Electronic Supplementary Information

Enhanced theranostic efficacy of epirubicin-loaded SPION@MSN through co-delivery of an anti-miR-21-expressing plasmid and ZIF-8 hybridization to target colon adenocarcinoma

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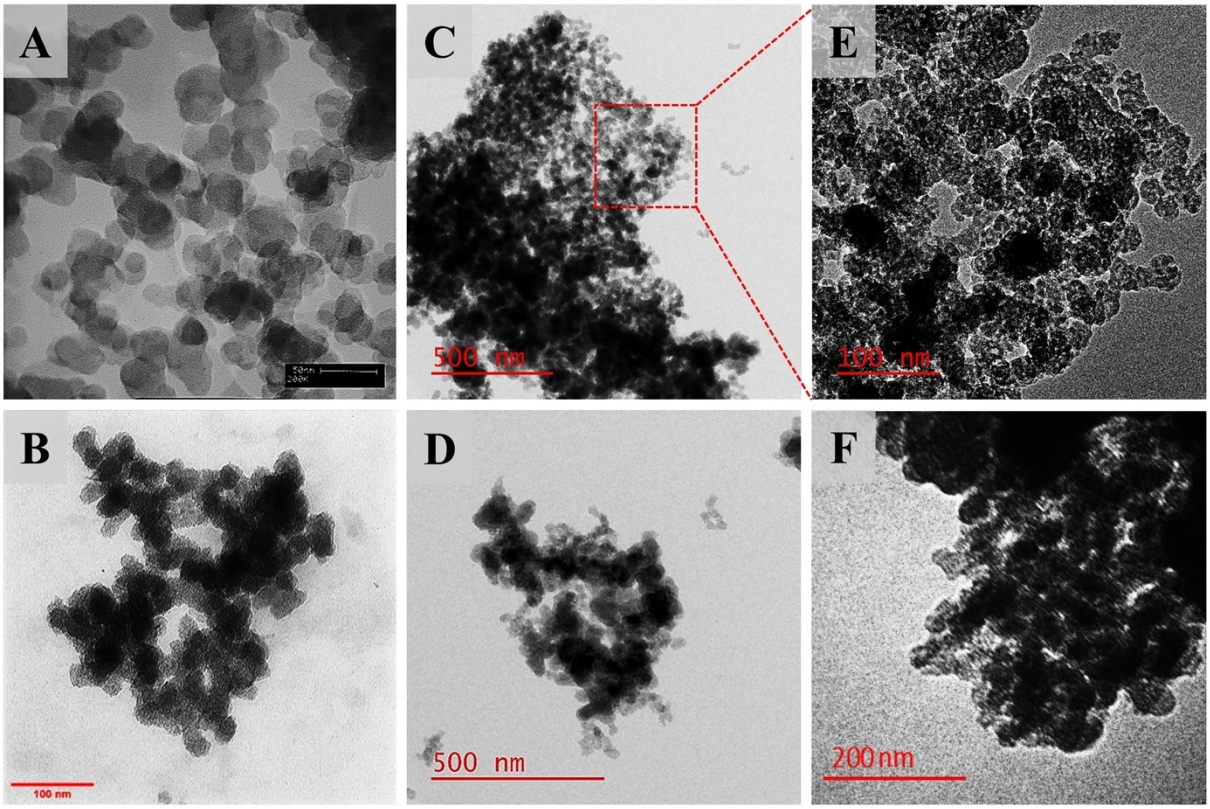

Fig. S1. Evaluation of structural and morphological characteristics of prepared nanoparticles. TEM micrograph of prepared SPION **(A)**, SPION@MSN **(B)**, and SPION@MSN-EPI/pDNA-ZIF-8 **(C-F)**. Abbreviations: *SPION*, superparamagnetic iron oxide nanoparticle; *MSN*, mesoporous silica nanoparticle; *EPI*, epirubicin; *pDNA*, pmiRZip-21 plasmid; *ZIF-8*, zeolitic imidazolate framework-8; *PEG*, polyethylene glycol; *TEM*, transmission electron microscopy.

