

SUPPLEMENTARY INFORMATION

**SINGLE-STEP CONTROLLED SYNTHESIS OF FLOWER-LIKE GOLD NANOPARTICLES STABILIZED BY CHITOSAN FOR SENSITIVE DETECTION OF HEPARIN USING SURFACE ENHANCED RAMAN SCATTERING METHOD**

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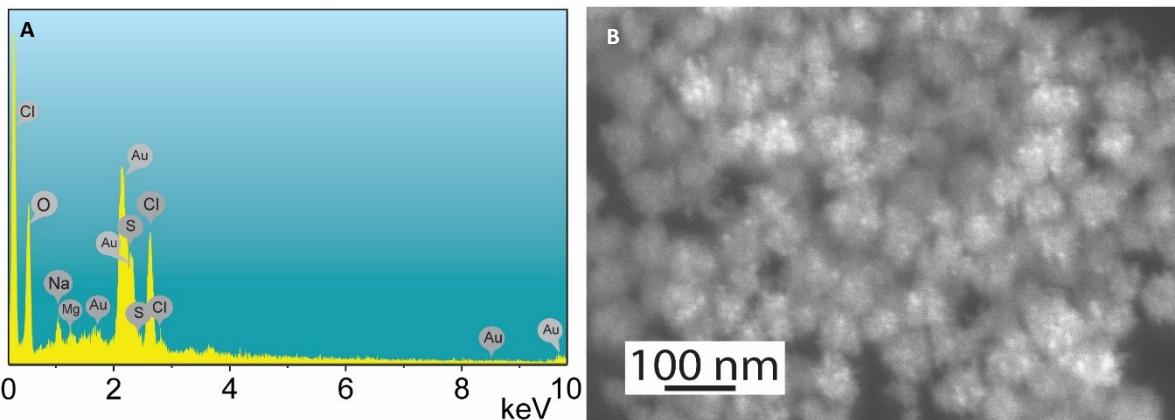


Fig. S1 (A) EDS spectroscopy and (B) corresponding SEM images of formed AuNFs-4-MBA@chitosan (scale bar 100 nm).

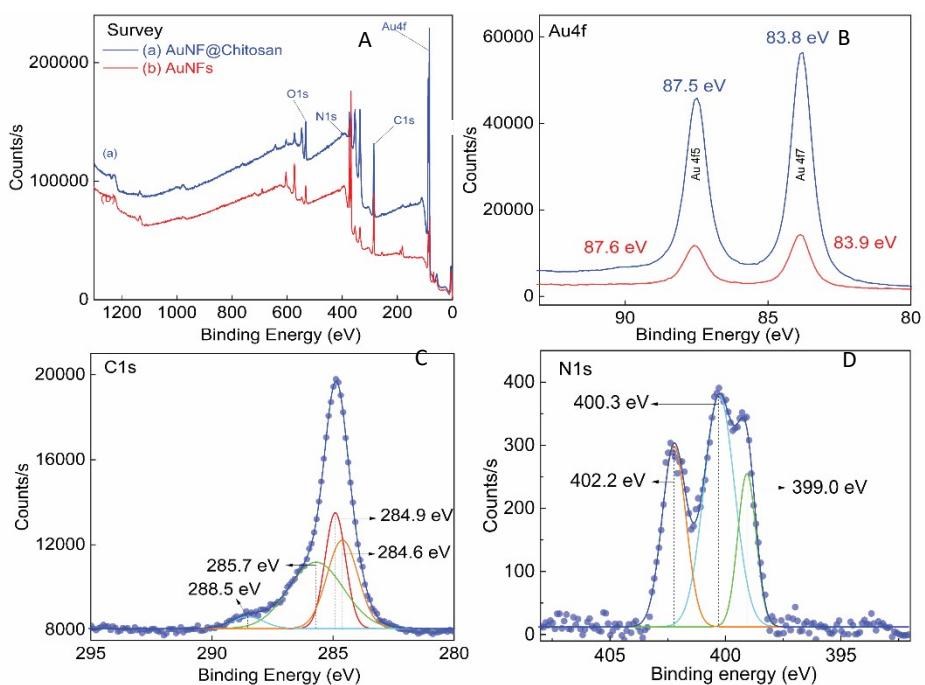


Fig S2. (A) XPS survey spectra of the AuNFs stabilized with chitosan, high-resolution XPS spectra of (B) Au4f, (C) C1s, and (D) N1s.

Table S1. FTIR band positions of AuNFs-chitosan, pure chitosan, pure heparin, and AuNF-chitosan-heparin.

