

Research Article

Diameter-dependent *in vitro* performance of biodegradable pure zinc wires for suture applicationH. Guo^a, R.H. Cao^b, Y.F. Zheng^{a,*}, J. Bai^{b,c}, F. Xue^{b,c}, C.L. Chu^{b,c}^a State Key Laboratory for Turbulence and Complex System and Department of Materials Science and Engineering, College of Engineering, Peking University, Beijing 100871, China^b School of Materials Science and Engineering, Southeast University, Nanjing 211189, China^c Key Laboratory for Advanced Metallic Materials, Southeast University, Nanjing 211189, China

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ABSTRACT

In this study, biodegradable pure zinc wires with 3.0 mm and 0.3 mm in diameter were prepared via hot-extrusion and subsequent cold-drawing process respectively. The microstructure, mechanical performance, corrosion behavior, *in vitro* cytocompatibility and antibacterial effect were comparatively studied. After cold-drawing, the mechanical property, especially the elongation of the $\phi 0.3$ mm pure Zn wire was improved significantly compared with the $\phi 3.0$ mm pure Zn wire. The *in vitro* corrosion study including immersion and electrochemical test showed acceptable corrosion resistance of these two materials in Hank's solution. The *in vitro* Human Umbilical Vein Endothelial Cells (HUVECs) viability assay showed obviously different results, in which the $\phi 0.3$ mm pure Zn wire demonstrated favorable cytocompatibility, while the $\phi 3.0$ mm wire exhibited severe cytotoxic effect with 100% extract concentration. Both of them exhibited partly antibacterial effect on *S. aureus*. These results demonstrated the feasibility of the prepared 0.3 mm pure Zn wire as the potential suture material with good absorbability.

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1. Introduction

Nowadays, biodegradable metals (BMs) [1] have received more and more attention as promising temporary implants, such as orthopedic, cardiovascular [2] and other medical applications, due to their favorable mechanical behaviors and biocompatibility. Spanning the last decade, the researches have focused on magnesium (Mg) [3–5] and iron (Fe) [6,7] and their alloys as BMs. Magnesium is one of the essential element abundant in human body, and plays an important role in many biological reactions for human life. However, the rapid corrosion resulting in hydrogen evolution, rapidly accumulated degradation products and loss of mechanical integrity, has restrained the clinical application for Mg and its alloys. In contrast, Fe and its alloys represent good mechanical performance and without hydrogen evolution during the degradation [7], yet exhibit relatively slow corrosion rate, therefore might cause problems similar to those found in permanent metallic implants.

Zinc (Zn) has a standard corrosion potential of -0.76 V, intermediate between Mg (-2.37 V) and Fe (-0.44 V), implying higher corrosion resistance than Mg, but faster corrosion rate in comparison to Fe. Moreover, Zn is also an essential element for human body and involved in large various aspects of cellular metabolism, immune and nervous systems and wound healing. It also promotes normal growth and a proper sense of smell and taste. The recommended dietary allowance (RDA) for zinc is 15 mg/day and the upper limit is about 40 mg/day [8]. Till now, pure zinc [9,10] and Zn-Mg [11–17], Zn-Ca [12,13], Zn-Sr [12,13], Zn-Mn [18], Zn-Li [19] and Zn-Cu [20,21] biodegradable alloys had been developed.

Due to the enormous application potential of temporary medical devices, there arises the requisition for biodegradable metallic fine wires [22,23], which are expecting to replace the permanent sutures made of stainless steel or titanium alloys so as to avoid the second surgery and potential complication. These biodegradable metallic wires can be employed as surgical staples for wound closure, and be knitted into various kinds of tubular mesh stents, as well as the reinforcement to support the polymer composite for orthopedic surgery [24], and so on. For example, Seitz et al. [25] manufactured four kinds of Mg alloys wires (AX30, AL36, MgCa0.8, and ZEK100) with 0.3–0.5 mm in diameter, which could be tightening knotted and met the parameter required for a medical suture.

