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Development and evaluation of a magnesium–zinc–strontium alloy for biomedical applications — Alloy processing, microstructure, mechanical properties, and biodegradation

Ren-guo Guan [a], Aaron F. Cipriano [b], Zhan-yong Zhao [a], Jaclyn Lock [b], Di Tie [a], Tong Zhao [c], Tong Cui [a], Huinan Liu [b,d,*]

[a] School of Materials and Metallurgy, Northeastern University, Shenyang 110004, China
[b] Department of Bioengineering, University of California at Riverside, Riverside, CA 92521, USA
[c] Department of Internal Medicine, Hospital of Liaoning University of Traditional Chinese Medicine, Shenyang 110032, China
[d] Materials Science and Engineering Program, University of California at Riverside, Riverside, CA 92521, USA

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ABSTRACT

A new biodegradable magnesium–zinc–strontium (Mg–Zn–Sr) alloy was developed and studied for medical implant applications. This first study investigated the alloy processing (casting, rolling, and heat treatment), microstructures, mechanical properties, and degradation properties in simulated body fluid (SBF). Aging treatment of the ZSr41 alloy at 175 °C for 8 h improved the mechanical properties when compared to those of the as-cast alloy. Specifically, the aged ZSr41 alloy had an ultimate tensile strength of 270 MPa, Vickers hardness of 71.5 HV, and elongation at failure of 12.8%. The mechanical properties of the ZSr41 alloy were superior as compared with those of pure magnesium and met the requirements for load-bearing medical implants. Furthermore, the immersion of the ZSr41 alloy in SBF showed a degradation mode that progressed cyclically, alternating between pitting and localized corrosion. The steady-state average degradation rate of the aged ZSr41 alloy in SBF was 0.96 g/(m^2·hr), while the pH of SBF immersion solution increased. The corrosion current density of the ZSr41 alloy in SBF solution was 0.41 mA/mm^2, which was much lower than 1.67 mA/mm^2 for pure Mg under the same conditions. In summary, compared to pure Mg, the mechanical properties of the new ZSr41 alloy improved while the degradation rate decreased due to the addition of Zn and Sr alloying elements and specific processing conditions. The superior mechanical properties and corrosion resistance of the new ZSr41 alloy make it a promising alloy for next-generation implant applications.

1. Introduction

Magnesium (Mg) stands as a prime candidate for medical implants and devices because it is naturally found in the human body, where it plays essential roles in metabolic pathways as enzyme catalysts [1–9], in cell structure and function [10–18], and in bone formation and growth by promoting calcium deposition [19,20]. Studies reported increased osteoblast adhesion on the surface of bioceramics (such as hydroxyapatite) and collagen when Mg ions were incorporated. As a result, the gene expression of signaling proteins increased and the bone-implant integration improved [21]. Additionally, Mg ions can be absorbed into the apatite crystal lattice to accelerate the adhesion of bone cells to apatite and hence promote the growth of hemopoietic bone tissue [22]. In animal studies, it was found that Mg supplements administered at early animal development stages could accelerate the transition of callus to osteogenesis, and promote osseous maturity and biomechanical functions [23–25]. Lastly, Mg also plays an important role in the healing of bone fractures, improving bone mineral density, and stabilization of implants [25–30]. In addition to superior biological properties, Mg has physical and mechanical properties that are comparable to that of natural bone. The density of Mg, 1.78–2.0 g/cm^3, is close to that of human bone, 1.8–2.1 g/cm^3 [31]. The elastic modulus of pure Mg (41–45 GPa) is closer to that of natural bone (3–20 GPa), while that of titanium alloys (110–117 GPa) or cobalt–chromium alloys (230 GPa) are much greater than bone [31]. As a result, Mg-based implants can effectively reduce stress-shielding effects on surrounding bone.

