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Potentiality of the "Gum Metal" titanium-based alloy for biomedical applications

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ABSTRACT

In this study, the "Gum Metal" titanium-based alloy (Ti–23Nb–0.7Ta–2Zr–1.2O) was synthesized by melting and then characterized in order to evaluate its potential for biomedical applications. Thus, the mechanical properties, the corrosion resistance in simulated body fluid and the in vitro cell response were investigated. It was shown that this alloy presents a very high strength, a low Young's modulus and a high recoverable strain by comparison with the titanium alloys currently used in medicine. On the other hand, all electrochemical and corrosion parameters exhibited more favorable values showing a nobler behavior and negligible toxicity in comparison with the commercially pure Ti taken as reference. Furthermore, the biocompatibility tests showed that this alloy induced an excellent response of MC3T3-E1 pre-osteoblasts in terms of attachment, spreading, viability, proliferation and differentiation. Consequently, the "Gum Metal" titanium-based alloy processes useful characteristics for the manufacturing of highly biocompatible medical devices.

1. Introduction

Metals and alloys for medical applications typically require a combination of different properties such as excellent biocompatibility with no adverse tissue reactions and adapted mechanical properties. For use as bone substitutes, the mechanical properties of a biocompatible alloy must be as close as possible to those of bone, especially Young's modulus. Decreasing Young's modulus of metallic implants minimizes the bone atrophy due to the stress shielding effect and increases the durability of the implant [1].

Titanium and titanium alloys are widely used as biomaterials, due to their low density, interesting mechanical properties and biocompatibility. Standard Ti-based biomaterials for orthopedic implants are commercially pure CP-Ti (grade 2) and Ti–4Al–6V (grade 5 ELI) alloy. However, their high Young's modulus (respectively, 105 and 114 GPa), caused by the α or α + β microstructure, affects the long-term performances in service. Moreover, a perfect biocompatible Ti-based alloy must be composed of non-cytotoxic elements. The use of the Ti–6Al–4V alloy in medicine is then a subject of controversy because aluminium ions released are suspected to be associated with long term health problems like neurological pathologies and vanadium oxide, V_2O_5, which is also known to be cytotoxic [2,3].

Since the β microstructure in Ti alloys exhibits a significantly lower modulus than α or α + β microstructure, there is still a tremendous scope for improvement in terms of alloy design for an ideal orthopedic implant. Consequently, new generation of low modulus β-titanium alloys, which are free of vanadium and aluminium, is made with β-stabilizing and biocompatible elements such as Ta, Nb, Mo, and Zr via optimization of alloy compositions and thermo-mechanical treatments [4–8].

Among the beta-type Ti-based alloys, the multifunctional Ti–23Nb–0.7Ta–2Zr–1.2O alloy composition (mol%), called "Gum Metal", was shown to possess "super" properties such as very high strength, low Young's modulus, super elasticity and super plasticity at room temperature [9]. These properties make this alloy an excellent candidate for various applications and particularly in the biomedical sector.

In this study, we have synthesized this alloy composition by a melting process contrary to the original alloy which was elaborated by sintering. The objective of this study is to show if the "super" properties of this alloy composition are still obtained by this alternative way of processing and to investigate its biocompatibility as this alloy could be potentially very interesting for biomedical applications. One can noticed that the biocompatibility of the specific "Gum Metal" alloy composition was never investigated until now. Thus, the corrosion resistance in

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simulated body fluid (Ringer–Brown and Ringer solutions) and the in vitro cell response (cell attachment, spreading and morphology, cell proliferation, differentiation) of the "Gum Metal" titanium alloy were investigated in this work.

2. Materials and methods

2.1. Synthesis and characterization of alloys

As titanium, zirconium, tantalum and niobium have different melting points and densities, the synthesis of the "Gum Metal" Ti–23Nb–0.7Ta–2Zr–1.2O (mol%) alloy composition (named GM in this paper) was realized by the cold crucible semi-levitation melting (CCLM) technique under high vacuum, using a high-frequency magnetic induction generator heating system (CELES). With this method, the alloying elements are fully mixed into the melt without contamination, thanks to the restricting contact points between the melt and the cold crucible [10].

The added elements are raw solid metals, except oxygen, introduced through titanium oxide (TiO_2) powder. After a homogenization treatment at 950 °C for 16 h, samples were cold rolled until 90% of reduction in thickness. To finish, all samples were solution treated at 850 °C for 0.5 h in the β-phase field and water quenched. The aim of this treatment is to restore a fully recrystallized β-phase microstructure from the cold rolled state with a reduced β-grain size.

The commercially pure CP-Ti (grade 2, provided by Goodfellow) was used as reference for the experimental investigations in this study.

The phase analysis of both CP-Ti and GM alloy was investigated by X-ray diffraction (XRD) with a Philips diffractometer with $CuK_{\alpha 1}$ radiation ($\lambda = 1.54060$ Å). The microstructures were visualized by electron backscattered diffraction (EBSD) in a JEOL JSM 6400 scanning electron microscope equipped with a TSL EBSD system. To be observed, samples were successively mechanically polished with different SiC abrasive papers until grade 4000. The "mirror polished" state was obtained using a colloidal silica suspension (particle size: 50 nm). A short chemical etching in a solution composed of 5% HF, 5% HNO_3 and 90% H_2O (vol.%) was done to remove the superficial deformed layer.

