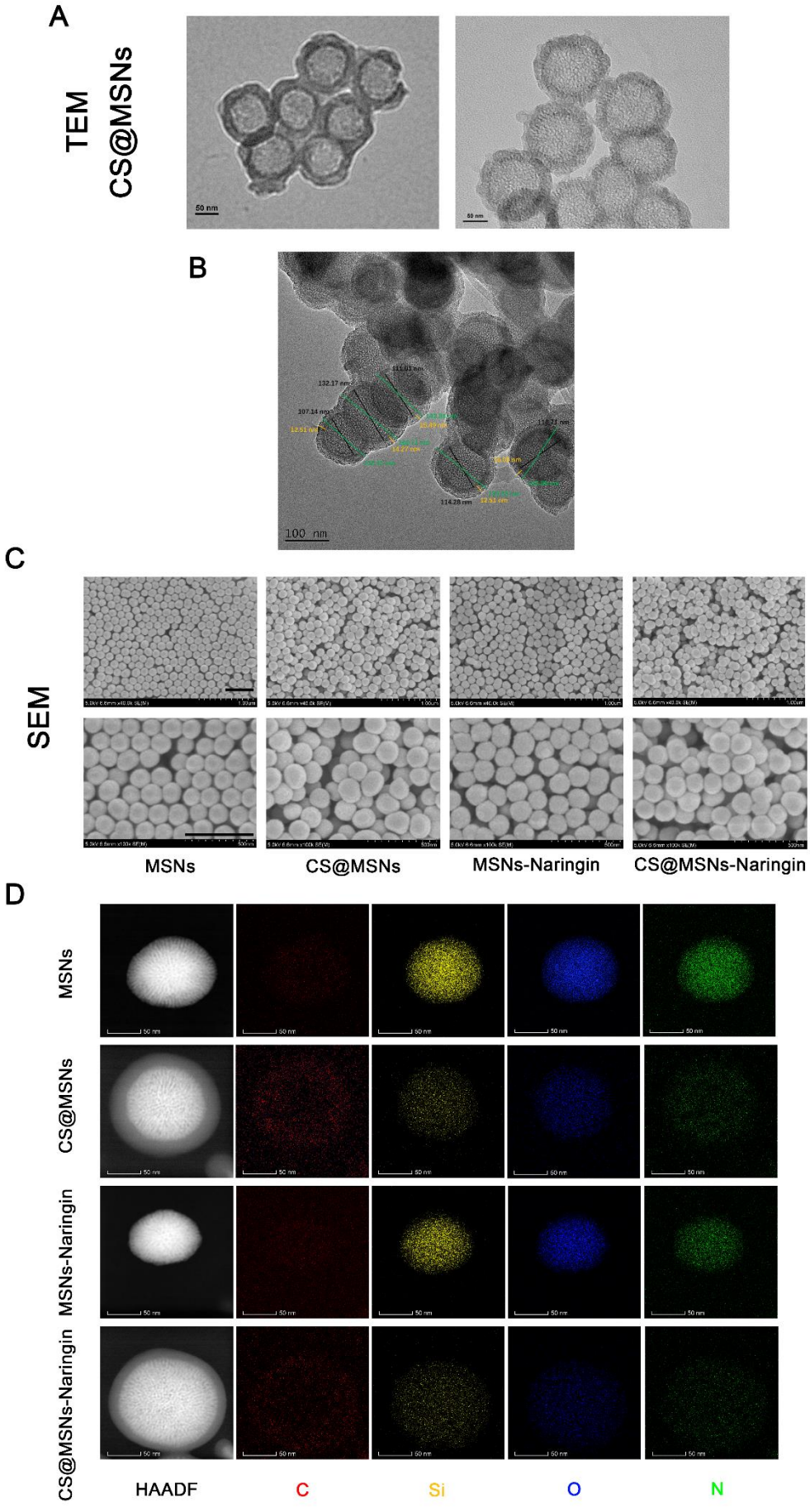
