

Supplementary data

# Nitric Oxide-Scavenging Hyaluronic Acid Nanoparticles for Osteoarthritis Treatment

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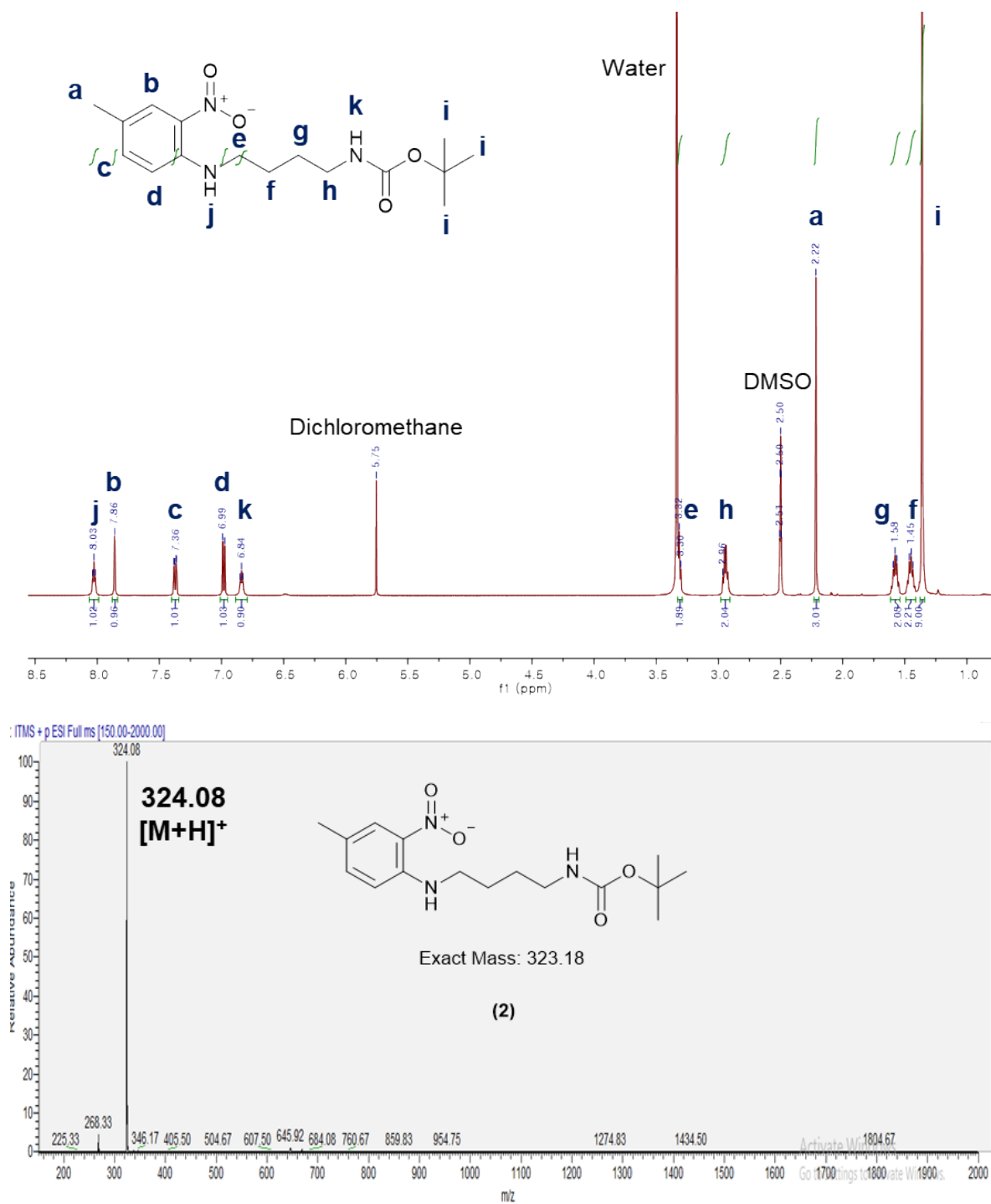
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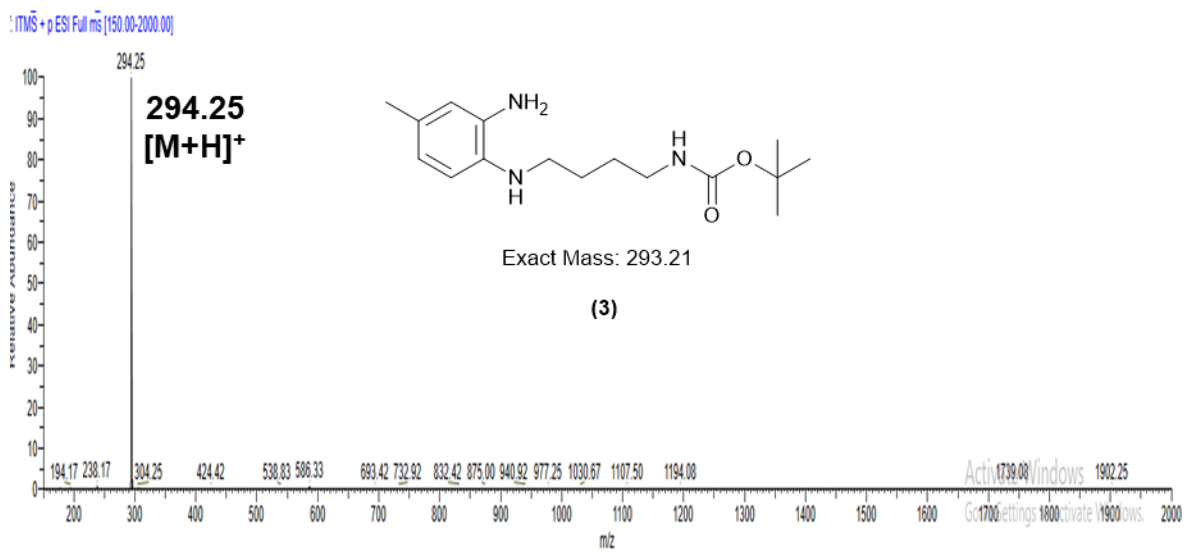
