Supporting Information:

In Vitro and *In Vivo* Mechanism of Tumor Inhibition by Selenium-Doped Bone Mineral Nanoparticles

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Table S1. Average particle size, polydispersity index (PDI) and zeta potential of the synthesized nanoparticles.

Groups	Particle size (nm)	PDI	Zeta potential (mV)
HANs	71.02 ± 0.51	0.084	-37.40 ± 0.62
3%Se-HANs	77.47 ± 0.12	0.078	-37.90 ± 0.24
6%Se-HANs	79.89 ± 0.56	0.110	-38.43 ± 0.88
10%Se-HANs	78.55 ± 0.20	0.117	-37.13 ± 0.63

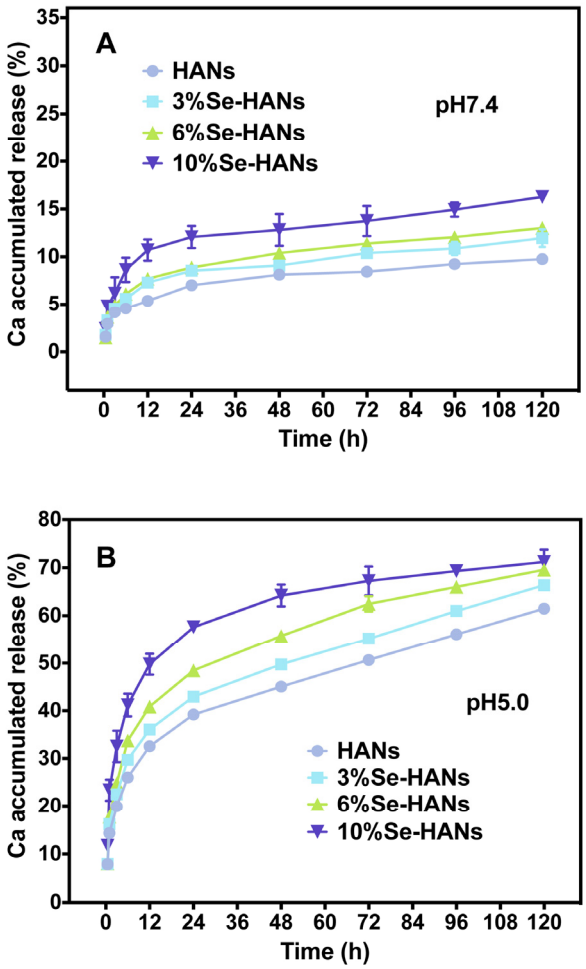

Figure S1. Accumulated release of Calcium in PBS of pH 5.0 or pH 7.4. Release of Ca^{2+} ions was highly associated with the degradation kinetics of as-prepared nanoparticles and was sensitively influenced by pH value. The results showed that nanoparticle degradation was greater in acidic condition of pH 5.0 than that in neutral condition of pH 7.4, and the degradation rate was significantly elevated with the increase of selenium content in different compounds.

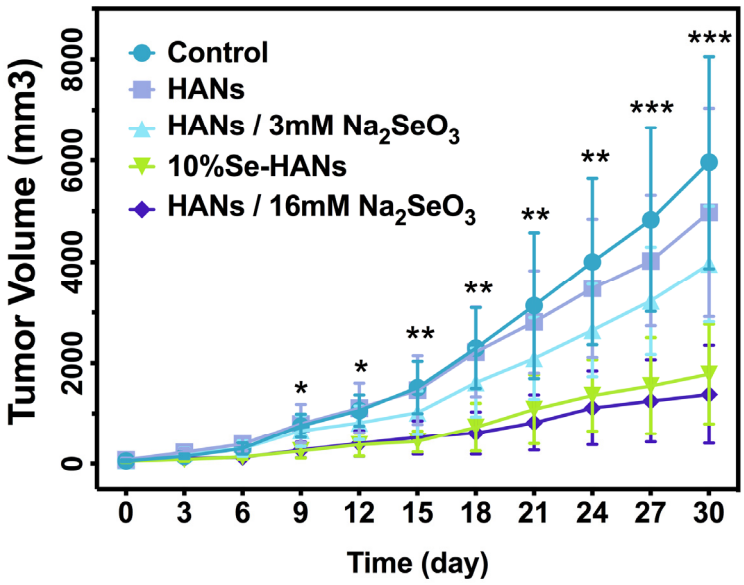

Figure S2. Time course of the growth in tumor volume. 10%Se-HANs group shows significant tumor growth inhibition from day 9 to day 30 (mean ± SD, n=6, *$p < 0.05$, **$p < 0.01$ and ***$p < 0.001$ compared to the control.)

