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Surface structure and in vitro apatite-forming ability of titanium doped with various metals

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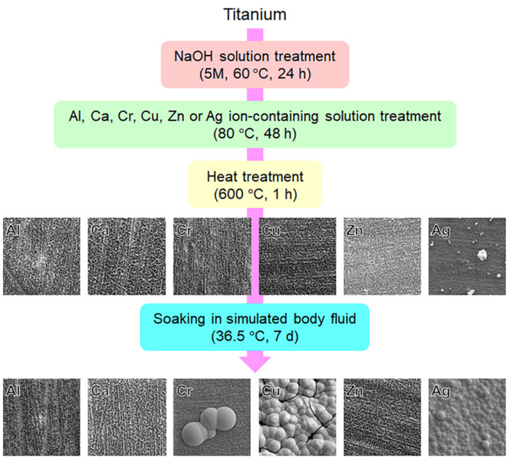
GRAPHICAL ABSTRACT



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ABSTRACT

Surface modification by sodium hydroxide (NaOH) and subsequent heat treatment can provide titanium and its alloys an apatite-forming ability in simulated body fluid (SBF), and is used clinically to treat titanium alloy hip joints in Japan. However, there is no systematic study on the relationship between the amount and chemical state of metals incorporated into titanium and the apatite-forming ability in SBF. We have studied this relationship herein by treating NaOH–modified titanium with aqueous solutions containing different types (aluminum, calcium, chromium, copper, zinc, and silver) and concentrations (0.01, 0.1, and 1 M) of metal ions. As a result, we found that formation of anatase and the chemical states of the metals incorporated into titanium control the apatite-forming ability. Further, the chemical states of the metals can be interpreted in terms of the ionization tendency. These findings would aid future design of metal-doped bioactive titanium for orthopedic or dental implants.

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1. Introduction

Titanium and its alloys are frequently used as orthopedic and dental implants due to their good biocompatibility. However, the osteoconductivity of untreated titanium has scope for improvement. Various surface modifications have been applied to titanium and its alloys to induce bone-bonding ability (i.e., bioactivity). Of these, hydroxyapatite is the most representative; however, sodium hydroxide (NaOH) and subsequent heat treatment can also induce bioactivity to titanium and its alloys [1], and this technique has been used to produce bioactive titanium alloy hip joints that have been clinically used in more than 20,000 patients in Japan since 2007 [2]. Titanium and its alloys treated with NaOH and heat can form an apatite surface layer, through which they can bond to living bone when they are implanted into bone defects [3]. Apatite formation on titanium and its alloys can be reproduced in vitro in simulated body fluid (SBF) [4] with ion concentrations nearly equal to those of human plasma [5]. Although in vitro apatite-forming ability in SBF does not always lead to in vivo bone-bonding ability of artificial materials [6], it is often a good indicator.

Since the development of the NaOH and subsequent heat treatment, additional surface modifications using metal ion-containing aqueous solutions have been proposed to fabricate bioactive titanium with new functions such as antibacterial activity and enhanced osteoconductivity [7–13]. Antimicrobial activity can be induced in titanium by the incorporation of silver [7–9,13], and osteoconductivity can be enhanced by the incorporation of calcium or strontium [10,11]. Further, introducing zinc to the NaOH-modified titanium surface, by treatment with a solution containing $[Zn(OH)_4]^{2-}$ complex, has been shown to result in modified titanium implants with significantly stronger bone fixation [12].

The apatite-forming ability of surface-modified titanium is attributed to the formation of Ti−OH groups and surface charge [2], but there have been no systematic studies on the relationship between the amount and chemical state of doped metals and their apatite-forming ability in SBF. In this study, aqueous solutions containing different of metal ions (aluminum, calcium, chromium, copper, zinc, or silver) were prepared in concentrations of 0.01, 0.1, or 1 M, to investigate the relationship between the amount and chemical state of doped metals and apatite-forming ability in SBF as fundamental research. Like silver, copper can show antibacterial activity [14], and an antibacterial Ti-Cu alloy has been proposed [15,16]. Aluminum is added to titanium to produce alloys with high mechanical strength, such as Ti-6Al-4 V [17,18]. Chromium is also an important alloy ingredient of Co-Cr-Mo alloys and offers excellent corrosion resistance [18,19]. Considering this, despite the fact that some of the resultant samples are unlikely to be used in clinical applications—aluminum oxide (Al_2O_3), a major chemical compound of aluminum, cannot show osteoconductivity [20], and hexavalent chromium ion (Cr^{6+}) is highly toxic [21]—the present findings are expected to aid future design of metal-doped bioactive titanium for orthopedic or dental implants.

