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Effect of physical and chemical characteristics on the washout resistance of calcium sulfate pellets

Pei-Yi Hsu[a], Man-Ping Chang[a], Wei-Hsing Tuan[a,*], Po-Liang Lai[b,*]

[a] Department of Materials Science and Engineering, National Taiwan University, Taipei 106, Taiwan
[b] Department of Orthopedic Surgery, Bone and Joint Research Center, Chang Gung Memorial Hospital at Linkou, College of Medicine, Chang Gung University, Taoyuan 333, Taiwan

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ABSTRACT

The washout resistance of bone substitute in body fluid is essential for its medical application. In the present study, the effect of physical and chemical characteristics of calcium sulfate pellets on the washout resistance is investigated. Special attention is paid to the effect of crystalline structure. A calcium sulfate hemihydrate powder was used as the starting material, then heated to a temperature up to 1225 °C. Using a synchrotron X-ray diffractometer, the phase evolution from hemihydrate to anhydrite is characterized. The washout resistance of hemihydrate is very poor under the attack of a large amount of simulated body fluid (SBF). The anhydrite can be categorized into III, II and I; the resistance of anhydrite III is also poor. Nevertheless, the anhydrite II shows an excellent resistance to washout. Furthermore, the preosteoblast MC3T3-E1 cells can attach and proliferate on the surface of anhydrite II pellet. The washout resistance of anhydrite I is poor for the formation of microcracks.

1. Introduction

Synthetic bone substitute has received a lot of attention with increasing orthopedic application, such as traumatic bone defect, bone tumor reconstruction, arthroplasty and spinal fusion [1]. The bone substitute can be generally divided into two groups, one group is degradable and the other is non-degradable. For the degradable bioceramic, it has to exhibit the ability of resisting the attack of a large amount of physiological solution. To take the case of bone cancer as the example, the scenario for the use of degradable ceramics is as following. The bone cancer mass is first removed from the host; a large amount of physiological saline is used to wash and clean the surgical site. The osteoconductive and degradable bioceramics as well as supplementary osteoinductive growth factors are then implanted into the void that left behind by the tumor [2]. The muscle fasciae are sutured to secure the bone graft in place. The bone substitute is not allowed to dis-integrate at this stage. Therefore, the resistance of the degradable bioceramic to the washing of a large amount of tissue fluid is a must. Such resistance is also termed as washout resistance.

Two degradable bioceramics are available from the market, tricalcium phosphates and calcium sulfates. Though calcium sulfate hemihydrate, frequently referred as the plaster of Paris, has been used as bone substitute for more than 100 years [3], and its popularity has suffered from its fast degradation rate [4]. Un-expected dis-integration during operation has also been found on occasion. Based on the amount of crystallized water, calcium sulfate exhibits three chemical forms, dihydrate, hemihydrate and anhydrite [5]. There are two forms for calcium sulfate hemihydrate, α– and β– forms; three forms for calcium sulfate anhydrite: III, II and I. Nevertheless, the phase identification on these forms is challenging. Though α-hemihydrate and β-hemihydrate exhibit significantly difference on their reactivity to water [5]; their crystalline structure is very similar. Through the use of X-ray diffraction (XRD), ^{1}H nuclear magnetic resonance (NMR) and infrared spectra (IR) techniques, the difference between the α- and β-hemihydrate is negligible [6]. Though the medical application is using hemihydrate mainly, recent studies indicated that the degradation rate of anhydrite was slower than that of hemihydrate [7,8]. To the best knowledge of the present authors, no detailed investigation has been conducted on the structure of anhydrite I, II and III. Furthermore, the effect of crystal structure on the degradation behavior was not examined either.

