Electronic Supplementary Information (ESI)

One-Pot Synthesis of Folic Acid Encapsulated Upconversion Nanoscale Metal Organic Frameworks for Targeting, Imaging and pH Responsive Drug Release

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Synthesis of upconversion metal organic framework nanocomposite (UCNP@ZIF-8)

Upconversion nanoparticles encapsulated Zeolite imidazolate framework (ZIF-8) was synthesized by the following procedure. In brief, 0.055 g of previously prepared $NaYF_4$: Yb^{+3}, Er^{+3} (UCNPs) and zinc nitrate hexahydrate (0.125 g) was dispersed in 15 mL of dry methanol. Then, a solution was prepared by dissolving 0.25 g of 2-methyl imidazole were dissolved in 15 mL of dry methanol. After that, 2-methyl imidazole solution were drop-wise added into the methanolic solution of zinc nitrate hexahydrate. The reaction was continued for 30 min at 25 ºC. Gradually a white color product was obtained. The product was centrifuged and washed several times by ethanol and finally dried at 50 ºC in a vacuum oven for 12 h.

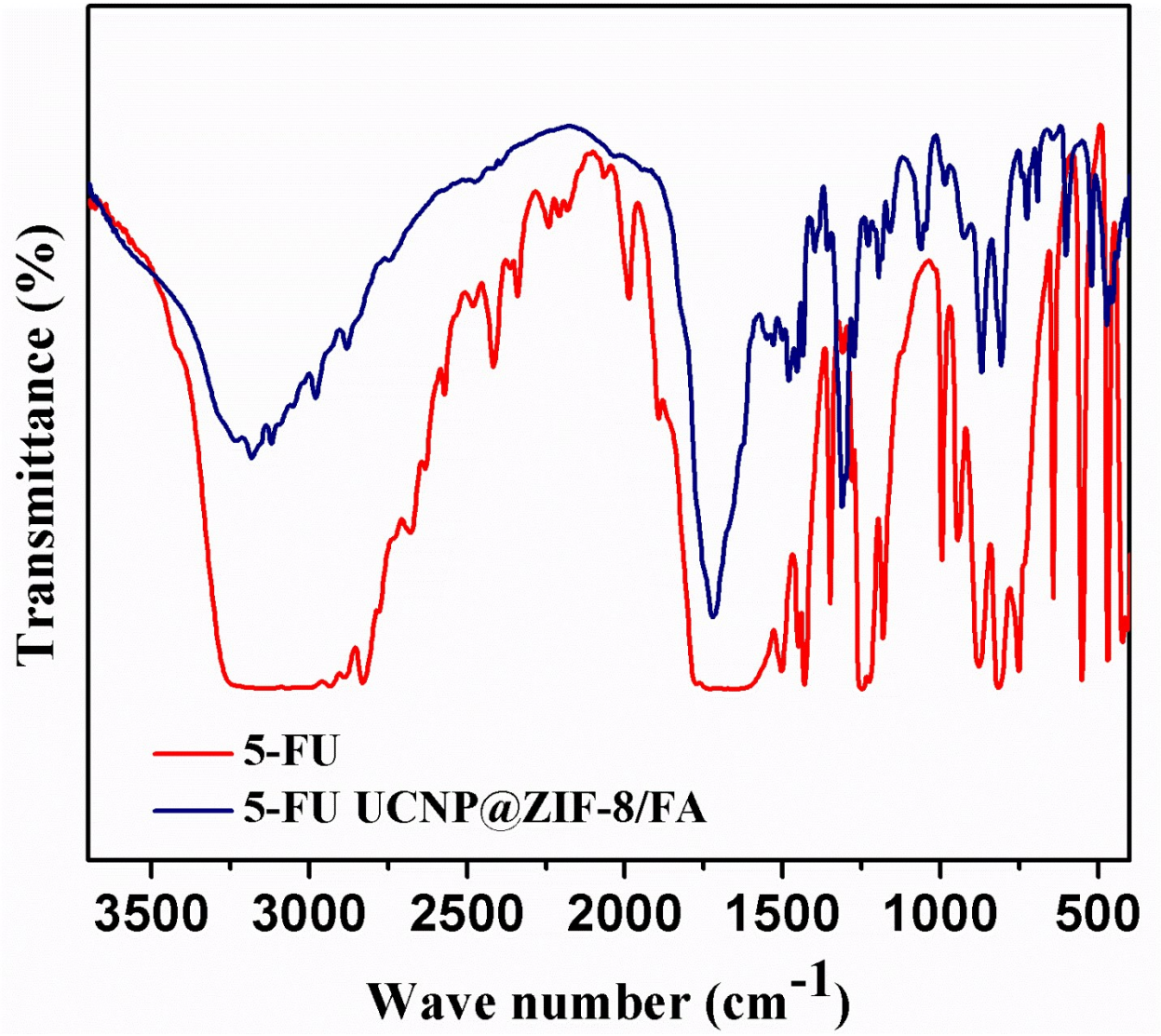


Figure S1. FTIR spectra of 5-FU loaded UCNP@ZIF-8/FA and only 5-FU.

