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Titanium-niobium pentoxide composites for biomedical applications

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ABSTRACT

The strength of titanium scaffolds with the introduction of high porosity decreases dramatically and may become inadequate for load bearing in biomedical applications. To simultaneously meet the requirements of biocompatibility, low elastic modulus and appropriate strength for orthopedic implant materials, it is highly desirable to develop new biocompatible titanium based materials with enhanced strength. In this study, we developed a niobium pentoxide (Nb_2O_5) reinforced titanium composite via powder metallurgy for biomedical applications. The strength of the Nb_2O_5 reinforced titanium composites (Ti-Nb_2O_5) is significantly higher than that of pure titanium. Cell culture results revealed that the Ti-Nb_2O_5 composite exhibits excellent biocompatibility and cell adhesion. Human osteoblast-like cells grew and spread healthily on the surface of the Ti-Nb_2O_5 composite. Our study demonstrated that Nb_2O_5 reinforced titanium composite is a promising implant material by virtue of its high mechanical strength and excellent biocompatibility.

1. Introduction

Titanium (Ti) has shown the greatest potential to be the material basis of load-bearing implant applications due to its excellent mechanical strength, biocompatibility over alternative biomaterials, such as polymers and ceramics [1,2]. It also possesses a relatively low elastic modulus and excellent corrosion resistance compared with other metal biomaterials, such as SUS316L stainless steel and Co–Cr–Mo alloys. However, pure titanium used today is in its solid forms and often much stiffer than human bone as the elastic modulus of titanium implants is much higher than that of natural bone [1,2]. This mismatch of elastic modulus causes stress shielding, leading to implant loosening and eventual failure [1,3].

The elastic modulus of titanium can be tailored through the introduction of a porous structure [4,5]. A porous structure may also provide new bone tissue ingrowth ability and vascularization, which make porous titanium as a promising scaffold biomaterial for bone tissue engineering. However, the strength of porous titanium decreases dramatically with the introduction of porosity, and becomes lower than that of natural bone when with high porosity [3,5]. To be a successful implant, it is necessary to simultaneously meet the requirements of low elastic modulus, appropriate strength and excellent biocompatibility for load-bearing implant materials.

Particulate-reinforced metal matrix composites (MMCs) are known to provide a higher strength and hardness, and better wear resistance, compared to unreinforced metals [6–8]. The appropriate selection of reinforcement and metal matrix systems are of critical importance for ensuring a property combination of biocompatibility, high strength and high wear resistance. Volume fraction, shape, size, and orientation of the reinforcement phase in metal matrix play an essential role in determining the properties of MMCs. A wide range of metal systems and reinforcements are available for MMCs, including, for example, Al, Mg, Ni, Ti, Cu, Fe, etc., and reinforcement systems in the form of whiskers, fibers, and particulates, for instance, boron, carbon fiber, carbon nanotubes, Kevlar, silicon carbide and various metal oxides. Particulate-reinforced metal matrix composites have attracted extensive attention as a result of their relatively low costs and characteristic isotropic properties.[8] Silicon carbide, boron carbide, titanium carbide, titanium diboride, zirconium diboride, and aluminum oxide are commonly used to produce reinforced titanium composites [9]. However, for particulate-reinforced MMCs for biomaterials

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applications, they should have not only enhanced mechanical properties but also excellent biocompatibility. Silicon carbide, boron carbide, titanium diboride, zirconium diboride, and aluminum oxide may be of insufficient biocompatibility according to their Material Safety Data Sheets [10]. To ensure the particulate-reinforced MMCs with excellent biocompatibility, the selected particle reinforcements should be biocompatible [11–13].

Niobium pentoxide (Nb_2O_5) is considered biocompatible [10]. The titanium alloy coated with Nb_2O_5 by using a sol–gel technique can significantly improve its biocompatibility, bioactivity and corrosion resistance [14,15]. It has been reported that particulate-reinforced titanium metal matrix composites using metal oxides as reinforcements, such as TiO_2, SiO_2, ZrO_2 and SrO, show promising mechanical properties and excellent biocompatibility for orthopedic implant materials [16–18]. In this study, to simultaneously achieve high strength and excellent biocompatibility for load-bearing applications, we attempt reinforcing titanium metal matrix with Nb_2O_5 particulate to fabricate a Ti-Nb_2O_5 composite for biomedical applications. The mechanical properties and the microstructure of the particulate-reinforced Ti-Nb_2O_5 composite were evaluated using compression tests and scanning electron microscopy (SEM). The in vitro biocompatibility and cell adhesion behavior of the Ti-Nb_2O_5 composite were assessed by using human osteoblast-like SaOS2 cells.

2. Experimental methods

Processing methods for MMCs play a crucial role in the properties of the final titanium-metal oxide composites. Powder metallurgy has several advantages in the processing of metal matrix composites since it can synthesize a wider range of compositions with relatively low costs and characteristic isotropic properties [3,5]. Typical powder metallurgy process to fabricate MMCs is schematically shown in Fig. 1.

