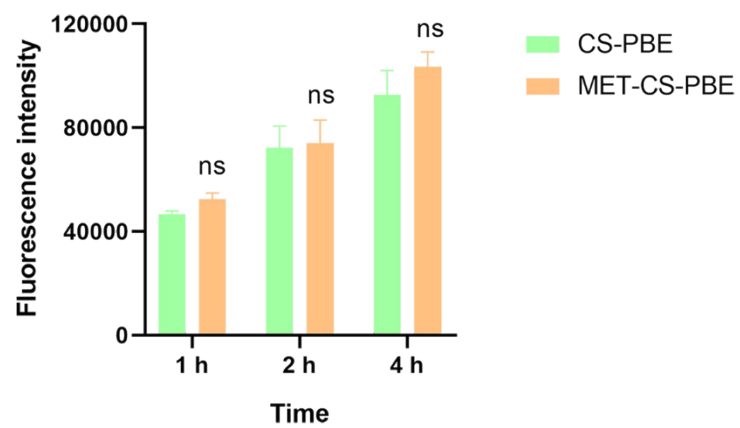


Fig. S3. The uptake efficiency of MET-CS-PBE and CS-PBE micelles in RAW 264.7.

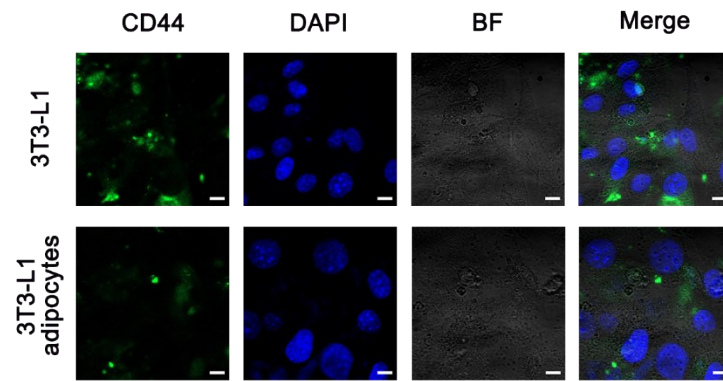


Fig. S4. Confocal microscopic images of CD44 expression difference on 3T3-L1 and 3T3-L1 adipocytes.

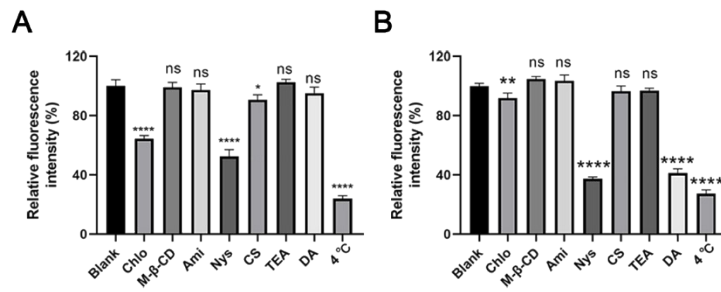


Fig. S5. The fluorescence intensity of 3T3-L1 preadipocytes accumulation of micelles after 2 h incubation in the presence of different inhibitors of distinct cell endocytosis mechanisms.

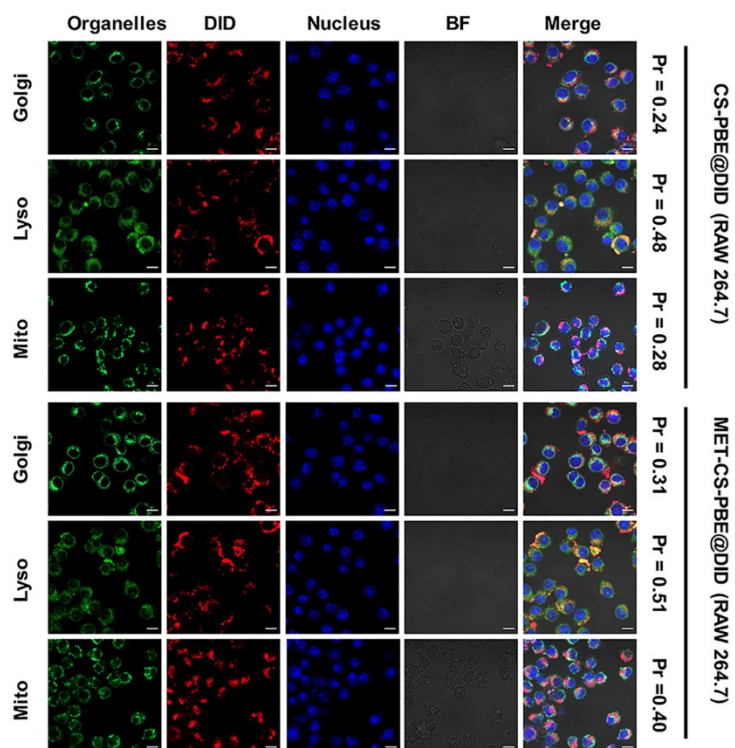


Fig. S6. The intracellular distribution of CS-PBE micelles and MET-CS-PBE micelles in RAW 264.7. Scale bar, 10 μm .