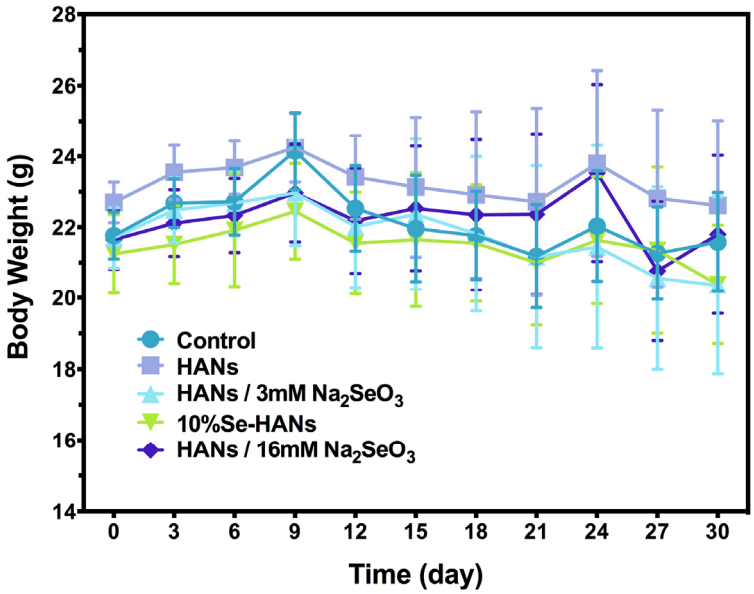

Figure S3. Body weight variety of nude mice bearing osteosarcoma through 30 days.

All mice survived to the experimental endpoint of day 30, and did not show significant difference in body weight.

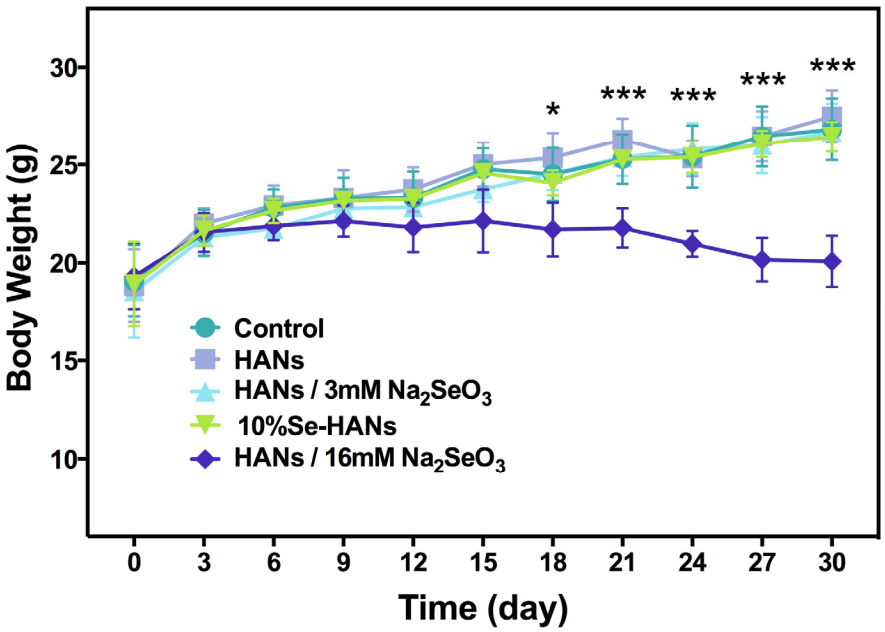

Figure S4. Body weight of normal BALB/c mice. All mice survived to the experimental endpoint of day 30. HANs/16 mM Na_2SeO_3 significantly inhibited ponderal growth after treatment for 18 days, and no significant difference was found between 10%Se-HANs and control (saline). (mean ± SD, n=6, *$p < 0.05$, ***$p < 0.001$, 10%Se-HANs compared to HANs/16 mM Na_2SeO_3)