	Wavenumber ( $\text{cm}^{-1}$ )			Assignment	Ref
AuNFs-4-MBA@CS	Pure CS	Pure HEP	AuNFs-4-MBA@CS after adding HEP		
3523	3447			O-H overlapped with N-H stretch	1, 2
3311					
2916	2921			C-H stretch	1, 3
1753	1700			Amide II stretch	
1628	1657			C=O stretching in amide I acetyl amino in heparin	1, 3
		1620	1621		4
		1539	1539	N-H stretch (amide II)	1, 2, 5
1392	1409			Asymmetric C-H stretch bending of $\text{CH}_2$ group	1
1369				Amide III	
1319	1313			C-O stretch, S=O	6
	1233	1233		N-sulphonate	7-9
1112				C-H symmetrical bending	10
1018	1066			Skeletal vibration C-O bridge (glucosamine)	1, 10
869		890		OH in-plane bending	10
				Coupling of C-O-S and ring C-O-C	11

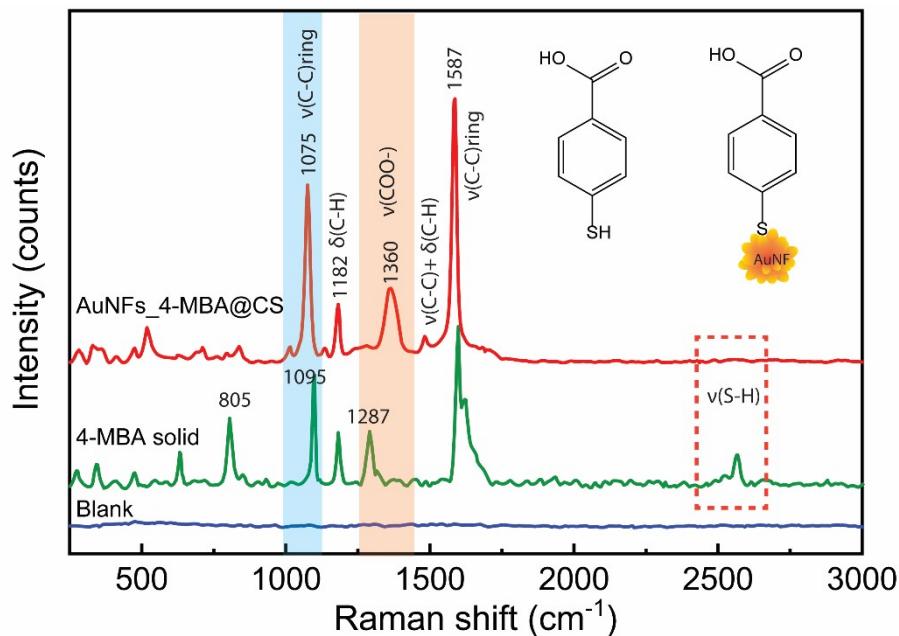


Fig S3. Compared SERS spectroscopy of (A) 4-MBA solid and (B) AuNFs-MBA@CS after adding chitosan.

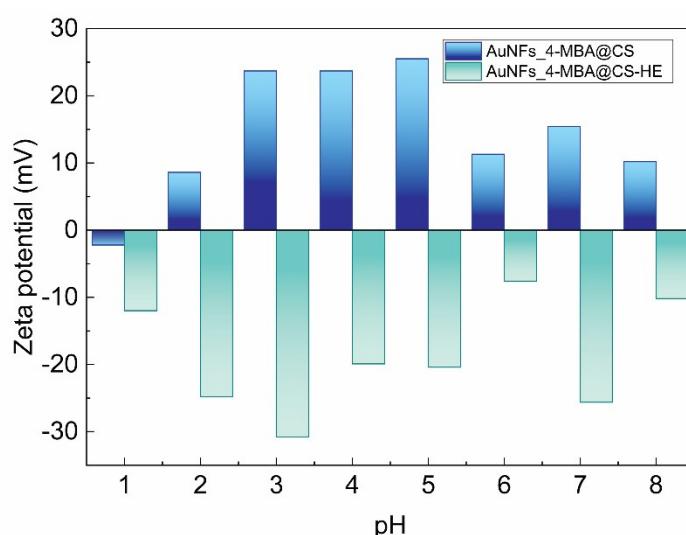


Fig S4. Zeta potential of AuNFs-chitosan (blue column), and AuNFs-4-MBA@chitosan-heparin (green-column).