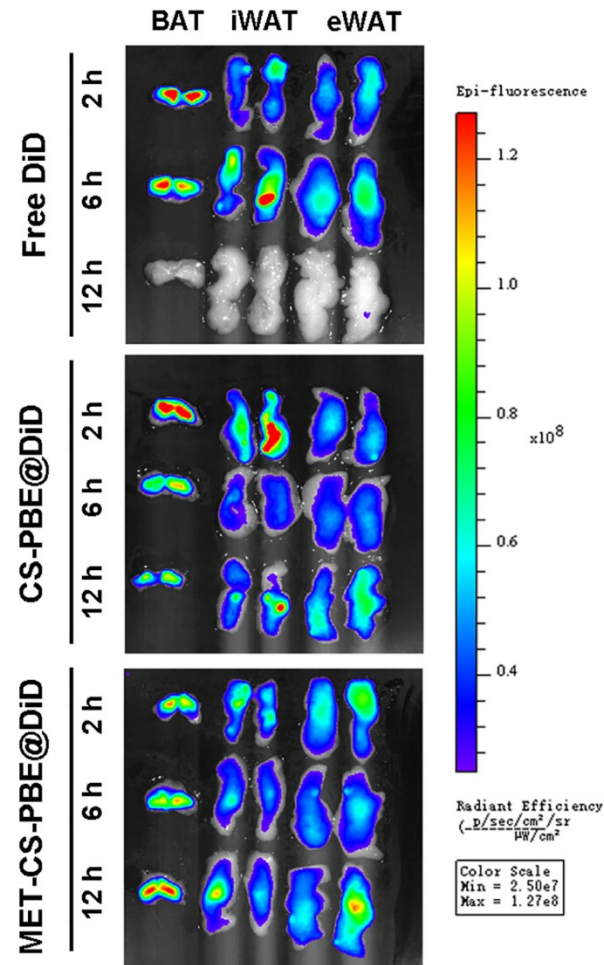


Fig. S7. *In vivo* IVIS images of adipose tissues after intravenous injection for 2, 6, 12 h.

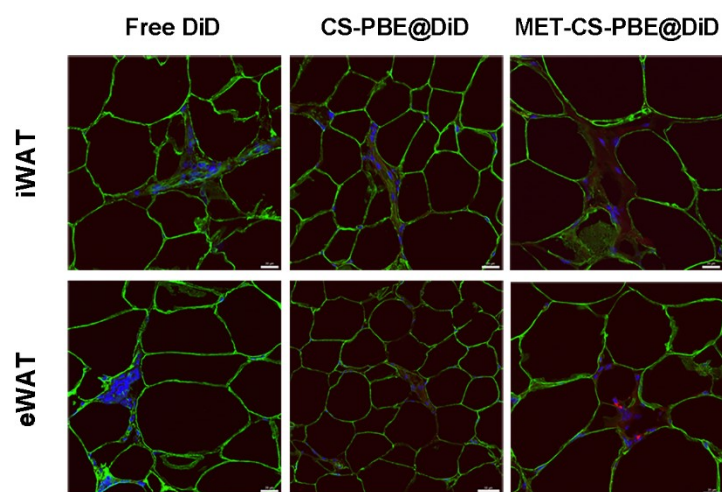


Fig. S8. Immunofluorescence image of the localization of DiD-loaded micelles within iWAT and eWAT. Red, Free DiD, CS-PBE@DiD, or MET-CS-PBE@DiD micelle. Green, caveolin. Blue, cell nuclei. Scale bar, 20 μm .

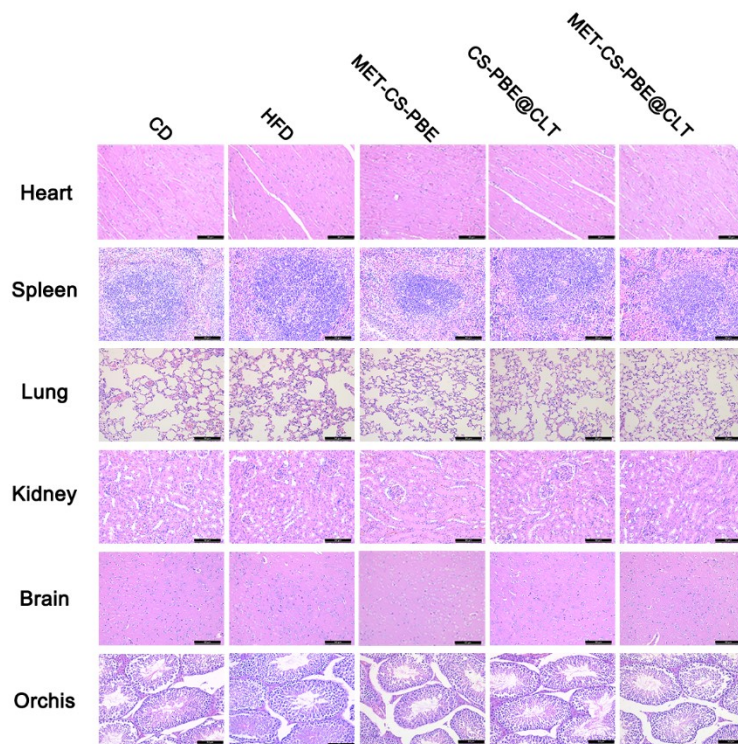


Fig. S9. Representative H&E histological images of major organs from treatment groups. Scale bar, 50 μ m.