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Supporting Information

Non-peptidic guanidinium-functionalized silica nanoparticles as selective mitochondria-targeting drug nanocarriers

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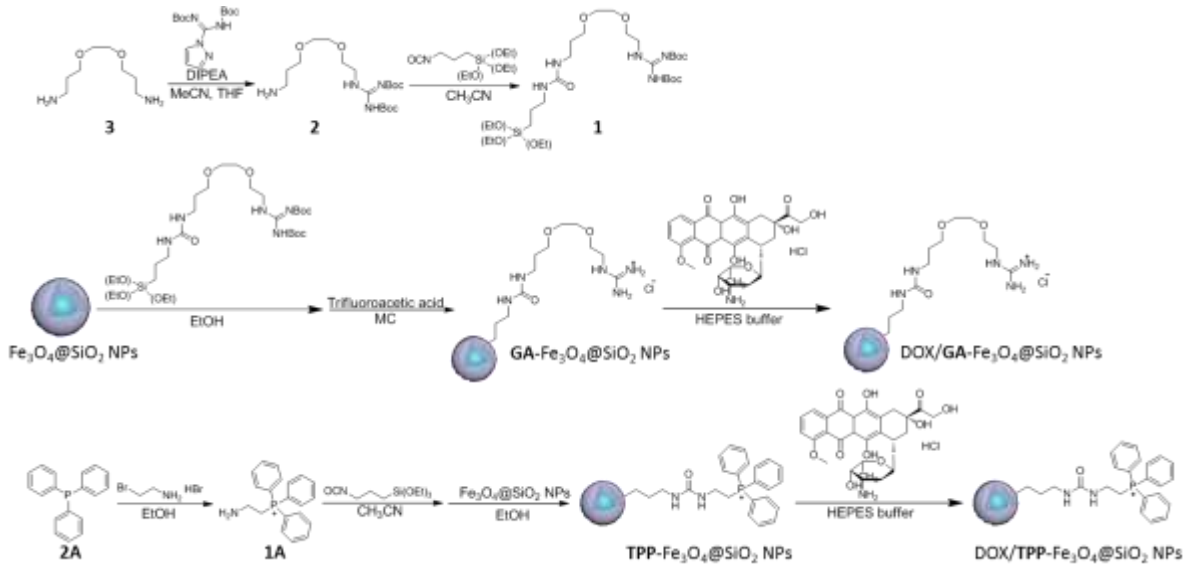


Scheme S1. Synthetic routes of DOX/GA-Fe_3O_4@MSNs and DOX/TPP-Fe_3O_4@MSNs.