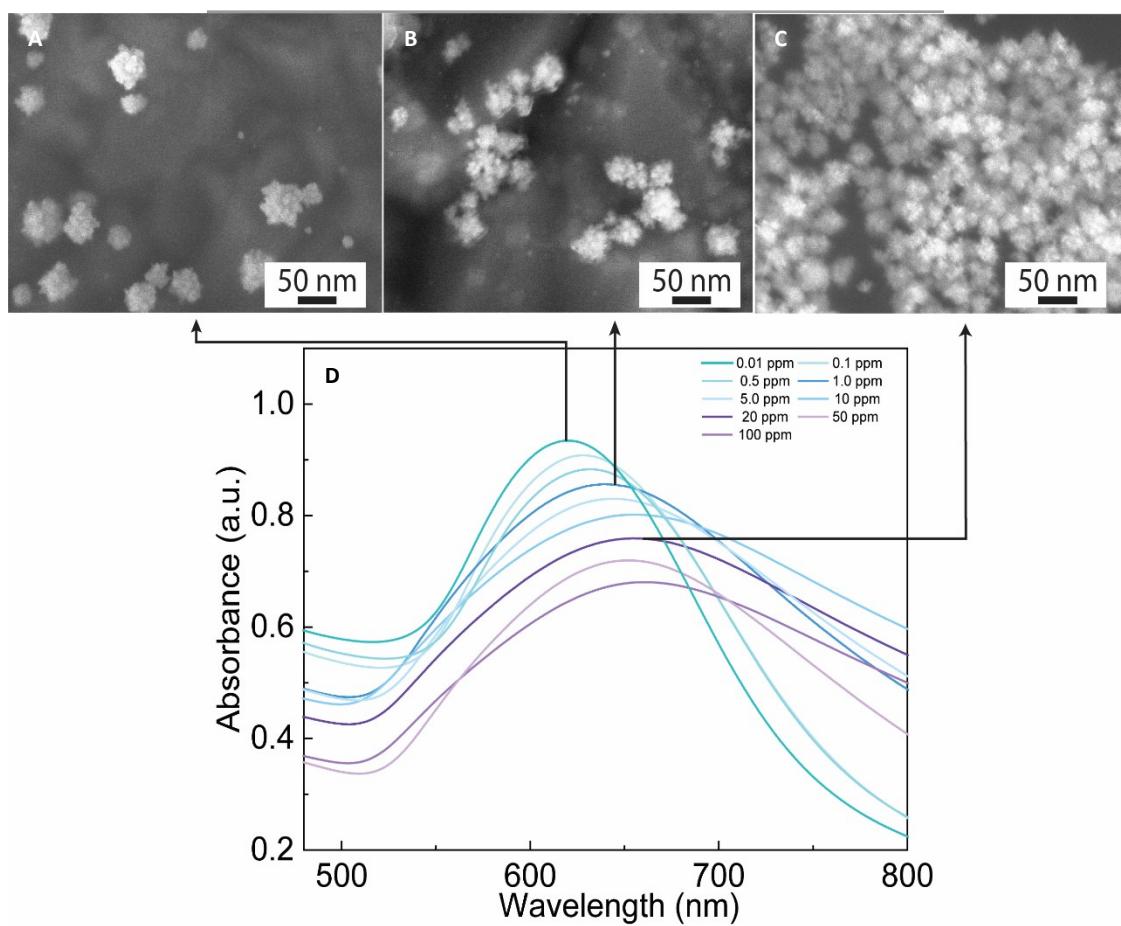


Fig S5. (A), (B), (C) SEM images of colloidal SERS tags after adding 0.01, 1.0, and 20 ppm concentration of heparin, and (D) UV-Vis spectrum of AuNFs-4-MBA@Chitosan colloids added with different heparin concentrations ranging from 0.01 to 100 ppm