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In this paper, pure zinc wire with diameter of 0.3 mm was prepared from the 3.0 mm diameter extruded Zn wire via sequent cold-drawing process. The objective of the present work is to comparatively investigate the diameter-dependent properties, including microstructure, mechanical property, *in vitro* biodegradation behavior and cytotoxicity, and finally evaluate the feasibility of the as-prepared pure zinc wire as the potential biodegradable suture.

2. Materials and methods

2.1. Material preparation

The pure Zn (99.98%, Nanjing yunhai Special Metals Co., Ltd, China) ingots were used as raw materials. After hot extruded at a temperature of about 200 °C with an extrusion ratio of 25:1, the Zn wire with 3.0 mm in diameter was prepared. Then via cold-drawing process through a series of wire-drawing steel dies with reducing diameters, the pure Zn wire with a diameter of 0.3 mm was finally prepared. For all samples used in the experiment, they were ultrasonic cleaned in acetone, absolute ethanol and distilled water for 10 min, respectively. For *in vitro* cytocompatibility and antibacterial testing, the wires with 3.0 mm and 0.3 mm in diameter were both sterilized by ultraviolet radiation for at least 4 h.

2.2. Microstructure characterization

X-ray diffractometer (XRD, Rigaku DMAX 2400, Japan) using Cu K α radiation with scanning range from 10° to 90° at a scan rate of 4°/min operated at 40 kV and 100 mA at room temperature was employed for the phase identification of the two kinds of pure Zn wires. For the sample preparation, pure Zn wires of 3.0 mm in diameter were cold-mounted into the epoxy resin, ground with #800, #1200 and #2000 grit SiC papers and polished with 0.5 μ m diamond pastes, whereas ten ϕ 0.3 mm pure Zn wires were stacked closely and scanned by XRD due to the very small diameter.

The wires of 3.0 mm and 0.3 mm in diameters for microstructure observation were cut from the cross-sectional direction, cold-mounted into the epoxy resin, ground with #800, #1200 and #2000 grit SiC papers and polished with 0.5 μ m diamond pastes, and then chemically etched by a solution of 4% HNO₃/alcohol solution. Their metallographic microstructures were observed by SEM (S-4800, Hitachi, Japan).

2.3. Mechanical property test

The tensile mechanical property test was carried out in a universal material test machine (Instron 5969, USA) at a displacement rate of 1 mm/min at room temperature. Specimens with 100 mm gauge length were used for mechanical property tests. Five parallel samples were taken for each group.

With the same sample preparing method as mentioned in Section 2.2, the hardness of the specimens was determined by the digital Vickers microhardness tester (HNV-2 T, Shimadzu Corporation, Japan) with a 0.98 N load and 15 s dwell time. Five indentations were applied for each sample.

For the bending curvature test of ϕ 3.0 mm pure Zn wire, we wound them around different cylinders with diameters in 40 mm, 20 mm, 18 mm and 16 mm, corresponding to the deformation strain of 3.8%, 7.5%, 8.3% and 9.4%, respectively. The knotting test of ϕ 0.3 mm wire was implemented by tying them into closed knots, as well as loops. The tensile property after knotted was also carried out with the same machine and method mentioned above in this section.

2.4. In vitro corrosion test

2.4.1. Immersion test

In this experiment, 10 mm was used as the standard length for calculation. The segmented pure Zn wires with geometric dimensions of ϕ 3.0 mm $\times$ 10 mm and ϕ 0.3 mm $\times$ 10 mm were immersed in Hank's solution at 37°. The ratio of solution volume to sample surface area was 20 ml/cm² according to ASTM G31-72 standard. Five parallel samples were taken for each group. After different immersion times, the samples were removed from Hank's solution, gently rinsed with distilled water, and dried at room temperature. Then the corrosion products were removed by ultrasonic cleaned in chromic acid solution (200 g/L Cr₂O₃) at 40° for 5 min, and the corrosion rates were estimated using the weight loss method. The surface morphologies before and after removing corrosion products were observed using SEM (S-4800, Hitachi, Japan) with energy-disperse spectrometer (EDS) attachment.