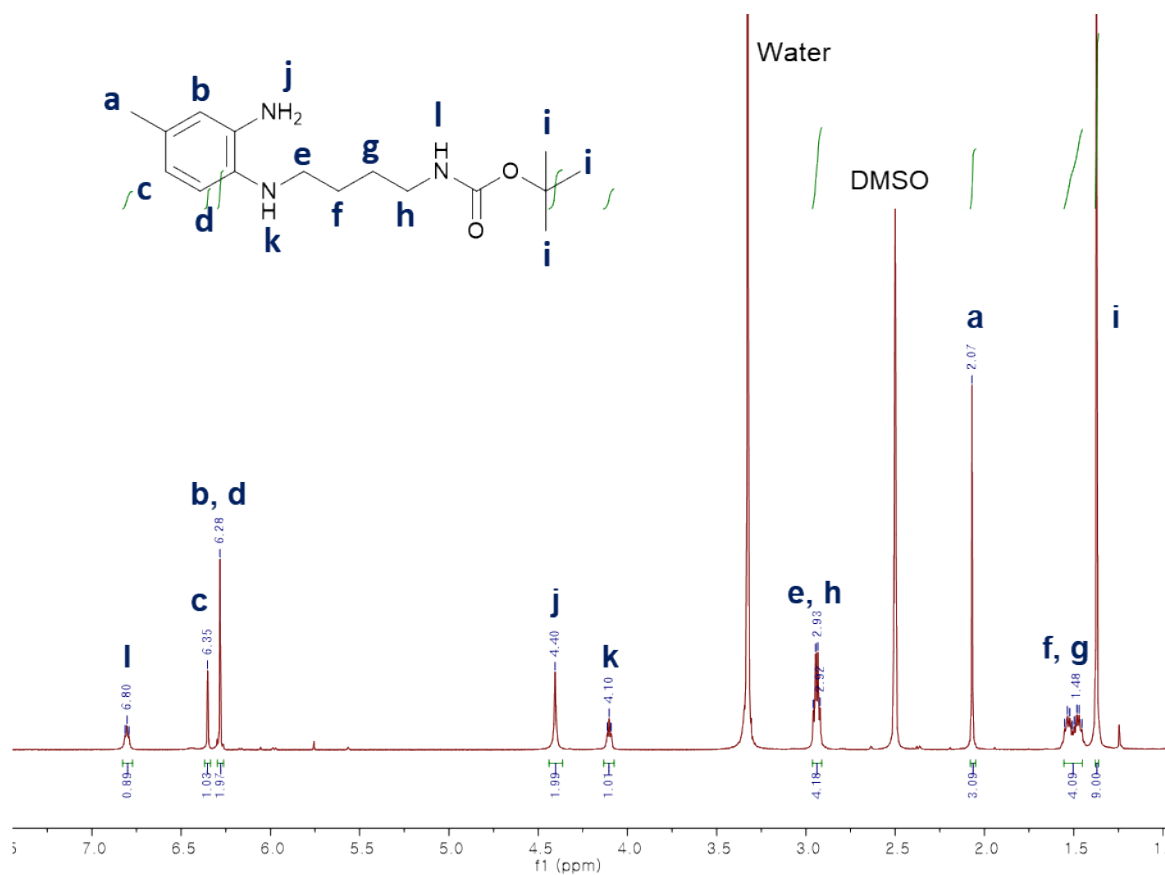
E-mail address: [wjkim@postech.ac.kr](mailto:wjkim@postech.ac.kr)

**Table S1.** IC<sub>50</sub> values of HA, NSc, HA-NSc, and HA + NSc mixture against LPS (-) and LPS (+) RAW 264.7 cells.

