

## Supplementary Information

**L-Arginine/L-Lysine functionalized chitosan-casein core-shell and pH-responsive nanoparticles: Fabrication, characterization and bioavailability enhancement of hydrophobic and hydrophilic bioactive compounds**

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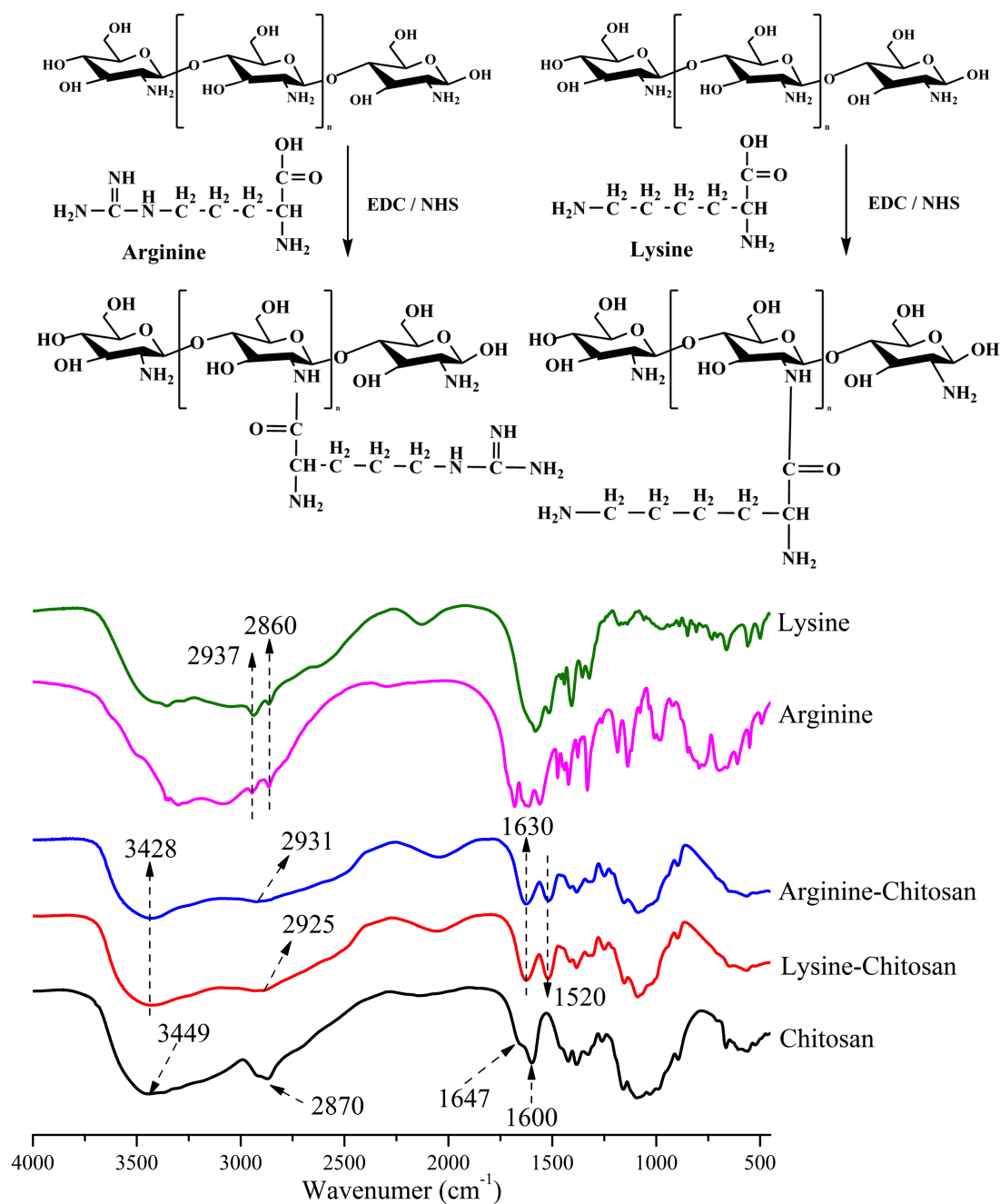


Figure S1. Schematic diagram for synthesis of Arg-CS and Lys-CS. FTIR spectra of Arginine, Lysine, Arginine-Chitosan, Lysine-Chitosan, and chitosan.

