

Supplementary Information

Smart pH-Responsive Magnetic Iron Oxide Nanoflower–Chitosan Nanogels for Controlled Drug Delivery in Cancer Therapy

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S1. Additional information about TEM and DLS analysis of CS coated seed iron oxide nanoflowers

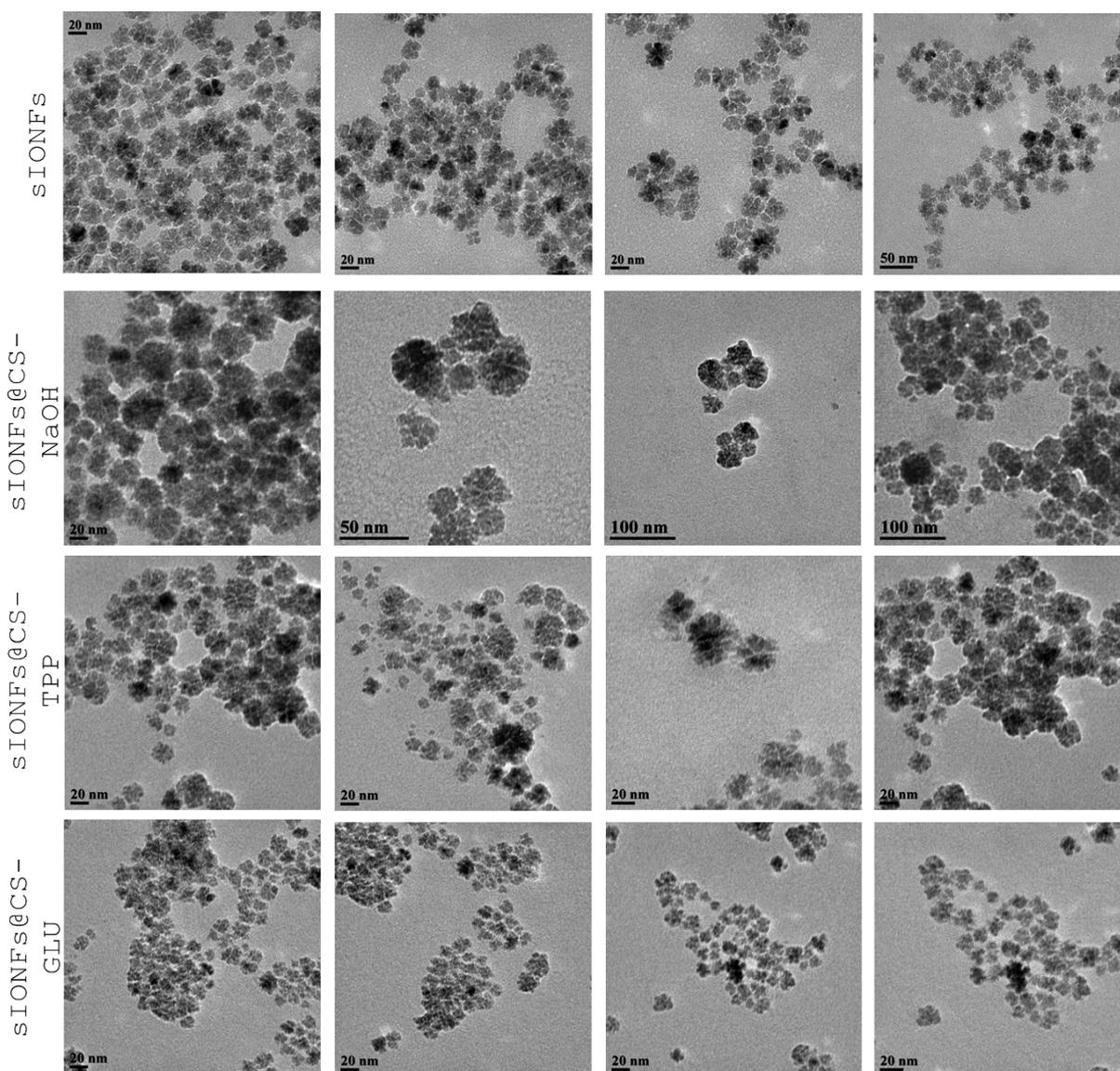


Figure S1. TEM images at different magnification for sIONFs, sIONFs@CS-NaOH, sIONFs@CS-TPP, and sIONFs@CS-GLU samples.

