In vitro characterization of ZM21 mini-tube used for biodegradable metallic stent

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A B S T R A C T

Feasibility of a ZM21 mini-tube to be used as biodegradable stent applications was studied mainly focusing on its microstructure, mechanical property and corrosion behaviors. This mini-tube was composed of α-Mg, a small amount of Mn0.815Si0.185 and possibly some undissolved Mn. Compressive yield strength, ultimate compressive strength and compressive strain of this mini-tube were 86.5 ± 4.9 MPa, 347.7 ± 15.0 MPa and 10.9 ± 0.4%, respectively. It exhibited decent corrosion resistance in Hank’s solution with a degradation rate of 0.26 mm/y. ZM21 mini-tube exhibited great potential to be used as biodegradable stents. But before that, localized corrosion should be well solved through impurity control and microstructure control.

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1. Introduction

Magnesium alloys have been studied as promising biodegradable stent materials [1]. In 2016 the first clinically-proven magnesium-based drug-eluting scaffold (Magmaris, BIOTRONIK) was approved with CE mark [2]. Superior to traditional metallic stents (non-biodegradable), blood vessels are set free from the metallic cage after full degradation of magnesium-based stents. In addition, mechanical properties (radial strength, deformability, deliverability, et al.) of magnesium-based stents are superior to those of biodegradable polymeric stents [3].

ZM21 is a commercial magnesium alloy with approximate 2.0 wt% Zn and 1.0 wt% Mn. Zn is responsible for the improvement of mechanical properties, especially ductility. Meanwhile, Mn is effective in increasing the corrosion resistance in the presence of Fe as an impurity in magnesium [4]. Zn and Mn are essential for human and therefore unlikely to cause harmful effects at fairly low concentrations [5]. ZM21 alloy exhibits good formability and it has been successfully fabricated into mini-tube, which makes it a promising candidate for biodegradable stent material since mini-tube is the precursor of stent fabrication. In present study, in vitro performance of ZM21 mini-tube to be used as biodegradable stent was investigated, mainly focusing on its microstructure, mechanical property and corrosion behaviors in Hank’s solution.

2. Material and methods

A ZM21 mini-tube (ID = 2.625 ± 0.004 mm, OD = 3.156 ± 0.004 mm) was cut into pieces, 10 mm in length, and polished in Jiangyin Fasten-PLT Materials Science Company Ltd. Details about the preparation of ZM21 mini-tube could be found in our previous work [6]. An X-ray diffractometer (XRD, X’Pert Pro MPD) was employed to identify the constituent phases. The test was performed by using a Mono-Capillary PreFix Module operated at 45 kV and 40 mA with Cu Kα radiation, at a step size of 0.017° over a range of 10–90°. Microstructure was observed under a scanning electron microscope (SEM, HITACHI S-4800, Japan) equipped with an energy dispersive spectrometer (EDS) after etched in 4% nitric acid alcohol solution. Compressive test of the tube sections was performed on a universal material testing machine (Instron 5969, USA) at a crosshead speed of 0.5 mm/min. Immersion test was carried out in Hank’s solution (H1025, Solarbio) at 37 ± 1°C with an exposure ratio of 20 mL/cm², according to ASTM-G31-72 [7]. The pH value during immersion was monitored by using a pH meter (PB-10, Sartorius), with normal Hank’s solution as control. Ion concentrations (Mg, Ca and P) in Hank’s solution after immersion were measured by an inductively coupled plasma emission spectrometer (ICP-OES, iCAP 6000, Thermo). Corrosion products on the
Fig. 1. (a) Typical microstructure of ZM21 mini-tube under SEM and second phases found in the alloy matrix; (b) element distribution in Fig. 1(a) particle C; (c) EDS results corresponding to particles A, B and C in Fig. 1(a), presence of Au was derived from Au-sputtering during sample preparation; (d) XRD pattern of ZM21 mini-tube; (e) compressive stress–strain curve of ZM21 mini-tube, insert indicating the failure mode.
Fig. 2. (a) X-ray and micro-CT examination of ZM21 mini-tube after immersion for 7 days; (b) surface morphologies of ZM21 mini-tube before & after immersion (before and after removing corrosion product), and corresponding locally enlarged details; (c) typical cross-section morphology of ZM21 mini-tube after immersion and corresponding elements distribution.
Sample surface were characterized by Fourier transform infrared spectroscopy (FTIR, Nicolet iS 50, Thermo Scientific) and XRD. FTIR spectrum was recorded from 4000 to 650 cm\(^{-1}\) at 1 cm\(^{-1}\) resolution. The corroded samples were examined under a high resolution micro-CT scanner (Skyscan1172, Bruker) at a spatial resolution of 10 \(\mu\)m. Samples were also observed under SEM before and after removing the corrosion products in chromic acid [8]. Corrosion rate was calculated according to the following equation, 
\[
CR = \frac{3.65\Delta W}{\rho t}
\]
by measuring the weight loss.