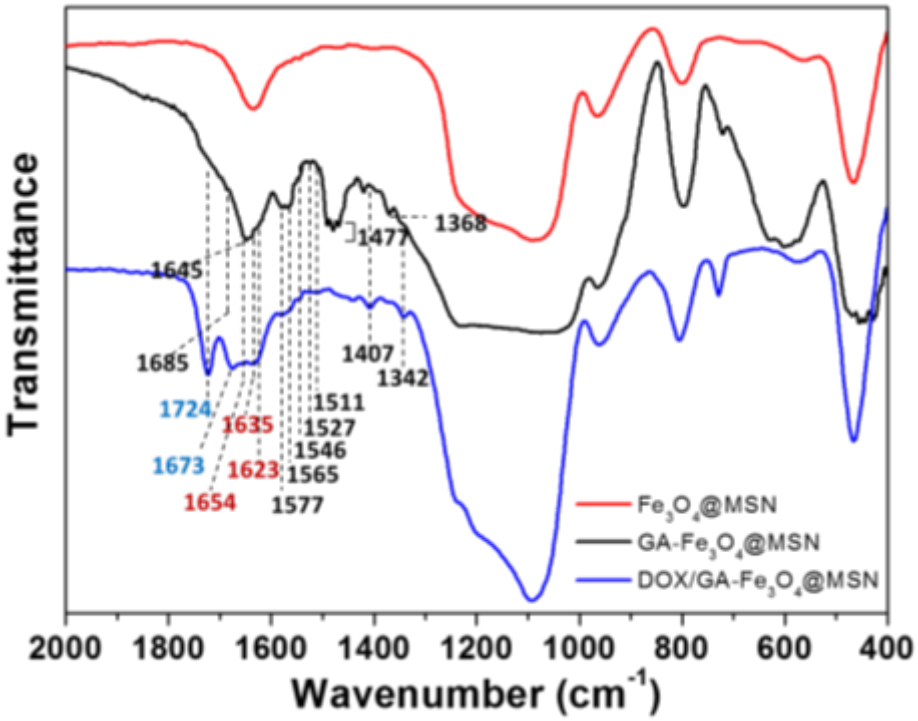
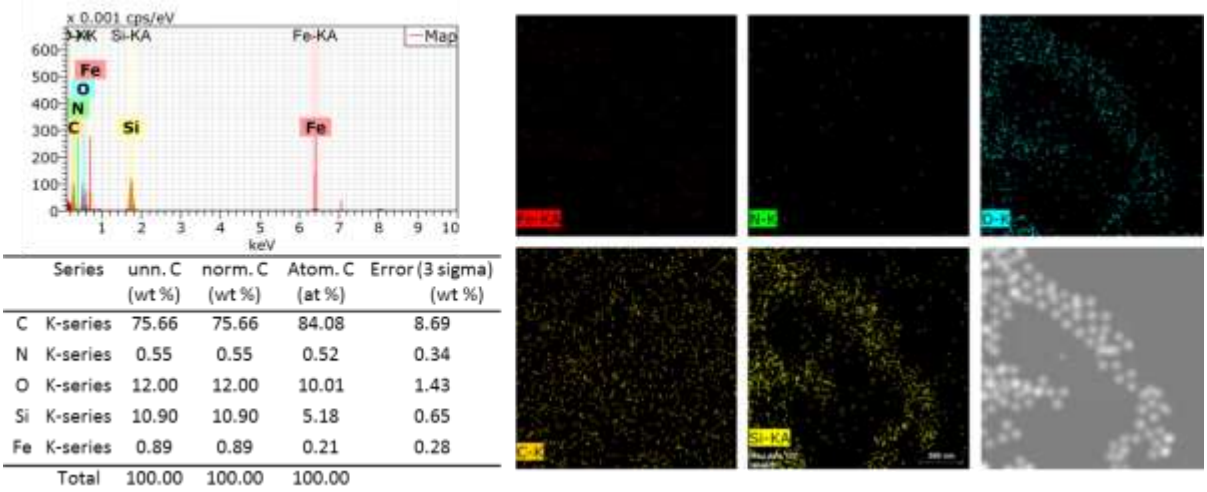


Figure S1. IR spectra of Fe_3O_4@MSNs, GA-Fe_3O_4@MSNs, and DOX/GA-Fe_3O_4@MSNs.



	Series	unn. C (wt %)	norm. C (wt %)	Atom. C (at %)	Error (3 sigma) (wt %)
C	K-series	75.66	75.66	84.08	8.69
N	K-series	0.55	0.55	0.52	0.34
O	K-series	12.00	12.00	10.01	1.43
Si	K-series	10.90	10.90	5.18	0.65
Fe	K-series	0.89	0.89	0.21	0.28
	Total	100.00	100.00	100.00	

Figure S2. TEM-EDS of GA-Fe_3O_4@MSNs. (Cu-supported carbon/formvar grid was used for GA-Fe_3O_4@MSNs sampling)