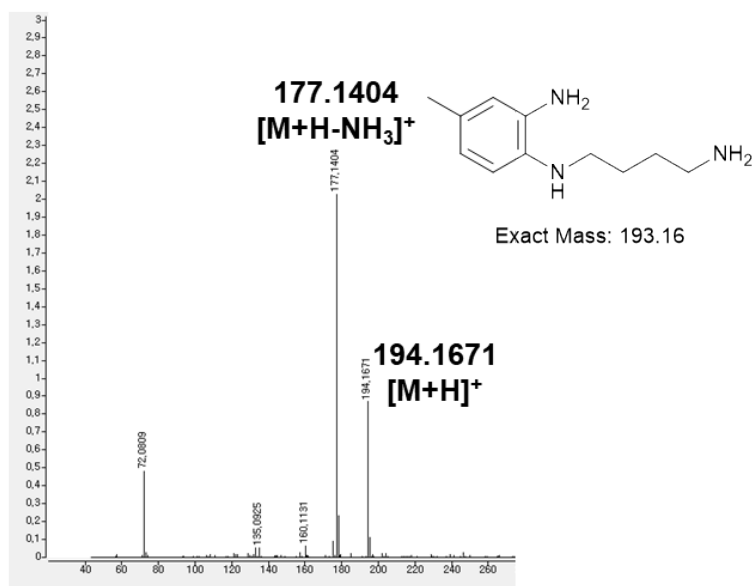
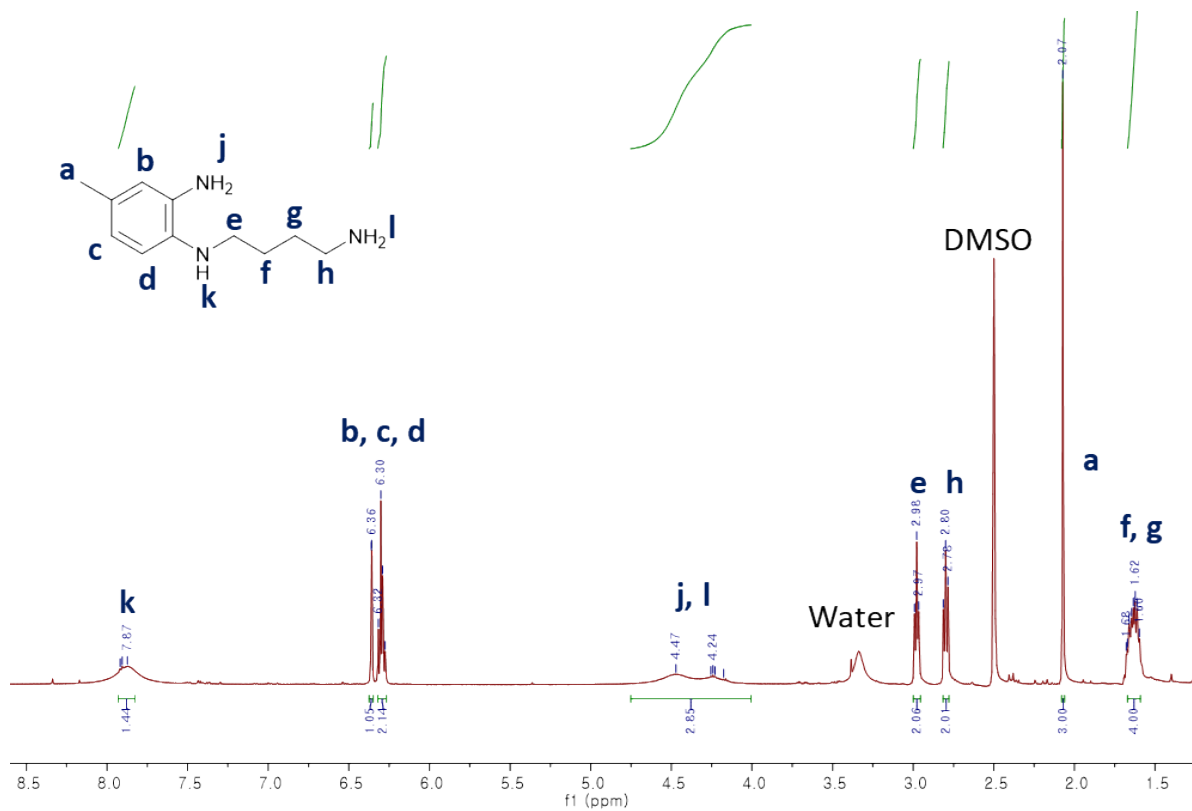
IC <sub>50</sub>	HA	NSc	HA + NSc	HA-NSc
LPS (-) RAW 264.7	-	0.659 ± 0.012	0.447 ± 0.010	1.27 ± 0.045
LPS (+) RAW 264.7	-	0.438 ± 0.009	0.460 ± 0.007	1.352 ± 0.173