In this study, titanium powder (purity of 99.8%, average particle size ~ 45 μm, Atlantic Equipment Engineers, USA), and Nb_2O_5 particles (purity of 99.9%, average particle size < 45 μm, Sigma-Aldrich, Australia) were used as the starting materials. The morphologies of the starting materials are shown in Fig. 2. Powder mixtures for the niobium pentoxide reinforced titanium composites containing 2%, 3%, and 4% of Nb_2O_5 (weight percent, hereafter) were blended in a planetary ball mill for 2 h at a weight ratio (balls to powder) of 10:1 and a rotation speed of 100 rpm. The mixtures of titanium powder and Nb_2O_5 particles were consolidated using a cold presser at 300 MPa and then sintered at 1000 °C in a vacuum furnace at 10^{-6} torr to obtain the MMCs. Titanium composite disc samples with a diameter of 9 mm and thickness of 2 mm were cut from the sintered products for microstructure characterization, phase analysis, and in vitro biocompatibility assessments. Cylinder composite samples with a diameter of 3 mm and a height of 6 mm were used for evaluating the mechanical properties under compression. Compressive tests were performed at room temperature at an initial strain rate of 10^{-3} s^{-1} using an Instron universal tester equipped with a video extensometer (Instron 5567, Norwood, MA). Characterization of the microstructures of the Ti-Nb_2O_5 composites was performed by scanning electron microscopy (Quanta 200, USA).

Osteoblast-like cells (SaOS2, a human osteosarcoma cell line with osteoblastic properties, Barwon Biomedical Research, Geelong Hospital, Victoria, Australia) were used to assess the in vitro biocompatibility of the Ti-Nb_2O_5 composites based on a direct contact method [3,11]. SaOS2 cells were cultured in a modified minimum essential medium (MMEM) at 37 °C in a humidified atmosphere of 5% CO_2 in air. MMEM composed of minimum essential medium (MEM, Gibco, Invitrogen, Mulgrave, VIC, Australia), 10% fetal bovine serum (Bovogen Biologicals, Essendon, Victoria, Australia), 1% non-essential amino acid (Sigma-Aldrich, Castle Hill, NSW, Australia), 10,000 units/mL penicillin-10,000 μg/mL streptomycin (Gibco), and 0.4% amphostat B (In Vitro Technologies, Auckland, New Zealand). The culture medium was changed every 3 days. When cells become confluent, they were harvested by using 0.1% Trypsin-5 mM EDTA (Sigma-Aldrich, Australia) and collected for use.

For the in vitro assessment, all samples were sterilized in an autoclave. The samples were then placed in a 48-well cell culture plate with each well containing one sample covered with 200 μl MMEM. SaOS2 cells were seeded at a density of 5×10^3 cells per well. After incubating the cells in a humidified atmosphere with 5% CO_2 in air at 37 °C for 7 d, MTS assay was performed to measure the cell number in the wells. The respective medium in each well was replaced by 150 μl phenol red free MEM. MTS/PMS solution of 50 μl was added in each well and the cell culture plate was incubated for 1 h at 37 °C in a humidified atmosphere of 5% CO_2 in air. Then, 100 μl from each well was transferred to a 96-well plate for absorbance reading at 490 nm using a spectrophotometer (GENios Pro, Tecan, Mannedorf, Switzerland).

The cell morphology of the osteoblast-like cells (SaOS2) on the surfaces of the Ti-Nb_2O_5 composite samples was observed using a confocal microscope (Leica SP45, Germany) and scan electron microscopy (SEM). For confocal microscopy observation, the cell-seeded discs after cell culture were fixed in 2% paraformaldehyde and permeabilised with 0.2% (v/v) triton-X100 in phosphate-buffered saline (PBS) (Sigma-Aldrich, Australia) each for 10 min at room temperature. The discs were then incubated with 1%

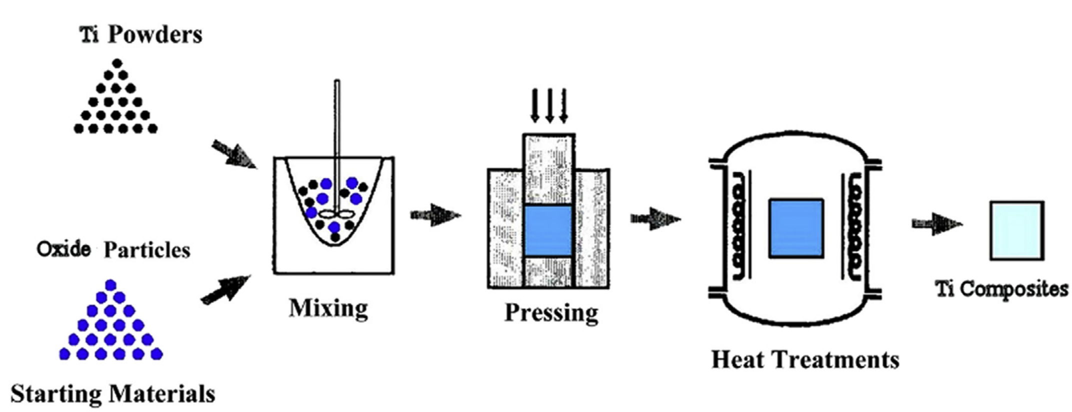

Fig. 1. Schematic illustration of powder metallurgy process in the fabrication of particulate reinforced metal matrix composites (MMCs).