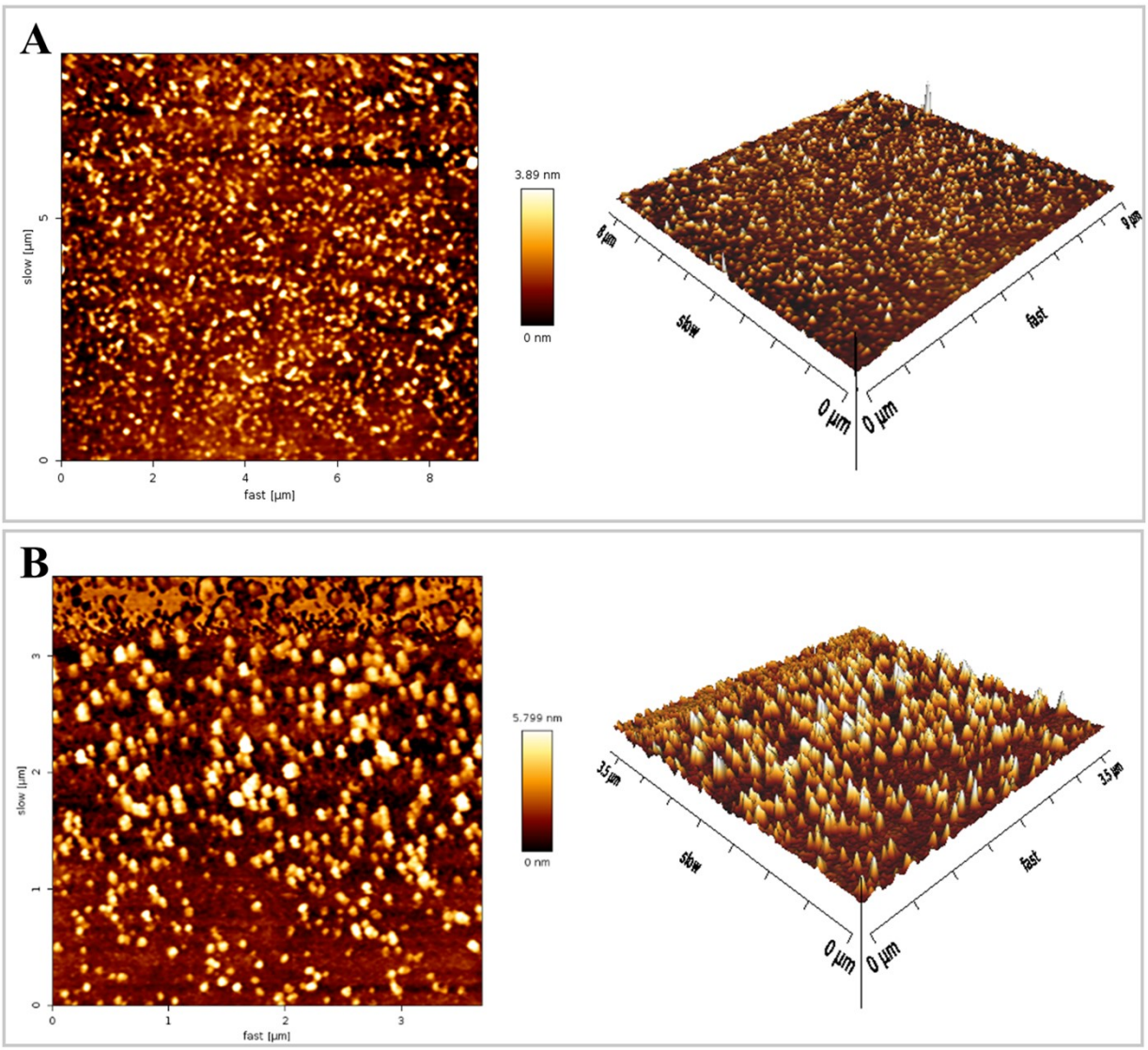

Fig. S2. Morphology and dispersity of SPION@MSN **(A)**, SPION@MSN-EPI/pDNA-ZIF-8 **(B)** are illustrated using AFM. Abbreviations: *SPION*, superparamagnetic iron oxide nanoparticle; *MSN*, mesoporous silica nanoparticle; *EPI*, epirubicin; *pDNA*, pmiRZip-21 plasmid; *ZIF-8*, zeolitic imidazolate framework-8; *PEG*, polyethylene glycol; *AFM*, atomic force microscopy.