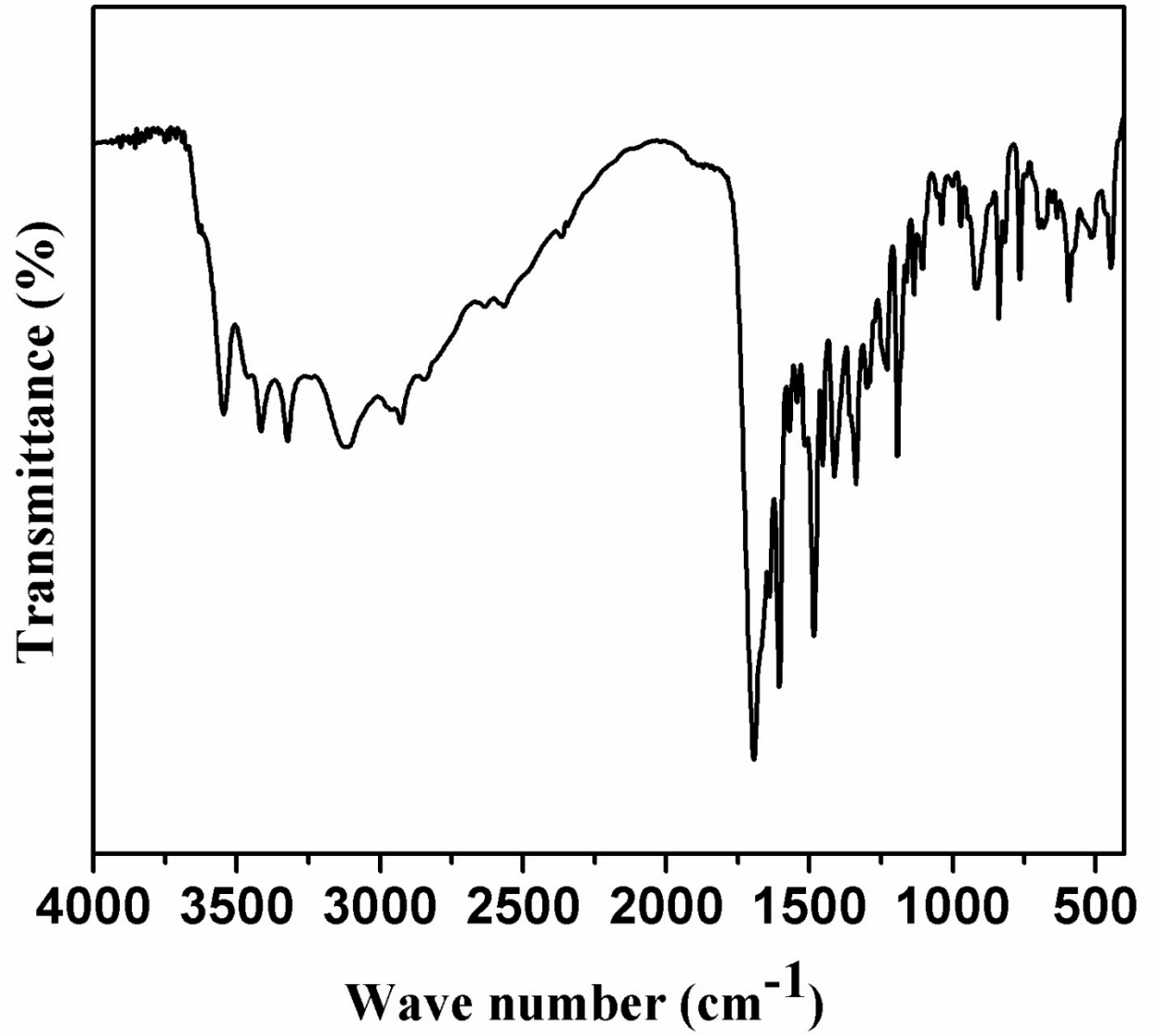


Figure S2. FTIR spectra of free folic acid.