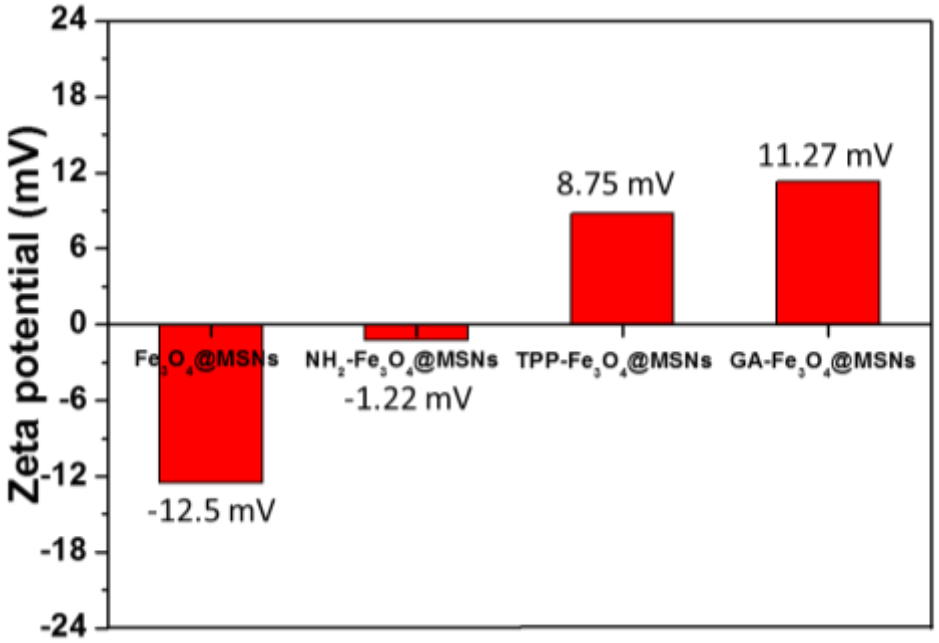


Figure S3. Zeta potentials of Fe_3O_4@MSNs, NH_2-Fe_3O_4@MSNs, TPP-Fe_3O_4@MSNs and GA-Fe_3O_4@MSNs at 25 ℃ in HEPES buffer (0.01 M, pH 7.4).

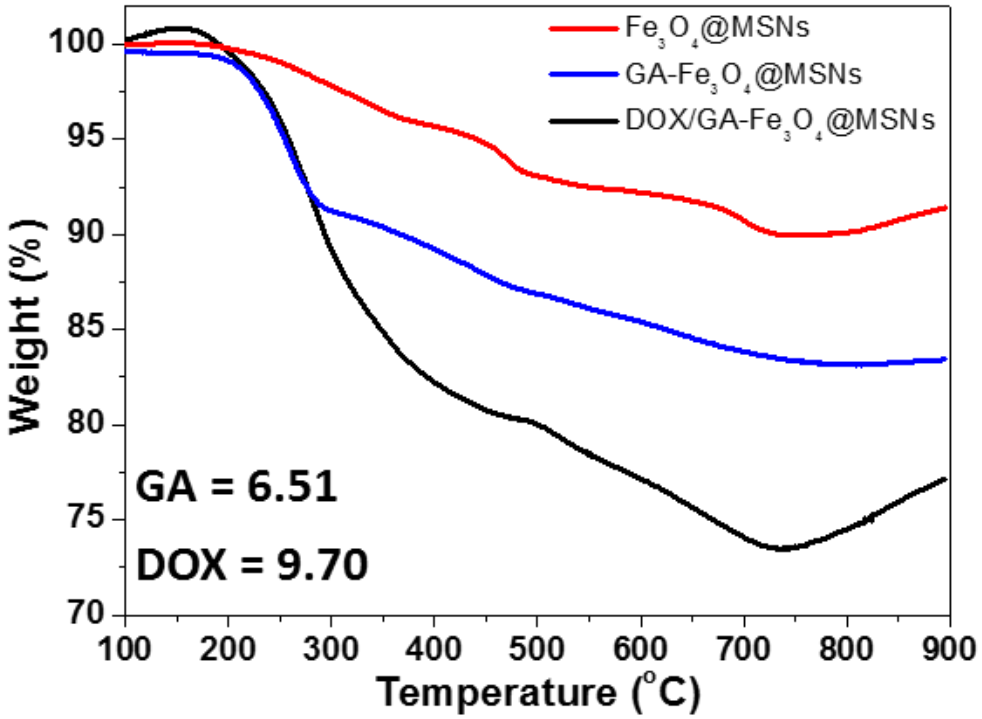


Figure S4. Theromogravimetric analyses of Fe_3O_4@MSNs, GA-Fe_3O_4@MSNs and DOX/GA-Fe_3O_4@MSNs (N_2 flow: 20 mg/min, heating rate: 5°C/min).