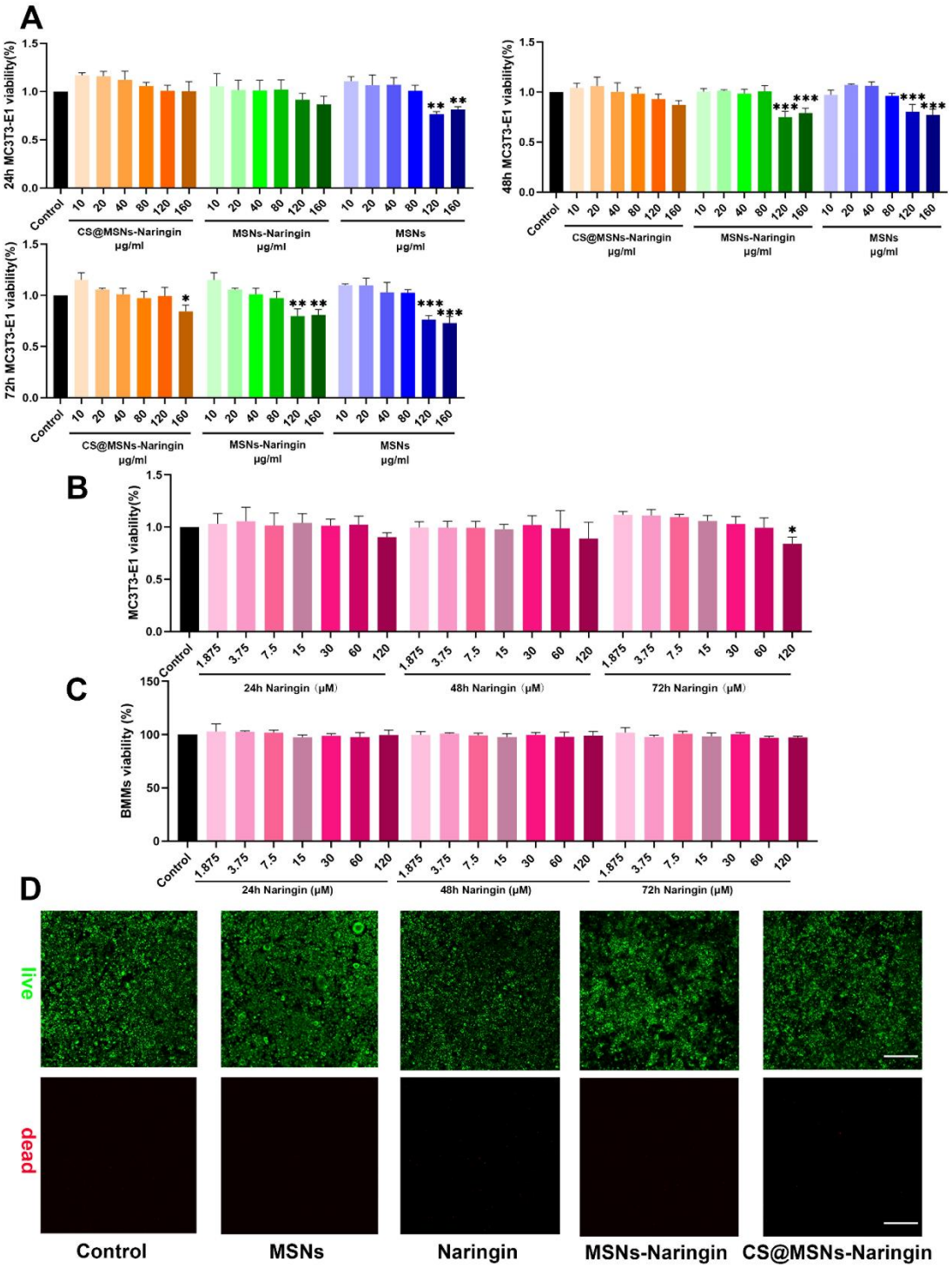