Despite the advantageous biological, physical, and mechanical properties, the degradation rate of pure Mg and currently available Mg-based biocompatible alloys is too rapid in physiological environments for medical applications. Abundant chlorine (Cl^-) ions found in body fluids could accelerate Mg degradation. According to the Mg degradation reactions, rapid degradation leads to fast release of Mg

* Corresponding author at: Department of Bioengineering, Materials Science and Engineering Program, Materials Science and Engineering Building 227, University of California at Riverside, 900 University Avenue, Riverside, CA 92521, USA. Tel.: +1 951 827 2944; fax: +1 951 827 6416.
E-mail address: huinan.liu@ucr.edu (H. Liu).

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ions accompanied by associated hydrogen release and subsequent accumulation in blood as well as increase of local pH [32]. This rapid increase in local concentration of Mg ions and pH can lead to cell death and tissue inflammation. The results of previous research revealed that a moderate Mg ion concentration could persistently induce new bone formation around the implants, but excessive Mg ion concentration and high pH induced by Mg degradation products resulted in the dissolution of local bone [33–35].

In order to take full advantage of the biological and mechanical properties of Mg, it is critical to develop engineering solutions to control Mg degradation in body fluids. Surface coatings have been developed in recent years to improve the degradation of Mg and Mg-based alloys. For example, hydroxyapatite (HA) coatings have demonstrated improved biocompatibility and therefore have been studied as a coating material for Mg-based implants [36]. However, studies have shown that the effectiveness of HA coatings on corrosion protection is highly dependent on both surface morphology of the underlying Mg alloy substrate and on the coating technique [37]. While surface coatings have provided a possible solution to improve Mg degradation, the key challenge resides in improving the degradation properties of the metallic substrate to avoid coating delamination issues. Current commercially available Mg-based alloys (such as AZ31, AZ91, and WE43) were originally designed for industrial rather than medical applications, and they may release harmful aluminum ions or rare earth elements. Moreover, their long-term toxicity to humans is still unknown.

The objective of this study is to develop a biocompatible Mg alloy to address the issues related to current Mg alloys and improve the mechanical and degradation properties. Biocompatibility is one of the key criteria for designing biomedical alloys. Zn and Sr were chosen as alloying elements because both of them are naturally present in the human body, are likely to satisfy the requirements of biocompatibility, and their degradation products can be metabolized and released from the body. Specifically, Zn takes an active part in the synthesis of many enzymes in the human body and is related to the activities of more than 300 enzymes. If Zn becomes deficient in the body, DNA replication slows down and as a result, protein synthesis is restrained [38]. Sr is a natural component in bones and teeth and can promote osteoid formation and bone growth, as well as adjust calcium metabolism [39]. Recent studies have found that Sr is essential and irreplaceable for the embryonic development of several mollusks [40]. Furthermore, Sr ranelate (a Sr compound) has been clinically used to promote osteoid formation and bone growth [39]. It has been reported that low doses of stable Sr compounds can reduce bone absorption, maintain high rate of bone formation, promote the synthesis and metabolism of bone, and have therapeutic effects on the treatment of osteoporosis [41]. In addition, recent research has shown that appropriate addition of Sr in Mg–Zr–Sr alloys can enhance osteoblastic activity and bone formation [42]. Therefore, we hypothesized that Sr in our designed Mg–Zn–Sr alloys would have similar benefits. Future studies on in vivo bone formation around Mg–Zn–Sr alloys are still needed in order to confirm this.

A second reason for choosing Zn and Sr as alloying elements resided in the fact that each of them can potentially improve the mechanical and corrosion properties when alloyed with Mg [43,44]. Zn has the same crystal structure as Mg and a 6.2 wt.% maximum solubility in Mg, where the solubility decreases as the temperature decreases. Thus, Zn can provide the advantages of solution strengthening and aging strengthening. Furthermore, solid solution of Zn in the α-Mg matrix phase increases the electric potential of the matrix and improves corrosion resistance. Although Sr has a limited solid solubility (0.11 wt.%; equivalent to 0.03 at.%) at the Mg–Sr eutectic temperature of 585 °C, the addition of Sr can form Mg–Sr intermetallic compounds in Mg alloys, refine the microstructure, increase the mechanical properties, improve the creep properties, and increase corrosion resistance of Mg alloys [45–47].