The degradation behavior of degradable bioceramics is a complicate issue. It depends on the chemical and physical characteristics of bioceramics. Copious body tissue fluid usually exists in the bone void after orthopedic surgery due to local inflammation. The impact of body tissue fluid on the chemical and physical properties of calcium sulfates remains unknown. In the present study, the effect of physical characteristics of calcium sulfate on the degradation behavior is investigated; its biocompatibility with preosteoblast cells is also

* Corresponding authors.
E-mail addresses: tuan@ntu.edu.tw (W.-H. Tuan), polianglai@gmail.com (P.-L. Lai).

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evaluated. Extra attention is paid to the washout resistance to a large amount of simulated body fluid (SBF).

2. Experimental procedures

A calcium sulfate hemihydrate powder (CSH, $CaSO_4{\cdot}0.5H_2O$, Avantor Performance Materials, LLC, PA, USA) was used as the starting material in the present study. The process started with the milling of the powder in ethanol for 24 h. The milling media was zirconia balls with diameter of 10 mm. After milling, the slurry was dried in a rotary evaporator, then in an oven at 90 °C for 12 h. Dried powder cake was crushed with an agate mortar, then sieved through a #150 plastic mesh. The green discs were formed using die-pressing technique under a uniaxial pressure of 28 MPa. The dimensions of the discs were 13.1 mm in diameter and 2.5 mm in height. The heat treatment was carried out in a box furnace at 200–1225 °C for 1 h. The heating and cooling rates were 3 °C/min. The weight change of heated disc before and after heat treatment was monitored. At least 10 discs were prepared for each heat treatment condition.

The crystalline structure of the discs was characterized with X-ray powder diffraction (XRD) technique. The X-ray source was generated from a synchrotron beam line (BL-12B2, National Synchrotron Radiation Research Center, Hsin-Chu, Taiwan) at 18 KeV. The scanning angle (2θ) varied from 10° to 80°. Microstructure observation was carried out using a scanning electron microscope (SEM, JEOL 6510, Japan).

The resistance of the calcium sulfate discs to physiological solution was evaluated. The test was conducted by soaking the discs in a plastic dish containing simulated body fluid (SBF; phosphoric buffered saline, NaCl 8000 mg/L; KCl 200 mg/L; KH_2PO_4 200 mg/L; Na_2HPO_4 2160 mg/L, Sigma-Aldrich Co., USA). The weight of the calcium sulfate discs was fixed at 2.5 g; the volume of SBF was 25 ml. The dish was vibrated horizontally at a frequency of 12 Hz in a chamber. The temperature in the chamber was 37 °C. The morphology of the discs was monitored during the test.

The biocompatibility and cell attachment of pre-osteoblast cells, MC3T3-E1, to the specimen was evaluated. The disc was heat treated at 1100 °C for 1 h. Firstly, the discs were immersed in α-minimum essential medium (α-MEM, Gibco, Life Technologies, USA) for 3 days. Secondly, the medium was removed and the discs were placed into a 24-well plate. Then 10^4 cells were loaded onto each disc. Finally, α-MEM was added for culturing in an incubator humidified with 95% air and 5% CO_2 at 37 °C for 72 h. To examine cell morphology, the cultured discs were fixed in a mixed solution of 3% glutaraldehyde and dehydrated through a series of ethanol solution (30%, 50%, 70% and 95%). The discs were vacuum-dried overnight, coated with platinum–palladium sputtering, and examined with a scanning electron microscope (Hitachi, S-5000, Japan).

3. Results

The morphology of the starting calcium sulfate hemihydrate powder is shown in Fig. 1. The shape of the calcium sulfate particles is angular; their size distribution shows a bimodal style. After pressing the hemihydrate powder into cylindrical disc, the specimens were heat treated at various temperatures. Fig. 2 shows the weight loss after heating the disc at the indicated temperatures for 1 h. A weight loss of ~ 1% is noted after heating to 200 °C. The weight loss increases rapidly in the temperature range from 200 °C to 400 °C; then increases slightly in the temperature interval from 400 °C to 600 °C. The weight loss remains unchanged after heating from 700 °C to 1050 °C. The weight loss increases its value again in the temperature interval from 1050 °C to 1180 °C. The weight loss drops above 1180 °C.

