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Addition of a small amount of glass to improve the degradation behavior of calcium sulfate bioceramic

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Abstract

Calcium sulfate is a degradable bioceramic; its pellets have been used as bone void fillers for more than 100 years. However, the use of calcium sulfate bioceramic as a bone graft substitute is limited by its low strength and rapid degradation rate. In the present study, a small amount of glass (1 wt%) is incorporated into calcium sulfate powder. Dense glass-doped calcium sulfate pellets are prepared by sintering at 900 °C for 1 h. Though the amount of glass is low, the compressive strength of the pellets is enhanced by 40%; the degradation rate is reduced by nearly an order of magnitude.

Keywords: A. Sintering; B. Microstructure-final; C. Strength; E. Biomedical applications

1. Introduction

Four types of bone grafts are available: autografts, allografts, xenografts, and synthetic bone grafts [1]. Since nothing is better for grafting than the patient's own bone, an autograft is the most suitable bone graft for a transplant operation. However, there are many disadvantages of using an autograft, including limited supply, donor site morbidity and so forth. As for allograft and xenograft, the possibility of disease transmission and quality variation have limited their use [1,2]. Various synthetic bone graft substitutes have thus been developed. Though the use of bone grafts to repair bone defects is well accepted in clinical applications nowadays, many improvements are still needed. The development of new bone grafts has therefore attracted a great deal of attention.

The use of synthetic bone grafts should facilitate osteogenesis and prevent fibrous scar tissue at bone defect sites. To achieve this goal, the best scenario involves the degradation of the bone graft and the substitution of new bone tissue at the location of implantation. Since the new bone is similar to the patient's existing bone tissue, its proper function is assured. Calcium sulfate ($CaSO_4$, or CS) exhibits excellent biocompatibility; its pellets were used as bone void fillers as early as 1892 [3]. However, previous studies have indicated that the biodegradation of CS pellets is much faster than the growth rate of new bone [4,5]. The CS pellets collapse within days after their implantation; they thus fail to provide sufficient support for the newly forming bone. Reducing the degradation rate of CS pellets is thus important to their use as bone graft substitutes.

Several approaches have been adopted to reduce the degradation rate of CS. One approach involves the addition of hydroxyapatite (HAp) particles [6–8]. The incorporation of HAp particles induces the formation of calcium phosphate layer on the surface during degradation. Nevertheless, while the degradation rate of the CS pellets decreases, the compressive strength of the pellets decreases as well. The strength decrease of CS–HAp composite could be solved through the addition of silica particles at the nanometer scale [5]. However, the risks of using nanoparticles within the human body are not yet well understood. An alternative is needed to reduce the degradation rate of CS pellets.

The strength of ceramics depends strongly on the quantity of pores [9]. For example, the compressive strength of a CS pellet

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is increased by reducing its surface porosity [10]. Due to the unique self-setting characteristics of CS, the pellets can be prepared through mixing with water. The self-setting process at room temperature is straightforward; thus, little attention has been given to the sintering of CS pellets. In fact, sintering is one of the most popular techniques to reduce porosity in ceramics. Common practice for sintering involves the use of high temperatures and the addition of small amounts of sintering aids. The major function of sintering aids is the enhancement of densification and the retardation of grain growth [11]. Kuo et al. demonstrated that the sintering technique was helpful in increasing the density of CS pellets [12]. A value of 90% was reported for the relative density of the pellets after sintering at 1100 °C. The addition of several sintering aids, $NaHCO_3$, CaO, P_2O_5 and SiO_2, further enhanced the densification. The result was a higher compressive strength for the sintered CS pellets. More importantly, the degradation rate was reduced [12]. The sintered CS pellets with sintering additives exhibited low cytotoxicity [12]. Nevertheless, the sintering additives formed fine particles between the CS grains. The size of these particles is in the range of tens of nanometers. They may be released into their surroundings along with the resorption of CS grains. The release of such nano-sized particles may induce inflammatory reactions in host tissues [13]; the alternative, to improve the densification and reduce the degradation rate of CS pellets, is thus of interest.

