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Preparation and drug release behavior of TiO_2 nanorod films with incorporating mesoporous bioactive glass

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ABSTRACT

For orthopedic implant coatings, excellent biological performance and anti-infective property have been both increasingly required for implantation surgery. In this work, TiO_2 nanorod films with good cellular responses and mesoporous bioactive glass (MBG) with good drug loading and release ability were adopted, and MBG-incorporated TiO_2 nanorod films were prepared by the sol–gel technique. The effects of TiO_2 nanorod density and MBG composition on the formation of the incorporated films were investigated. The results show that T-MBG ($SiO_2/CaO/P_2O_5/TiO_2 = 80/5/5/10$) tightly cohered to TiO_2 nanorods in the films, and the degree of T-MBG incorporation ranged from about 100 nm to 300 nm of exposed TiO_2 nanorods in height. T-MBG incorporation had a positive role in the cytocompatibility of the films. Importantly, T-MBG incorporation improved greatly the drug release behavior of the TiO_2 nanorod films. The present work provides an approach to build organized nanostructure films on implant surfaces with satisfactory biological performance and essential anti-infective ability.

1. Introduction

For orthopedic implants, biological performance, anti-infective capability and excellent mechanical properties have been increasingly required for implantation surgery [1–6]. Metallic implants, such as tantalum implants, are widely used in orthopedic implantation due to their good biocompatibility and excellent mechanical properties to withstand or transfer loads. Surface modification is frequently adopted to further improve the implantation through physical, chemical or biological methods. From a biomimetic viewpoint, a biomaterial coating composed of microscale or nanoscale topography could provide a desirable surface for cell functions and osteogenesis responsiveness [7–9].

Many materials, such as natural biological molecules [10,11], hydroxylapatite [12–15], calcium phosphate [16] and TiO_2 [17–23], can be fabricated into the microscale or nanoscale topography with high osteogenesis responsiveness. TiO_2 has versatile nanostructures, such as nanodots [17], nanowires [18–20], nanotubes [21], and nanorods [22,23], and these topological structures have been more suitable for cell growth. Since nanorod topography has the characteristics of a pseudo-3D structure [24] with controlled nanorod density and size [25], TiO_2 nanorods could provide a more appropriate microenvironment for cell growth. Admittedly, bacterial infection in implantation surgeries has been a matter of concern, because the infections seriously retard osseointegration, and even result in implantation failure [4,5]. Thus, a good antibacterial microenvironment is also necessary during the osseointegration process [26]. Local drug delivery is safer and more effective than systemic administration, and is the most promising method for antibacterial efficacy [27–30]. However, TiO_2 nanorod films with high biological responsiveness have rod-like structures, leading to limited drug loading capacity and fast release behavior. Thus, the improvement in drug loading and release behaviors for such films is challenging.

Mesoporous materials with pore sizes of 2–50 nm have a high specific surface area and pore volume, bringing about a higher adsorption and slower release rate of drugs [31,32]. Many researches have shown that mesoporous bioactive glass (MBG) is considered to have both excellent bioactivity and drug loading/release ability [31–35]. However, the surface topological structure of MBG provides too small morphological change to be "perceived" by cells.

In this work, we attempted to incorporate MBG into TiO_2 nanorod films on the tantalum substrates by sol–gel technique, letting the films, which were optimized in micro-nanostructure and biological stability, improve cytocompatibility and drug release behaviors. Besides, the density and the height of TiO_2 nanorods grown on the tantalum substrates are likely to regulate, which is so significant for MBG incorporation, because

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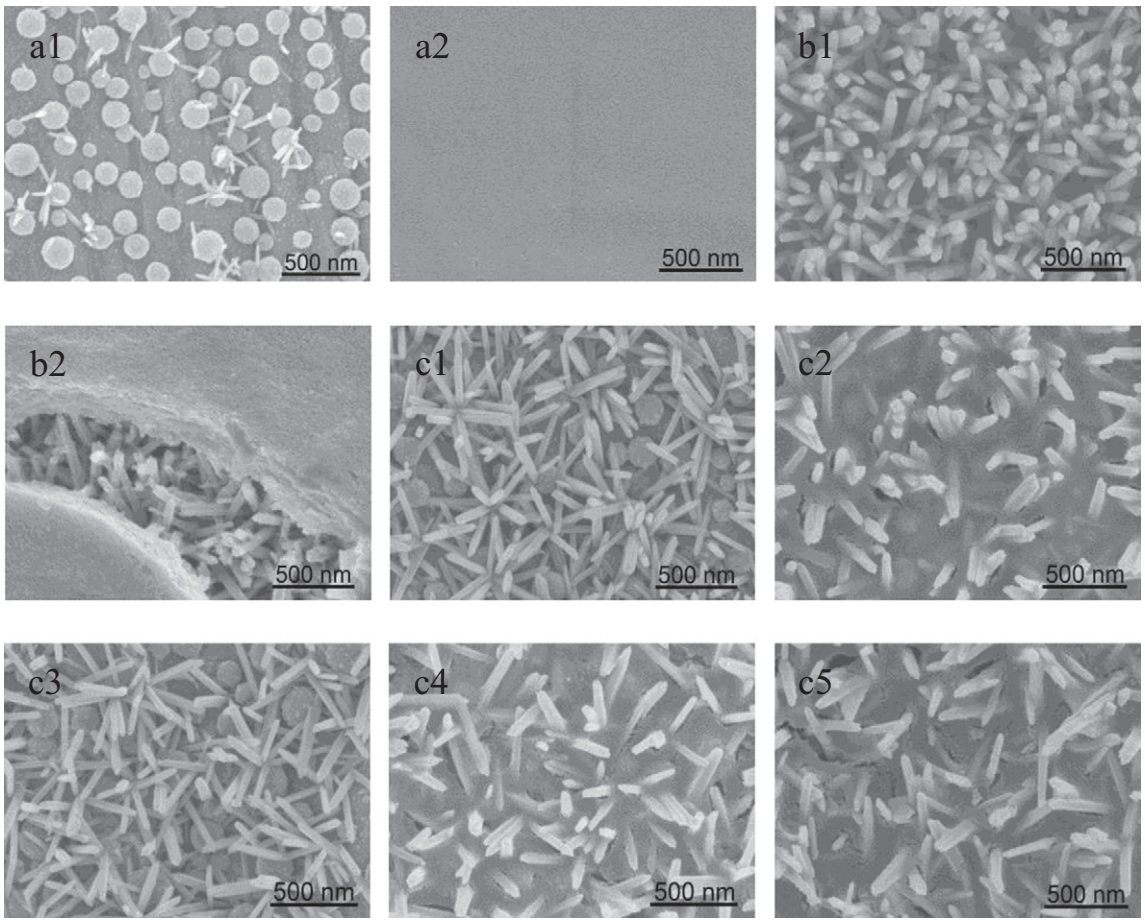