2.4.2. Electrochemical test

The electrochemical tests were conducted with an electrochemical working station (Autolab, Metrohm, Switzerland) at room temperature in Hank's solution. A three-electrode cell with the platinum counter electrode and the saturated calomel electrode (SCE) reference electrode were employed. For working electrode, we implemented an electrode holder to fix the one end of the Zn wires vertically and the rest parts of the wires can be immersed in the electrolyte. We ensured the length of each sample immersed in Hank's solution was 10 mm. The open-circuit potential (OCP) of each specimen was monitored for 1800 s. Afterwards, potentiodynamic polarization tests were carried out at a scanning rate of 1 mV/s and with the potential window of 500 mV above and below the OCP [26]. Each group was taken in five copies. By linear fit and Tafel extrapolation, corrosion parameters including open-circuit potential (OCP), corrosion potential (E_{corr}) and corrosion current density (i_{corr}) were analyzed [27]. After tests, the surface morphologies of the specimens were observed by SEM (S-4800, Hitachi, Japan).

2.5. In vitro cytocompatibility evaluation

Cell viability and proliferation evaluation was conducted according to ASTM 10993-5: 2009. Human Umbilical Vein Endothelial Cells (HUVECs) were utilized and cultured in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% fetal bovine serum (FBS), 100 U/ml penicillin and 100 μ g/ml streptomycin, in a humidified atmosphere, with 5% CO₂ at 37°. The extracts of the two kinds of wires were obtained by incubating them in the same culture medium mentioned above for 24 h respectively, with an extraction ratio of 1.25 cm²/mL and collecting the supernatants. After that, by adding a certain amount of the DMEM to dilute the extracts, the 50% and 10% concentration extracts were prepared. The cytocompatibility assays were evaluated using the 100%, 50% and 10% concentration extracts of the two kind of pure Zn wires. Cells were incubated in 96-well culture plates at a density of 3×10^3 cells/well and incubated for 24 h to allow cell attachment. Then the medium was replaced with the different concentration extracts of the specimens, with the DMEM medium as negative control. After incubating for 1, 3 and 5 days, the cell viability and proliferation were valued with a Cell Counting Kit-8 (CCK-8, Dojindo, Japan). The spectrophotometric absorbance of each well was measured with a microplate reader (Bio-RAD680) at 450 nm wavelength. The zinc ion concentrations in extracts of the specimens were measured by Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES, iCAP6300, Thermo).

To evaluate the influence of the extracted zinc ions on the cell morphology, HUVECs were seeded on the glass slide (0.17 mm

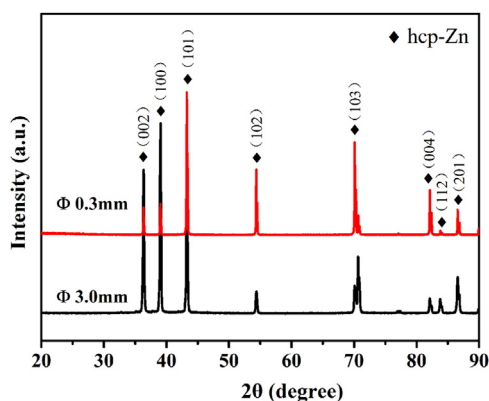


Fig. 1. XRD results of ϕ 3.0 mm and ϕ 0.3 mm pure Zn wires.

in thickness) in 24-well plates at a density of 5×10^4 cells with the extracts for 24 h. Cells cultured in normal DMEM were used as control. Then the cells were washed by PBS and fixed in 4% paraformaldehyde for 10 min at room temperature. 0.1% Triton was added and reacted for 7 min. After that, 5 μ g/ml FITC-phalloidin dye was added and incubated for 30 min at room temperature. Finally, the cell nuclei were stained by DAPI dye. The cell morphologies with different concentration extracts and samples were visualized with the confocal laser scanning microscope (A1R-si, Nikon). Each group was prepared in triplicate for observation.