In the present study, instead of ceramic particles, two glasses are used as sintering additives. These glasses are prepared through conventional melting processes. They are then incorporated into CS pellets to improve their sintering. The amount of glass added is low: 1 wt%. The degradation behavior and strength of the glass-doped CS pellets are then evaluated.

2. Experimental procedures

The glass powders were prepared by melting silicon dioxide (SiO_2, Ceramet Co., Taiwan), phosphorus pentoxide (P_2O_5, Acros Organics, USA), calcium oxide (CaO, Acros Organics, USA) and sodium hydrogen carbonate ($NaHCO_3$, Nacalai Tesque Inc., Japan) powders at 1600 °C. The starting composition of the two glasses is listed in Table 1. The glass melt was quenched in water, followed by ball milling in ethanol for 4 h. The milling medium was zirconia balls.

Reagent-grade calcium sulfate hemihydrate powder ($CaSO_4 \cdot 1/2H_2O$, J. T. Baker Co., New Jersey, USA) was ball-milled with 1 wt% glass powder in ethanol for 4 h. The slurry was dried in a rotary evaporator to remove the ethanol, and then sieved through a #150 plastic mesh. The mixed powders were consolidated into pellets 10 mm in diameter and 3.3 mm in thickness under a uniaxial pressure of 25 MPa. The glass-doped CS pellets were prepared by sintering at 900 °C for 1 h (unless otherwise stated below). The heating and cooling rates were 3 °C/min. Pellets composed of glass only or of CS only were also prepared with the same firing profile, except the pure CS pellets were sintered at 1100 °C for 1 h.

After sintering, the composition of the sintered pellets was analyzed using electron-probe micro-analyzer (EPMA; JXA-8200, JEOL Co., Japan) and energy-dispersive spectroscopy (EDS, EDAX Co., NJ, USA). The phase analysis was carried out using X-ray diffractometry (XRD; Rigaku Co., Tokyo, Japan) at 50 kV and 22 mA at a scanning rate of 3°2θ/min. The microstructure was observed using scanning electron microscopy (SEM; JSM6510, JEOL Co., Tokyo, Japan). Transmission electron microscopy (TEM; FEI Tecnai G^2 F20, Philips Co., Oregon, USA) was also used to characterize the microstructure. The TEM foil was prepared using an environmental dual-beam focused-ion-beam system (FIB; FEI Helios 600i, Philips Co., Oregon, USA). The accelerating voltage of the ions was 0.5–30 kV. After FIB thinning, the thickness of foil was less than 100 nm. The chemical analysis near the grain boundary was conducted using X-ray energy-dispersive spectroscopy (XEDS; EDAX Inc., New Jersey, USA).

The compressive strength of pellets with a diameter-to-height ratio of 1:1 was measured using a universal testing machine (MTS 810, MTS Co., USA). The displacement rate was 0.16 mm/s. Five specimens were used to calculate the average value and its standard deviation. For the measurement of degradation rate, the pellets were soaked in Hank's solution (H9269, Sigma Co., Missouri, USA) in test tubes. The test tubes were placed in a water bath at 37 °C and shaken at a speed of 60 rpm. Table 2 shows the composition of the Hank's solution. Five pellets were used for each test. The ratio of pellets to Hank's solution was kept at 1 g to 10 mL. The Hank's solution was replaced with fresh solution every 24 h. The weight loss of the pellets and the pH value of the solution were monitored daily. The pH value of the Hank's solution without pellets was also measured daily for comparison purposes. After soaking the pellets, the concentration of silicon and calcium ions in the solution was measured with inductive coupled plasma mass spectroscopy (ICP–MS; SCIEX ELAN 5000, Perkin Elmer, USA).

3. Results

3.1. Characteristics of glasses

Fig. 1 shows the morphology of the glass powders. The size of the glass particles varies from 1 μm to 50 μm, a relatively

Table 1
Starting composition for the glasses prepared in the present study.

	SiO_2 (wt%)	P_2O_5 (wt%)	CaO (wt%)	$NaHCO_3$ (wt%)
Glass-1	56.0	11.0	21.0	12.0
Glass-2	31.7	4.2	17.3	46.8