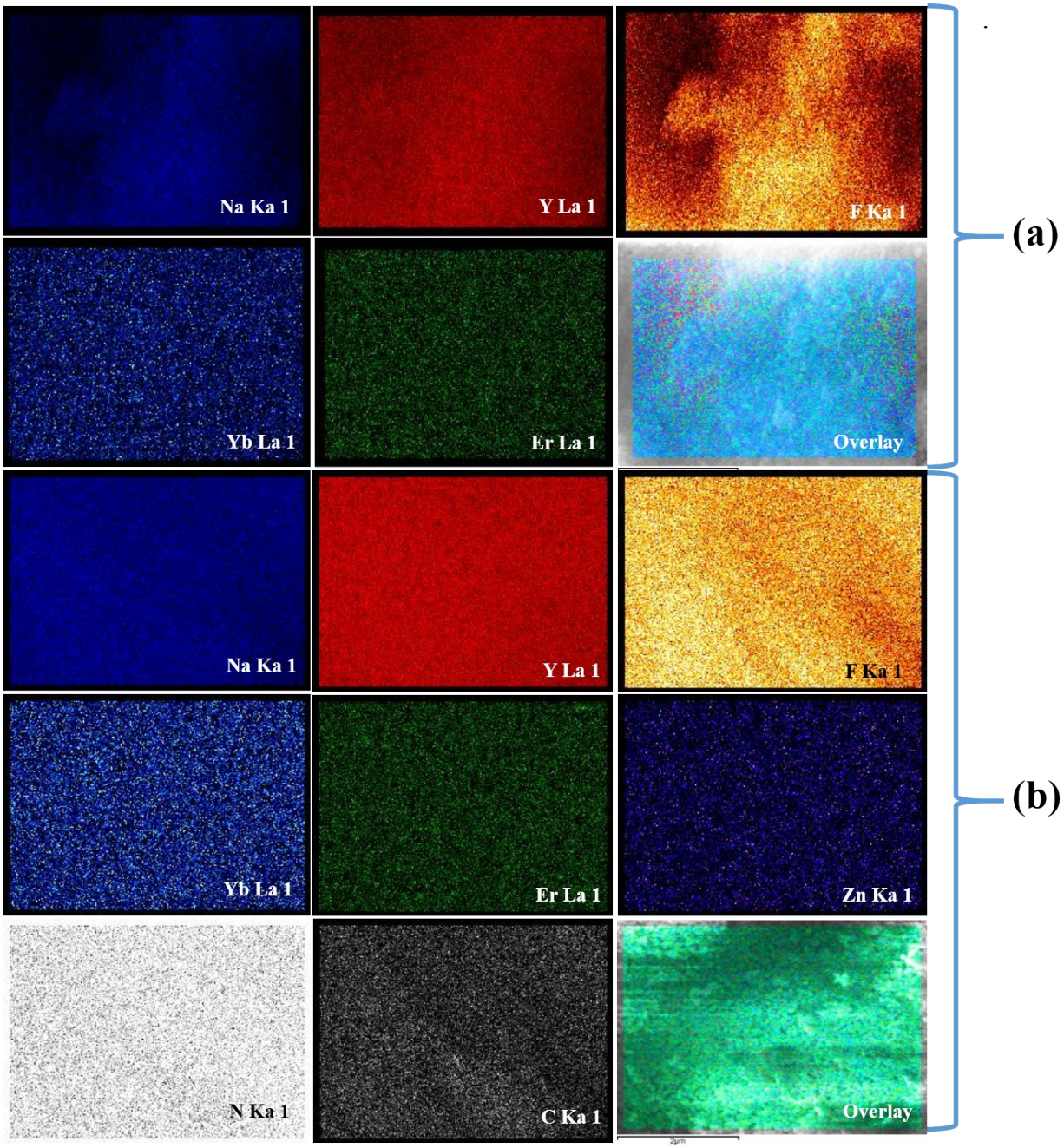
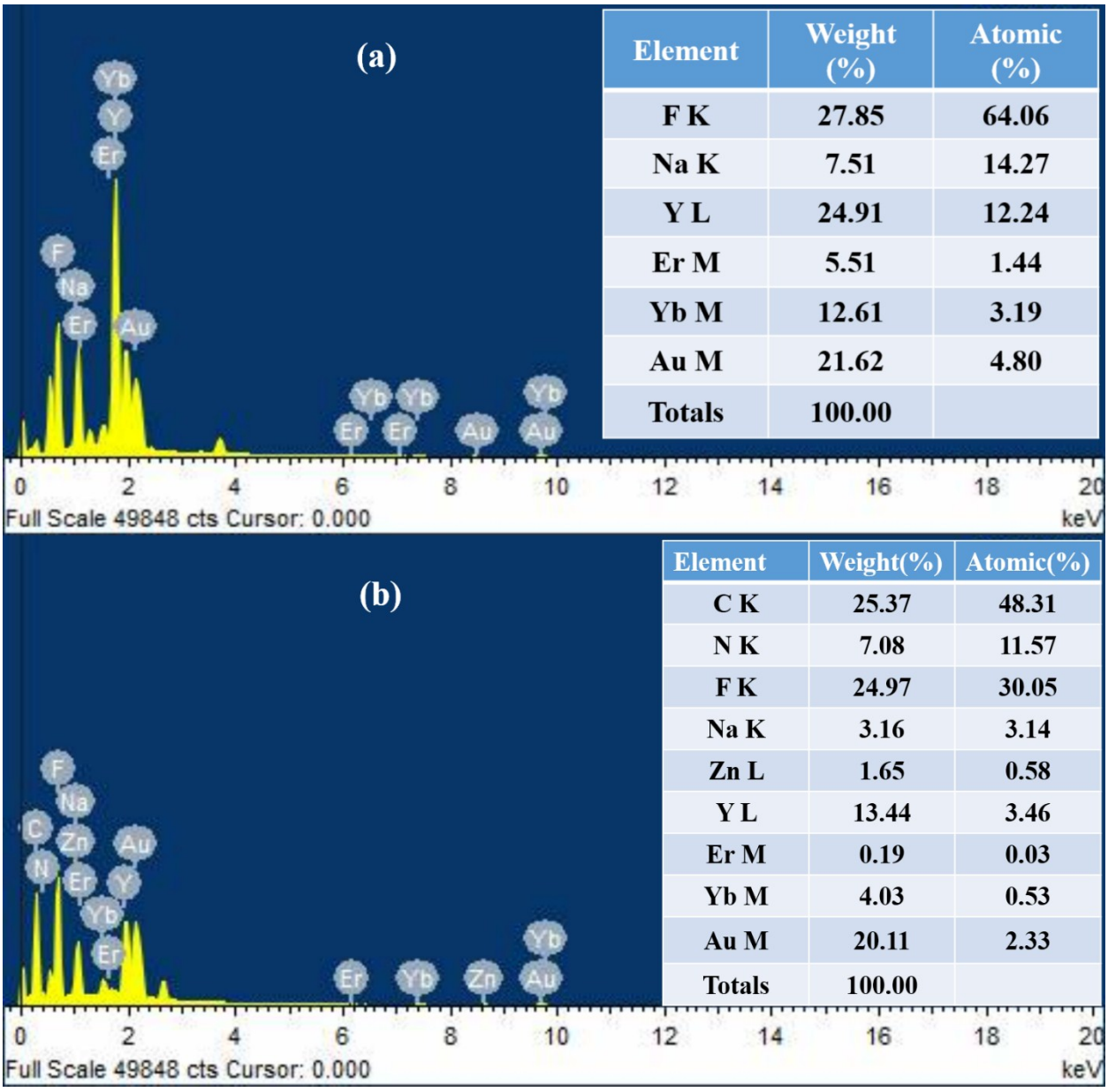

