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A Ni-free high-zirconium-based bulk metallic glass with enhanced plasticity and biocompatibility

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ABSTRACT

A novel Ni-free high-zirconium-based bulk metallic glass (BMG) of $Zr_{65}Ti_{2.5}Al_{10}Fe_{7.5}Cu_{10}Ag_5$ was fabricated by copper mold casting. The mechanical behavior and initial *in vitro* biocompatibility of BMG were investigated. The newly developed BMG exhibited excellent room temperature plasticity and toughness with compressive plastic strain over 12% and notch toughness of 95.8 ± 7.5 MPa $m^{1/2}$. Live/dead staining and WST-1 assay results revealed higher cell viability and proliferation activity of mouse MC3T3-E1 cell on the BMG substrate than on Ti–6Al–4V alloy and pure Zr. The combination of enhanced mechanical properties and *in vitro* biocompatibility demonstrated its promise for biomedical applications.

1. Introduction

Zirconium-based bulk metallic glasses (BMGs) exhibit a unique combination of high glass-forming ability (GFA), high specific strength, high hardness, low Young's modulus, excellent corrosion resistance and biocompatibility, which motivates their potential applications as biomaterials, including as orthopedic implants [1–5]. As potential biomedical materials two principal aspects of compatibility should be taken into consideration: mechanical compatibility and biocompatibility between implant alloys and bone. From the perspective of mechanical properties, low Young's modulus of Zr-based BMGs can facilitate reducing the concern of bone resorption caused by the mismatch of Young's modulus between implants and bone [6]. Meanwhile, good plasticity is required for BMGs to increase the reliability by preventing catastrophic failure in load-bearing conditions. Recently, high-zirconium-based BMGs (≥65 at.% Zr) have attracted great interest owing to their superior mechanical properties, such as lower Young's modulus and larger plasticity, compared to the conventional Zr-based BMGs (40–60 at.% Zr) [7–9]. The previous studies showed that high-zirconium-based BMGs, such as $Zr_{70}Al_8Ni_{16}Cu_6$ and $Zr_{72}Ni_{7.5}Cu_{13}Al_{7.5}$ alloys [7,8], exhibited low Young's modulus of about 70 GPa, which was closer to that of human bone (about 30 GPa) than commercial orthopedic implant alloys including Co–Cr alloy (about 230 GPa), 316 L stainless steel (about 200 GPa) or Ti–6Al–4V alloy (about 110 GPa), with a potential consequent reduction in stress shielding [10]. On the other hand, it was found that the plasticity of Zr-based BMGs increased with increasing in Zr content. The toughness of BMGs was correlated with their Poisson's ratio ν [11]. A large ν was regarded as an indicator of the plastic character of a BMG and could therefore be used to identify plastic BMGs [12]. By tailoring compositions in Zr–Al–Ni–Cu and Zr–Al–Fe glass-forming systems, $Zr_{75}Al_{7.5}Fe_{17.5}$ and $Zr_{70}Al_7(Ni_{1/3}Cu_{2/3})_{23}$ high-zirconium-based BMGs were developed by copper mold casting [9,13]. Those BMGs exhibited excellent room temperature compressive plasticity and high notch toughness, which was related to their high Poisson's ratio of about 0.4.

Before any material can be used *in vivo*, its biocompatibility is a subject requiring a great number of investigations. However, many elements known to favor the glass formation are not necessarily biologically compatible, which then puts constraint on the alloy design of biocompatible glassy alloys. For example, Ni and Cu are commonly found in Zr-based BMGs. However, both elements are highly allergenic and/or toxic while Ni is possibly carcinogenic and should be avoided in implant applications [14]. In the last decade, research focus has been devoted to develop Ni-free Zr-based BMGs, such as Zr–Al–Fe [9], Zr–Al–Fe–Cu [15], Zr–Al–Co–Ag [5], Zr–Al–Fe–Cu–Ag [16], Zr–Ti/Nb–Al–Fe–Cu [17], Zr–Al–Cu–Nb–Pd [18], Zr–Al–Cu–Ti [19], and Zr–Al–Cu–Ag [20] systems. *In vitro* studies found that Zr-based BMGs supported similar or better cell adhesion and proliferation of cells compared with commercial biomedical alloys [15–20]. *In vivo* assessments revealed a common foreign body response and non-toxicity of BMGs in animal tests [17,21]. However, those alloys still contain high content of Cu (>20%). In the case of long term usage of implant alloys in physiological environment, high concentration of Cu ion could be released by

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corrosion, which is potentially dangerous to biomedical application [22]. Therefore, a Cu-free or at least a Cu-reduced BMG should be regarded as a more promising biomedical implant.