Figure S1 exhibits the characteristic FTIR spectra of CS and the arginine (Arg) or lysine (Lys) functionalized CS conjugate. The peak at 1647  $\text{cm}^{-1}$  (amid I) and 1600  $\text{cm}^{-1}$  (amid II) in CS all shift to 1630  $\text{cm}^{-1}$  in Arg or Lys functionalized CS, which could be ascribed to the characteristic carbonyl stretching ( $\text{C}=\text{O}$ ) owing to the formation of amide bonding<sup>1</sup>. The new peak in Arg or Lys functionalized CS appears at 1520  $\text{cm}^{-1}$  could be attributed to the bending vibration and stretching vibration of secondary amide. Furthermore, the peak between 3300 and 3450  $\text{cm}^{-1}$  can be attributed to the vibration of hydroxyl, amino and amide groups in CS<sup>2</sup>. Intermolecular and intramolecular hydrogen bonding between these groups in CS

greatly limits its solubility. However, the peak becomes much narrower and weaker in Arg or Lys functionalized CS, which suggested that their conjugation to CS destroys the hydrogen bonds in CS then increases its solubility<sup>3</sup>. All these results indicates the linkage of Arg or Lys to CS.

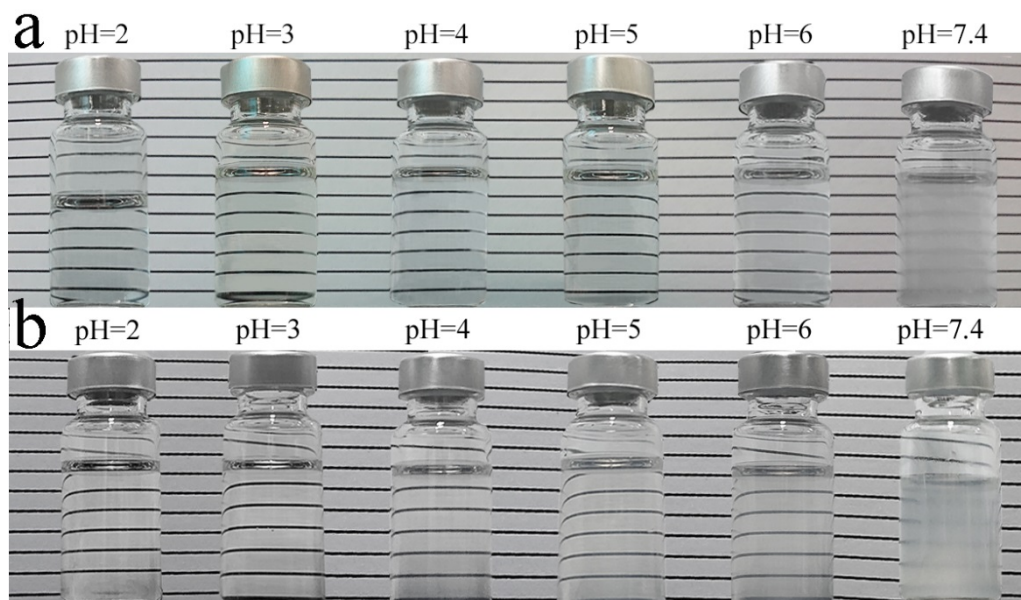


Figure S2. Sample images of Arg-CS-CA NPs (a) and Lys-CS-CA NPs (b) under different pH values.

