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Rapid screening of potential metallic glasses for biomedical applications

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ABSTRACT

This paper presents a rapid screening process to select potential titanium and zirconium based metallic glasses (MGs) for bio-material applications. Electrochemical activity of 7 MGs including 6 bulk metallic glasses and 1 thin-film deposited MG in simulation body and human serum is first inspected. A low-voltage potential state test is also developed to simulate the cell membrane potential that the implant MGs will suffer. Results show that the MGs composed of $Ti_{65}Si_{15}Ta_{10}Zr_{10}$ and $Ta_{57}Zr_{23}Cu_{12}Ti_8$ exhibit excellent electrochemical stability in both simulation body fluid and human serum. In addition, the copper content in the MGs plays an important role on the electrochemical activity. MGs with the copper content higher than 17.5% show significant electrochemical responses. The cytotoxicity of the solid MG samples and the corrosion released ions are also evaluated by an in-vitro MTT test utilizing the murine bone marrow stem cells. Results indicate that all the solid MG samples show no acute cytotoxicity yet the corrosion released ions show significant toxicity for murine bone marrow stem cells. The rapid screening process developed in the present study suggests that the $Ti_{65}Si_{15}Ta_{10}Zr_{10}$ metallic glass has high potential for biomedical applications due to its good electrochemical stability and very low cytotoxicity.

1. Introduction

Materials used in medical devices either contact or are temporarily inserted or permanently implanted in the body, are typically described as biomaterials and have unique design requirements [1]. Biocompatibility of the implanted materials is one of the most important issues needed to be considered first while developing biomaterials. Biocompatibility of implanted materials depends on the time that it is exposed to the human body and the location in the body where it is applied or implanted. The implanted materials which contact with tissues must avoid inducing any toxic, irritating, inflammatory, allergic, or any carcinogenetic actions [2–5]. Recently, some metals such as cobalt chromium alloys, tantalum (Ta), niobium (Nb) and titanium (Ti) have been used for implants, since they have excellent corrosion resistance [6]. Titanium (Ti) is the most popular metal for producing long-term implantable devices due to its excellent biocompatibility. However, the lower strength and low hardness of commercial pure titanium (CP Ti, typically ~300–500 MPa for tensile strength and ~1.5 GPa for hardness) are issues for some clinical applications. In this regard, a number of titanium alloys were developed for biomedical applications. However, some studies have reported that lower wear resistance of titanium alloys may produce toxic debris after long-term usages [7,8]. In Ti alloy (Ti–6Al–4V), it was reported that aluminum (Al) and vanadium (V) were dissolved [9]. Al is a growth inhibitor of bone and a possible cause of Alzheimer's disease [10] and V has strong cytotoxicity. Cytotoxicity is often dependent on the ionization tendency of the metals. Highly corrosive materials in the body may release cytotoxic ions and cause cell apoptosis and necrosis after long-term use [11]. Therefore, some metallic glassy materials were studied for biomedical applications in the recent years since there is no grain boundary in the amorphous structure of metallic glasses (MGs). The metallic glass materials have become new candidates for developing potential orthopedic implants due to the high wear resistance for load-bearing applications [12]. Nevertheless, the undesired electrochemical corrosion between the grain boundaries might be suppressed or eliminated while using these amorphous structures [13]. Therefore, to realize the potential electrochemical responses for the newly developed MG materials is essential prior to the practical applications for these new materials.