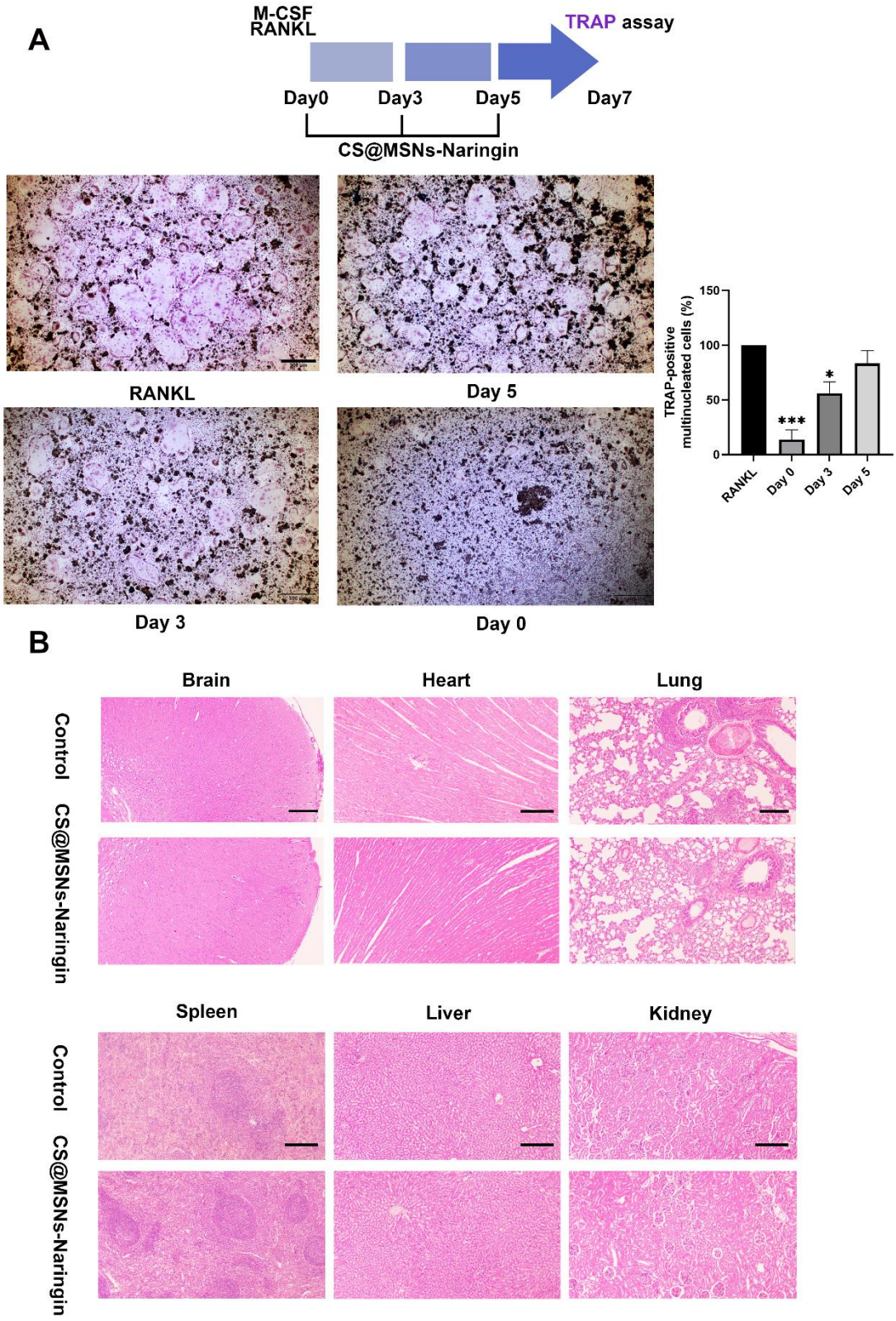