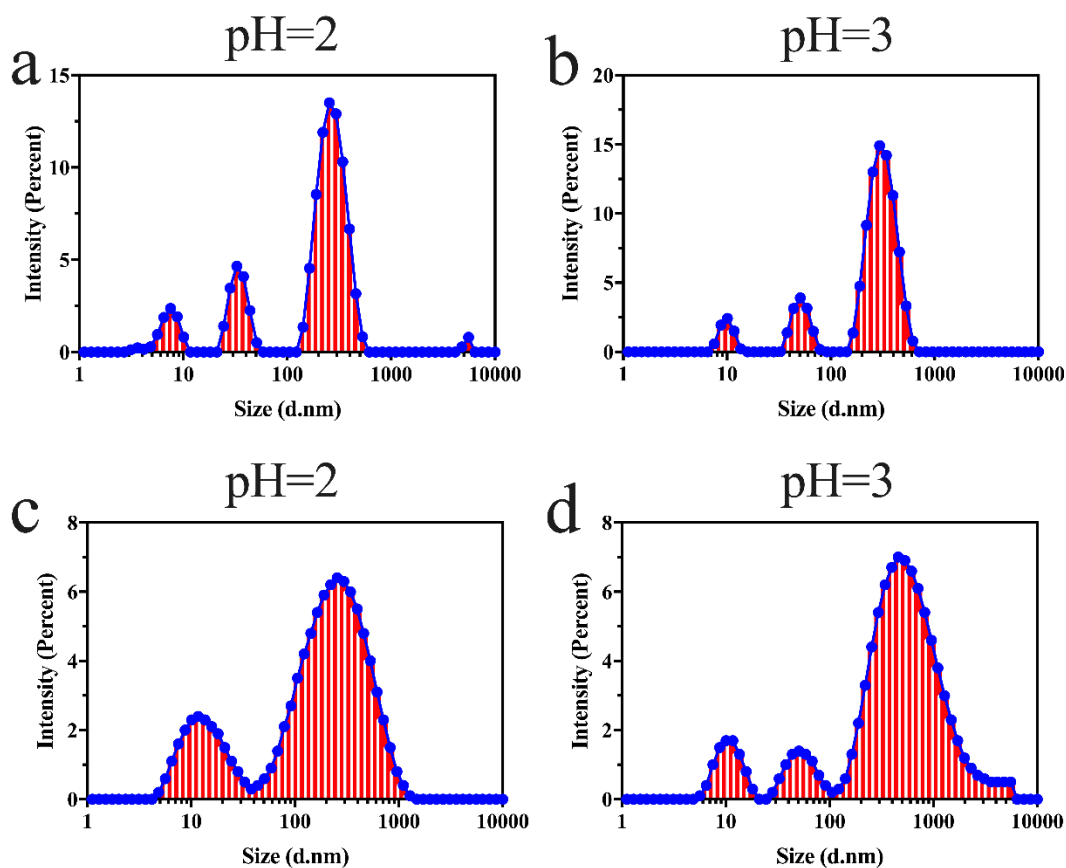


Figure S3. Size distribution of Arg-CS-CA NPs (a, b) and Lys-CS-CA NPs (c, d) at pH 2 and 3, respectively.

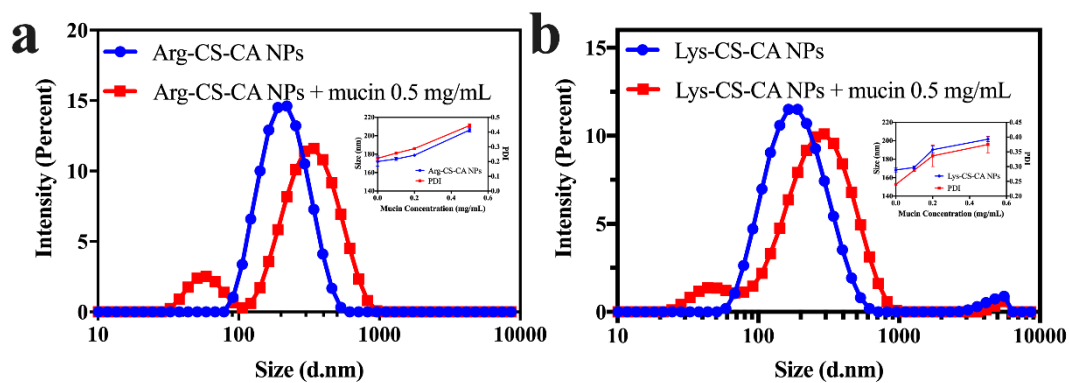


Figure S4. Interaction between Arg-CS-CA (a) and Lys-CS-CA (b) NPs and mucin at pH 5.