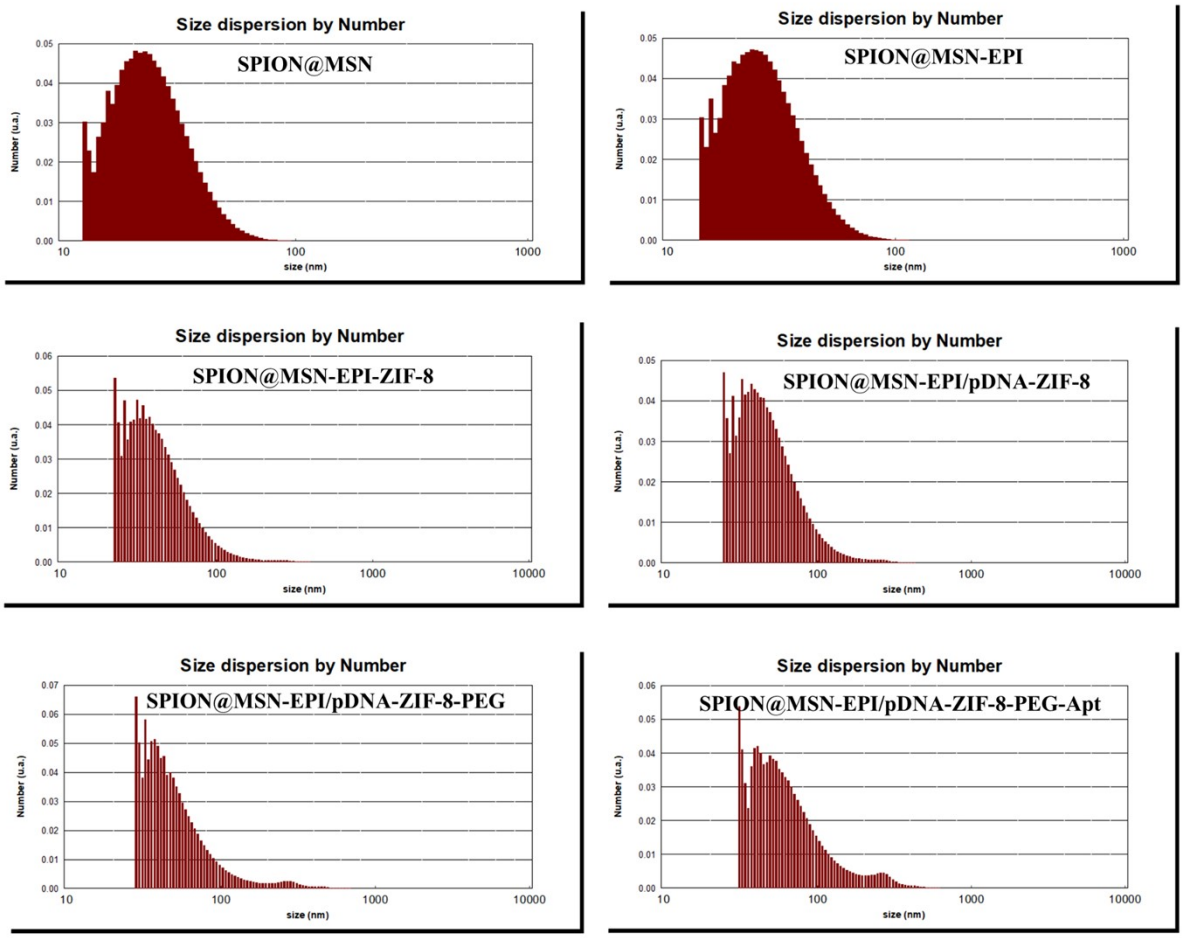

Fig. S3. Illustration of nanoparticle size distribution by number using DLS histograms. Abbreviations: *SPION*, superparamagnetic iron oxide nanoparticle; *MSN*, mesoporous silica nanoparticle; *EPI*, epirubicin; *pDNA*, pmiRZip-21 plasmid; *ZIF-8*, zeolitic imidazolate framework-8; *PEG*, polyethylene glycol; *Apt*, aptamer; *DLS*, dynamic light scattering.

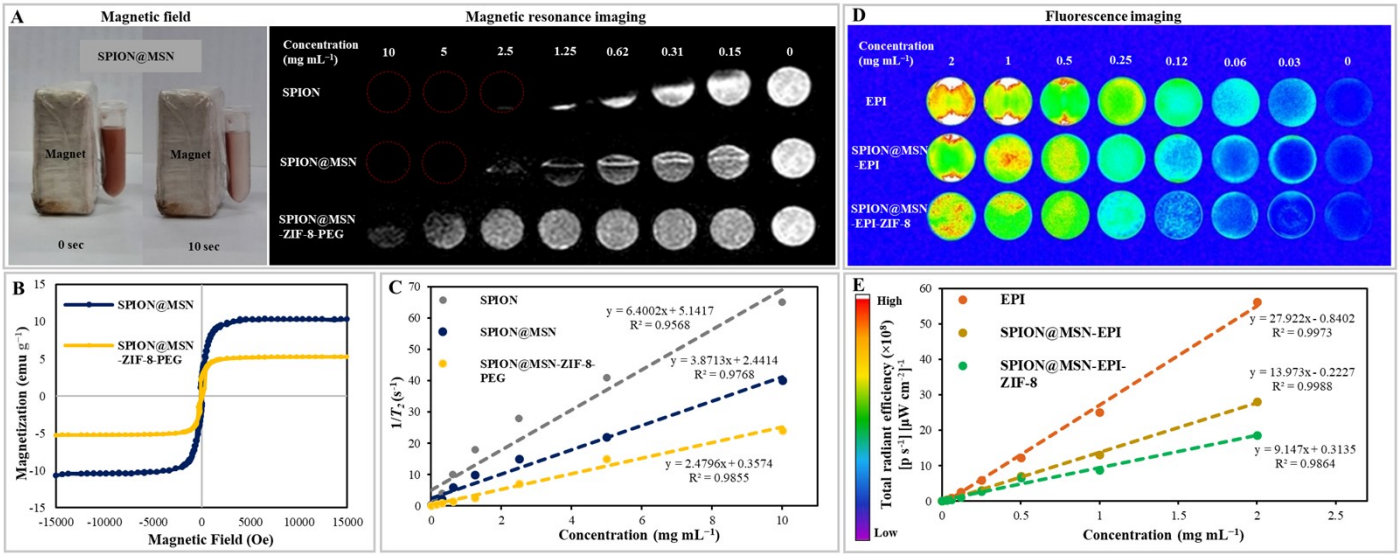

Fig. S4. Characterization of prepared nanoparticles by different methods. The behavior of prepared NPs against magnetic field and MR imaging (A). Assessing the magnetic properties of SPION@MSN and SPION@MSN-EPI/pDNA-ZIF-8-PEG using VSM technique (B). The linear relationship between T_2 relaxation rate ($1/T_2$) versus nanoparticles concentration (C). Fluorescence emission of different concentrations of EPI and nanoparticles under fluorescence imaging (D) and their associated total radiant efficiency (E). Abbreviations: *SPION*, superparamagnetic iron oxide nanoparticle; *MSN*, mesoporous silica nanoparticle; *EPI*, epirubicin; *ZIF-8*, zeolitic imidazolate framework-8; *PEG*, polyethylene glycol; *VSM*, vibrating-sample magnetometer.