A
TEM
CS@MSNs
50 nm
50 nm
B
100 nm
C
SEM
MSNs
CS@MSNs
MSNs-Naringin
CS@MSNs-Naringin
D
MSNs
CS@MSNs
MSNs-Naringin
CS@MSNs-Naringin
HAADF
C
Si
O
N

Supplementary Figure 1. Complementary characteristic analysis of nanoparticles. **(A)** TEM of CS@MSNs. Scale bar = 50 nm. **(B)** Chitosan thickness measurement. The black line is the diameter of MSNs, the green line is the diameter of CS@MSNs-Naringin, and the yellow line is the thickness of chitosan. **(C)** SEM representative figures of different nanoparticles. Scale bar = 500 nm. **(D)** TEM-EDS of different nanoparticles. Scale bar = 50 nm.



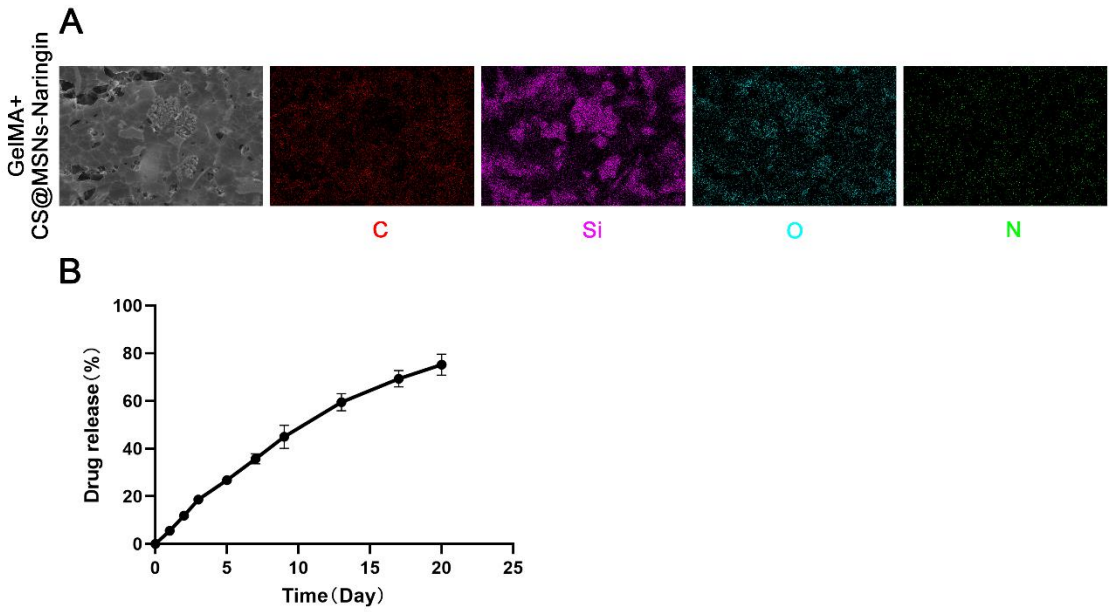
Supplementary Figure 2. Cytotoxicity of nanoparticles and naringin for the BMMs and MC3TC-E1. **(A)** Cytotoxicity of CS@MSNs-Naringin, MSNs-Naringin, and MSNs to MC3TC-E1 at 24, 48, 72h. **(B and C)** Cytotoxicity of Naringin to MC3TC-E1 and BMMs at 24, 48, 72h. *: $p<0.05$; **: $p<0.01$; ***: $p<0.001$ compared to the control group. **(D)** Results of dead/alive

staining of BMMs by naringin and different nanoparticles. Living cells are labeled green and dead cells are labeled red. Scale bar = 200 μm.



Supplementary Figure 3. The specific time period of CS@MSNs-Naringin inhibition of

osteoclast formation and in vivo biosafety. **(A)** BMMs were incubated with 50 ng/ml M-CSF and 100 ng/ml RANKL plus 80 μg/mL CS@MSNs-Naringin addition at the indicated time points (day 0, 3, or 5). Cells were fixed and TRAP staining was performed. Scale bar = 500 μm. *: $p<0.05$; ***: $p<0.001$ compared to the RANKL group. **(B)** HE staining of major metabolic organs in rats. Scale bar = 400 μm.



Supplementary Figure 4. Complementary characteristic analysis of GelMA. **(A)** TEM-EDS of GelMA+CS@MSNs-Naringin. **(B)** Cumulative release of naringin in GelMA+CS@MSNs-Naringin.

Supplementary Table 1 Real-time PCR primers

Genes	Forwad primer	Reverse primer
c-Fos	GTACTGTAGTCCTTCAGCGTCAATG	ATGTCGAAAGACCTCAGGGTAGAA
TRAP	GTCGGCTTCTTCTCCAATCAG	CTTATCCTCACAGCTTGTCCAG
Cathepsin K	GAGTTGACTTCCGCAATCCTTAC	CAGAAACTTGAACACCCACATCC
DC-STAMP	GCTGTGGACTATCTGCTGTATCG	ACACTGAGACGTGGTTTAGGAATG
NFATc1	CATCCTTGCCTGCCCTTGAC	GCTGCCTTCCGTCTCATAGTG
GAPDH	CCTACCCCCAATGTGTCCGTC	GTAGCCCAAGATGCCCTTCAGT