Zr-based BMGs are usually multi-component alloys to achieve high glass forming ability (GFA). The choice of alloying elements could be of significant importance to the biocompatibility of BMGs. The ideal alloying additions for a Zr-based metallic glass implant should not only increase the GFA of the alloy but must also be biocompatible to avoid any adverse reaction of the human body. Recent study showed that the addition of Ag in Zr-based BMGs can not only improve the GFA and mechanical properties but also enhance the corrosion resistance and biocompatibility of alloys [5,16,20,23]. Similar results have been found in Zr-based BMGs with a certain amount of Ti addition. The $Zr_{61}Ti_2Cu_{25}Al_{12}$ BMG with large GFA and good toughness exhibited a superior biocompatibility compared with CP-Ti and Ti–6Al–4V alloys [17,19].

Among the components of Zr-based BMGs, Zr is one of the highly biocompatible elements. Thus, it can be predicted that BMGs with higher content of Zr, substituting those less compatible elements in former glass-forming compositions, would exhibit better biosafety due to the excellent biocompatibility of Zr element. Meanwhile, the high-zirconium-based BMGs exhibit excellent mechanical compatibility which favors their biomedical application. Thus, in this work, we have developed a novel Ni-free high-zirconium-based BMG with the composition $Zr_{65}Ti_{2.5}Al_{10}Fe_{7.5}Cu_{10}Ag_5$. Compared with other high-zirconium-based BMGs, this BMG contains a reduced Cu content of 10 at.% and a certain amount of Ti and Ag in order to further improve its biocompatibility. The mechanical properties and cellular responses of the BMG were investigated to evaluate the initial biocompatibility. All of the results provide the foundational information of this Ni-free high-zirconium-based BMG for further biomedical applications.

2. Materials and methods

Master alloys with a nominal composition of $Zr_{65}Ti_{2.5}Al_{10}Fe_{7.5}Cu_{10}Ag_5$ (in at.%) were prepared by arc melting the mixtures of pure Zr, Ti, Al, Fe, Cu, and Ag metals under Ti-gettered high-purity argon atmosphere. Amorphous specimens were prepared by injection copper mold casting under high-purity argon atmosphere. The amorphous structure of the as-cast alloy samples was examined by X-ray diffraction (XRD) with the Cu-Kα radiation and high-resolution transmission electron microscopy (HRTEM). TEM specimens were prepared by a two-jet electropolishing method using a chemical solution of 4% $HClO_4$ ethanol. Thermal properties including glass transition temperature, supercooled liquid region, and crystallization of the glassy alloy were investigated by differential scanning calorimetry (DSC) at a heating rate of 0.33 K/s.

Compressive and notch toughness tests were carried out using an Instron mechanical testing system with a strain rate of 2.1×10^{-4} s^{-1} at room temperature. The specimen gage sections for compressive tests were 2 mm in diameter and 4 mm in length. Rectangular beam specimens were prepared for notch toughness measurements with a thickness of 2 mm, a width of 2 mm, and a length of 30 mm. The notch toughness of BMG was examined by three-point bending test with 20 mm span. The notch with a depth of about 1 mm and root radius of about 200 μm was cut by a slow diamond saw. At least five samples were measured to ensure statistical reliability of the data. The error bars of mechanical property tests mark the standard deviations of the measurements. The morphology of samples after deformation was examined with a scanning electron microscope (SEM).

The *in vitro* biocompatibility of the BMG was evaluated by characterizing the initial attachment and viability and the proliferation behavior of a mouse MC3T3-E1 pre-osteoblasts (ATCC, USA). All samples for cell behaviors tests were prepared to have a size of about 5 mm × 5 mm × 1 mm with the square surface being well polished to #2000. Cell attachment and viability were examined by a live/dead staining assay. Cells were seeded on triplicate samples (n = 3) at a density of 1×10^4 cells cm^{-2} in 24-well culture plates. The labeled cells were viewed under a Zeiss Axio Observer A1 inverted fluorescent microscope. Viable cells were stained with calcein (green), while non-viable cells were stained with EthD-1 (red).