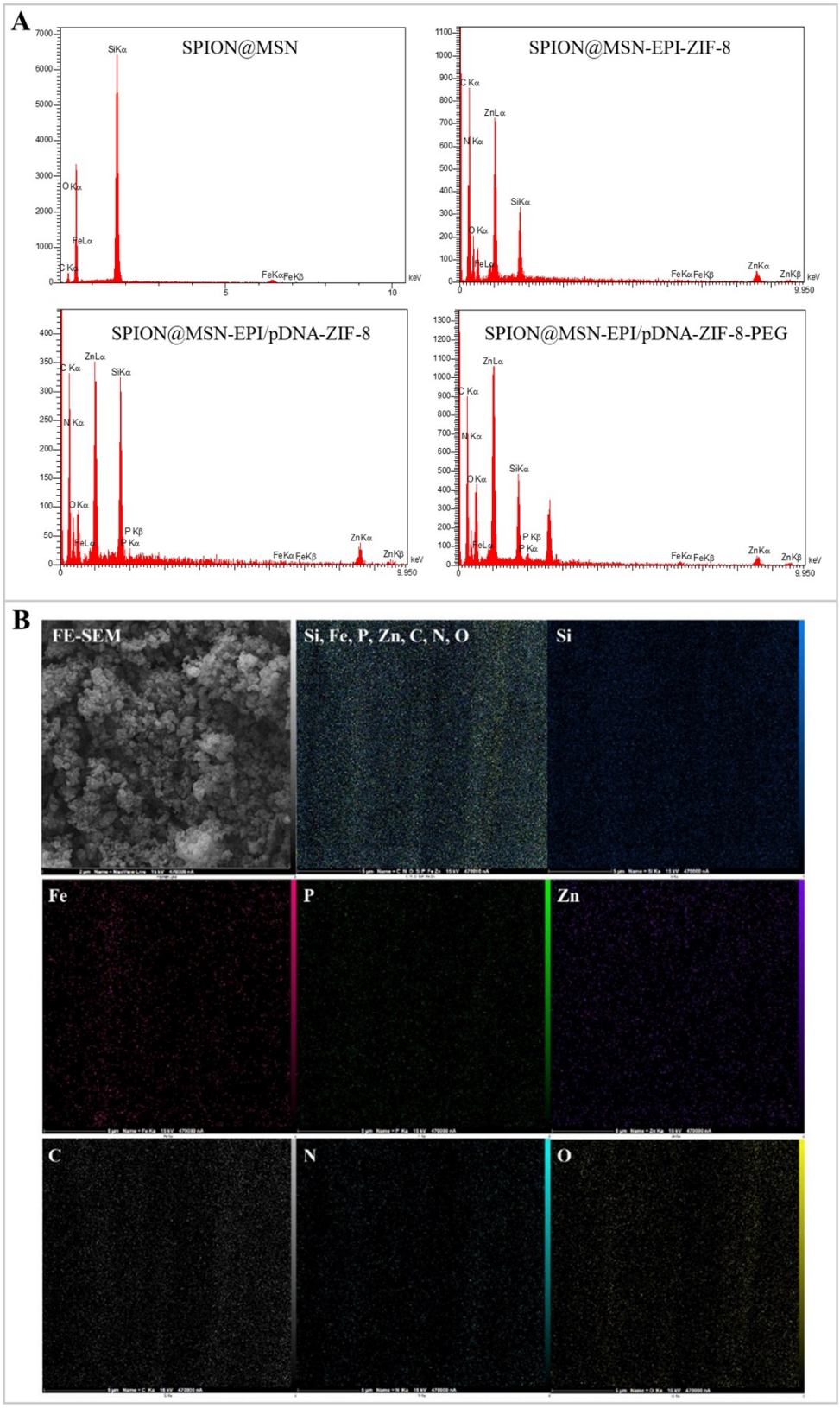

Fig. S5. Compositional characterization of prepared nanoparticles. Energy-dispersive X-ray (EDX) spectroscopy analysis of different formulations **(A)**. EDX mapping of SPION@MSN-EPI/pDNA-ZIF-8 illustrated an equivalent distribution of the main elements **(B)**. Abbreviations: *SPION,* superparamagnetic iron oxide nanoparticle; *MSN,* mesoporous silica nanoparticle; *EPI,* epirubicin; *pDNA,* pmiRZip-21 plasmid; *ZIF-8,* zeolitic imidazolate framework-8; *PEG,* polyethylene glycol.