2.6. In vitro antibacterial assay

The strains of bacteria used in this experiment were *S. aureus* (*Staphylococcus aureus*, Gram positive, ATCC 6538) and *E. coli* (*Escherichia coli*, Gram negative, ATCC 25922). The experimental specimens with dimensions Φ 3.0 mm $\times$ 5 mm and ϕ 0.3 mm $\times$ 5 mm were sterilized by ultraviolet radiation, respectively. The strains were prepared to 1×10^6 colony forming units (CFUs)/ml in Luria-Bertani (LB) medium. 2 ml prepared bacteria suspension (1×10^6 CFUs/ml) was added to each well in 24-well plate contained specimens, then incubated at 37 °C for 24 h. In the test, the planktonic bacteria in the culture medium were analyzed by the spread plate method and the LB medium was used as a blank control. The active bacteria were counted according to the National Standard of China GB/T 4789.2 protocol and the antibacterial ratio was calculated as follows: $\frac{(A-B)}{A} \times 100\%$, where A is the average number of bacteria on the control sample (CFU/sample) and B is the average number of bacteria on the testing samples (CFU/sample).

2.7. Statistical analysis

Statistical analysis was conducted with SPSS 17.0. Differences between groups were analyzed using one-way ANOVA followed by Turkey test.

3. Results

3.1. Phase and microstructure characterization of pure Zn wires

The constitutional phases for two kind of pure Zn wires were characterized by XRD, as shown in Fig. 1. The XRD patterns show that the two samples are composed of zinc phase with hexagonal close packed (hcp) crystal structure, without other phase being detected. It's worth noting that the intensity of the (004) planes of ϕ 0.3 mm Zn wires are particularly stronger than that of the (112) planes. We inferred that the stacking mode of the ϕ 0.3 mm Zn wires may cause the preferred orientation of the XRD pattern.

The microstructures of the two specimens are illustrated in Fig. 2. Extruding and drawing directions were labelled in the image respectively. As we can see, both wires exhibit puzzle shaped microstructures and no obvious preferred orientations, which are consistent with the inference about the XRD pattern above. The ϕ 3.0 mm Zn wire is composed of almost equiaxed grains with 5–10 μ m in size, while the ϕ 0.3 mm Zn wire has finer grains with around 2 μ m. During the drawing process, the dynamic recovery and recrystallization occurred and after that, the grain size had been decreased.

3.2. Mechanical properties of pure Zn wires

The mechanical properties of the Φ 3.0 mm and Φ 0.3 mm pure Zn wires are displayed in Fig. 3. The yield strength (YS), ultimate tensile strength (UTS) and elongation of two kind specimens were 45.95 ± 10.83 MPa, 74.01 ± 4.18 MPa, $3.15 \pm 1.51\%$ and 73.62 ± 4.76 MPa, 100.09 ± 6.46 MPa, $15.95 \pm 2.18\%$, respectively. The microhardness values (HV) of the two specimens were 45 ± 2 and 48 ± 4 , with no apparent difference between them. As can be seen, the overall mechanical performances of pure Zn wire with ϕ 0.3 mm diameter were superior to that of ϕ 3.0 mm, especially in the elongation. This can be broadly ascribed to the lower average grain diameter due to the drawing process [25].

For the potential application of wound closure, the knot feasibility and security of suture is also required in surgery to provide adequate tension. At the end of wound closure, the suture is knotted in specific ways. Apart from the tensile strength, the knots must also be securely sustained and be simple and easy to handle [25,28]. Hence, we investigated the knot properties of the two kind of pure Zn wires. When the ϕ 3.0 mm wires were wound along the cylin-