Cell proliferation was assessed using a WST-1 (a water-soluble tetrazolium salt) assay on triplicate samples (n = 3). Cells were cultured on the substrates in 96-well plates in a final medium volume of 100 μl. The seeding density was 5×10^3 cell cm^{-2}. After incubation, 10 μl of cell proliferation reagent WST-1 (Roche Applied Science, USA) was added to each well and incubated at 37 °C in a 5 vol.% CO_2 balanced air atmosphere for 4 h. Afterwards, the media were mixed thoroughly for 1 min on a shaker. The absorbance of the supernatants was measured against a background control blank at 440 nm, using a BioTek Synergy 2 Multi-Mode Microplate Reader. The error bars of tests denote the standard deviations of the measurements.

3. Results

Fig. 1(a) shows the XRD pattern of the transverse cross-section of as-cast $Zr_{65}Ti_{2.5}Al_{10}Fe_{7.5}Cu_{10}Ag_5$ rod with a diameter of 4 mm. The

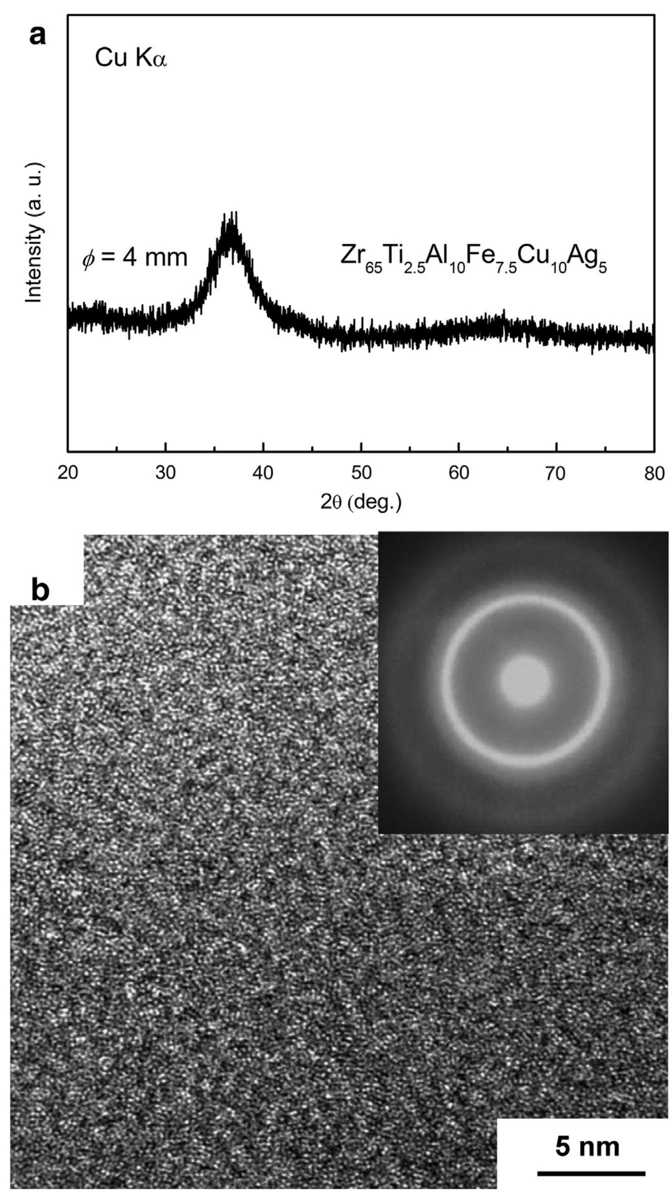

Fig. 1. (a) XRD pattern of the transverse cross-section of as-cast $Zr_{65}Ti_{2.5}Al_{10}Fe_{7.5}Cu_{10}Ag_5$ cylinders with a diameter of 4 mm, and (b) HRTEM image and selected area electron diffraction pattern of this BMG.