Na Ka 1
Y La 1
F Ka 1
Yb La 1
Er La 1
Overlay
(a)
Na Ka 1
Y La 1
F Ka 1
Yb La 1
Er La 1
Zn Ka 1
N Ka 1
C Ka 1
Overlay
(b)

Figure S3. Elemental mapping of (a) UCNP (b) UCNP@ZIF-8/FA.



Element	Weight (%)	Atomic (%)
F K	27.85	64.06
Na K	7.51	14.27
Y L	24.91	12.24
Er M	5.51	1.44
Yb M	12.61	3.19
Au M	21.62	4.80
Totals	100.00	

Element	Weight(%)	Atomic(%)
C K	25.37	48.31
N K	7.08	11.57
F K	24.97	30.05
Na K	3.16	3.14
Zn L	1.65	0.58
Y L	13.44	3.46
Er M	0.19	0.03
Yb M	4.03	0.53
Au M	20.11	2.33
Totals	100.00	

Figure S4. EDAX spectrum of (a) UCNP (b) UCNP@ZIF-8/FA [Nanoparticles were coated with gold (Au) before EDAX analysis].

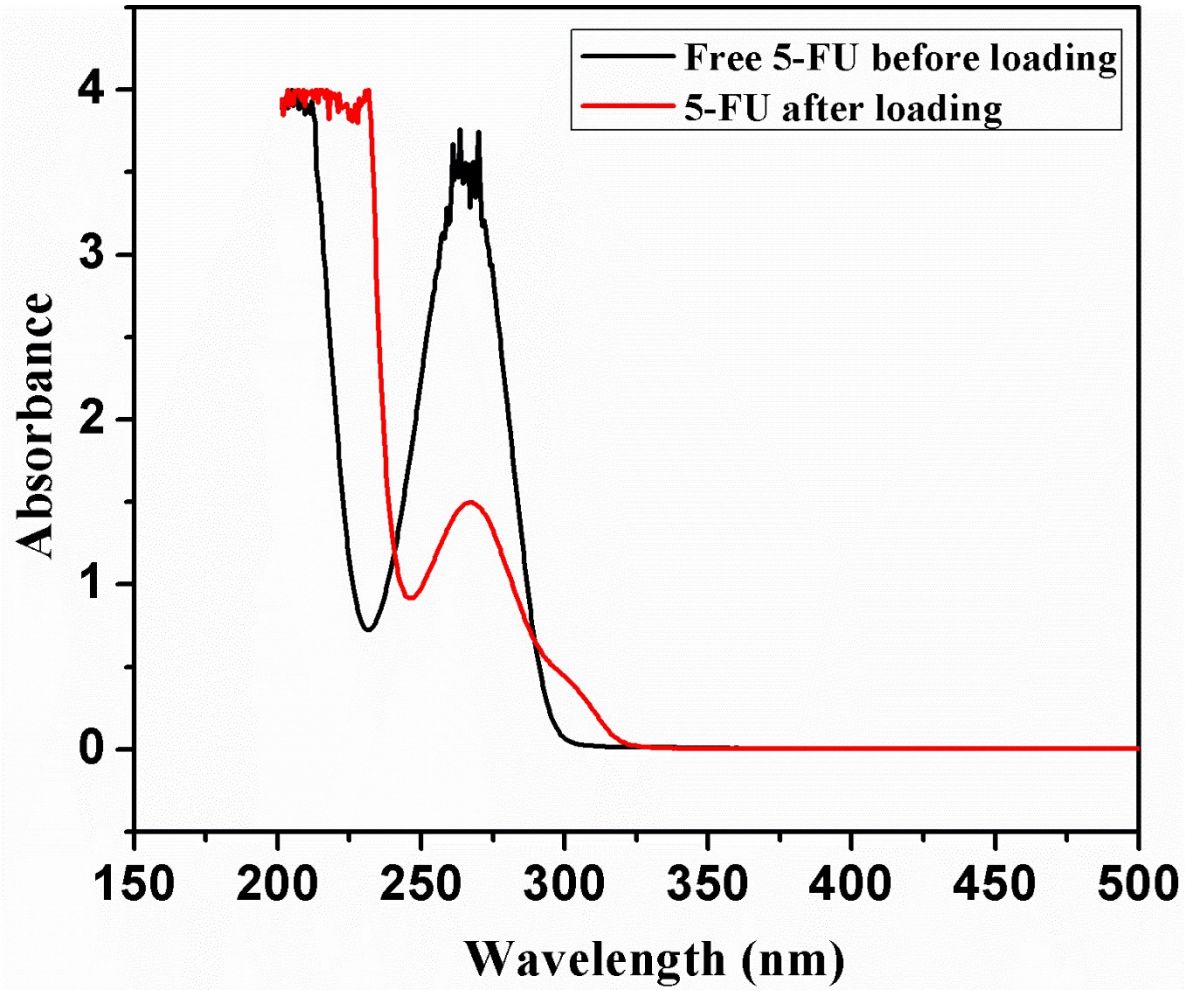


Figure S5. UV-Vis spectroscopy of free 5-FU and 5-FU after loading into UCNP@ZIF-8/FA.

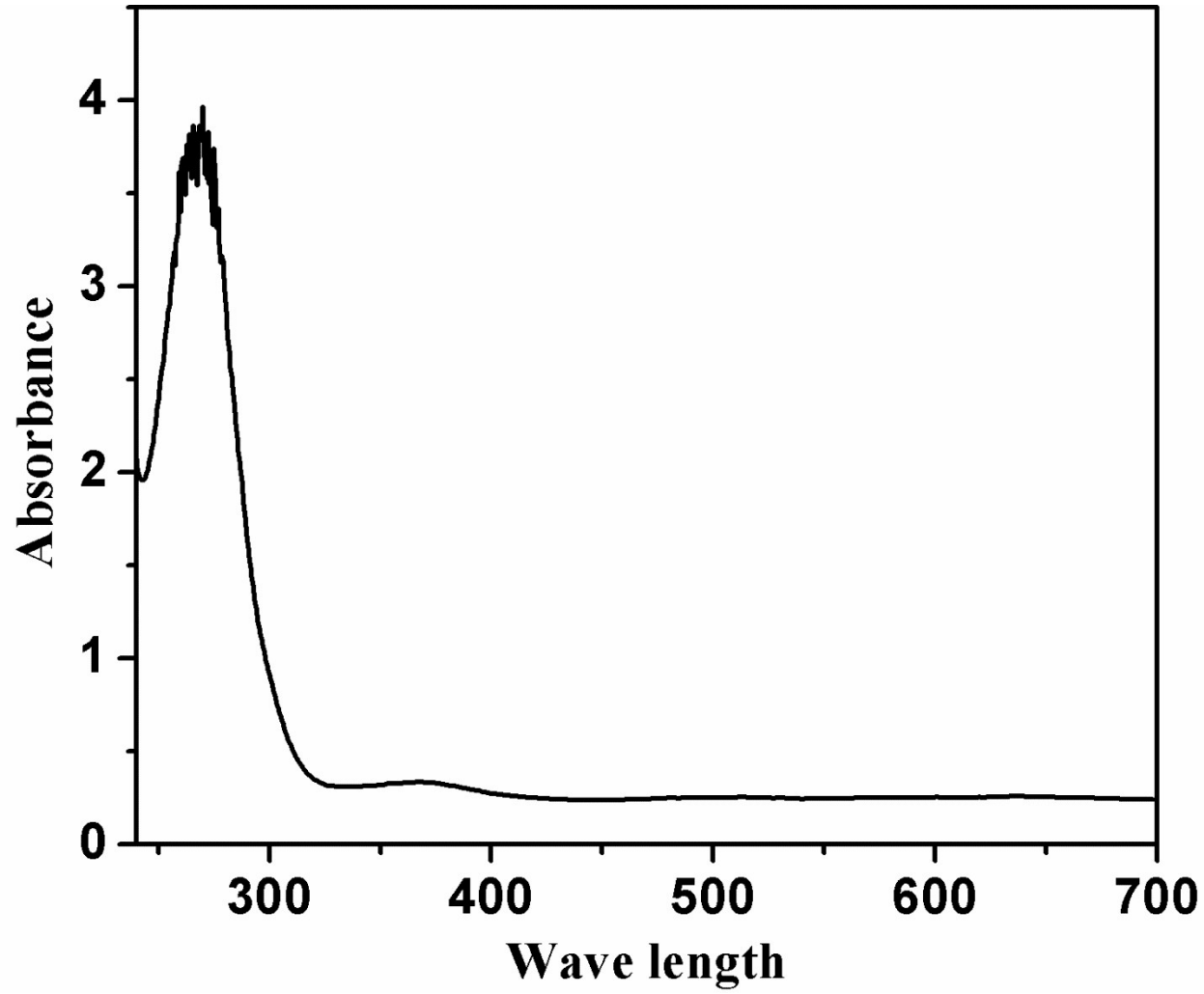


Figure S6. UV-Vis spectroscopy of 5-FU loaded into UCNP@ZIF-8/FA.

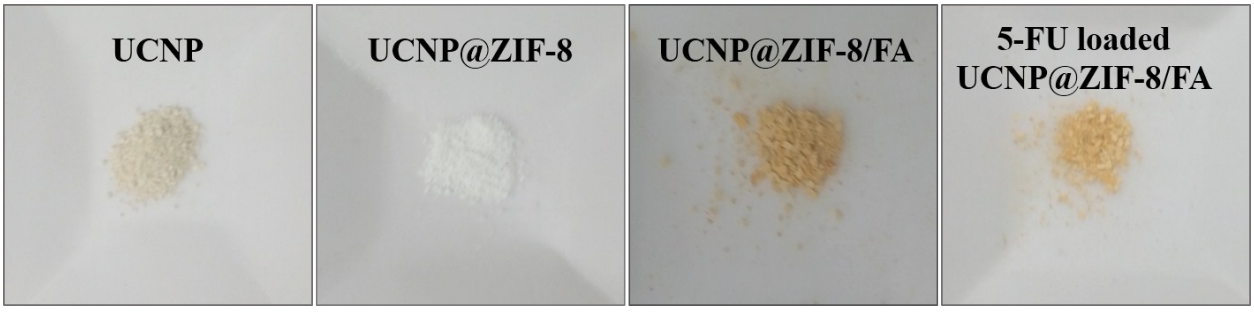


Figure S7. Camera photo image of solid state UCNP, UCNP@ZIF-8, UCNP@ZIF-8/FA, 5-FU loaded UCNP@ZIF-8/FA.