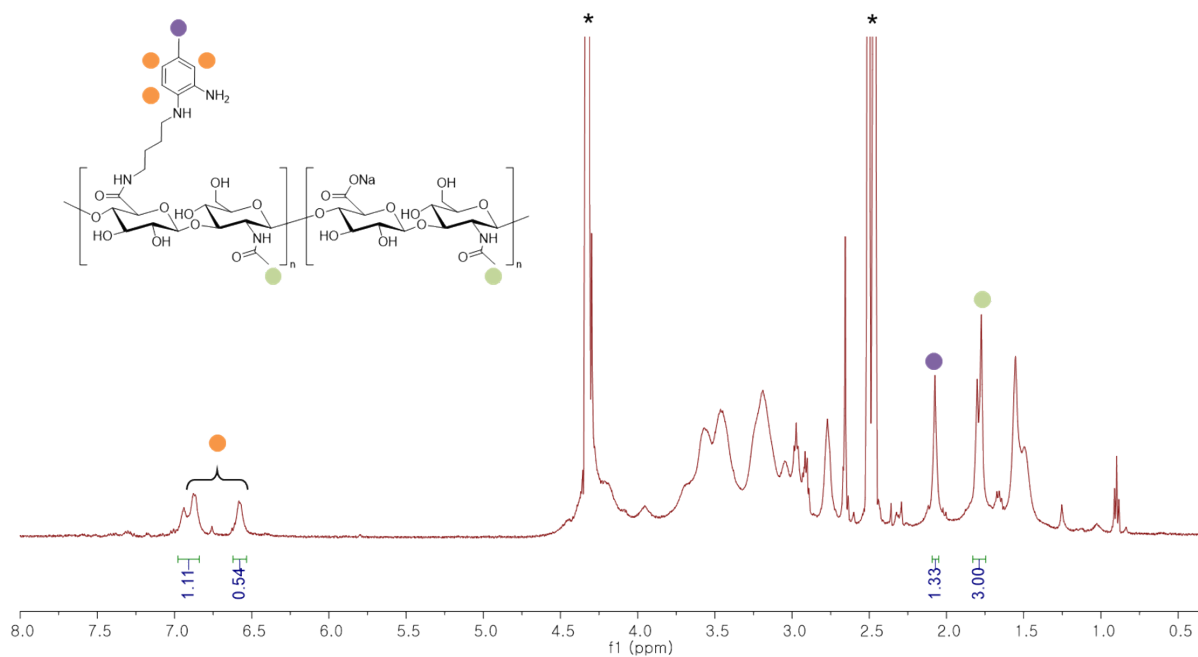
**Fig. S1** The <sup>1</sup>H NMR in DMSO-*d*<sub>6</sub> and ESI-MS spectra of compound 2.



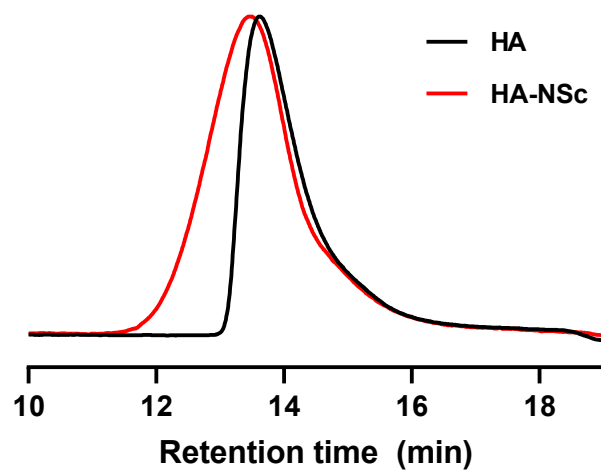
**Fig. S2** The <sup>1</sup>H NMR in DMSO-*d*<sub>6</sub> and ESI-MS spectra of compound 3.