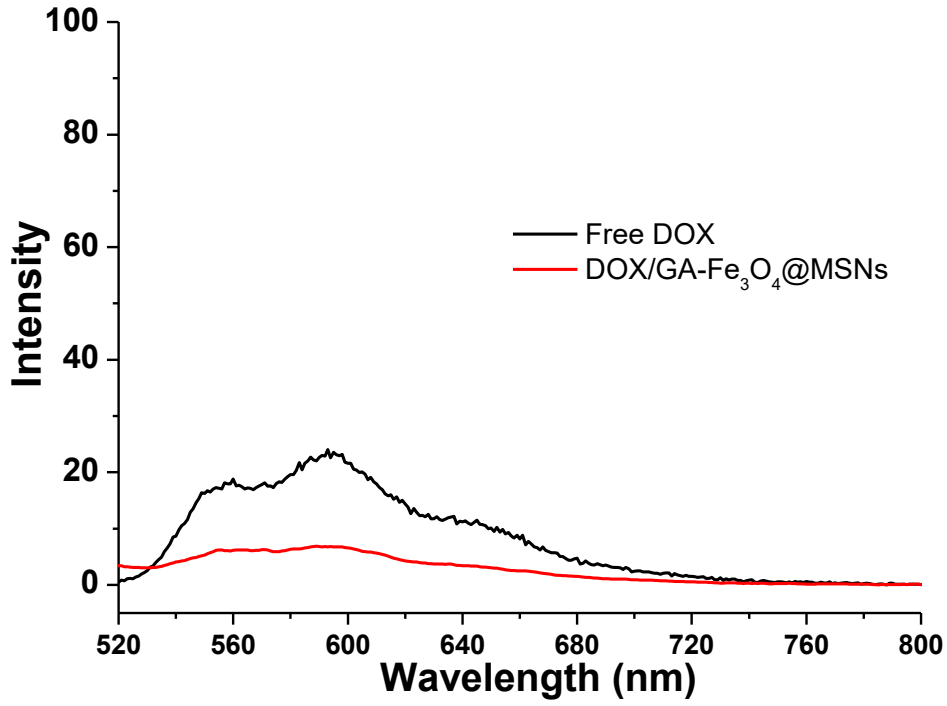


Figure S5. Fluorescence spectra of DOX (2.7 μM) and DOX/GA-Fe_3O_4@MSNs (0.33 mg/ml). (Excitation wavelength: 490 nm)

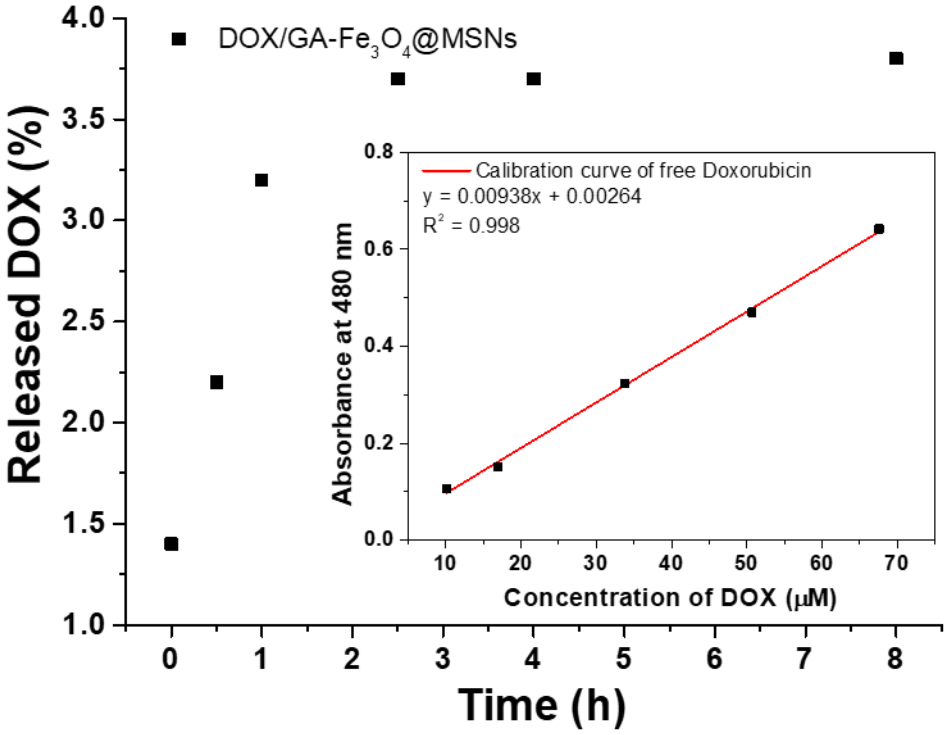


Figure S6. Time dependent release monitoring of DOX leaked out from DOX/GA-Fe_3O_4@MSNs in HEPES buffer (0.01 M, pH 7.4) at 37 ℃, inset: calibration curve of free DOX.

Table S1. Accumulation times for mitochondria-targeting probes from previously reported results.