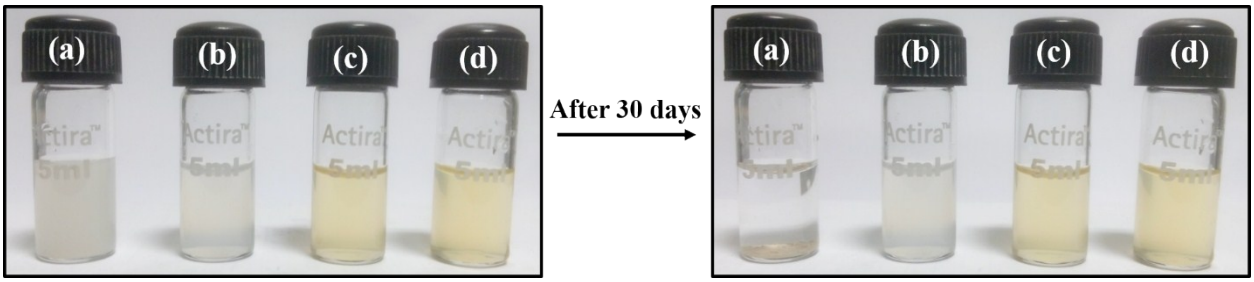


Figure S8. Stability study of (a) UCNP (b) UCNP@ZIF-8 (c) UCNP@ZIF-8/FA (d) 5-FU loaded UCNP@ZIF-8/FA.

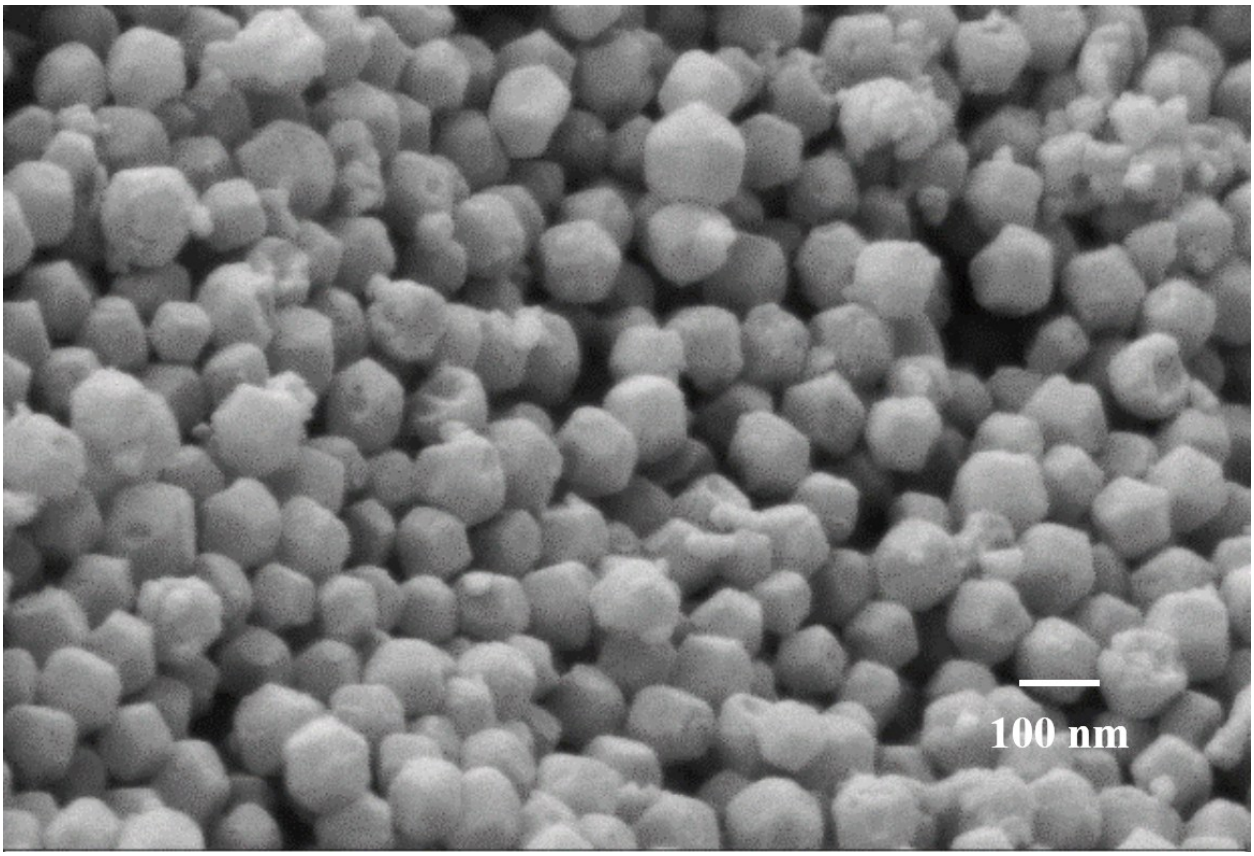


Figure S9. FESEM image of 5-FU loaded UCNP@ZIF-8/FA.

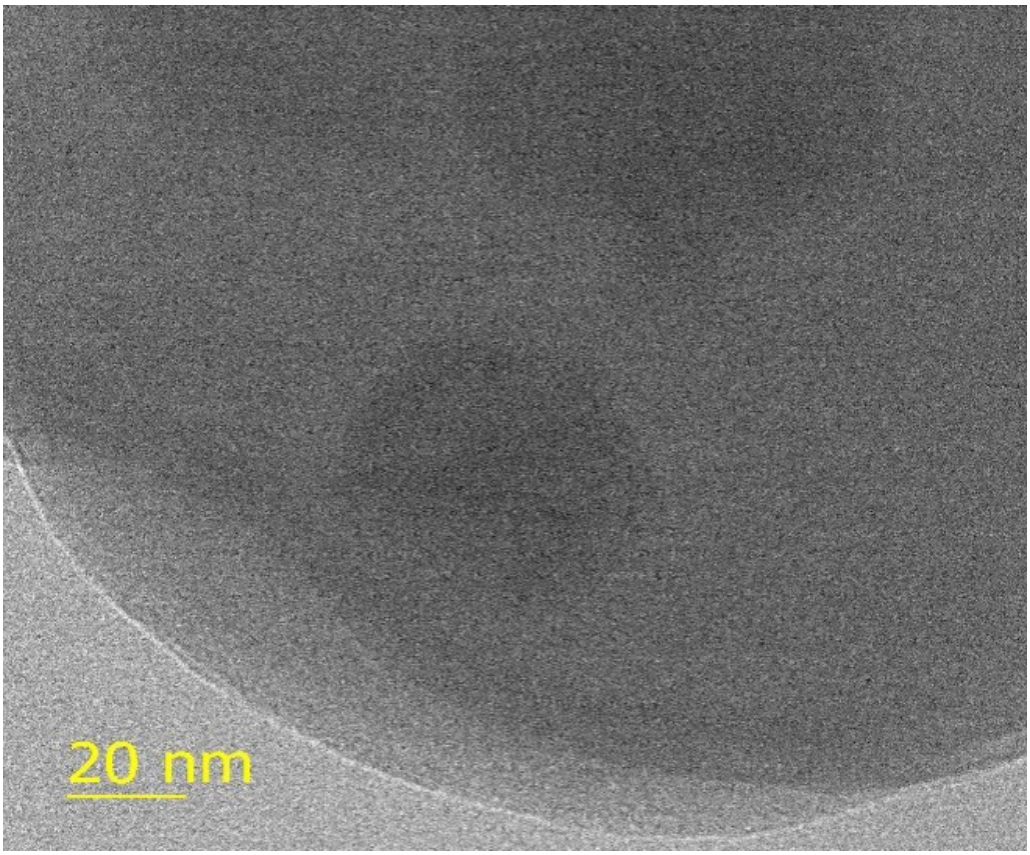


Figure S10. HRTEM (high resolution) image of UCNP@ZIF-8/FA.

