Supporting Information

Controlled *in situ* Synthesis of Surface Functionalized BaSO₄ Nanoparticles for Improved Bone Cement Reinforcement

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Experimental

Materials

K₂S₂O₈ (Aladdin, 99.5%), BaCl₂H₂O (Alfa Aesar, 99%), 2-(Methacryloyloxy) ethyl dimethyl-(3-sulfopropyl) ammonium hydroxide (MSAH) (Aldrich, 98%), KOH (Sinopharm, 98%), and benzoyl peroxide (BPO, Aladdin, 99%) were used as received. Methyl methacrylate (MMA) (Aladdin, 99%), Dimethyl-*beta*-propiothetin hydrochloride (DMPT) (Sinopharm, 98%), hydroquinone (HQ) (Aladdin) were distilled before use. Poly (methyl methacrylate) (PMMA) was purchased from Altuglas V045I. De-ionized water was used as solvent.

Synthesis of MSAH-coated BaSO₄ nanoparticles

MSAH solution was obtained by dissolving certain amount of MSAH in 50 mL de-ionized water. In a typical preparation procedure, 200 mL BaCl₂ aqueous solution (0.25 mol/L) were added into the aqueous solution of MSAH with stirring. Then 200 mL aqueous solution of K₂S₂O₈ (0.25 mol/L) were added into 50 mL aqueous solution of KOH (0.5 mol/L) with stirring. Thereafter, the K₂S₂O₈ solution was added drop wise into the BaCl₂ solution at 60 °C and with the steady drop rate of 4 mL/min with a stirring rate of 400 rpm. The molar ratio of MSAH/BaCl₂ was varied from 0 to 0.656. After the K₂S₂O₈ solution was totally added to the MSAH/BaCl₂ solution, the reaction was carried out at the same condition until the pH value of the solution reached around 7. The formed precipitates were separated from the solution by centrifugation, followed by washing with de-ionized water for three times, and dried at 60 °C in vacuum overnight. BaSO₄ nanoparticles without MSAH used in bore

cement were synthesized with the same method but burnt at 900 °C for 24 hours in air to remove the MSAH. μ m-sized BaSO₄ particles used in bone cement were prepared as following: certain amount BaCl₂ was dissolved in 200 mL de-ionized water (0.25 mol/L), followed by addition of Na₂SO₄ solution (0.25 mol/L) dropwise with a stirring rate of 400 rpm. The formed precipitates were separated from the solution by centrifugation, followed by washing with de-ionized water for three times, and dried at 60 °C in vacuum overnight.

Fabrication of PMMA-based bone cement

The experimental bone cements were formulated by adding the liquid component to the solid component at room temperature (25 °C) followed by hand mixing without vacuum evacuation. The solid component consisted of PMMA powder (79 wt. %), benzoyl peroxide (BPO) (1 wt. %) and the as-synthesized BaSO₄ nanoparticles (20 wt. %). The liquid component consisted of MMA (as the base monomer) (99.9 wt. %), DMPT (accelerator) (0.05 wt. %) and HQ (inhibitor) (0.05 wt. %). A mass ratio of the solid component to the liquid component was kept at 1.2 in all bone cement samples.

Characterization

The size and morphology of the BaSO₄ nanoparticles were characterized using a S4800 Scanning Electron Microscope (SEM, Tokyo, Japan) at an accelerating voltage of 15.0 kV. The sample powder was put on a conductive tape and sputtered with gold before imaging. The presence of MSAH layer was determined by Transmission Electron Microscopy (TEM). A drop of aqueous suspension containing the MSAH-coated BaSO₄ nanoparticles was cast on a copper grid and measured with

