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Aligned porous barium titanate/hydroxyapatite composites with high piezoelectric coefficients for bone tissue engineering

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ABSTRACT

It was proposed that the piezoelectric effect played an important physiological role in bone growth, remodelling and fracture healing. An aligned porous piezoelectric composite scaffold was fabricated by freeze casting hydroxyapatite/barium titanate (HA/BT) suspensions. The highest compressive strength and lowest porosity of 14.5 MPa and 57.4% with the best parallelism of the pore channels were achieved in the HA10/BT90 composite. HA30/BT70 and HA10/BT90 composites exhibited piezoelectric coefficient d_{33} of 1.2 and 2.8 pC/N, respectively, both of which were higher than the piezoelectric coefficient of natural bone. Increase of the solid loading of the suspension and solidification velocity led to the improvement of piezoelectric coefficient d_{33}. Meanwhile, double-templates resulted in the coexistence of lamellar pores and aligned macro-pores, exhibiting the ability to produce an oriented long-range ordered architecture. The manipulation flexibility of this method indicated the potential for customized needs in the application of bone substitute. An MTT assay indicated that the obtained scaffolds had no cytotoxic effects on L929 cells.

1. Introduction

In 1960s, Fukada et al. [1] observed that the stress-induced piezoelectric effect in bone was due to the slipping of collagen fibres past one another. The bone tissue exhibited a very low piezoelectric coefficient of 0.7 pC/N [2] and was demonstrated to be biologically active and would respond to micromechanical stress such as the movement of the body itself, leading to the generation of an electrical dipole [3]. The calcium (Ca^{2+}) and phosphate (PO_4^{3-}) ions in the body fluid can be attracted to the electrical dipole with an opposite electric charge [4], which can stimulate bone growth and enhance the integration of the implant material with the host bone, resulting in the development of callus in living bone. It is therefore of great interest to examine the electromechanical behaviour of potential bone substitute materials for improving the implant performance.

Due to the environment and biocompatibility concerns, many efforts were made to improve the bone healing response by using lead free piezoelectric ceramics, such as $(Li_{0.06}Na_{0.5}K_{0.44})NbO_3$ (LNKN) [5], potassium sodium niobate (KNN) [6] and barium titanate [7]. Barium titanate ($BaTiO_3$, BT) is the most studied lead-free material used in the bone replacement and repair for more than 30 years [7]. It exhibits excellent biocompatibility [7], and ability to form a strong interfacial strength with bone [8]. More importantly, its piezoelectric property could be used as a charge supply to stimulate the bone implant healing process, which was similar to the phenomenon of stress generated potentials of collagen molecule in the bone. So far, all the piezoelectric ceramics used in vivo and vitro were in the dense bulk form [9]. However, owing to the interconnected pores to provide a favourable environment for bone ingrowth and osseointegration [10], a functional bone implant should be in a porous form, which was greatly favourable to the healing process in the bone replacement and substitute.

Recently directional freeze casting, also known as ice-templating process, was demonstrated as a new way for the fabrication of a porous ceramic with aligned lamellar architectures, which were formed as a replica of the ice crystals preferentially growing during unidirectional freeze [11,12]. For the purpose of utilizing the piezoelectric effect in bone applications, a stronger bone interface would be induced in HA/piezoelectric composites than pure piezoelectric ceramics. To our best of knowledge, there is no report so far on the piezoelectric properties of aligned porous piezoelectric ceramics for bone replacement and repair. In this study, porous HA/BT composites were obtained by the ice-templating method. In order to provide the thorough information and find the most useful combination of the different properties used for in vitro study, the morphologies, porosities, piezoelectric and mechanical properties were investigated according to the processing parameters, i.e. HA/BT contents in volume fraction, solid loadings of the suspensions, cooling rates and packing densities of fibres.

2. Material and methods

HA powder with the median grain size $d_{50} = 1$ μm and a purity of 99% (according to the manufacturer's data, Nanjing Emperor Nano

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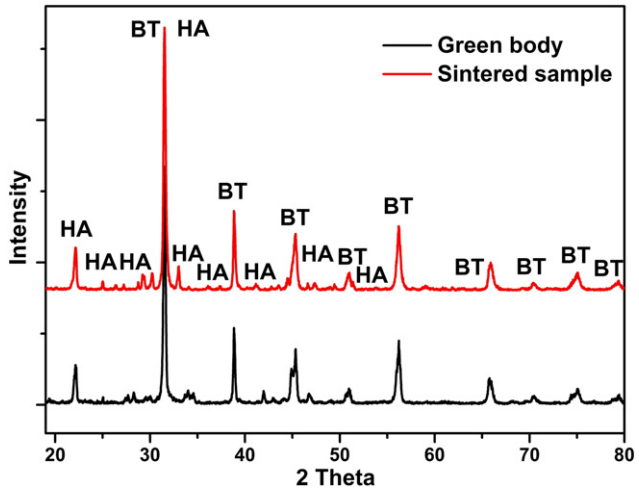

Fig. 1. XRD patterns of green body and sintered HA/BT piezoelectric composite.

Material Co., Ltd., PR China), BT powder with a spherical-like morphology of the median grain size $d_{50} = 0.29$ μm and a purity of 99.5% (according to the manufacturer's data, Shanghai Dianyang Industry Co., Ltd., P. R. China), deionized water, polyvinyl alcohol (PVA, 420, Kuraray Co. Ltd, Japan) and ammonium polyacrylate (HydroDisper A160, Shenzhen Highrun Chemical Industry Co. Ltd, PR China) were used as the starting materials, freezing vehicle, the binder and the dispersant, respectively.