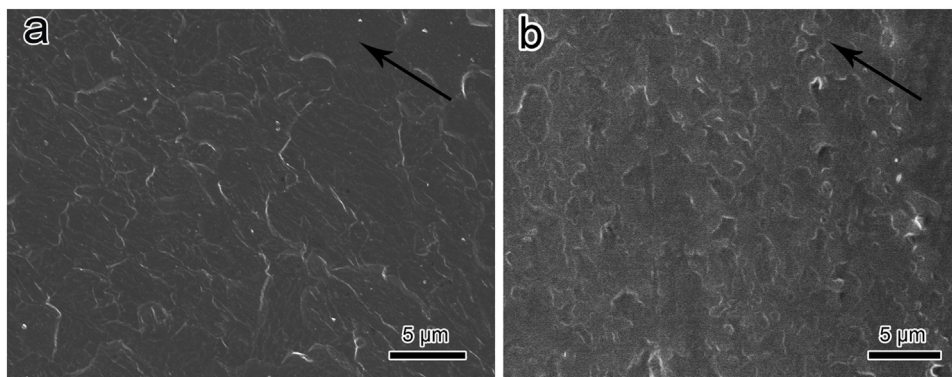


Fig. 2. Microstructures of (a) ϕ 3.0 mm and (b) ϕ 0.3 mm pure Zn wires observed by SEM. The extruding and drawing direction were labelled by black arrow.

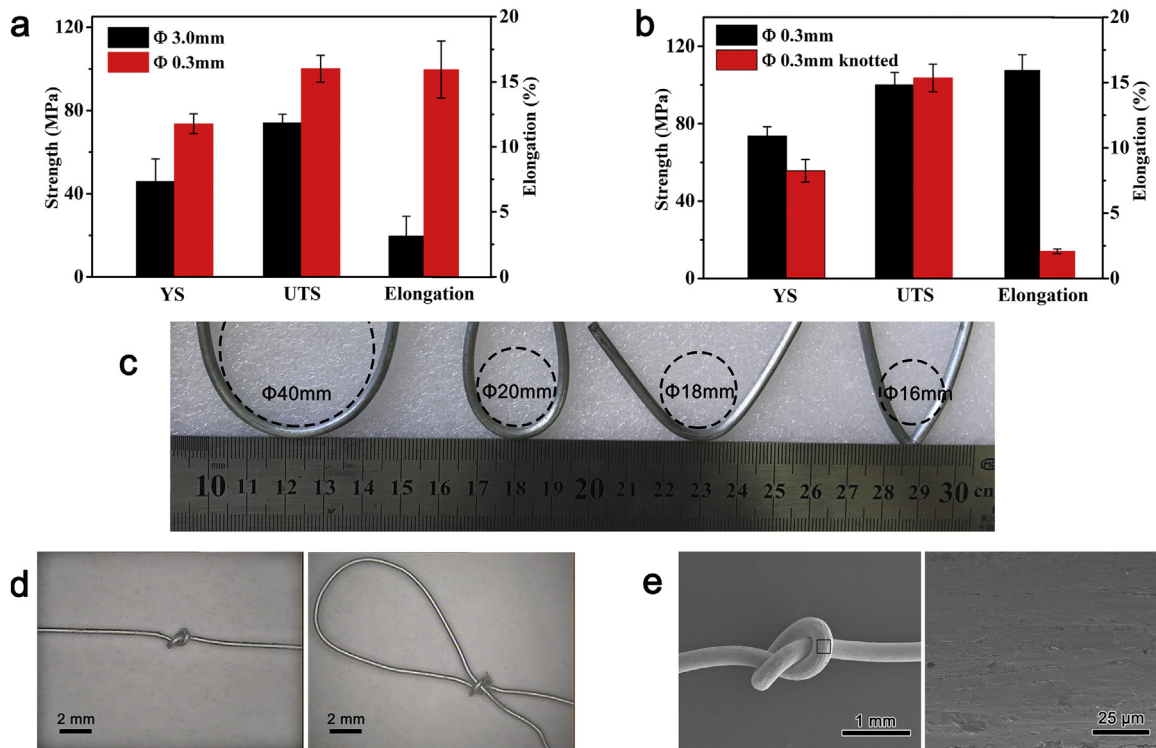


Fig. 3. Mechanical property parameters of $\phi 3.0$ mm and $\phi 0.3$ mm pure Zn wires. Tensile properties of (a) $\phi 3.0$ mm and $\phi 0.3$ mm pure Zn wires and (b) $\phi 0.3$ mm pure Zn wires before and after knotting. (c) images of $\phi 3.0$ mm pure zinc wires after being wound around cylinders with different diameters, (d) images of $\phi 0.3$ mm pure zinc wires with knot and loop, (e) microstructures of knotted $\phi 0.3$ mm pure zinc wires and some tiny hairline cracks can be seen in the knots by SEM.