Fig. 1. FESEM images of the films: (a1) low-density TiO_2 nanorod films; (a2) low-density TiO_2 nanorod films with incorporating M80S15C-MBG; (b1) high-density TiO_2 nanorod films; (b2) high-density TiO_2 nanorod films with incorporating M80S15C-MBG; (c1) medium-density TiO_2 nanorod films; TiO_2 nanorod films with incorporating M80S15C-MBG before (c2) and after (c3) immersing in PBS for 24 h; TiO_2 nanorod films with incorporating T-MBG before (c4) and after (c5) immersing in PBS for 7 days.

the titanium source is provided by the solution instead of the substrates. Compared with other methods, the sol–gel technique can prepare uniform MBG without high temperature and incorporate MBG into TiO_2 nanorod films in a controlled manner. The cytocompatibility was evaluated using pre-osteoblastic MC3T3-E1 cells by MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium) assay, and the films were loaded with vancomycin hydrochloride as a model of a water-soluble drug to study the drug release behavior. The role of MBG in the films for improving the drug release behavior was analyzed in the view of release kinetics.

2. Experimental details

2.1. Materials

Metal tantalum (Ta, Baoji Lihua Non-ferrous Metals Co., Ltd.) substrates (1 cm × 1 cm) were rinsed in turn with acetone, ethanol and deionized water by ultrasonic cleaning, and dried in ambient air. Acetylacetone (AcAc, Aladdin), tetrabutyl titanate (TBOT, Aladdin), polyvinyl pyrrolidone (PVP, Aladdin) with a molecular weight of 30,000 and ethanol were mixed to prepare nanodot layers on Ta substrates [17]. TBOT and hydrochloric acid were used to prepare hydrothermal solutions [25]. Triblock copolymer poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) (P123, $M_r = 5800$, Sigma-Aldrich), tetraethyl orthosilicate (TEOS, Aladdin), calcium nitrate tetrahydrate ($Ca(NO_3)_2 \cdot 4H_2O$, Aladdin), triethyl phosphate (TEP, Aladdin), TBOT, hydrochloric acid and ethanol were mixed to prepare MBG sol [36]. Mouse calvaria-derived, pre-osteoblastic cells (MC3T3-E1, CRL-2594, ATCC) were used in this study. Vancomycin hydrochloride (VH, No. 0990, 1% (w/v), Amresco) was adopted as a model of a water-soluble drug. All chemicals were of analytical reagent grade and were used without further purification. All aqueous solutions were prepared using deionized water.

2.2. Hydrothermal growth of TiO_2 nanorods

Our research group developed a phase-separation-induced self-assembly method for the preparation of TiO_2 nanodot layers. In brief,

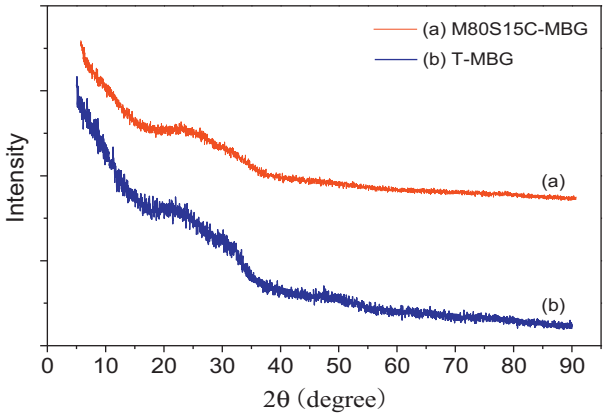

Fig. 2. XRD patterns: (a) M80S15C-MBG; (b) T-MBG.