Last but not least, the purity of Mg plays an important role on the corrosion rate. Although Mg with super high purity (>99.99% purity) may have better corrosion resistance than some alloys (certainly not all alloys), producing Mg with super high purity is too costly to be practical for implant applications. Moreover, pure Mg offers less control over mechanical properties to meet the clinical requirements. Therefore, the focus of this research is to search for better Mg alloys instead of trying to produce Mg with super high purity.

In this study, a Mg–Zn–Sr alloy composed of 4.0 wt.% Zn and 1.0 wt.% Sr (ZSr41) was designed and produced through metallurgical processing, including casting, rolling and heat treatment. Subsequently, the microstructures, and mechanical and degradation properties of the alloy were evaluated and compared with those of pure Mg control.

2. Experimental

2.1. Preparation and processing of ZSr41 alloy

A metallurgical process consisting of melting, casting, rolling, and heat treatment was used to produce the ZSr41 alloy. First, a stainless steel crucible was preheated to 690–700 °C. Pure Mg ingots with a purity of 99.95% were melted in the stainless steel crucible while blowing argon (Ar) gas into the crucible at a flow rate of 6 L/min. When the Mg ingots reached approximately 720 °C, preheated metallic Zn and Sr were added and the mixture was stirred slightly to facilitate reaction between alloying elements. Throughout the melting of Mg and the addition of Zn and Sr, Ar gas was used continuously to protect the alloy from oxidation. The melted mixture was then held at 690–700 °C for 30 min, deslagged, and cast as ingots at 720 °C. ZSr41 ingots were rolled at 380 °C into 2 mm thick sheets. The pure-Mg control was produced similarly using Mg ingots of the same purity. Because the objective of this study was to compare the Mg–Zn–Sr alloy with a pure Mg control, we kept Mg purity as a constant in order to remove the influence of Mg purity on the results. That is, we used the same Mg source with a constant purity of 99.95% for producing Mg–Zn–Sr ingots and Mg control.

Furthermore, for mechanical testing, degradation studies in simulated body fluid (SBF), and potentiodynamic measurements, the ZSr41 alloy sheets were aged at 175 °C for 4–16 h. The aged ZSr41 alloy sheets and pure Mg control were cut into 20 × 20 mm squares, and polished using 1200 grit silicon carbide abrasive papers (Ted Pella, Inc.) to remove surface oxides. After removal of surface oxides, ZSr41 and pure Mg samples had a silver-white color. Each sample was subsequently ultrasonically cleaned (VWR, Model 97043-036) for 15 min in 200 proof ethanol (Koptec), and individually weighed (W_0).

2.2. Microstructural characterization of ZSr41 alloy

An optical microscope (OLYMPUS, PMG51) and a scanning electron microscope (SEM; Model SSX-550) were used to observe the microstructures and surface morphology of the ZSr41 alloy samples at different processing stages as well as those of pure Mg. An energy dispersive X-ray spectrometer (EDS; EDAX9100) was used to determine the distribution of elements on the surface of the alloy at different processing stages. EDS data was used to compare the elemental composition in different surface features. Both SEM and EDS were also used to characterize the surface features and elemental composition of ZSr41 and pure Mg after degradation in SBF. Additionally, X-ray diffraction (XRD; PANalytical, X'Pert Pro) was used to analyze the crystal structures of the distinct constituent phases present on the surface of the as-cast ZSr41 alloy.

2.3. Mechanical testing of ZSr41 alloy

The mechanical testing system (MTS China, CMT5105) was used to determine tensile strength, Vickers hardness, and elongation at