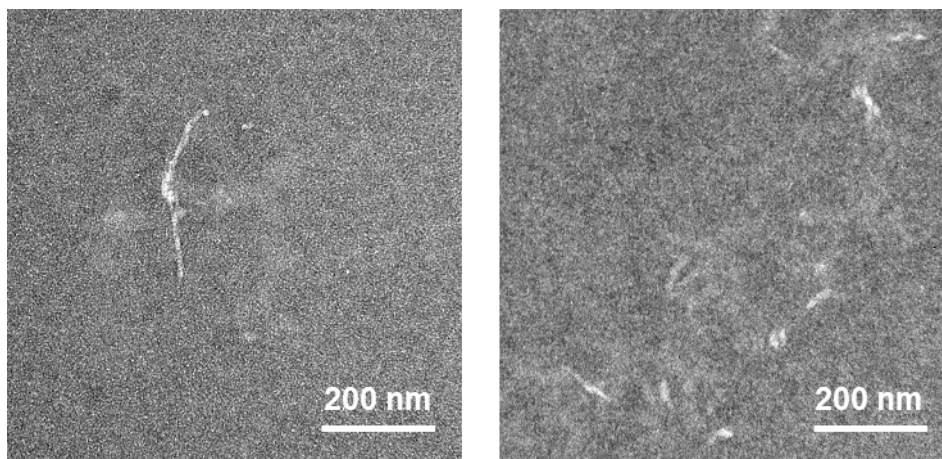
**Fig. S3** The <sup>1</sup>H NMR in DMSO-*d*<sub>6</sub> and ESI-MS spectra of NSc.



**Fig. S4** The <sup>1</sup>H NMR spectrum of HA-NSc conjugate in DMSO-*d*<sub>6</sub>/*D*<sub>2</sub>O. The asterisks indicate solvent residual peak.