Types of Carrier	Targeting-Probe	Name of carriers	Accumulation time	Reference
Polymer-based carrier	N-(2-hydroxypropyl) methacrylamide-guanidine copolymer	P-GPMA-KLA	4 hours	*ACS Appl. Mater. Interfaces* 2017, **9**, 27563−27574.
	Poly(lactic-co-glycolic acid)-TPP	GGA loaded PLGA NPs	1 hour	*Biomater. Sci*. 2017, **5**, 1800-1809.
	Methoxy polyethylene glycol (mPEG)−TPP conjugate	mPEG−(ss-$TPP)_2$/DOX NPs	4 hours	*Biomacromolecules*, 2017, **18**, 1074−1085.
	TPP-amphiphilic polymer (C_{18}-PEG_{2000}-TPP)	PTX-PLGA/CPT/DSSP	24 hours	*Nanoscale*, 2017, **9**, 17044-17053
	Thioketal linker-camptothecin-PEG_{1K}-TPP block copolymer	ZnPc/CPT-TPP NPs	6 hours	*Theranostics*, 2016, **6**, 2352-2366
Hydroxyapatite-based carrier	Without targeting probe	HAPNs	24 hours	*ACS Appl. Mater. Interfaces*, 2016, **8**, 25680−25690.
Ceria-based carrier	Atto 647N	Pt-Ceria-8-atto NPs	10 minutes	*Nanoscale*, 2016, **8**, 13352–13367.
Graphene-based carrier	Integrin αvβ3 monoclonal antibody	PPa-NGOmAb	4 hours	*Nanoscale*, 2016, **8**, 3530–3538.
Silica-based carrier	Without targeting probe	R-P@MSN–DTX	4 hours	*Nanoscale*, 2017, **9**, 314-325.
	Without targeting probe	ACML	1 hour	*Acta Biomaterialia*, 2016, **39**, 94–105.
	DNA-binding Ru^{2+}-complex	UCSRF	12 hours	*Biomaterials*, 2017, **141**, 86-95.
	Mitochondrial locating signals (MLS)-peptides	2-ME/mtMSN	12 hours	*Nano Research*, 2014, **7**, 1103-1115.
	TPP	MSNPs-PPh_3-FITC	12 hours	*ACS Appl. Mater. Interfaces*, 2016, **8**, 34261–34269.
	TPP	MMCN	4 hours	*Small*, 2016, **12**, 4541-4552.
	TPP	J-MSN	2 hours	*ACS Appl. Mater. Interfaces*, 2017, **9**, 26697-26706.
	TPP	MSNP-PPh_3-DOX	4 hours	*Nanoscale*, 2015, **7**, 16677-16686.
	A guanidinium derivative	DOX/GA-Fe_3O_4@MSN	5 minutes	This work

TPP: triphenylphosphonium, PEG: polyethylene glycol

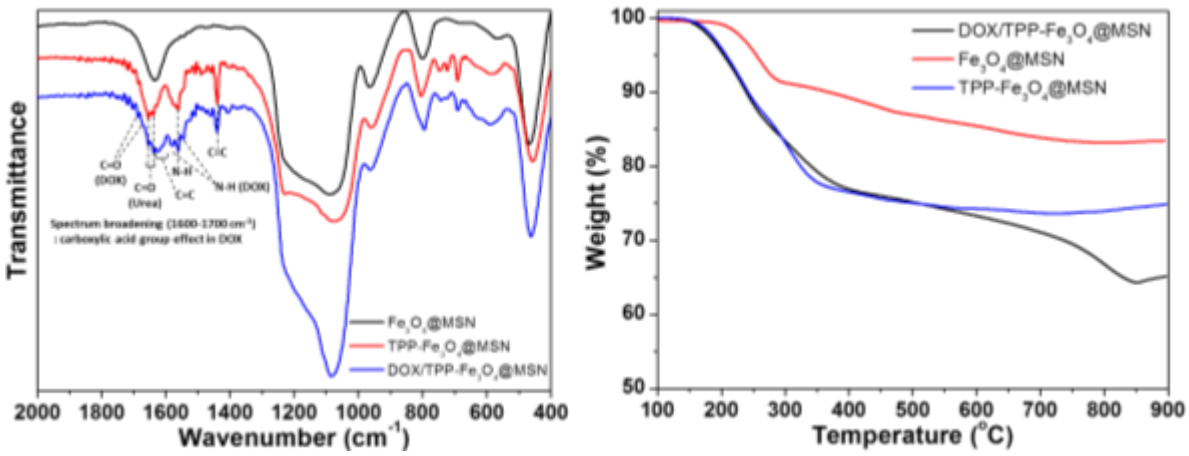


Figure S7. IR spectra and theromogravimetric analyses of Fe_3O_4@MSNs, TPP-Fe_3O_4@MSNs and DOX/TPP-Fe_3O_4@MSNs.