Metallic glasses (MG) have a unique atomic structure, so they do not contain the microstructural defects such as vacancies, dislocations, twins or grain boundaries. Metallic glasses usually have more promising corrosion-resistant properties [14–17], high mechanical strength in the range of 800–3000 MPa and some plasticity [18–21], and superplastic processing capabilities within the super-cooled

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liquid temperature region [22,23], making them highly feasible for biomedical implant applications. For example, the strength of $Ti_{40}Cu_{36}Pd_{14}Zr_{10}$ [24] is about three times higher than pure Ti [25] and its elastic modulus is closer to bones. The surface structure of $Ti_{40}Cu_{36}Pd_{14}Zr_{10}$ can be modified by laser pulses to make cells attach. $Mg_{60}Zn_{35}Ca_5$ [26] or $Fe_{73}Nb_3Si_7B_{17}$ [27] MGs are being investigated as degradable functional materials. Unlike traditional steel or titanium, $Mg_{60}Zn_{35}Ca_5$, as a biomaterial for implantation into bones as screws, pins, or plates, to fix fractures, can dissolve in organisms at a rate of roughly 1 mm per month and is replaced with bone tissue. Metallic glasses of the Cu-, Ni- or Al-based alloys contain abundant harmful Cu, Ni or Al as their matrix element. The Pd- or Au-based BMGs are unlikely to be accepted for their high cost. The more promising candidates might still be the Ti-, Zr-, or Ta-based MGs, with no Be or Ni and minimum Cu or Al. It is known that implants with a high Young's modulus may cause more significant stress shielding effect. The Young's modulus of conventional implant materials of Ti and Co–Cr alloy are 121 GPa and 241 GPa, respectively, which are much higher than the human cortical bone of around 3–20 GPa [26,28]. The modulus mismatch between the implants and the bond tissue may cause stress shielding effect and may result in the decrease of the bone density (osteopenia) and even bone fractures. In contrast, the Young's modulus of metallic glasses is around 90 GPa for Ti–Zr–Cu–Pd MG and 48 GPs for Mg–Zn–Ca MG [29,30], which are much lower than the typical Ti or Co based implant materials due to the free volume inside the amorphous structure. Once the metallic glasses are made into porous foams, the modulus can be further lowered to around 10 GPa [31], close to that of human bones. Hence, that is the reason why developing MG-based implant materials is important for future prosthesis studies.

As long-termed bio-implant materials, in addition to suitable mechanical and biocompatibility performance, bio-corrosion response in human body fluids is also critical. In this study, we developed a novel electrochemical test by measuring the cyclic voltammetry response of various MGs in the simulation body-fluid (SBF) and human serum for the first screening. In addition, to examine the electrochemical stability of various MGs, a simulation cell potential test under a given potential can reveal the response in terms of induced current versus time. Through the cyclic voltammetry assay and the cell potential test, the MGs which present obvious electrochemical activity and large current variation can be eliminated for subsequent biocompatibility tests. If some metal ions are released from MGs, the cyclic voltammetry response would show larger current changes, indicating the instability and potential cytotoxicity. Such MG surfaces would also be accompanied by significant corrosion pits, unsuitable for bio-implant applications. The novel methods developed in this study provide a simple and fast way to screen potential metallic glasses for bio-applications.

2. Experimental

2.1. Material preparation and characterization

In the present study, seven potentially promising MGs in Ti-, Zr-, or Ta-based were used for the rapid screening processes, and compared with the reference, i.e., pure Ti. Our previous report [32] showed that the MGs composed of magnesium exhibited high electrochemical responses in solutions, such that magnesium was excluded from this study. Six various metallic glass ribbons, with nominal compositions of $Ti_{65}Si_{15}Ta_{10}Zr_{10}$, $Ti_{40}Cu_{36}Pd_{14}Zr_{10}$, $Ti_{45}Cu_{35}Zr_{20}$, $Zr_{53}Cu_{30}Al_8Pd_{4.5}Nb_{4.5}$, $Zr_{53}Cu_{30}Ni_9Al_8$, and $Zr_{61}Cu_{17.5}Ni_{10}Al_{7.5}Si_4$ (all in atomic percent) were produced utilizing the standard melt spinning process. All the composition were started with pure elements of Ti (99.99 wt.%), Cu (99.999 wt.%), Pd (99.9 wt.%), Zr (99.9 wt.%), Ni (99.9 wt.%), Al (99.9 wt.%), Si (99.99 wt.%), Nb (99.999 wt.%), and Ta (99.99 at.%). The MG ribbons were prepared firstly by induction melting, followed by rapid quenching via single roller melt-spinning under argon atmosphere [33], resulting in alloy ribbon samples with about 0.1 mm in thickness and about 10 mm in width. One thin film metallic glass sample with the nominal compositions of $Ta_{57}Zr_{23}Cu_{12}Ti_8$ was also produced by co-sputtering various alloy metal targets on microscope glass slides, with base pressure below 5×10^{-7} Torr [34].