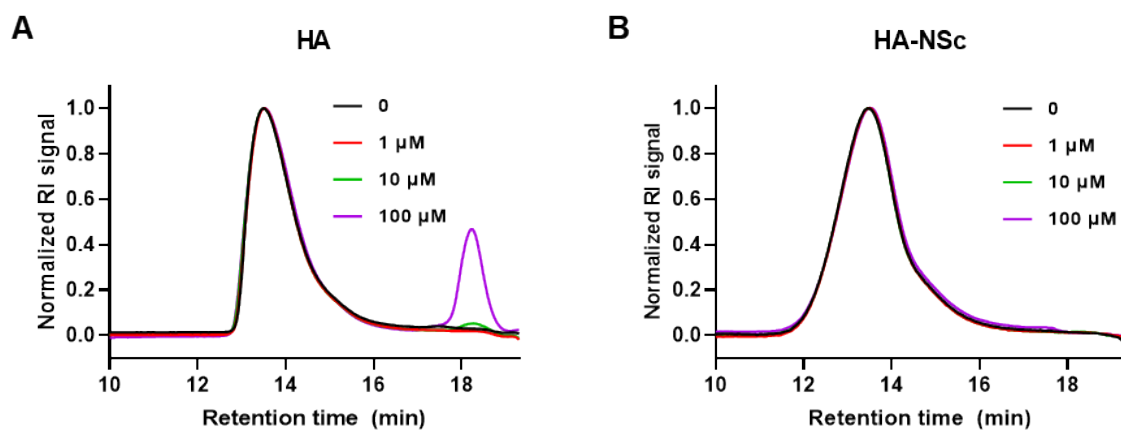


**Fig. S5** The GPC spectra of HA ( $M_n = 100\,000$  g/mol) and HA-NSc conjugate.

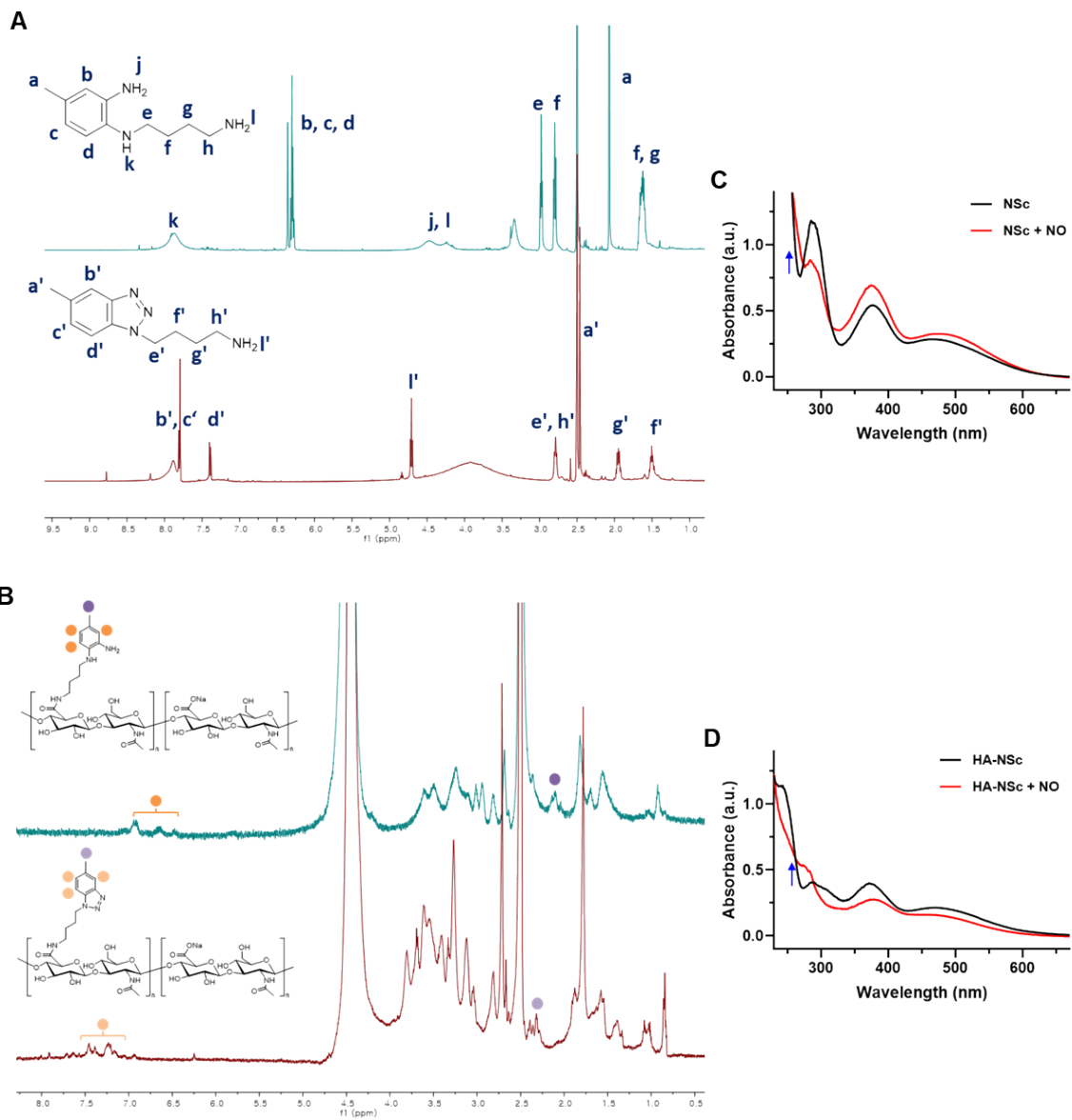


**Fig. S6** TEM images of HA (scale bar = 200 nm). Nanoparticles were not observed.