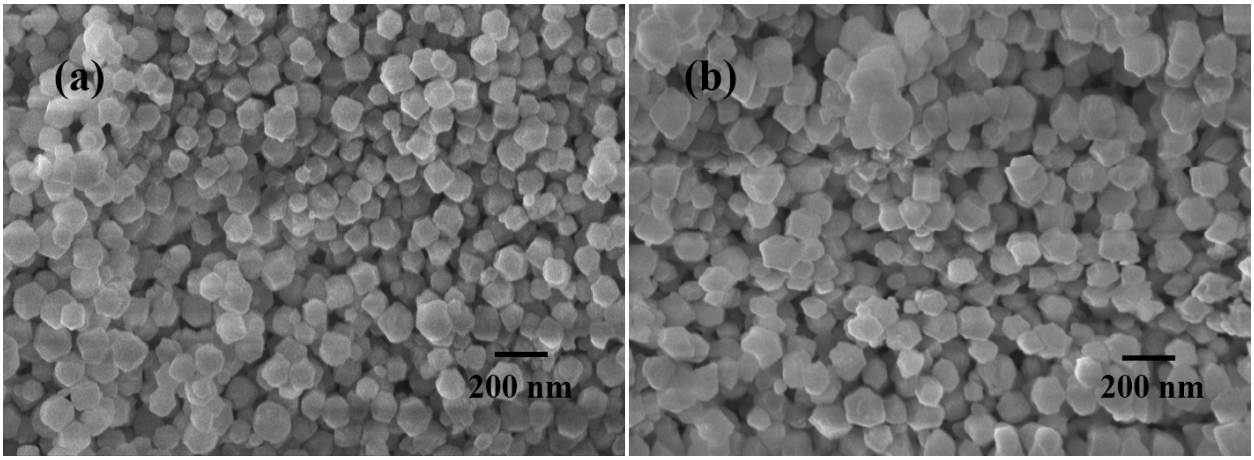


Figure S11. FESEM image of synthesized UCNP@ZIF-8/FA after drug release up to 12 h (a) and 24 h (b) in PBS at 37 ^{o}C [in pH 7.4].

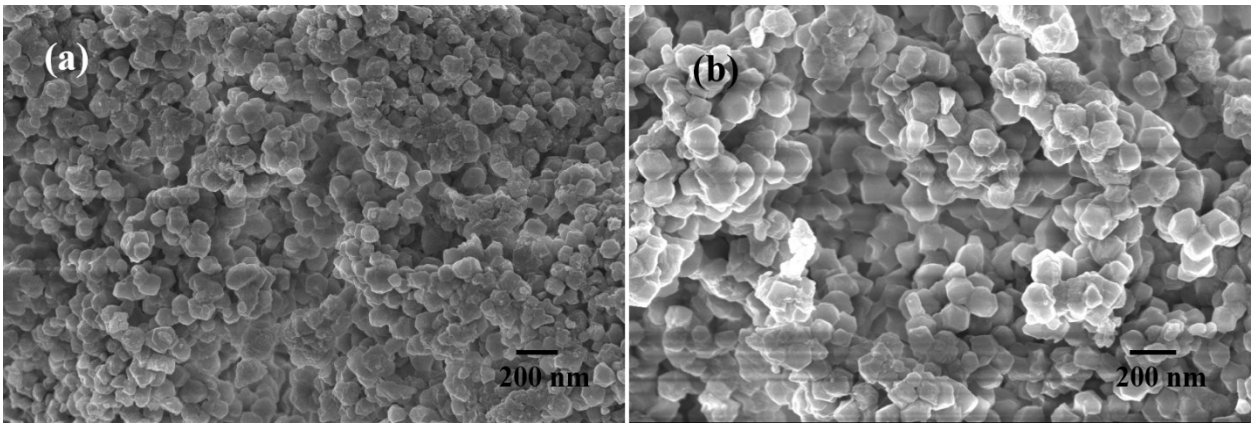


Figure S12. FESEM image of synthesized UCNP@ZIF-8/FA after drug release up to 12 h (a) and 24 h (b) at 37 ^{o}C [in pH 5.5].