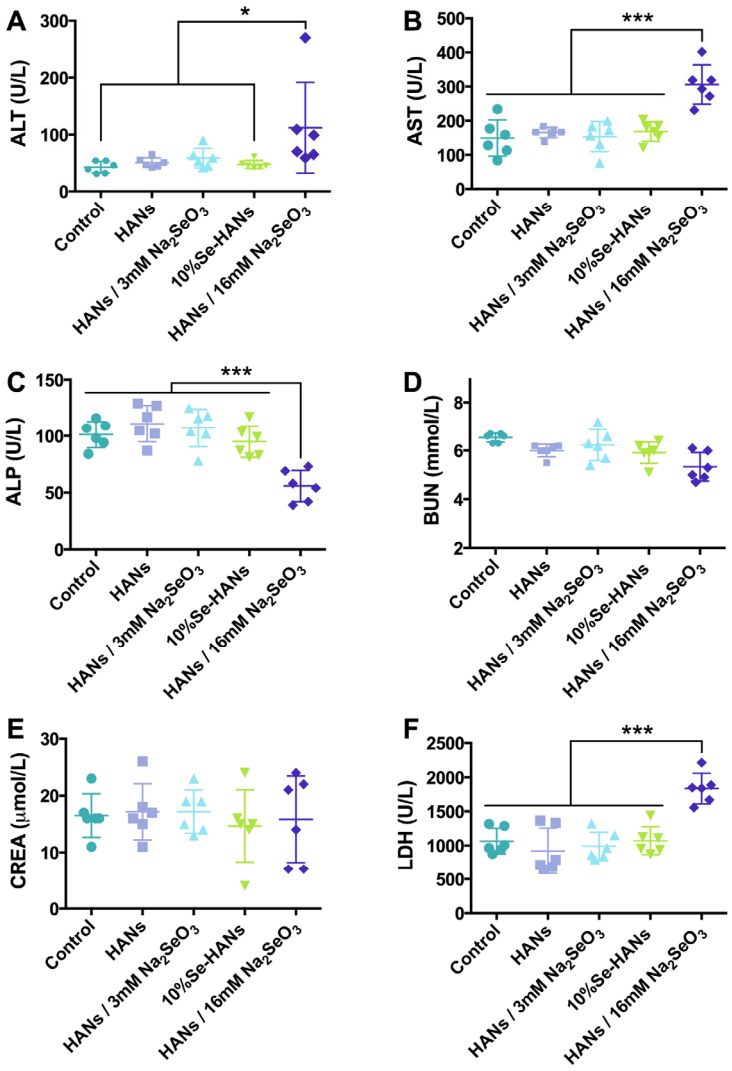

Figure S5. Blood biochemical analysis of normal BALB/c mice. 10%Se-HANs was nontoxic compared to the control (saline), while HANs/16 mM Na_2SeO_3 showed obvious systemic toxicity by significantly increasing the levels of AST, ALT, LDH and decreasing the level of ALP. (mean ± SD, n=6, *$p < 0.05$, ***$p < 0.001$)

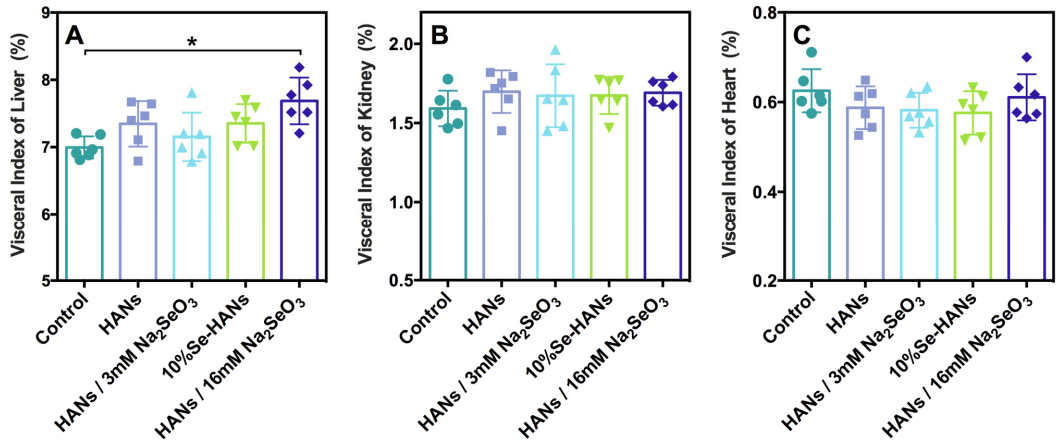

Figure S6. Visceral Index of normal BALB/c mice HANs/16 mM Na_2SeO_3 increased the visceral index of liver compared to the saline control, indicating the toxicity-induced hepatomegaly. 10%Se-HANs showed no noticeable effect on the visceral index. (mean ± SD, n=6, *$p < 0.05$)