HA/BT composites with different HA/BT contents in volume fraction, i.e. HA50/BT50, HA30/BT70, HA10/BT90 and solid loading ranging from 10 to 40 vol.%, were achieved by mixing HA powder, BT powder, 1 wt.% dispersant and 1 wt.% PVA binder in deionized water, followed by ball-milling for 24 h with zirconia media and de-aired by stirring in a vacuum desiccator, until complete removal of air bubbles. Freeze casting the suspension was carried out by pouring the suspension into a transparent cylindrical polydimethylsiloxane (PDMS) mould (10 mm diameter × 15 mm high), which was then transported to a copper double-side cooling setup which was cooled from room temperature by liquid nitrogen to −100 °C at 1–20 °C/min rates. Ring heaters were attached to the copper rods to control the cooling rate and temperature gradient between the copper rods. Meanwhile, polyamide (PA) fibre of circular cross-section with packing densities from 0 to 60 vol.% and ice solvent were used as structural double-templates simultaneously for the manufacture of HA/BT composites. Frozen samples were then demoulded and then placed in the vacuum chamber (<10 Pa) of a freeze-drier (FD-1A-50, Beijing Boyikang Medical Equipment Co., China) for 24 h to allow the ice to sublimate. The dried samples were heated at 550 °C for 3 h in order to burn out the organic additives and fibre templates and sintered at 1250 °C for 3 h.

X-ray diffractometer (Rigaku D/max2550pc, Japan) with monochromatic Cu Ka radiation (λ = 1.54178 Å) was used to characterize the crystalline phase of the green body and the sintered sample. Field emission scanning electron microscopy (FESEM, NOVA NANOSEM 230) with energy-dispersive spectroscopy (EDS, AZTec X-Max 80) was applied for the microstructural evaluation and composition analysis. The mechanical property was tested on samples of ~9 mm diameter and ~7 mm height at a crosshead speed of 0.2 mm/min using an Electronic Universal Testing Machine (KD11-2, Shenzhen KEJALI Technology Co. Ltd., China). The pore size distributions of the sintered ceramics were measured by mercury intrusion porosimetry (Poremaster 33, Quantachrome, Boynton Beach, Florida, USA). In order to measure the piezoelectric property, a corona poling [13]was conducted on the sintered porous samples at 110 °C using a pential of 28 kV and a point source height of 70 mm. The piezoelectric coefficient (d_{33}, which quantifies the volume change when a piezoelectic material is subject to an electric field, or the polarization on application of a stress) was measured using a quasi-static d_{33} meter (ZJ-4AN, Institute of Acoustics, Chinese Academy of Sciences, Beijing, China).

MTT cytotoxicity test was carried out according to a standard procedure ISO 10993-5:1999 [14] using murine fibroblast cells (L929 cell). Cells were cultured in the RPMI 1640 supplemented with 10% fetal calf serum at 37 °C in a humidified atmosphere of 5% CO_2. 96-well cell culture plates were employed for incubating cells. 2.5×10^7 cells/L of medium was placed in each well and incubated for 24 h for cell attachment. RPMI 1640 supplemented with 10% heat inactivated fetal calf serum and 8 mol/L phenol were used as negative and positive control group respectively, and 100% HA/BT extract was used during the test. After 3 days of incubation, 20 μL MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide, 500 μg/ml) in a concentration of 5 g/L was added to each well for other 4 h of incubation. After that, the MTT solution was removed and the insoluble formazan crystals were dissolved in 1.5×10^{-4} L dimethylsulfoxide (DMSO, Sigma), followed by homogeneous swirling for about 10 min by the shaker. The optical density (OD) of the solubilization product was spectrophotometrically measured at 490 nm by Microplate Spectrophotometer System (Elx-800,Bio-Tek instruments), and the relative growth rate (RGR) was calculated by equation, i.e. RGR = (OD value of experimental group / OD value of negative control proup) × 100%.

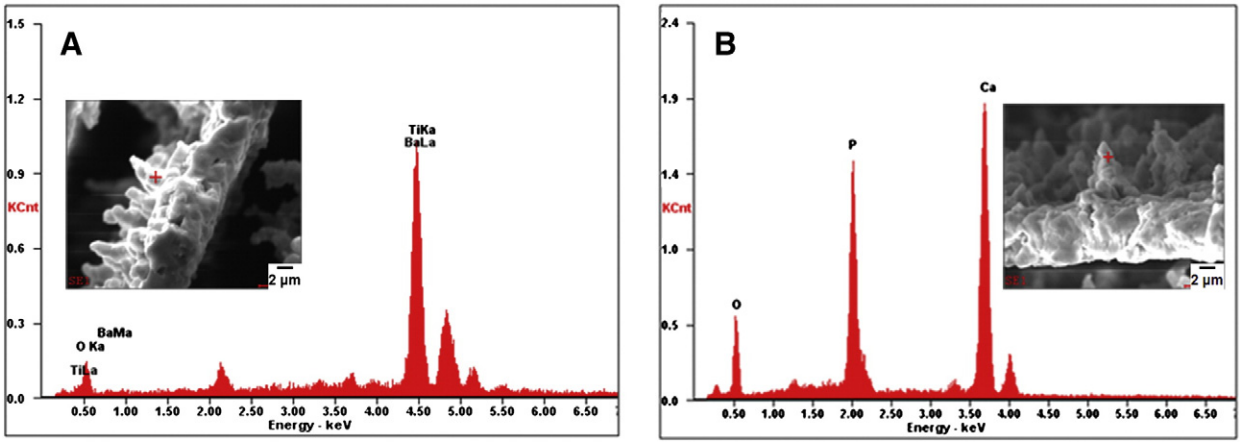

Fig. 2. EDS patterns of HA/BT piezoelectric composites.