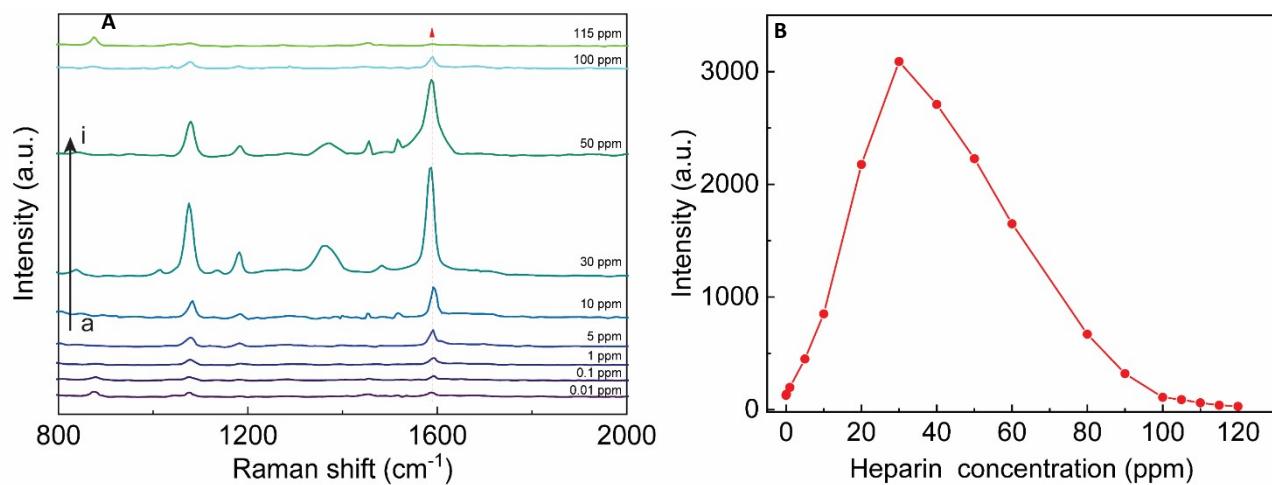


Fig S6. (A) SERS spectra of AuNFs-4-MBA@CS colloidal solution studied with different heparin concentrations (a-i: 0.01, 0.1, 1.0, 5.0, 10, 30, 50, 100, and 115 ppm); (B) Intensity change of Raman peak at  $1587 \text{ cm}^{-1}$  while changing the heparin concentration.

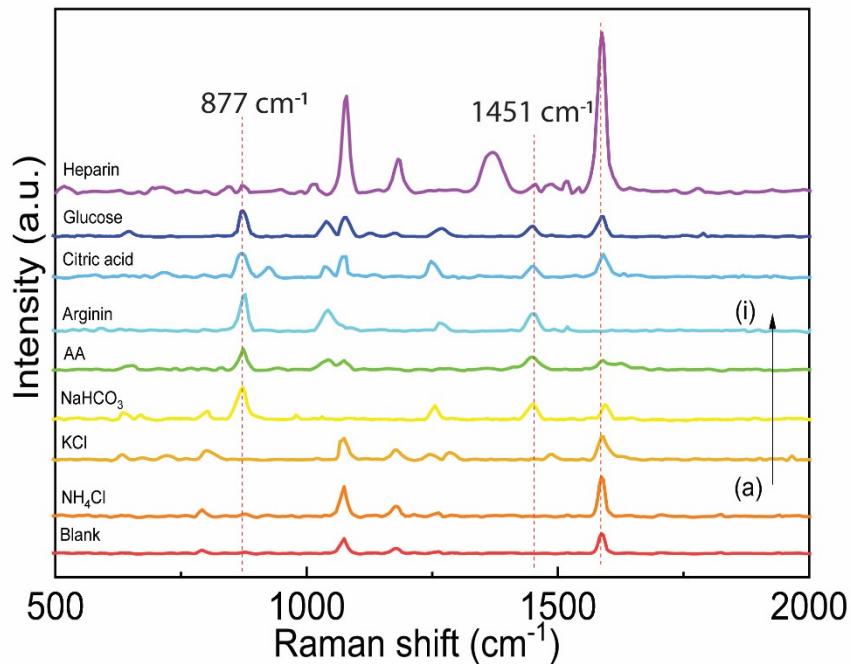


Figure S7. Compared SERS spectra of AuNFs-4-MBA@CS colloids after adding various substances (a-i: glucose, citric acid, arginine, ascorbic acid,  $\text{NaHCO}_3$ , KCl,  $\text{NH}_4\text{Cl}$ , and heparin) for studying the selectivity. The blank sample was investigated on the AuNFs-4-MBA@chitosan colloid without using any induced-aggregation substance.

## Reference

1. S. Kumar, J. Koh, H. Kim, M. K. Gupta and P. K. Dutta, *International journal of biological macromolecules*, 2012, **50**, 493-502.
2. S. Kumar and J. Koh, *Int J Mol Sci*, 2012, **13**, 6102-6116.
3. J. E. dos Santos, E. R. Dockal and É. T. Cavalheiro, *Carbohydrate polymers* 2005, **60**, 277-282.
4. R. Saravanan, S. Vairamani and A. Shanmugam, *Preparative biochemistry & biotechnology*, 2010, **40**, 305-315.
5. Q. K. Vo, D. D. Phung, Q. N. Vo Nguyen, H. Hoang Thi, N. H. Nguyen Thi, P. P. Nguyen Thi, L. G. Bach and L. Van Tan, 2019, **7**, 873.
6. A. Devlin, L. Mauri, M. Guerrini, E. Yates and M. Skidmore, *The use of ATR-FTIR spectroscopy to characterise crude heparin samples by composition and structural features*, 2019.
7. M. J. Harris and J. R. Turvey, *Carbohydrate Research*, 1970, **15**, 51-56.
8. D. Grant, C. Moffat, W. Long and F. Williamson, *Biochemical Society Transactions*, 1989, **17**, 498-500.
9. D. Grant, C. Moffat, W. Long and F. Williamson, *Biochemical Society Transactions*, 1989, **17**, 500-501.
10. s. Sashikala and S. Shafi, *Der Pharmacia Lettre*, 2014, **6**, 90-97.
11. F. Cabassi, B. Casu and A. S. Perlin, *Carbohydrate Research*, 1978, **63**, 1-11.

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