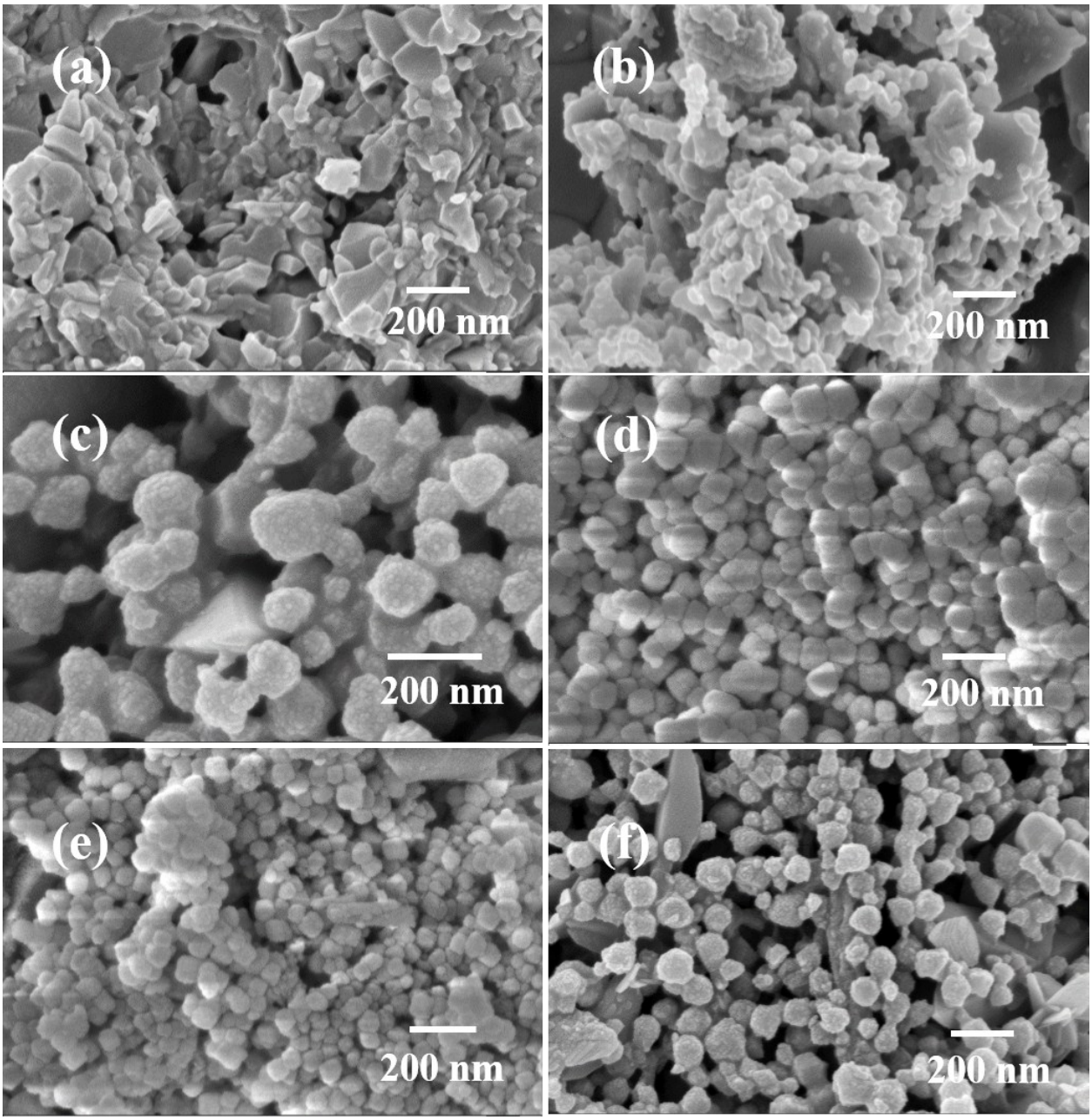


Figure S13. FESEM image (change of morphology) of synthesized UCNP@ZIF-8/FA in pH (a) 3.0 (b) 4.0 (c) 5.0 (d) 6.0 (e) 8.0 and (f) 9.0 after 24 h stirring at 37 ^{o}C.

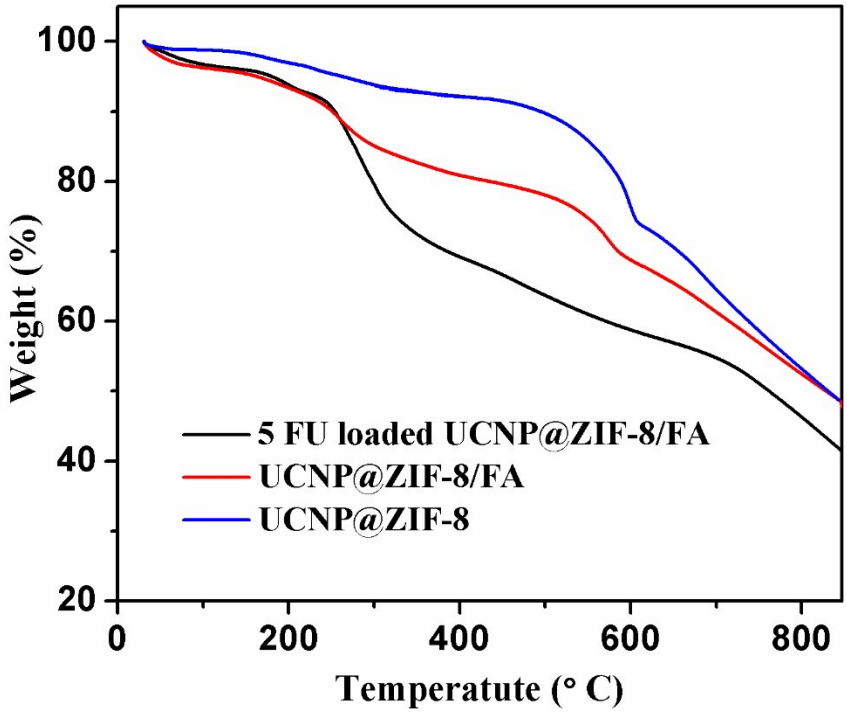


Figure S14. Weight loss curves (TGA thermograms) of UCNP@ZIF-8, UCNP@ZIF-8/FA, 5-FU loaded UCNP@ZIF-8/FA.

TGA analysis was carried out to confirm the amount of folic acid attached with the NMOFs, as the folic acid amount has the vital influence on the performance of targeting in cell. TGA result reveals that incase of UCNP@ZIF-8/FA, the weight loss near about 100 °C can be due to the loss of methanol molecules and moisture adsorbed into the ZIF-8 pores. After that, temperature around 230-450 °C, 8.94 % weight loss is responsible for the decomposition of folic acid from the UCNP@ZIF-8/FA, as shown in figure S14. The loading percentage of FA onto the UCNP@ZIF-8 is of 4.76 %. In case of 5-FU loaded UCNP@ZIF-8/FA, comparatively more

weight loss at around 300 °C confirms the attachment of 5-FU into the UCNP@ZIF-8/FA framework.