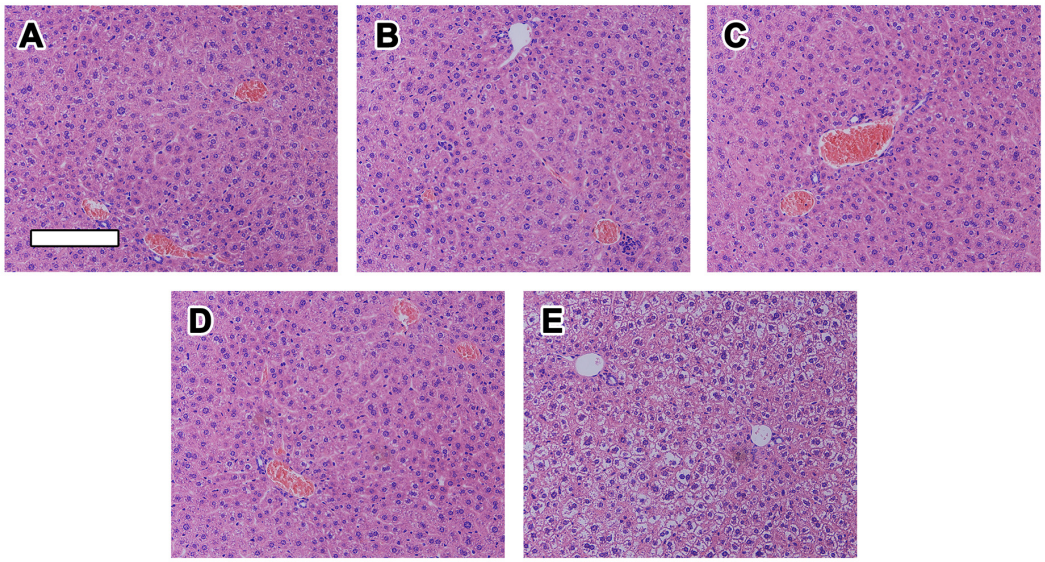

Figure S7. Histological analysis of liver tissues. Pathological changes of liver tissues showed obvious hepatic edema in mice treated with (E) HANs/16 mM Na_2SeO_3. However, (D) 10%Se-HANs showed no evident histological lesion compared to (A) saline control, (B) HANs and (C) HANs/3 mM Na_2SeO_3. Scale bar was 100 μm.

Experimental Section for Systemic Toxicity Evaluation of 10%Se-HANs

The *in vivo* systemic toxicity of 10%Se-HANs was individually studied without the interference of tumor malignancy in normal BALB/c mice (4-6 weeks). Animal proposal was approved by Institutional Animal Care and Use Committee (IACUC) of Huazhong University of Science and Technology. After three days, the mice were randomly divided into 5 groups (6 mice per group) including 10%Se-HANs (100 mg/mL 10%Se-HANs), HANs/16 mM sodium selenite (100 mg/mL HANs with 16 mM sodium selenite), HANs/3 mM sodium selenite (100 mg/mL HANs with 3 mM sodium selenite), HANs (100 mg/mL HANs) and the control (physiological saline). The mice were injected with 20 μL of test nanoparticles for each mouse at the left shoulder every other day, and weighted every three days. On day 30, 500 μL of blood was collected from tail vein for each mouse, and the blood serum was isolated for biochemical analysis of ALT, AST, ALP, BUN, Cr and LDH according to manufacturers' protocol (Nanjing Jiancheng Bioengineering Institute, China). Thereafter, all mice were euthanized and conducted with autopsy. The livers, hearts and kidneys were detached, weighted, and fixed with 10% neutral formalin. Visceral index of each mouse was calculated according to the following formula.

$$\text{Visceral index} = \text{organ weight} / \text{mice body weight} \times 100\%$$

Then the tissues were embedded with paraffin, sectioned at a thickness of 5 μm, mounted onto the slides and observed using Hematoxylin-eosin (HE) staining.