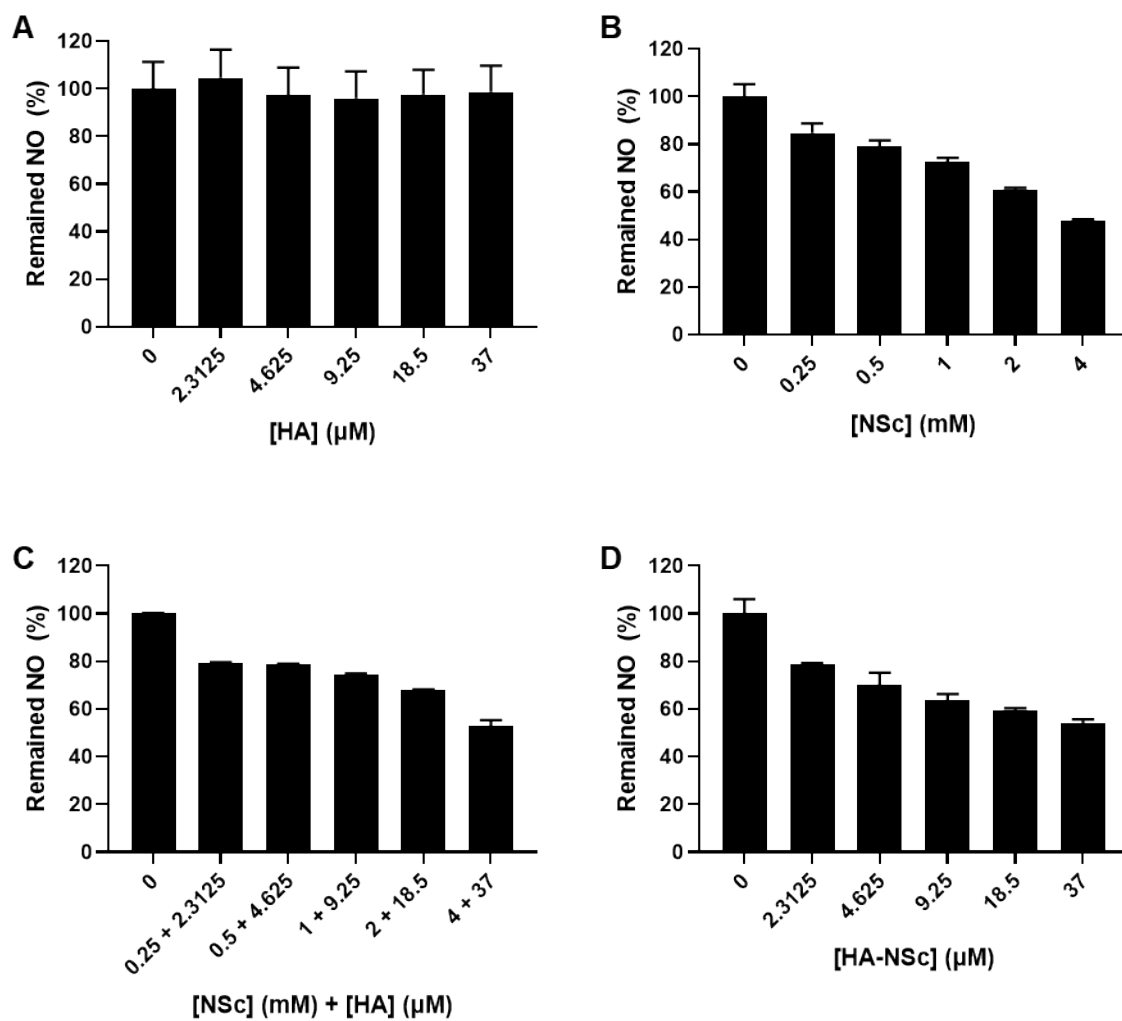




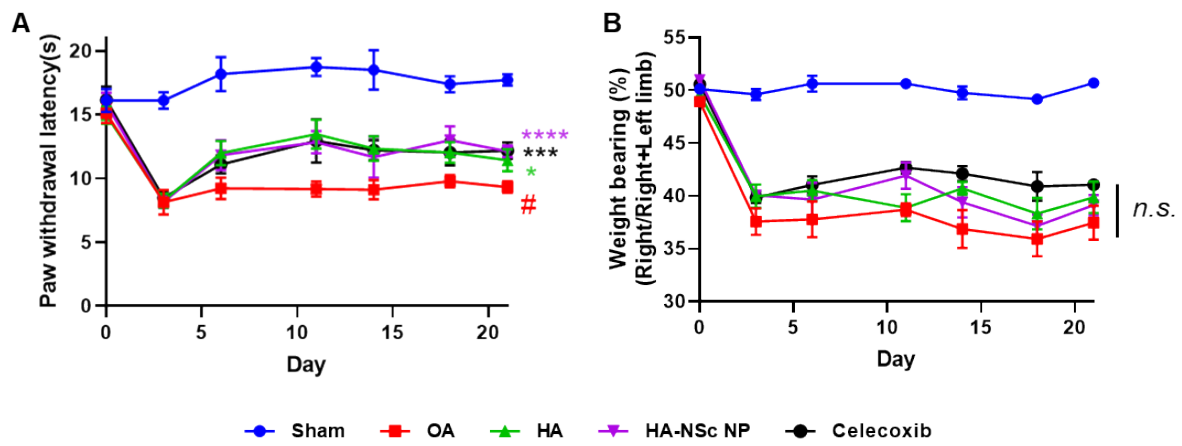
**Fig. S7** The decomposition of (A) HA and (B) HA-NSc conjugate was confirmed through GPC after incubation with NO solution of different concentrations for 24 h.



