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A Ni-, Al-, Be-free Zr-based metallic glass for biomedical applications

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ABSTRACT

Biomaterials are attracting an ever-increasing research interest. As part of this overall effort, we report herein the fabrication and characteristics of Zr-based ribbon samples with three different compositions: $Zr_{56}Co_{28}Ga_{16}$, $Zr_{56}Co_{28}Ga_{14}Si_2$, and $Zr_{56}Co_{28}Ga_{14}Sn_2$. The supercooled-liquid region $\Delta T = T_x - T_g$ of these materials is 16, 18, and 29 K, respectively, where T_x is the temperature of the onset of crystallization and T_g is the glass-transition temperature. The samples are thermally characterized by using differential scanning calorimetry and by determining the activation energy. The corrosion resistance is determined by immersing the materials for up to 20 days in a simulated body fluid, and the cytotoxicity is measured from the proliferation of osteoblast-like cells on the samples. Finally, the mechanical properties are investigated by nanoindentation. The Young's modulus is 112 GPa. These results all highlight the suitability of this metallic glass for biomedical applications.

1. Introduction

Metallic materials are widely used as biomaterials in applications involving implants or prostheses or for medical hardware such as screws or pins. Some of the best-known medical materials are Ti-based alloys, such as Ti-6Al-4 V, or CoCr-based alloys, and 316 L stainless steel. However, the medical use of crystalline metallic materials is restricted by demanding biomedical standards that prevent their use. Aluminum, in the form of released ions, is seen as a potential cause of Alzheimer and also as a bone-growth inhibitor [1, 2]. Vanadium is cytotoxic and chromium may have adverse health effects [3]. As an alternative, a new type of material with unique properties is attracting ever more attention in the materials science field: the so-called metallic glasses. Because these materials are amorphous and have no grain boundaries, dislocations, or other microstructure, they have unique properties, such as a high elastic limit and excellent resistance to corrosion and wear. Glassy alloys have a lower Young's modulus than their crystalline counterparts, which reduces stress shielding between human bone and implant. Moreover, because of the absence of long-range order, the homogeneous chemical structure of these materials is an advantage, especially for small devices. Since the first metallic glasses (MGs) $Au_{75}Si_{25}$ elaborated by Klement et al. [4], glassy alloys have been adapted to their target applications and now are based on Mg [4,5], Ca [6], Ti [7, 8], Pd [9], Co [10], Zn [10], Au [11,12], Cu [13], and Pt [14].

Among all the materials, Zr-based MGs are the most extensively studied for many applications. They are perfectly suitable as biomaterials because they are highly biocompatible and have a relatively low elastic modulus (50–110 GPa); much lower than CoCr alloys and steel [15, 16]. The tribological characteristics, which are due to the high mechanical strength and hardness of Zr-based BMGs, are excellent for medical purposes and have been widely investigated [17]. Nevertheless, Zr- and Pd-based alloys have the best glass-forming ability (GFA) and are easy to fabricate in sizes reaching several centimeters. The largest-diameter sample was a Pd-based sample made by Inoue et al. in 2002 [18]. To increase the GFA, the atomic size mismatch should be large, which may be achieved by adding small atoms such as Be, Ni, or Al, which also promotes the plastic deformation by generating multiple shear bands [19, 20]. However, Be and Ni are not desirable elements for the human body, the latter of which exerts an antiproliferative action in cell cultures and causes allergies in many people [21].

In 2002, Inoue and Wada reported on the Ni- and Be-free system Zr-Co-Al [22–25]. Based on this system, to replace Al, we propose a nearby element in the periodic table that should have properties similar to Al; namely, Ga, which has advantageous properties compared to crystalline systems. The melting temperature is 29.78 °C and the boiling temperature is 1983 °C, making Ga the element with the largest liquid range, which is an advantage during processing. The expansion upon solidification is about 3.4% and the density is 5.9 g/cm^3. This element is

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mainly known as a component for semiconductor devices in the form of gallium nitride (GaN) or gallium arsenide (GaAs) or, because of its good chemical stability, for diagnostic tests for infection, inflammation, or tumors [26]. Since 1956, several studies have suggested replacing dental amalgam by Ga alloys [27, 28] because of their non-toxicity even if the Ga compounds such as GaN may present oral toxicity.

Below, we begin by discussing the development of a reliable Zr-based alloy without Ni, Cr, Be, Cu, or Al for good biocompatibility. Si and Sn are often used because their atomic radii differ from those of the other elements, thereby increasing the GFA [7, 29]. They also improve the corrosion characteristics [30–32]. We present three compositions: $Zr_{56}Co_{28}Ga_{16}$, $Zr_{56}Co_{28}Ga_{14}Si_2$, and $Zr_{56}Co_{28}Ga_{14}Sn_2$.

The second part of the paper discusses the characteristics of the proposed alloys, which were obtained notably by using x-ray diffraction (XRD) and differential scanning calorimetry (DSC), and how Si and Sn influence the GFA, corrosion resistance, and cytotoxicity.