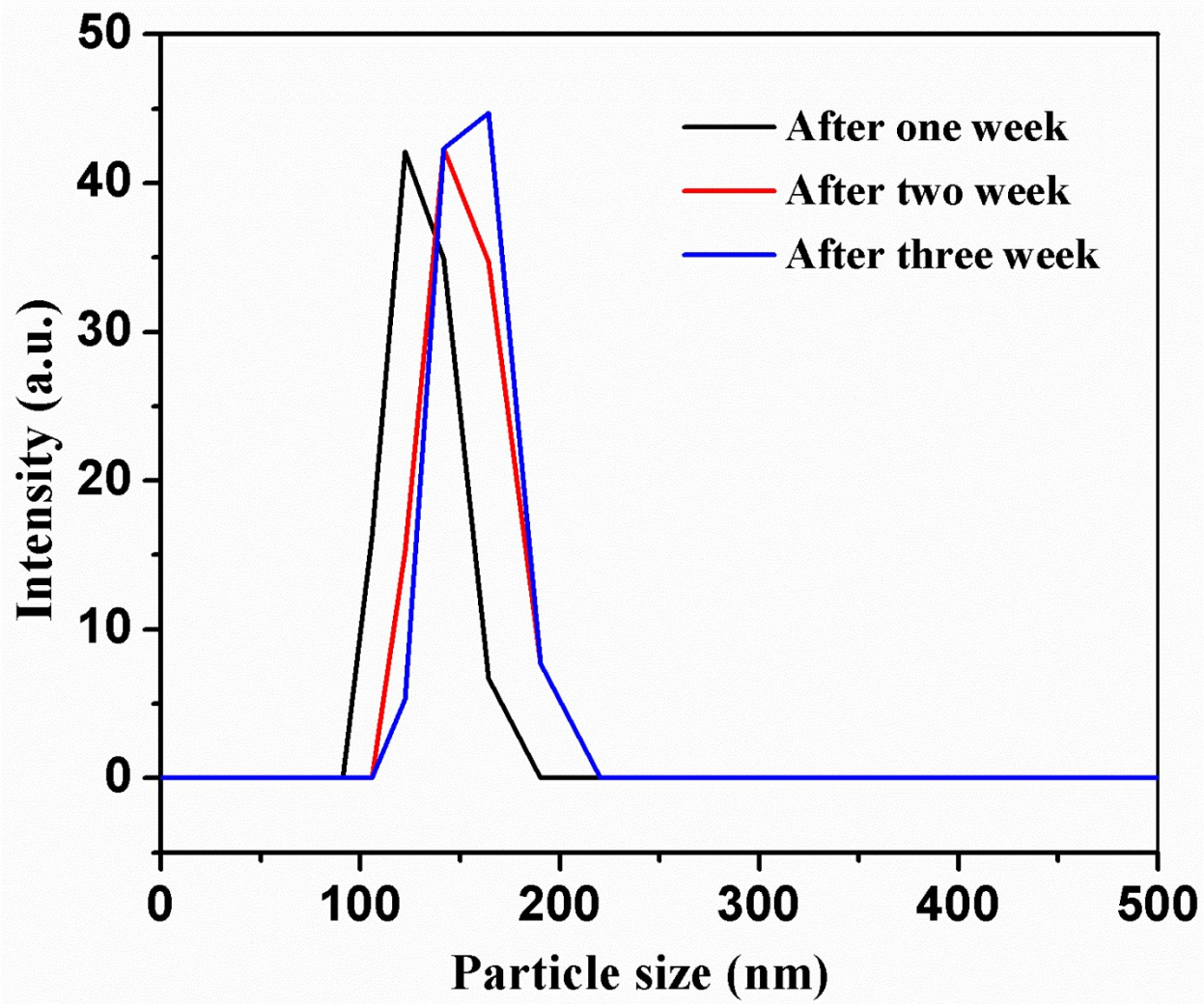


Figure S15. Stability of 5-FU loaded UCNP@ZIF-8/FA after several weeks in PBS at pH 7.4.

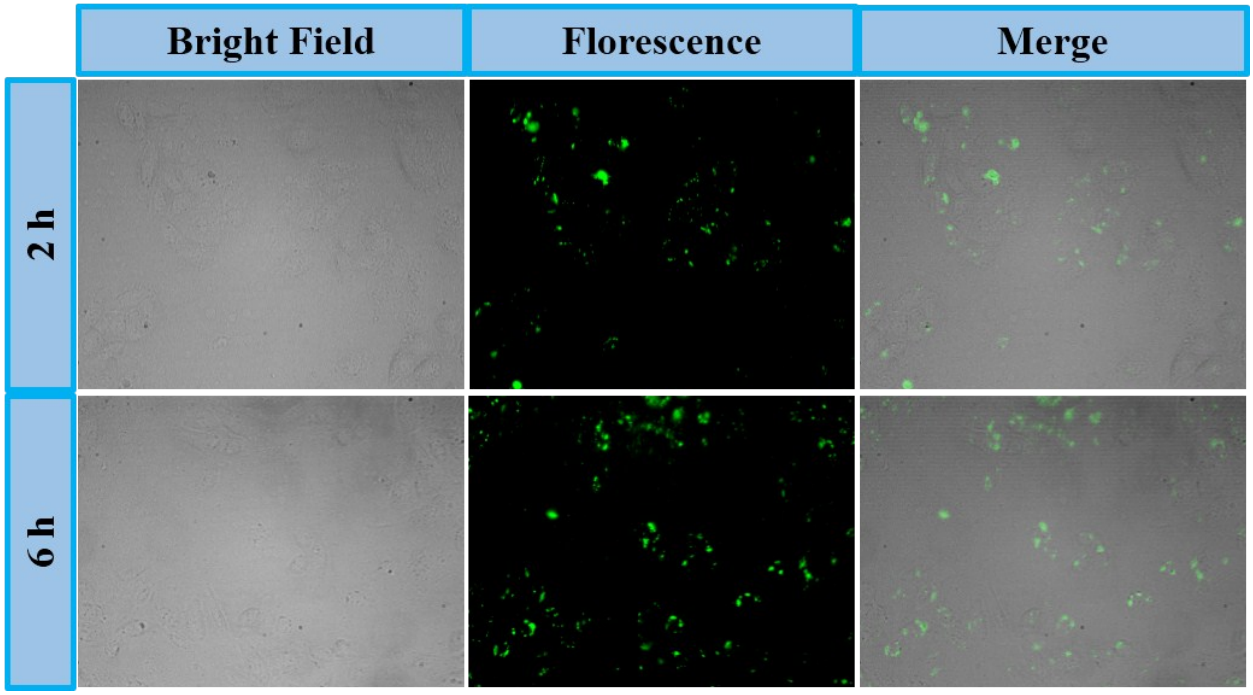


Figure S16. Fluorescence microscopic image of HeLa Cells incubated with 5 μg.mL^{-1} UCNP@ZIF-8 (without FA) for 2 h and 6 h at 37 °C with corresponding bright field and merge field.

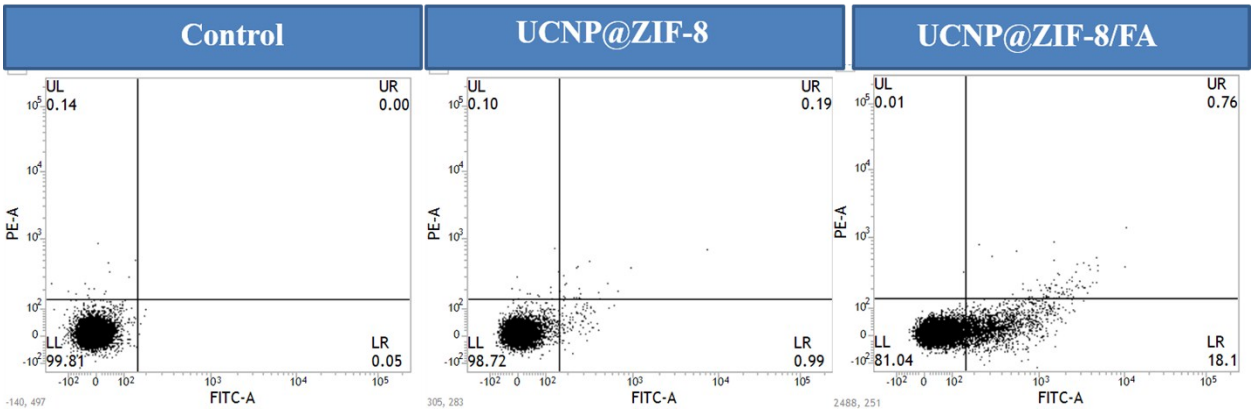


Figure S17. FACS study for intracellular uptake of the UCNP@ZIF-8 and UCNP@ZIF-8/FA exposed cancer cells (HeLa).