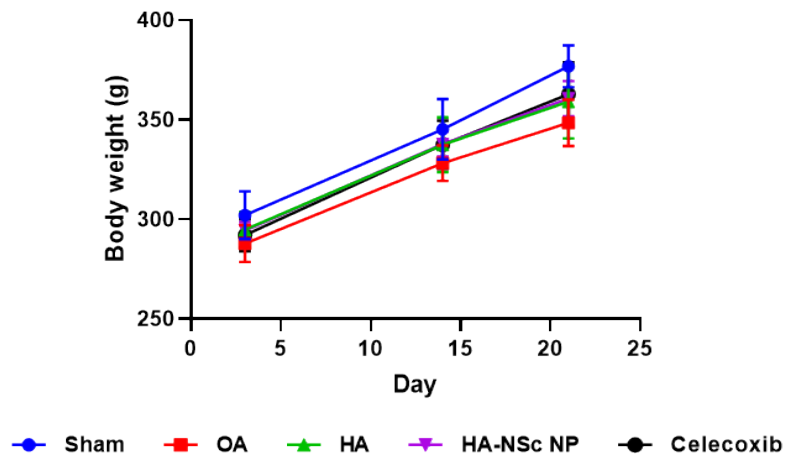
**Fig. S8** NO responsiveness of NSc and HA-NSc conjugate.  $^1\text{H}$  NMR spectra of (A) NSc and (B) HA-NSc conjugate before and after incubation with NO solution. UV-Vis absorption spectra of (C) Nsc and (D) HA-NSc conjugate before and after incubation with NO solution.



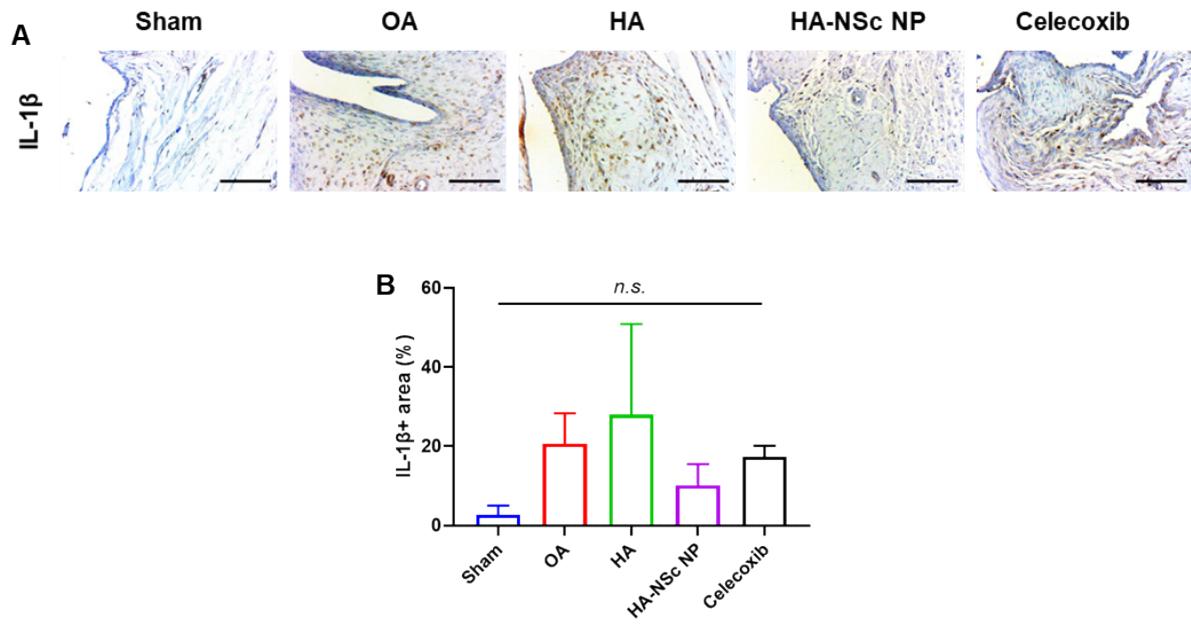
**Fig. S9** Confirmation of NO scavenging abilities of (A) HA, (B) NSc, (C) HA + NSc mixture and (D) HA-NSc conjugate according to their concentration ( $n = 5$ , mean  $\pm$  SD).



**Fig. S10** Measurement of therapeutic effect of HA-NSc NPs in MIA-induced OA rat model. (A) Paw withdrawal latency and (B) weight bearing measurements during monitoring period ( $n = 5$ , mean  $\pm$  SEM,  $*p < 0.05$ ,  $**p < 0.01$ ,  $***p < 0.001$ ).



**Fig. S11** Body weight measurements of each groups on Day 3, Day 14, and Day 21 after MIA injection ( $n = 5$ , mean  $\pm$  SD).



**Fig. S12** (A) Immunohistochemical staining images of IL-1 $\beta$  of isolated joints after monitoring (scale bar = 100  $\mu$ m) and (B) their quantitative analysis ( $n = 3$ , mean  $\pm$  SD).