2. Experimental procedure

2.1. Sample preparation

Ternary and quaternary ingots were prepared from the base materials Zr (99, 9%), Co (99, 9%), Ga (99, 9%), Si (99.9%), and Sn (99, 9%). A high-precision balance served to weigh the elements. Several preliminary tests were done to check for possible Ga vaporization, comparing the masses and EDX data before and after the processing, and no change in Ga composition has been observed. The master alloy was analyzed by energy-dispersive x-ray analysis (EDX) to check the homogeneity. Because the master alloy was homogeneous and the Ga had not evaporated, no pre-alloying was necessary, despite the low melting temperature of Ga. The master melt ingot was produced in a copper crucible under a high-purity argon atmosphere by using the arc melting. Ribbon samples of $Zr_{56}Co_{28}Ga_{16}$, $Zr_{56}Co_{28}Ga_{14}Si_2$, and $Zr_{56}Co_{28}Ga_{14}Sn_2$ were prepared by, first, induction melting of the master alloy, which was done in a custom-made melt-spinning device under an argon atmosphere. Once the ingot was melted (as indicated by its bright orange color and liquid behavior), it was ejected onto a single copper roller turning at 2500 rpm. The compositions of the three systems were also checked although, for samples with a small amount of Si or Sn, no accurate quantitative EDX analysis was possible. Thus Table 1 shows the EDX data only for the composition of the alloy $Zr_{56}Co_{28}Ga_{16}$.

The samples sizes are typical of ribbon samples: 1 mm wide and about 30 μm thick (see Fig. 1). For the DSC and XRD measurements, the samples were cut into small rectangles. The sample thickness was verified by using an optical microscope, and the width was measured by using calipers. Ribbons were used as samples because the GFA of these compositions prohibits bulk production.

2.2. Experimental methods

Room-temperature XRD was used to determine the amorphous character of the ribbon samples. To obtain sufficient signal, several small rectangular samples were placed next to each other on a Si support and exposed to Cu Kα radiation incident on the sample surface from 20° to 70° in a D8 Bruker device, with the x-ray tube operating at 40 kV and 40 mA. The diffraction patterns were analyzed by using the Bruker EVA software package.

Table 1
Elemental composition of $Zr_{56}Co_{28}Ga_{16}$ sample.

Elements	Amount (at. %)
Zr	53.6
Co	31.3
Ga	15.2

Once the alloys were verified to be amorphous, their thermal characteristics were obtained by using DSC. First, the supercooled-liquid region $\Delta T = T_x - T_g$, where T_x is the temperature of the onset of crystallization and T_g is the glass-transition temperature, was determined by measuring T_g and T_x of the metallic glass samples. For this, a PerkinElmer DSC was used under high-purity dry nitrogen at a flow rate of 20 mL/min for nonisothermal characterizations. During all measurements, the sample was sealed in an Al can and an empty can was used as a control. For better accuracy, samples of about 13 mg were weighed out for each measurement. The resistance to crystallization was determined by calculating the activation energy of the primary crystallization using the Kissinger [33] and Flynn–Wall–Ozawa laws [34, 35]– [36]. The heating rates used for this purpose were 10, 20, and 30 K/min.

The corrosion resistance was determined from immersion experiments. A centimeter-long sample was introduced in a simulated body-fluid solution (SBF) and then placed in the oven at 37 °C during 10 days and during 20 days. Next, XRD measurements were made to ensure that no crystallization occurred, the surface degradation was studied by using scanning electron microscopy (SEM), and energy-dispersive x-ray microanalysis was used to determine the corrosion products on the sample surface.

The Young's modulus was determined by using nanoindentation, which was done with a Nano Indenter G200 (Agilent Technologies) with a Berkovich tip using the CSM thin-film method [37, 38] with a depth limit of 500 nm and a surface-approach velocity of 10 nm/s. The ribbon sample was fixed to a resin substrate with a thin layer of conductive silver paint.

The sample biocompatibility was determined by cytotoxicity tests. Even if Ga is known to be nontoxic, because it was used to replace Hg in amalgam, only a few studies have investigated this question, and the addition of Ga into biomedical alloys presents a new use of the material [27, 28]. To elucidate this question, MG-63 osteoblast-like cells (Cell Culture Passage Number 41) (ATCC, Ref CRL-1427) were cultured in 24-well cell culture plates (Corning, NY, USA, ref. 3524) with RPMI 1640 medium (Dutscher, France, ref. L0498-500) (containing stable L-glutamine and phenol red) supplemented with 10% fetal bovine serum (Dutscher, ref. P040637100) and 5% antibiotic/antimycotic solution (Dutscher, ref SV30079.01) at 37 °C in a humidified atmosphere of 5% CO2. The samples were ribbon of some millimeters wide. The metallic ribbon was sterilized by UV for 20 min. A cellular suspension at 5000 cells was prepared using a cell counter (Millipore Scepter purchased at Dutscher, ref.: 053750). The Scepter cell counter uses the Coulter principle of impedance-based particle detection to reliably and accurately count every cell in the sample. The samples were placed in the 24-well cell culture plates (one sample in each well). Then, 50 μL of cellular suspension containing 5000 cells were deposited in the well, and cell culture plates were incubated 2 h at 37 °C under a humidified atmosphere of 5% CO2 to allow cell adhesion. After the addition of 2 mL of culture medium, cells were incubated until 10 days. The tests employed for measured the cell viability was Prestoblue technique (Invitrogen, Carlsbad, CA, USA) [39]. The resazurin, which is blue and non-fluorescent, is reduced by the metabolic mitochondrial activity of the cells into resorufin, a pink and fluorescent product, detectable by fluorometry. The cellular proliferation was evaluated after 4, 7 and 10 days. The culture medium was discarded and replaced by 1 mL of the culture medium without FBS, antibiotics and phenol red, but with 10% PrestoBlue put on each well. The samples were incubated 1.5 h at 37 °C under a humidified atmosphere of 5% CO2. Then, the plate was stirred, and 100 μL of each well were transferred in a 96 black-well plate and the fluorescence measured using an INFINITE PRO 200 fluorimeter (Tecan) with a wavelength of 535 nm for excitation and 615 nm for emission. After each measurement, cells were rinsed two times with RPMI, then 2 mL of medium were added and the plate incubated until the next measure (7 and 10 days). Each assay was done in triplicate. For each sample, a plastic control (cell culture treated polystyrene) was