## Electronic Supplementary Information (ESI)

## Chitosan-folate coated mesoporous silica nanoparticles as a smart and pH-

## sensitive system for curcumin delivery +

Mohammad Porgham Daryasari<sup>a</sup>, Mohammad Reza Akhgar<sup>a</sup>, Fatemeh Mamashli<sup>b</sup>, Bahareh Bigdeli<sup>b</sup>,

Mehdi Khoobi<sup>c,d,\*</sup>

This work is dedicated in memory of Prof. Abbas Shafiee (1937-2016)

<sup>a</sup>Department of Chemistry, Kerman Branch, Islamic Azad University, Kerman, Iran <sup>b</sup>Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran <sup>c</sup>Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran <sup>d</sup>Department of Pharmaceutical Biomaterials and Medical Biomaterials Research Center, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

\*Corresponding authors: E-mail: m-khoobi@tums.ac.ir (Mehdi.khoobi@gamil.com); Tel: +98-21-66406757; Fax:

+98-21-66461178.



Fig. S1 Representative photograph of MSNs: MSN (a), MSN-NH<sub>2</sub> (b), MSN-COOH (c), MSN-COOH-removed (d) and

MSN-COOH-CUR (e).



Fig S2 FT-IR spectra of LMSN (a), LMSN-removed (b) LMSN-NH<sub>2</sub> (c), LMSN-COOH (d), CUR loaded LMSN-COOH (e)

and CUR (f).



Fig. S3 <sup>1</sup>H NMR spectra of CS (a) and FA conjugated to CS (CS-FA) (b).



Fig. S4 Size distribution of LMSN (a), LMSN-NH<sub>2</sub> (b), LMSN-COOH (c), LMSN-COOH@CS (d) and LMSN-COOH@CS-FA

(e) by DLS.



Fig. S5 BJH pattern of NMSN (a), NMSN-removed (b), LMSN-removed (c).



**Fig. S6** N<sub>2</sub> adsorption/desorption isotherm of NMSN (a), NMSN-removed (b) and LMSN-removed (c).



Fig. S7 Calibration curve of APTES in the presence of ninhydrin.



Fig. S8 Standard calibration curve of CUR in DCM solution.



Fig. S9 Representative photograph of loading procedure: CUR loaded in MSNs (a) and primary CUR solution in DCM

(b).



**Fig. S10** Flow cytometric analysis of CUR, LMSN-COOH-CUR, LMSN-COOH-CUR@CS, and LMSN-COOH-CUR@CS-FA cellular uptake in (a) NIH-3T3 and (b) HeLa cells.



Fig. S11 Cytotoxicity of MSNs carrier as control, measured by MTT assay in NIH-3T3 cells after 24, 48 and 72h

Incubation. Data is expressed as mean  $\pm$  S.D. (n = 3).



Fig. S12 Cytotoxicity of MSNs carrier as control, measured by MTT assay in HeLa cells after 24, 48 and 72h

Incubation. Data is expressed as mean  $\pm$  S.D. (n = 3).





Fig. S13 Cytotoxicity of free and CUR loaded nanoparticles measured by MTT assay in NIH-3T3 (a) and HeLa (b) cells

after 24h Incubation. Data is expressed as mean  $\pm$  S.D. (n = 3).





Fig. S14 Cytotoxicity of free and CUR loaded nanoparticles measured by MTT assay in NIH-3T3 (a) and HeLa (b) cells

after 48h Incubation. Data is expressed as mean  $\pm$  S.D. (n = 3).



**Fig. S15** SDS-PAGE gel of human plasma proteins obtained from LMSN(a), LMSN-COOH(b), LMSN-COOH@CS-FA(c) and Mw of the proteins in the standard ladder (kDa) (A). Molecular weight histograms band intensity of proteins associated with same LMSNs in 10% plasma protein concentration (B) and in 100% plasma protein concentration



	LMSN	LMSN-NH2	LMSN-COOH	LMSN-COOH@CS	LMSN-COOH@CS-FA
Size distribution by Number [Diam. (nm)]	72.2	74.5	76.1	161	167
Zeta Potential (mV)	-19.8	+51	+20	+38.6	+20.4

Table S1 The zeta-potentials and size distribution of LMSN, LMSN-NH<sub>2</sub> and LMSN-COOH by DLS

**Table S2** The textural N2 adsorption and desorption parameters of MSN samples with normal and large pore sizes.

samples	Surface area (s, m <sup>2</sup> /g)	Pore diameter (d, Å)
NMSN	40.06	14.86
NMSN-removed	697.72	24.18
LMSN-removed	1096.05	36.37

<b>Table S3</b> Amine co	ontents of the sam	ples by ninhydrin assay
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samples	LMSN-NH <sub>2</sub>	LMSN-COOH	CS-FA	CS
NH <sub>2</sub> content (μmol/mg)	2.95	1.87	2.56	3.39

		pH 7.4 LMSN-COOH- CUR@CS-FA	pH 5.5 LMSN-COOH- CUR@CS-FA	pH 7.4 LMSN-COOH- CUR	pH 5.5 LMSN-COOH- CUR	pH 7.4 NMSN-COOH-CUR	pH 5.5 NMSN-COOH-CUR
Zero order	k <sub>0</sub>	3.0 × 10 <sup>-3</sup>	6. <sup>1 ×</sup> 10 <sup>-3</sup>	2.9 × 10 <sup>-3</sup>	4.4 × 10-3	4.9 × 10-3	5.5 × 10-3
	R <sup>2</sup>	0.87	0.78	0.31	0.38	0.30	0.36
First order	k <sub>1</sub>	2.1 × 10 <sup>-2</sup>	2.2 × 10 <sup>-2</sup>	4.0 × 10 <sup>-3</sup>	7.1 × 10-3	1.1 × 10 <sup>-2</sup>	1.3 × 10 <sup>-2</sup>
	R <sup>2</sup>	0.61	0.50	0.23	0.25	0.20	0.24
Korsmeyer- Peppas	n	0.53	0.54	0.12	0.22	0.23	0.43
	k <sub>P</sub>	3.2 × 10 <sup>-2</sup>	7.5 × 10-2	6.1 × 10-1	4.2 × 10-1	3.8 × 10 <sup>-1</sup>	1.9 × 10 <sup>-1</sup>
	R <sup>2</sup>	0.98	0.95	0.64	0.68	0.71	0.76

 Table S4 Release Mathematical models' correlation coefficients and exponents