2. Materials and methods

2.1. Sample preparation

Commercially available pure titanium plates (10 mm × 10 mm × 1 mm; purity, 99.9%; Kojundo Chemical Laboratory, Saitama, Japan) were abraded using No. 400 diamond abrasive paper and washed with pure acetone and ultrapure water in an ultrasonic cleaner. The Ti plates were then soaked in 5 mL of 5 M NaOH solution at 60 °C for 24 h followed by 7 mL of metal ion-containing aqueous solution at 80 °C for 48 h, and then gently washed with ultrapure water and dried. Special grade NaOH, aluminum nitrate nonahydrate ($Al(NO_3)_3{\cdot}9H_2O$), calcium nitrate tetrahydrate ($Ca(NO_3)_2{\cdot}4H_2O$), chromium(III) nitrate nonahydrate ($Cr(NO_3)_3{\cdot}9H_2O$), copper(II) nitrate trihydrate ($Cu(NO_3)_2{\cdot}3H_2O$), zinc nitrate hexahydrate ($Zn(NO_3)_2{\cdot}6H_2O$), and silver nitrate ($AgNO_3$) (Wako Pure Chemical Industries, Osaka, Japan) were used in this study. The concentration of metal ions in the aqueous solutions was fixed at 0.1 M for samples treated with $Al(NO_3)_3$, $Ca(NO_3)_2$, and $Cr(NO_3)_3$ aqueous solutions, but concentrations of 0.01, 0.1, and 1 M were used for treatment with $Cu(NO_3)_2$, $AgNO_3$, and $Zn(NO_3)_2$ aqueous solutions. Heat treatment of all samples was carried out at 600 °C. The samples were heated at a rate of 5 $°C{\cdot}min^{-1}$ in a desktop high-temperature muffle furnace (MSFS-1218, Yamada Denki Co., Ltd., Tokyo, Japan), held at 600 °C for 1 h, and then naturally cooled to room temperature in the furnace. The sample names are listed in Table 1 along with the metal ions and the concentrations of solutions used in this study.

Table 1
Sample names with the type and concentration of metal ions in solutions used in this study.

Sample name	Metal ion	Metal ion concentration [M]
01-Al	Al^{3+}	0.1
01-Ca	Ca^{2+}	0.1
01-Cr	Cr^{3+}	0.1
001-Cu	Cu^{2+}	0.01
01-Cu	Cu^{2+}	0.1
1-Cu	Cu^{2+}	1
001-Zn	Zn^{2+}	0.01
01-Zn	Zn^{2+}	0.1
1-Zn	Zn^{2+}	1
001-Ag	Ag^{+}	0.01
01-Ag	Ag^{+}	0.1
1-Ag	Ag^{+}	1

2.2. Characterization of sample surfaces

The surface structures of the treated titanium samples were investigated using a RINT-2200VL thin-film X-ray diffractometer (TF-XRD; Rigaku, Tokyo, Japan), a VE-8800 scanning electron microscope (SEM; Keyence, Osaka, Japan), and an AXIS Ultra DLD X-ray photoelectron spectrometer (XPS; Kratos Analytical, Manchester, U.K.). The following settings were used for the TF-XRD measurements: X-ray source, Ni-filtered Cu Kα radiation; X-ray power, 40 kV, 40 mA; scanning rate, 4° min^{-1}; sampling angle, 0.01°. The following settings were used for the XPS measurements: X-ray source, monochromatic Al Kα radiation (1486.7 eV); X-ray power, 15 kV, 10 mA. The binding energy was calibrated using the C_{1s} photoelectron peak at 284.8 eV as a reference. XPS peak analysis was performed using CasaXPS Version 2.3.15 software, and the Shirley background was subtracted from all spectra prior to fitting. The atomic concentration was calculated from the XPS spectra using the specific relative sensitivity factors for the Kratos Axis Ultra (O_{1s}, 0.780; Ti_{2p}, 2.001; N_{1s}, 0.477; C_{1s}, 0.278; Al_{2p}, 0.193; Ca_{2p}, 1.833; Cr_{2p}, 2.427; Cu_{2p}, 3.547; Zn_{2p}, 3.726; Ag_{3d}, 5.987).

2.3. Evaluation of the apatite-forming ability of samples in simulated body fluid

Treated titanium samples were soaked at 36.5 °C in 30 mL of simulated body fluid (SBF) containing ions at concentrations of: Na^+, 142.0 mM; K^+, 5.0 mM; Ca^{2+}, 2.5 mM; Mg^{2+}, 1.5 mM; Cl^-, 147.8 mM; $HCO_3{}^-$, 4.2 mM; $HPO_4{}^{2-}$, 1.0 mM; $SO_4{}^{2-}$, 0.5 mM. These values are nearly identical to those found in human blood plasma, according to the ISO 23317:2014 standard. After being immersed in SBF for 7 days, the samples were removed and gently washed with ultrapure water.

3. Results and discussion

3.1. Effect of metal type on surface structure and apatite-forming ability of samples

To discuss the effect of metal type on surface structure and apatite-