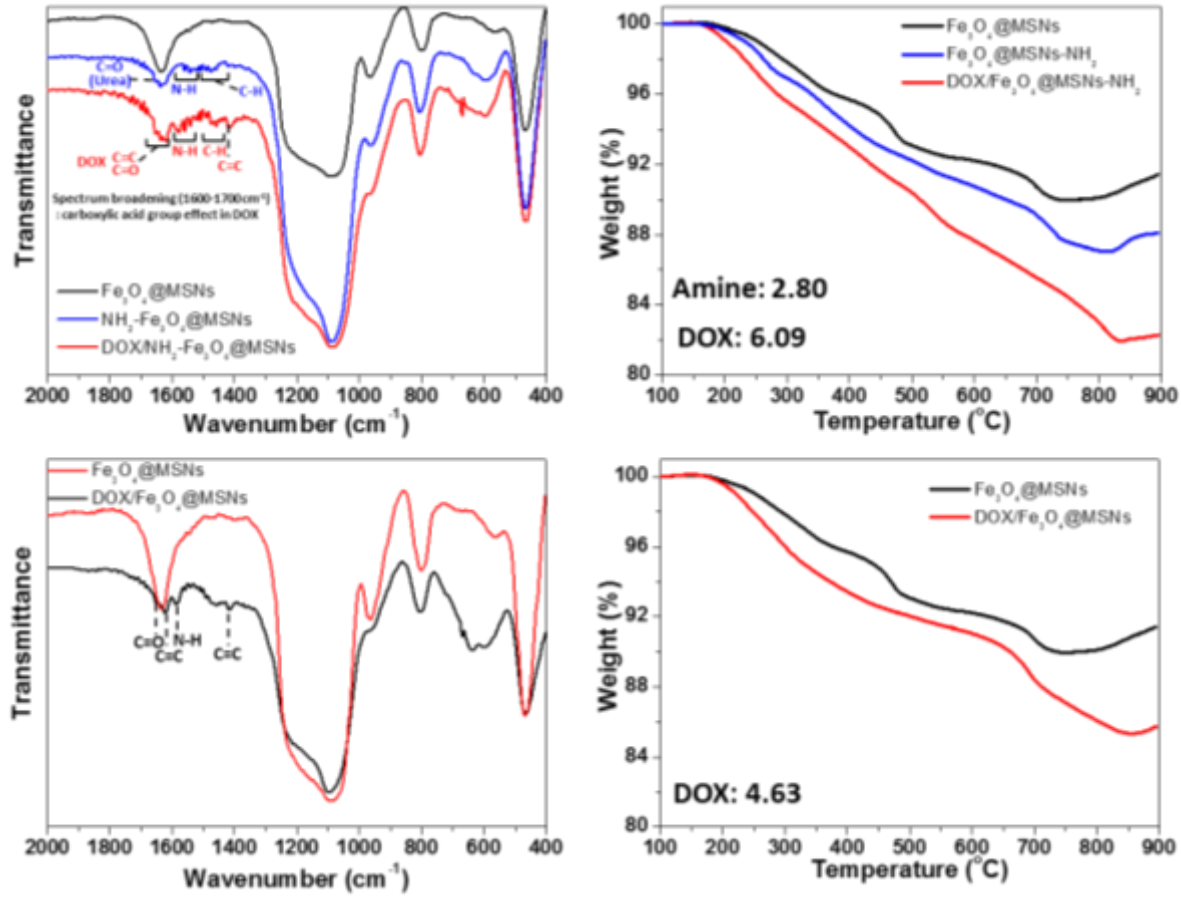


Figure S8. IR spectra and theromogravimetric analyses of DOX/NH_2-Fe_3O_4@MSNs and DOX/Fe_3O_4@MSNs.

Quantitative analysis of organic molecules in Fe_3O_4@MSNs by TGA

- Quantitative analysis of targeting ligand by TGA

$$\left[\frac{[(\text{Weight loss of GA-}Fe_3O_4\text{@MSN}) - (\text{Weight loss of }Fe_3O_4\text{@MSN})]}{100}\right] \div \text{Molecular weight of GA}$$

- Quantitative analysis of doxorubicin by TGA

$$\left[\frac{[(\text{Weight loss of DOX/GA-}Fe_3O_4\text{@MSN}) - (\text{Weight loss of GA-}Fe_3O_4\text{@MSN})]}{100}\right] \div \text{Molecular weight of DOX}$$