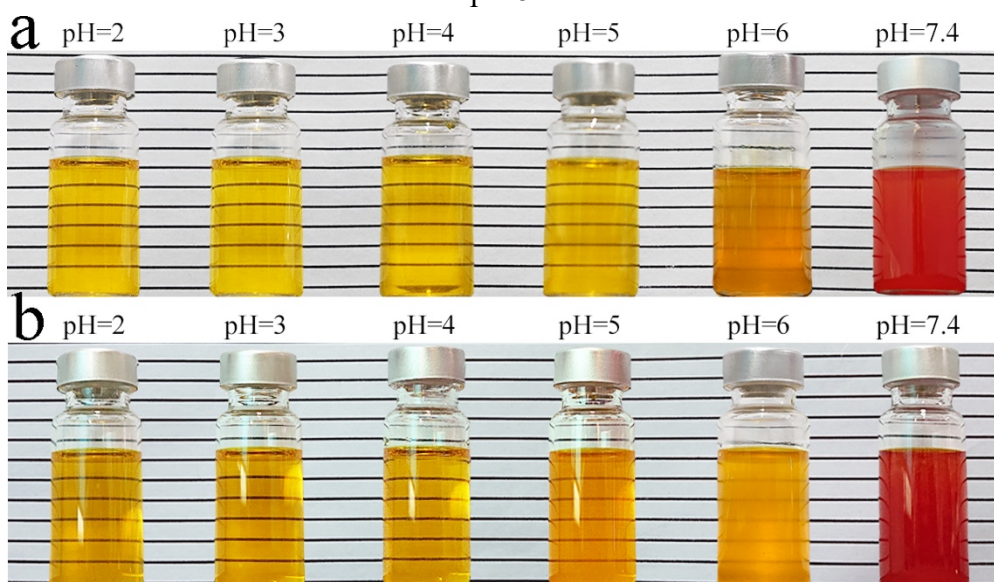


Figure S5. Sample images of curcumin entrapped in Arg-CS-CA NPs (a) and Lys-CS-CA NPs (b) under different pH values (containing 25% ethanol).

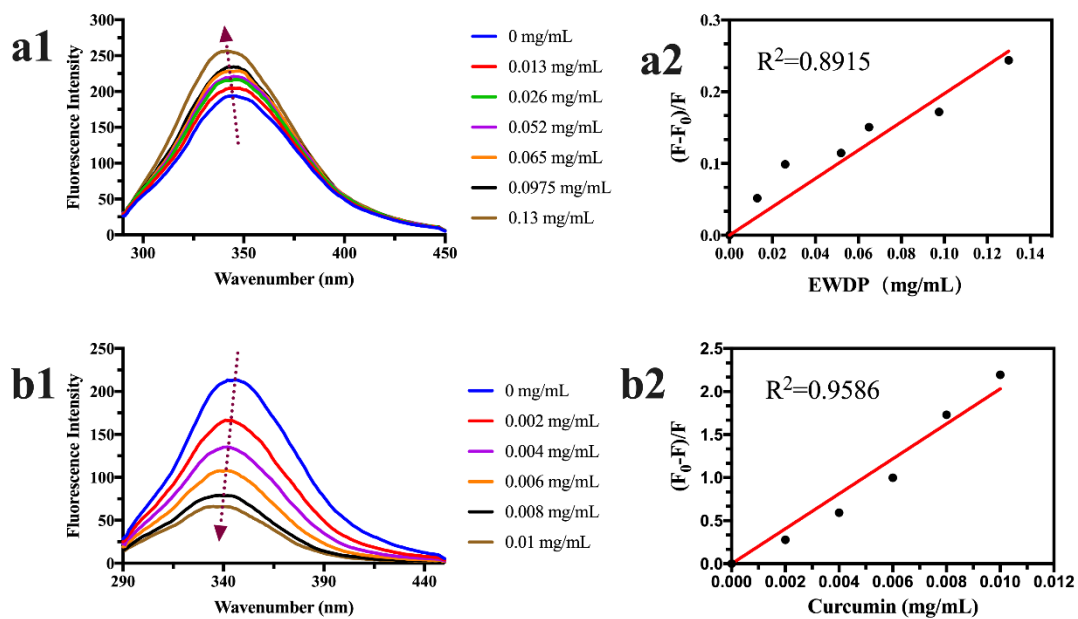


Figure S6. Fluorescence spectra of casein due to casein-EWDP (a)/curcumin (b) interaction.

## Reference:

1. C.-H. Chen, Y.-S. Lin, S.-J. Wu and F.-L. Mi, Multifunctional nanoparticles prepared from arginine-modified chitosan and thiolated fucoidan for oral delivery of hydrophobic and hydrophilic drugs, *Carbohydrate Polymers*, 2018, **193**, 163-172.
2. B. Hu, C. L. Pan, Y. Sun, Z. Y. Hou, H. Ye and X. X. Zeng, Optimization of fabrication parameters to produce chitosan-tripolyphosphate nanoparticles for delivery of tea catechins, *Journal of Agricultural and Food Chemistry*, 2008, **56**, 7451-7458.
3. K.-Y. Lu, C.-W. Lin, C.-H. Hsu, Y.-C. Ho, E.-Y. Chuang, H.-W. Sung and F.-L. Mi, FRET-Based Dual-Emission and pH-Responsive Nanocarriers for Enhanced Delivery of Protein Across Intestinal Epithelial Cell Barrier, *Acs Applied Materials & Interfaces*, 2014, **6**, 18275-18289.