Figure S1 showed the four representative nanoflowers groups (sIONFs, sIONFs@CS-NaOH, sIONFs@CS-TPP, sIONFs@CS-GLU) which were selected for morphology analysis. TEM analysis showed that all the IONFs samples kept a flower-shape; sample size increased after sIONFs core modification and reached 28.2 ± 7.3 nm for sIONFs@CS-TPP and 37.8 ± 8.6 nm for sIONFs@CS-NaOH (Figure S2).

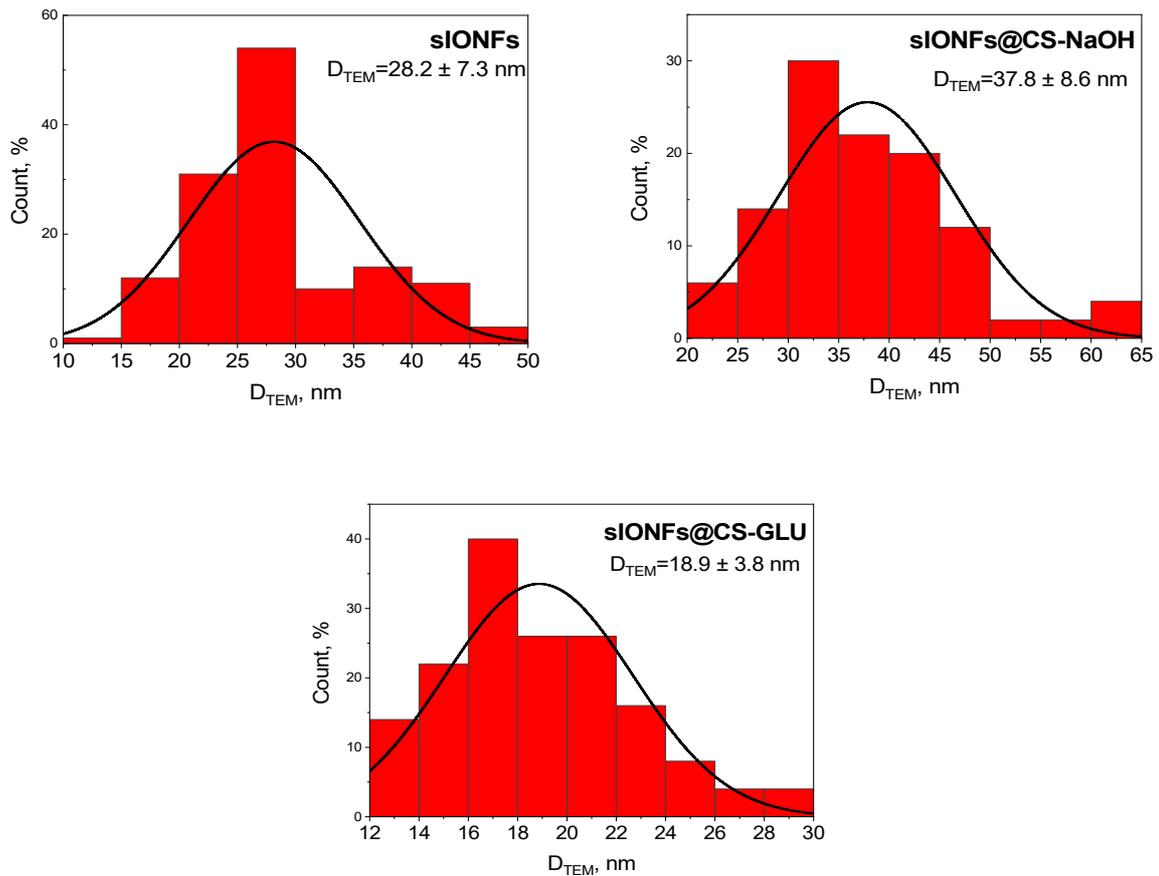


Figure S2. sIONFs, sIONFs@CS-NaOH, and sIONFs@CS-GLU samples of the particle size distribution curve obtained from TEM images for sIONFs, $n = 200$.