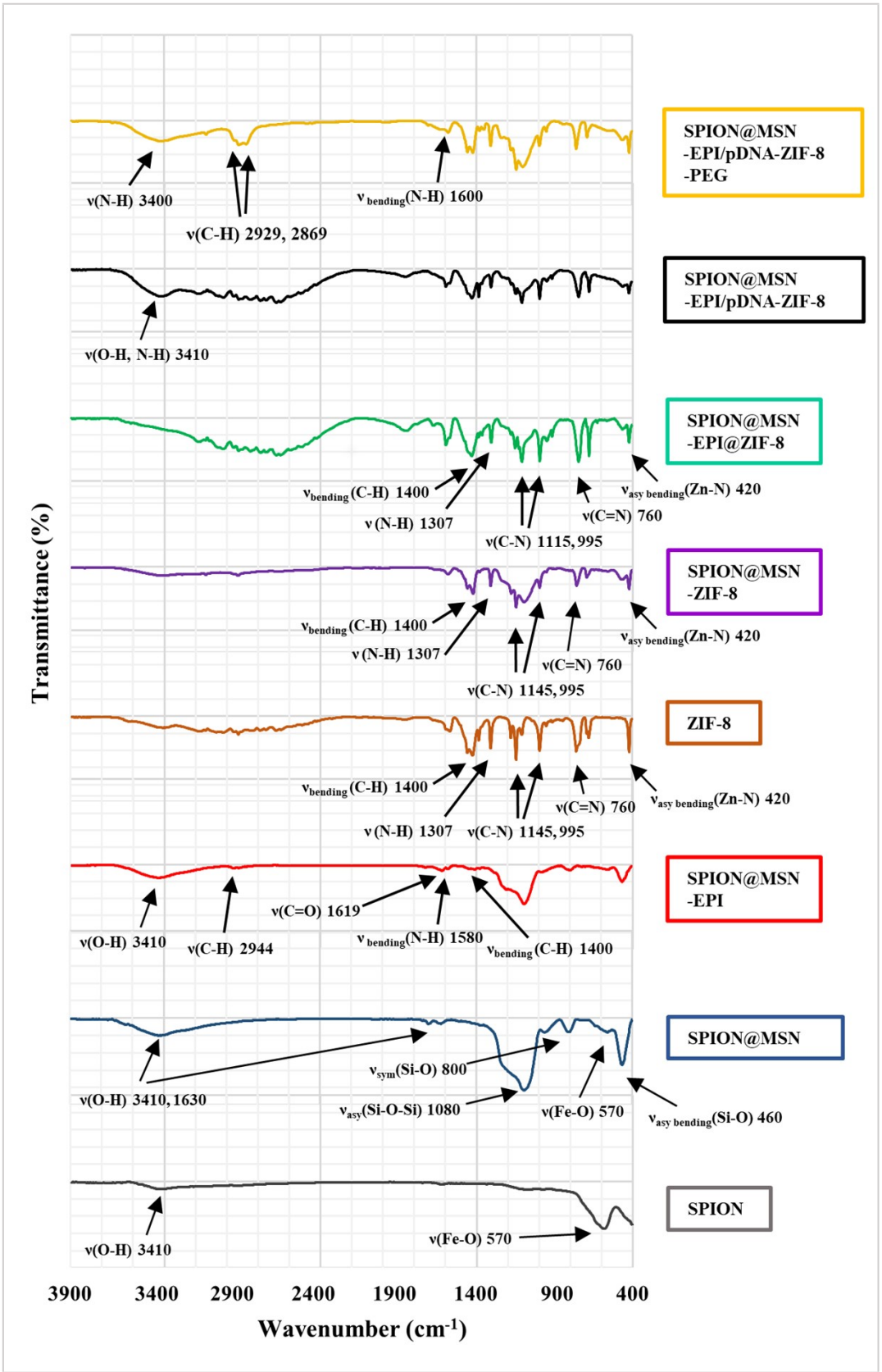

Fig. S6. Fourier transform infrared spectroscopy (FT-IR) spectra analysis in each step of nanoparticles' synthesis. Abbreviations: *SPION,* superparamagnetic iron oxide nanoparticle; *MSN,* mesoporous silica nanoparticle; *EPI,* epirubicin; *pDNA,* pmiRZip-21 plasmid; *ZIF-8,* zeolitic imidazolate framework-8; *PEG,* polyethylene glycol; *Apt*, aptamer.

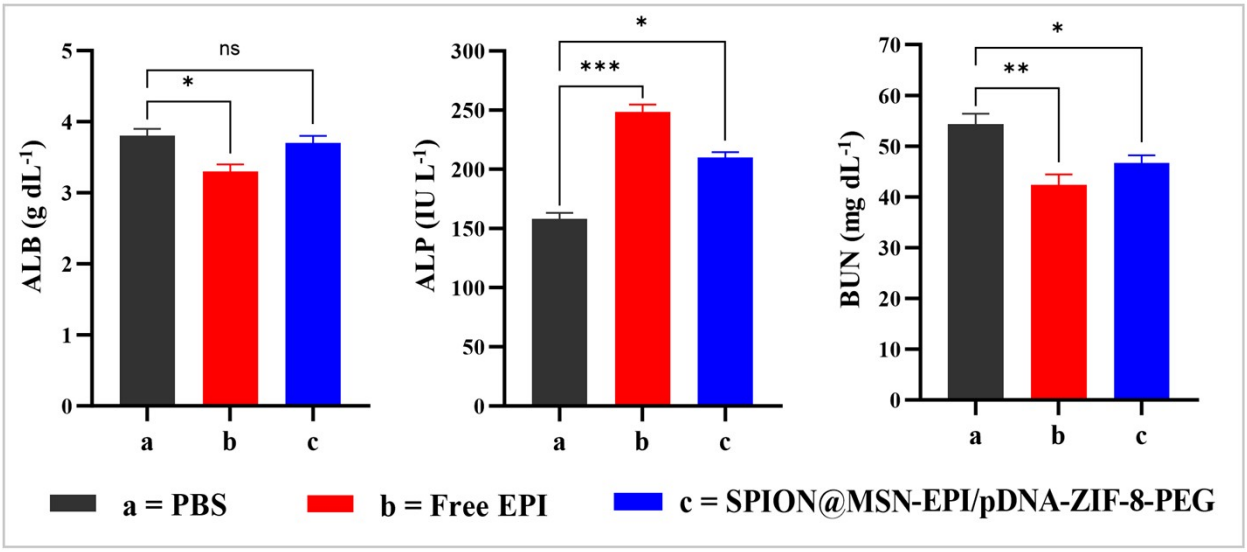

Fig. S7. Biosafety evaluation of the nanoparticles *via* biochemical assays to check the function of the liver and kidney. The levels of albumin (ALB), alkaline phosphatase (ALP), and blood urea nitrogen (BUN) were assessed three days after the administration of PBS, Free EPI, and SPION@MSN-EPI/pDNA-ZIF-8-PEG in healthy BALB/c mice. Data are expressed as mean ± SD, n = 3. ns, non-significant; * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$. Abbreviations: *SPION,* superparamagnetic iron oxide nanoparticle; *MSN,* mesoporous silica nanoparticle; *EPI,* epirubicin; *pDNA,* pmiRZip-21 plasmid; *ZIF-8,* zeolitic imidazolate framework-8; *PEG,* polyethylene glycol; *g* dL^{-1}, gram per deciliter; *IU* L^{-1}, international unit per liter; *mg* dL^{-1}, milligrams per deciliter.