Tensile tests were carried out until rupture with an Instron tensile machine and the strain rate used was 10^{-4} s^{-1}. In the elastic domain, the strain was measured with a 10 mm extensometer to evaluate precisely the Young's modulus. Tensile test samples used possess a normalized shape: 3 mm width, 0.5 mm in thickness and a gage length of 15 mm.

For the in-vitro biocompatibility tests, disc samples of each alloy (diameter: 13 mm, thickness: 2 mm) were cut out. Each sample was mechanically mirror polished as previously described. The polished samples were cleaned by immersion for 30 min in alcohol and 30 min in distilled water using an ultrasonic cleaner.

2.2. Electrochemical characterization methods

The corrosion of the metallic implant materials can produce ions and compounds released to the surrounding tissues which can cause problems, sometimes leading to the implant failure. The oxide layer on the titanium based alloy surface plays an important role because this layer is protective and remains intact for long-term. Therefore, the study of the interface between passive film on the alloy surface and simulated human body fluids has a great interest in the determination of the corrosion resistance of the implant materials.

The electrochemical and corrosion behavior of the GM alloy in comparison with that of commercially pure Ti was determined from cyclic potentiodynamic polarization curves, linear polarization measurements (Tafel representation) and monitoring of the open circuit potentials (E_{oc}) and corresponding open circuit potential gradients (ΔE_{oc}).

Prior to experiments, the mirror polished disc samples obtained from CP-Ti and GM alloy were rinsed with tap water, ultrasonic degreased in acetone and bi-distilled water, dried in air and mounted in the Stern–Makrides hold system.

The human biofluid was simulated by Ringer–Brown and Ringer solutions of the following compositions (g/L): Ringer–Brown (g/L), NaCl — 6.0; KCl — 0.4; $CaCl_2$ — 0.2; sodium lactate — 3.05; pH = 7.4; Ringer (g/L), NaCl — 6.8; KCl — 0.4; $CaCl_2$ — 0.2; $MgSO_4 \cdot 7H_2O$ — 0.2048; $NaH_2PO_4 \cdot H_2O$ — 0.1438; $NaHCO_3$ — 1; glucose — 1. The functional conditions of an implant implies the variation of the biofluid pH values due to the fact that in case of surgery, the pH value decreases till 5 or 3 points [11] and in the case of infections and inflammations, the pH value can increase till 9 points [12]. Also, for long-term, the oxides from passive film can hydrolyse, changing the local value of pH [13,14]. From this reason, we simulated the severe functional conditions of an implant by the use of Ringer solution of acid pH = 3.21, alkaline pH = 8.93 and neutral pH = 7.31. The temperature was kept at 37 °C ± 1 °C.

The electrochemical and corrosion behavior was studied in an electrochemical glass cell with three electrodes: working electrode — studied alloy, counter electrode — Pt grid, and reference electrode — saturated calomel electrode (SCE) connected to cell with Haber–Luggin capillary.

The cyclic potentiodynamic polarization curves were recorded with VoltaLab 80 equipment applying potential steps of 1 mV/s from −0.9 V till +2.0 V. From the obtained voltammograms, the principal electrochemical parameters were determined: E_{corr} — corrosion potential, like zero current potential, E_p — passivation potential at which the current density is constant; $|E_{corr} - E_p|$ difference represents the tendency to passivation (low values characterize a good, easy passivation); ΔE_p — passive potential range of the constant current; i_p — passive current density.

The linear polarization measurements were performed for ±50 mV around the open circuit potential with a scan rate of 0.1 mV/s; VoltaMaster 4 program adjusted the Tafel curves and directly supplied the main corrosion parameters: i_{corr} — corrosion current density; V_{corr} — corrosion rate; R_p — polarization resistance. The total quantity of the ions (ng/cm^2) released in the solution was estimated as follows [13–15]:

$$\text{ion release rate} = 1.016 \cdot V_{corr} \cdot 10^5 \tag{1}$$

where: V_{corr} = corrosion rate in mm/year.

The open circuit potentials E_{oc} were monitored for 1000 immersion h using a performing multimeter, Hewlett-Packard. The open circuit potential gradients ΔE_{oc} (pH), which can appear because of the pH differences on different zones of an implant were calculated as follows:

$$\Delta E_{oc1}(pH) = E_{oc}^{pH=3.21} - E_{oc}^{pH=7.31} \tag{2}$$

$$\Delta E_{oc2}(pH) = E_{oc}^{pH=3.21} - E_{oc}^{pH=8.93} \tag{3}$$

$$\Delta E_{oc3}(pH) = E_{oc}^{pH=7.31} - E_{oc}^{pH=8.93}. \tag{4}$$

Also, the gradient ΔE_{oc} (c), due to the composition difference of the human biofluid was simulated using neutral Ringer solution and neutral Ringer–Brown solution:

$$\Delta E_{oc4}(c) = E_{oc}^{\text{Ringer pH=7.31}} - E_{oc}^{\text{Ringer–Brown pH=7.4}}. \tag{5}$$

2.3. Cell biocompatibility testing

2.3.1. Cell culture

Although cell culture experiments do not exactly reproduce in vivo situations, they can give some idea of how different cell types might respond to an implant material.