Table S1. Hydrodynamic diameters and ζ -potentials of sIONFs@CS-NaOH, sIONFs@CS-TPP, and sIONFs@CS-GLU nanoparticles.

Sample	Dh (nm) / PDI (pH 4)	Dh (nm) / PDI (pH 5.5)	Dh (nm) / PDI (pH 7.4)	ζ -potential (mV)
sIONFs@CS-NaOH	1452.0 \pm 44.0 / 0.403	110.0 \pm 12.0 / 0.380	678.0 \pm 18.0 / 0.585	-25.8 \pm 4.5
sIONFs@CS-TPP	81.0 \pm 0.9 / 0.166	114.4 \pm 1.5 / 0.333	181.6 \pm 22.2 / 0.402	-31.9 \pm 8.4
sIONFs@CS-GLU	136.6 \pm 4.3 / 0.216	165.7 \pm 9.0 / 0.208	977.9 \pm 10.0 / 0.221	-15.1 \pm 5.2

Table S2. Hydrodynamic and TEM diameters of sIONFs, sIONFs@CS-NaOH, sIONFs@CS-TPP, and sIONFs@CS-GLU samples.

Sample	D _h (nm)	D _{TEM} (nm)
sIONFs	115 \pm 2.4	28.1 \pm 3.5
sIONFs@CS-NaOH	110 \pm 12	37.8 \pm 8.6
sIONFs@CS-GLU	165 \pm 7.9	18.9 \pm 3.8
sIONFs@CS-TPP	105 \pm 9.2	28.2 \pm 7.3

For in-vitro study sIONFs@CS-TPP sample was synthesised using the IONF cores with the best magnetic properties and a bigger size (IONFs $D_{TEM} = 28.1 \pm 3.5$ nm).

The TEM images at 30 k and 40 k magnification as shown in Figure S3 confirmed that coated and DOX loaded nanoflower still have a flower structure. Particles size increased after DOX loading from 49.1 ± 8.2 nm to 57.6 ± 11.5 nm respectively.