3. Results and discussion

**Fig. 1(a)** shows the typical microstructure and second phases in the matrix of ZM21 mini-tube. ZM21 exhibited a fully recrystallized microstructure composed of equiaxed grains with an average size of 25 \(\mu\)m determined by using the linear intercept method. Some white particles with size less than 2 \(\mu\)m were found throughout the \(\alpha\)-Mg matrix and they were rich in Zn and Mn, as depicted in **Fig. 1(c)**. Some particles with larger size (~5 \(\mu\)m) were also found to be embedded in the matrix and they were rich in Mn and Si. Besides, common impurities in magnesium, Fe and Al, were also detected in those particles, **Fig. 1(b)** and (c). According to the XRD pattern in **Fig. 1(d)**, second phase particles in ZM21 mini-tube should mainly be Mn\(_{0.815}\)Si\(_{0.185}\). A small amount of undissolved Mn could exist at the same time. **Fig. 1(e)** displays the compressive stress–strain curves of ZM21 mini-tube. The compressive yield strength, ultimate compressive strength and compressive strain at the maximum stress were 86.5 ± 4.9 MPa, 347.7 ± 15.0 MPa and 10.9 ± 0.4%, respectively. **Fig. 2(a)** presents the X-ray and micro-CT examinations of ZM21 mini-tube after immersion for 7 days. Some low-density areas could be observed under X-ray and they corresponded to the locally corroded areas under micro-CT examination, as indicated by red arrows. Before immersion, limited surface defects (pits) already existed on the sample surface and they should be derived from the chemical brightening process. Second phase particles or contamination with high contents of Fe, Cu and Al should be responsible for those defects, owing to their galvanic effect with the \(\alpha\)-Mg matrix. After immersion, a corrosion product layer mainly composed of Mg, O, Ca, P and Na was formed. At locally corroded sites, this layer was much thicker, **Fig. 2(b)** and (c). After removing the corrosion products, actual corrosion morphology of the matrix was revealed. At uniformly corroded area (area D), mild corrosion happened and pitting could still be found at micron level. Clear and intact grain boundaries could be observed at typically local corrosion area, such as area E, suggesting that grain boundary was not the vulnerable site during corrosion. For a stent with normal strut thickness of 150 \(\mu\)m, stent strut only consists of several grains. If grain boundaries were sensitive to corrosion, severe corrosion at grain boundaries would cause premature failure of stent. At severely corroded sites (area F), deep holes were revealed...
beneath the corrosion product layer. Non-uniform distribution of the second phase particles and high impurity contents at specific sites were believed to be responsible for the localized corrosion.

Cross-section element analysis revealed that Ca and P were enriched in the surface layer of the corrosion product layer, especially at the locally corroded sites, as revealed in Fig. 2(c). FTIR results indicated the presence of H2O, OH−, CO3− and PO4−, as shown in Fig. 3(a). Based on the FTIR and XRD results, constituent phases in the corrosion product layer could be identified. The corrosion products were mainly composed of Mg(OH)2, MgCO3·2H2O and Ca10(PO4)3(CO3)3(OH)2.

During the first day of immersion, pH value of Hank’s solution had a rapid increase (7.4–8.5), implying the fast degradation at the initial stage of immersion. Thereafter, it slowly increased and finally reached at a relatively stable value. The pH value kept lower than 8.8 during the whole 7-day-immersion, implying a low corrosion rate, as shown in Fig. 3(c). Mg releasing rate during 7-day-immersion was 2.14 ± 0.47 µg/(mL·d). Ca and P concentrations after immersion were lower than those in the normal control, indicating their deposition on the sample surface. Erinc et al. proposed that corrosion rate of magnesium alloys should be lower than 0.5 mm/y to satisfy the requirement for biodegradable stents [10]. Corrosion rate calculated by weight loss of the ZM21 mini-tube was 0.26 ± 0.07 mm/y, suggesting a reliable degradation rate for stent.

Generally, mechanical properties of magnesium stent are superior to polymeric materials which are developed for biodegradable stents due to its metallic nature [11]. ZM21 mini-tube exhibited a low yield strength ratio of 0.25. This endows the ability to be strengthened when plastic deformation is imposed during stent expansion. It should be favorable to stent radial support force. Besides element toxicity, corrosion rate and corrosion mode are two key aspects that mainly decide the reliability of stent. Even though ZM21 mini-tube exhibited a decent degradation rate (0.26 mm/y) in vitro, localized corrosion caused by impurities and non-uniformly distributed second phases should call for prompt attention. Otherwise, abrupt failure of the stent strut could impair mechanical supporting and implant reliability.

4. Conclusions

In the present study, microstructure, mechanical property and in vitro corrosion behaviors of a ZM21 mini-tube developed for biodegradable stents were systematically studied. ZM21 mini-tube consisted of α-Mg matrix, limited Mn0.815Si0.185, and a limited amount of undissolved Mn. It showed a decent corrosion rate of 0.26 mm/y in vitro, suggesting a satisfactory degradation rate for stents. Degradation products of ZM21 mini-tube were mainly Mg(OH)2, MgCO3·2H2O and Ca10(PO4)3(CO3)3(OH)2. All in all, localized corrosion induced by impurities or non-uniform second phase particles should be well solved before stent fabrication.

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