Supporting Information

Polymer coated MNPs scaffold for targeted drug delivery and improvement of Rheumatoid Arthritis

Seyedeh Mina Malaekehpoor,^a Katayon Derakhshandeh,^b Rasool Haddadi,^c Alireza Noorian,^d Ramin Ghorbani-Vaghei^{a,*}

^aDepartment of Organic Chemistry, Faculty of Chemistry, Bu-Ali Sina University, Hamadan 6517838683, Iran, Tel.: +98(813)8380709 E-mail: rgvaghei@yahoo.com (Ramin Ghorbani-Vaghei) ^bDepartment of Pharmaceutics, School of Pharmacy, Hamadan University of Medical Sciences, 6517838678, Hamadan, Iran ^cDepartment of Pharmacology & Toxicology, School of Pharmacy, Hamadan University of Medical Sciences, 6517838678, Hamadan, Iran ^dDepartment of Pathobiology, School of Veterinary Science, Bu-Ali Sina University, Hamadan, 6517658978, Iran

Synthesis of DHAA-Fe₃O₄ NPs

DHAA–Fe₃O₄ NPs were synthesized through the previous procedure [50]. In brief, (10 mL, 0.1 M) FeCl₃.6H₂O (aq) was added to (20 mL, 0.45 M) NaHCO₃ (aq) and, then, the suspension was stirred for 30 min. Subsequently, (10 mL, 0.01 M) vitamin C (aq) was added and, then, the mixture was stirred for another 10 minutes. Afterwards, it was transferred into an autoclave with a volume of (50 mL) and kept at 150 °C for 4 h in order to get DHAA–Fe₃O NPs. The synthesized nanoparticles were purified three times with *deionized* water (DI) and ethanol, were dried at room temperature for 24 hrs and eventually redispersed in DI water.

Synthesis of DHAA–Fe₃O₄@HA NPs

For the modification of DHAA–Fe₃O₄ NPs, at first, HA (0.01 g), EDC (4.1 mg) and DMAP (2.3 mg) were dissolved in purified water (4 mL) and stirred at room temperature for 1 h, then DHAA–Fe₃O₄ NPs (0.1 g) were dispersed (1 min) in DI water (6 mL), and, finally, they were added to the mixture and stirred at room temperature for two days. The resulting product isolation which was performed by an external magnet was washed with DI water (3 × 20 mL) and ethanol (3 × 20 mL). Finally, DHAA–Fe₃O₄@HA NPs were dried at room temperature for overnight and redispersed in DI water.

Synthesis of DHAA-Fe₃O₄@HA@SSZ NPs

For synthesizing DHAA–Fe₃O₄@HA@SSZ, firstly, SSZ (1 mg) was dissolved in DMSO (4 mL) and, then, EDC (0.4 mg) and DMAP (0.2 mg) were added into the solution. The mixture was stirred for 1 h. Then, DHAA–Fe₃O₄@HA NPs (10 mg), that were dispersed in DMSO (4 mL), were added to the reaction mixture and, finally, were continuously stirred at 38 °C for an overnight. The resulting product was collected through magnetic separation, washed with DMSO (2 × 20 mL) and DI water (2 × 20 mL) and, then, dried at room temperature for a day in order to obtain DHAA–Fe₃O₄@HA@SSZ. The resulting NPs were redispersed in DI water and PBS buffer.



Figure S1. EDS analysis of DHAA–Fe₃O₄ NPs.

Element	Line	Apparent	k Ratio	Wt%	Wt%	Atomic %
	Туре	Concentration			Sigma	
С	K series	1.17	0.01174	5.27	0.29	15.45
Ν	K series	0.43	0.00077	0.24	0.21	0.60
0	K series	22.50	0.07570	15.57	0.23	34.23
Fe	K series	53.60	0.53599	78.92	0.37	49.72
Total:				100.00		100.00

Figure S2. EDS analysis of DHAA–Fe₃O₄@HA NPs.

Element	Line	Apparent	k Ratio	Wt%	Wt%	Atomic %
	Туре	Concentration			Sigma	
С	K series	1.84	0.01837	7.60	0.30	16.95
N	K series	1.69	0.00300	0.94	0.26	1.79
0	K series	44.04	0.14821	31.07	0.31	51.99
S	K series	0.68	0.00585	0.91	0.07	0.76
Fe	K series	38.86	0.38862	59.49	0.40	28.52
Total:				100.00		100.00

Figure S3. EDS analysis of DHAA–Fe $_3O_4$ @HA@SSZ NPs.



Figure S4. (a), (b) FE-SEM images of DHAA–Fe₃O₄@HA NPs, (c) TEM images of DHAA–Fe₃O₄@HA@SSZ NPs, Scale bar: 75 nm, (d) FE-SEM images of DHAA–Fe₃O₄@HA@SSZ NPs.



Figure S5. (a) VSM of Fe $_3O_4$, (b) VSM of DHAA–Fe $_3O_4$ @HA NPs.





Figure S6. DLS size distribution of DHAA–Fe₃O₄@HA@SSZ NPs.



Figure S7. Zeta potential of DHAA–Fe₃O₄@HA NPs.



Figure S8. Zeta potential of DHAA–Fe₃O₄@HA@SSZ NPs.



Figure S9. (a) Particle size and (b) Zeta potential of DHAA–Fe₃O₄@HA@SSZ NPs in PBS at 37 °C.