Fig. 3 shows the XRD patterns for the calcium sulfate discs after heat treatment from 200 °C to 1200 °C. The XRD pattern for the starting powder is also shown. The major phase for the starting powder is

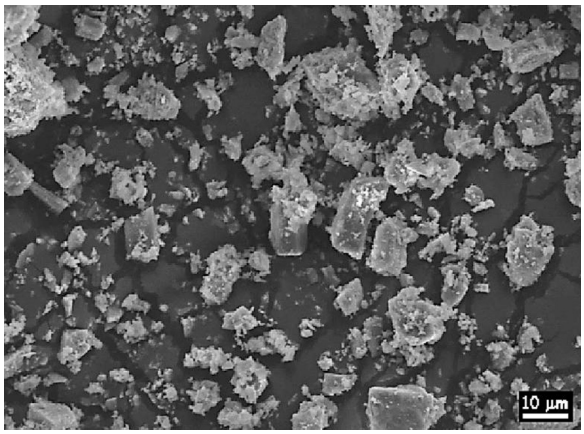

Fig. 1. Morphology of the starting calcium sulfate hemihydrate powder used in the present study.

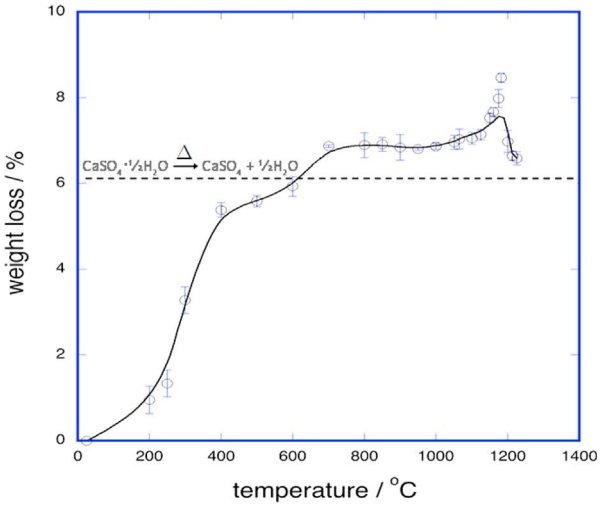

Fig. 2. Weight loss of the calcium sulfate discs after heating at the indicated temperatures for 1 h. The theoretical weight loss for the change from hemihydrate to anhydrite is also shown.

calcium sulfate hemihydrate (CSH); the minor one is calcium sulfate dihydrate (CSD). After heating to 200 °C, the amount of dihydrate is decreased. No dihydrate is found after heating to 400 °C. Only a minor residual hemihydrate is found. As the heat treating temperature is higher than 500 °C, anhydrite is the only phase detected.

The density of the disc after heat treatment is shown in Fig. 4. The green density of the discs is 1.6 g/cm^3. The density remains the same in the temperature interval from 200 °C to 300 °C; then increases slightly in the temperature range from 400 °C to 700 °C, then jumps to a value above 2.7 g/cm^3 after heating to 950 °C. Since the anhydrite is the only phase detected, Fig. 3, the relative density can be estimated. For the disc heated at 1100 °C, the relative density is about 96%. A density drop is then noted after heating above 1200 °C.

Fig. 5 shows the fracture surfaces of the calcium sulfate discs after heating to various temperatures. The size of calcium sulfate grains is much larger than that of the starting particles. Furthermore, the calcium sulfate grains are no longer angular after the heat treatment. The calcium sulfate grains with a size larger than 40 μm are observed in the disc heated at 1100 °C. The grains in the disc heated at 1200 °C are even larger. It is of interest to note that many cracks and pores are found within the grains.

In order to estimate the washout resistance, the heated cylindrical disc is soaked into the SBF. The integrity of the disc is taken as the index for washout resistance, as demonstrate in Fig. 6. The disc is fully