an FEI Tecnai F20 instrument (TEM, Oregon, USA) with 200 kV field emission gun. The average size of the BaSO₄ nanoparticles was measured by Dynamic Light Scattering (DLS, Zetasizer Nano 2S, Malvern, UK). The as-synthesized BaSO₄ powder (0.1 mg/ml) was dispersed in de-ionized water using ultrasonic liquid processor (Scientz-IID, China, 325 W, 15 minutes). Before measurement started, the sample solution was kept still for 120 seconds. For each sample, at least two sample solutions were prepared and measured. For each test, three parallel measurements were conducted. The standard deviation of the average size was calculated based on the total data points collected. The pH of the solution was measured by a pH-meter (pHS-3c). The crystallographic phase of the BaSO₄ nanoparticles was investigated by X-ray diffraction (XRD) (Bruker AXS D8 Advance, λ =1.541 Å, 2.2 kW) with 20 ranged from 20 $^{\circ}$ to 70 $^{\circ}$. The presence of MSAH on the surface of the BaSO₄ nanoparticles was studied by Fourier-transform infrared (FT-IR). Solid powder KBr pellets were prepared and the spectra were recorded on Thermo Nicolet 6700 spectrometer (Madison, America) with the wavenumber ranging from 4000 cm⁻¹ to 400 cm⁻¹. The spectrum of each sample was an average of 32 scans with 4 cm⁻¹ resolution. The content of MSAH was quantitatively determined by thermo gravimetric analyzer (TGA, Mettler Toledo, Switzerland) with the temperature from 50 to 900 °C at 20 °C/min ramp rate. Cuboid bone cement samples (approximately 75 mm * 10 mm * 3.3 mm) were prepared and tested in bending mode using Instron 5567 mechanical testing machine (Instron, Boston, USA). With reference to the standard protocol of ISO5833:2002, five samples were tested for each set (n=5). A

crosshead speed of 5.0 mm/min was used. Cylindrical $BaSO_4$ samples (approximately 6 mm in diameter and 12 mm long) were prepared and tested in unconfined compressive mode using Instron 5567 mechanical testing machine. Five samples were tested for each set (n=5). A crosshead speed of 20.0 mm/min was used. The compression limit was set as 90% strain to protect the load cell.



Figure S1. Representative DLS profiles of the MSAH-coated BaSO₄ nanoparticles (three parallel measurements, synthesized with the MSAH/BaCl₂ molar ratio of 0.164).



Figure S2. XRD of the MSAH-coated $BaSO_4$ nanoparticles synthesized with the MSAH/BaCl₂ molar ratio of 0.082. All of the peaks can be indexed as orthorhombic crystallographic phase according to JCPDS No.80-0512.



Figure S3. FTIR spectra of the BaSO₄ nanoparticles without (red) and with (black) MSAH coating (4.2 % by mass determined by TGA). The profile of the MSAH-coated BaSO₄ nanoparticles shows absorption peaks at 873 cm⁻¹ (v (C-H)), 1370 cm⁻¹ – 1385 cm⁻¹ (v (CH₃)) and 1630 cm⁻¹ (δ (C=C)), which confirms the presence of MSAH on the surface of the BaSO₄ nanoparticles.



Figure S4. TEM image of the MSAH-coated BaSO₄ nanoparticles prepared with the MSAH/BaCl₂ molar ratio of 0.328. The gray area marked by arrows indicates the MSAH coating layer surrounding the BaSO₄ nanoparticles.



Figure S5. pH change of the solution with increasing reaction time at the reaction temperature of 60 °C.

$$(y-y_0)^{\chi} = K(x-x_0)$$

Figure S6. Equation used for fitting the size change of the MSAH-coated BaSO₄ nanoparticle with increasing reaction time. $y_0 = 26.95$, $x_0 = 10$, $\chi = -0.3785$, K = 21.6.



Figure S7. SEM image of the μ m-sized bare BaSO₄ particles.



Figure S8. Bending modulus (a) and compressive modulus (b) of the bone cements prepared with different types of BaSO₄ nanoparticles. Blue column (sample S0): μ m-sized bare BaSO₄ particles; black column: MSAH-coated BaSO₄ nanoparticles; red column: bare BaSO₄ nanoparticles. Sample S1 – sample S4: BaSO₄ nanoparticles synthesized with the MSAH/BaCl₂ molar ratios of 0, 0.041, 0.082, 0.164, and 0.328.