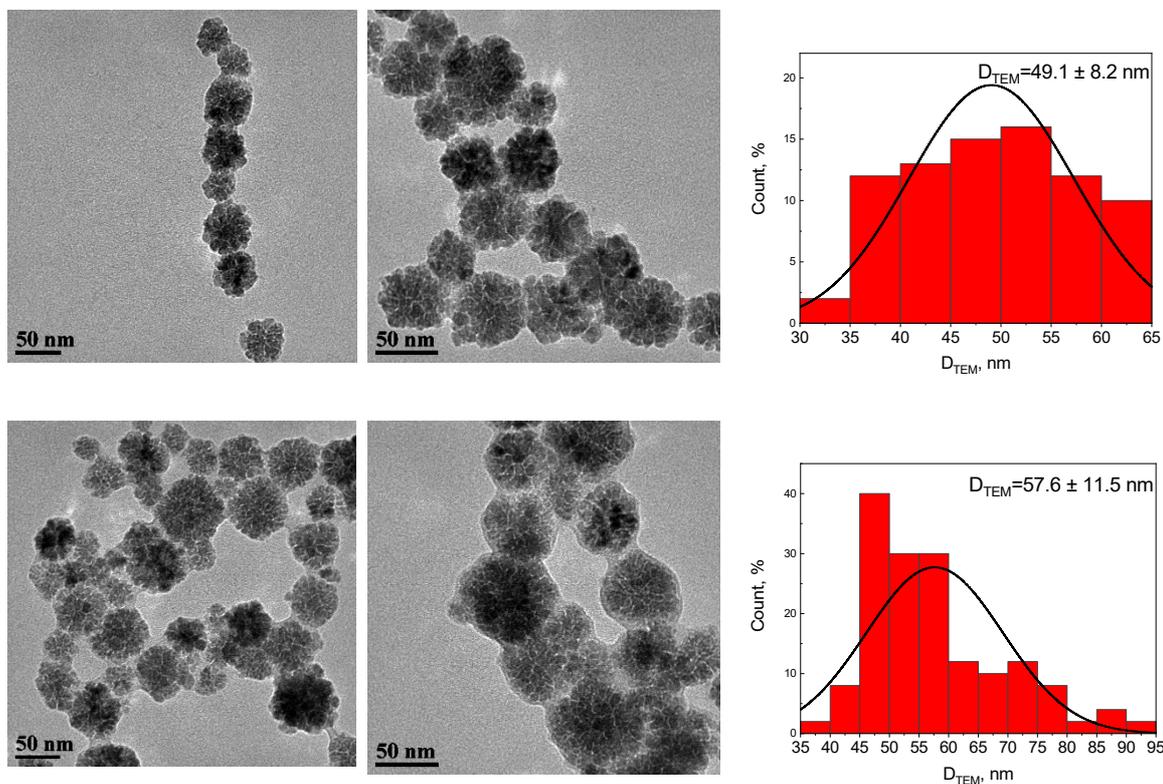


Figure S3. TEM images and particle size distribution curve obtained from TEM images for sIONFs@CS-TPP (top) and IONFs@CS-TPP-DOX (bottom) samples; n = 200.

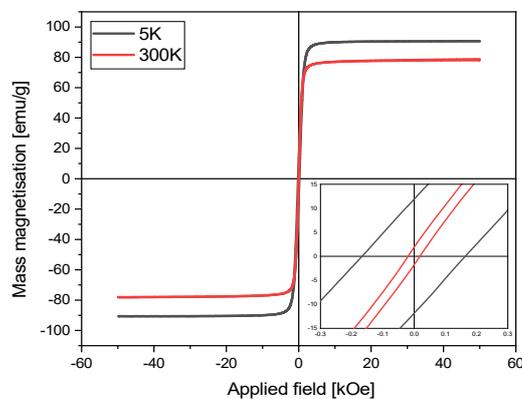
In order to compare the particle size of samples prior to and after DOX conjugation, we conducted a two-tailed unpaired Student's t-test using GraphPad Prism 9.3.1 statistical software. The resultant p-value = 0.0028, indicates that there is a significant difference between the two samples. The findings suggest that the modification process statistically significantly impacted the particle size of the samples, highlighting the effectiveness of the modification method.

Table S3. Hydrodynamic and TEM diameters of sIONFs@CS-TPP and sIONFs@CS-TPP-DOX samples.

Sample	D_h (nm)	D_{TEM} (nm)
sIONFs@CS-TPP	114.4 ± 1.5	49.1 ± 8.2
sIONFs@CS-TPP-DOX	181.0 ± 22.2	57.6 ± 11.5

S12. Magnetic properties of IONFs.

a)



b)

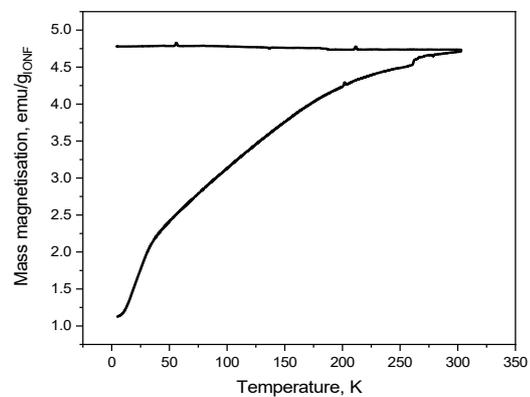


Figure S4. a) Hysteresis curves of IONFs at 5 K and 300 K. The insets show the magnified hysteresis loop at low field strengths. b) ZFC-FC magnetisation versus temperature curves in 100 Oe of IONFs.

Magnetic hysteresis curves recorded at 5 K and 300 K (Figure S3) show that IONFs were nearly superparamagnetic with coercivities of 160 Oe and 27 Oe and saturation magnetisation of 90.3 emu/g_{IONPs} and 72.5 emu/g_{IONPs} respectively.