The amorphous nature of the produced MG ribbons and thin films was inspected using Siemens D5000 X-ray Diffractometer (XRD) with Cu-K_α radiation. The thermal properties of the MG samples were characterized by Mettler Toledo DSC1 differential scanning calorimeter (DSC) and Netzsch DSC404 high temperature differential scanning calorimeter (HTDSC). JEOL JSM-6330 scanning electron microscopy (SEM) equipped with energy dispersive spectrometry (EDS) was used to observe the morphology and to verify the composition of the produced MGs before and after tests.

2.2. Electrochemical activity evaluation

The electrochemical activity of MGs was investigated using a three-electrode electrochemical cell. A standard Ag/AgCl electrode and a platinum wire were used as the reference and counter for the electrochemical tests, respectively. The electrochemical analysis was performed using a commercial electrochemical analyzer (CHI 611c, CH Instruments Inc., USA) at a controlled temperature of 37 °C. The Hank's SBF solution composed of 0.137 M of NaCl, 5.4 mM of KCl, 0.25 mM of Na_2HPO_4, 0.44 mM of KH_2PO_4, 1.3 mM of $CaCl_2$, 1.0 mM of $MgSO_4$, and 4.2 mM of $NaHCO_3$ was adopted. Identical test was also performed in human serum to further investigate the electrochemical response of MGs in real body condition. The electrochemical responses between the MGs and solution were characterized using a standard cyclic voltammetry (CV) with the scanning potential from +1 V to −1 V and a scan rate of 0.1 V/s. This potential range includes the oxidation potentials for most of the metals used in this study. The possible electrochemical response would be induced in this scan potential range such that a rapid screening for the potential MG samples with a low electrochemical response can be achieved. This rapidly obtained information can be used as a reference for further potentiodynamic polarization or cyclic polarization tests.

In addition, the MG materials may contact cell tissue in practical applications. A low-voltage of 80 mV (around the membrane potential of cell) was applied in another electrochemical test. The electrochemical stability can be examined by tracing the induced current versus time. This low-potential electrochemical test was used to mimic the contact condition of the MGs and cells to predict the cell potential induced corrosion of the metals. A standard potential state assay was used to monitor the induced current right after immersing the MGs into the simulation body fluid. The duration for this test was 30 min at a controlled temperature of 37 °C.

2.3. In-vitro cell viability testing

The cell viability test was performed using a standard MTT assay [35]. Pluripotent murine mesenchymal cells, D1 (ATCC) cloned from Balb/c mouse bone marrow stem cells [36] were used in the vitro cell culture experiment. D1 bone marrow stem cells were cultured in low glucose Dulbecco's modified Eagle's medium (DMEM) containing 10% fetal bovine serum (FBS), 1.5 g/L sodium bicarbonate, 1% NEAA, 1% vitamin C and 1% penicillin and streptomycin [37]. The culture medium was prepared at 37 °C in a humidified atmosphere with 5% of CO_2. The D1 cells for this in-vitro test were prepared in a 6-well cell culture dishes, cloned with the cell density of 5×10^4 cells/mL. The produced MGs and the reference pure Ti with the weight of 20 mg were firstly washed by 75% alcohol for antisepsis then immersed into the culture dishes with 5 mL of medium with D1 cells and then cultured for 72 h. It is noted that the group tested with