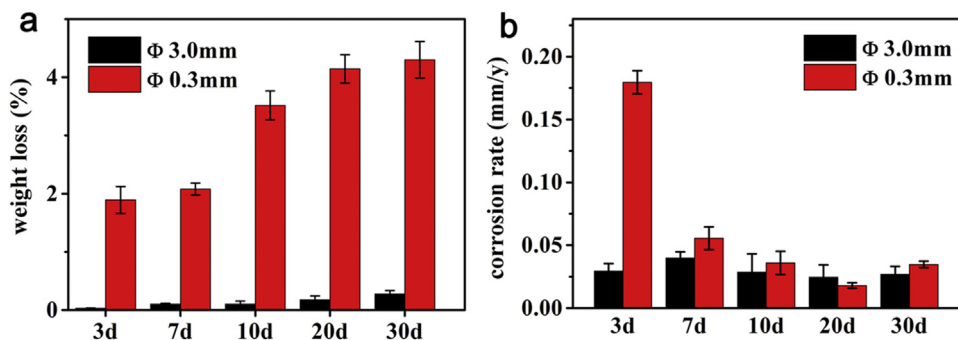


Fig. 4. (a) Weight loss and (b) corrosion rate of $\phi 3.0$ mm and $\phi 0.3$ mm pure Zn wires after immersion in Hank's solution for different days.

ders with different diameters, as shown in Fig. 3(c), they could be easily bent into U-shaped curvature around the $\phi 40$ mm, $\phi 20$ mm, $\phi 18$ mm cylinders. But fracture happened while wrapping along the $\phi 16$ mm cylinder, with the deformation strain around 9.4%. As for the $\phi 0.3$ mm wires, they could be easily tied into a closed knot with which loops could even be realized (Fig. 3(d)). After being knotted, the tensile strength of $\phi 0.3$ mm wires before and after knotted exhibited no apparent difference, while the elongation had reduced significantly (as shown in Fig. 3(b)). Some tiny hairline cracks can be observed from the microstructures of the knots (Fig. 3(e)), which can influence the mechanical properties and corrosion behaviors of the wires and need further investigation.

3.3. Corrosion behaviors of pure Zn wires

3.3.1. Corrosion behaviors during immersion test

Fig. 4 shows the corrosion results of the two kinds of pure Zn wires, calculated from the weight loss after immersion test. With the extension of immersion time, the weight loss rates of

the two kinds of pure Zn wires were both increasing continuously, while the corrosion rate decreased sharply after 7 days immersion for $\phi 0.3$ mm wire, and the $\phi 3.0$ mm wire showed relatively stable corrosion rate, as shown in Fig. 4. During the immersion in Hank's solution for 30 days, the $\phi 3.0$ mm pure Zn wire ($0.28 \pm 0.06\%$ weight loss ratio, 0.027 ± 0.006 mm/year corrosion rate) showed superior corrosion resistance compared with the $\phi 0.3$ mm wire ($9.52 \pm 0.31\%$ weight loss ratio, 0.035 ± 0.002 mm/year). The morphologies of the two specimens after 7 d and 30 d immersion time are exhibited in Fig. 5. All of the specimens were covered with layers of corrosion products and cracks could be observed on the surface due to dehydration process. The representative EDS analysis indicated that the corrosion products were mainly composed of Zn, C, O, P and Ca elements, which might be the zinc (calcium) phosphates, zinc (calcium) carbonates and zinc hydroxide.

In addition, we investigated the thickness of the corrosion layers of the two specimens through the cross-section. As shown in Fig. 5, the corrosion layer thickness was increasing slowly as immersion time increased. The thickness of $\phi 3.0$ mm pure Zn wire was around

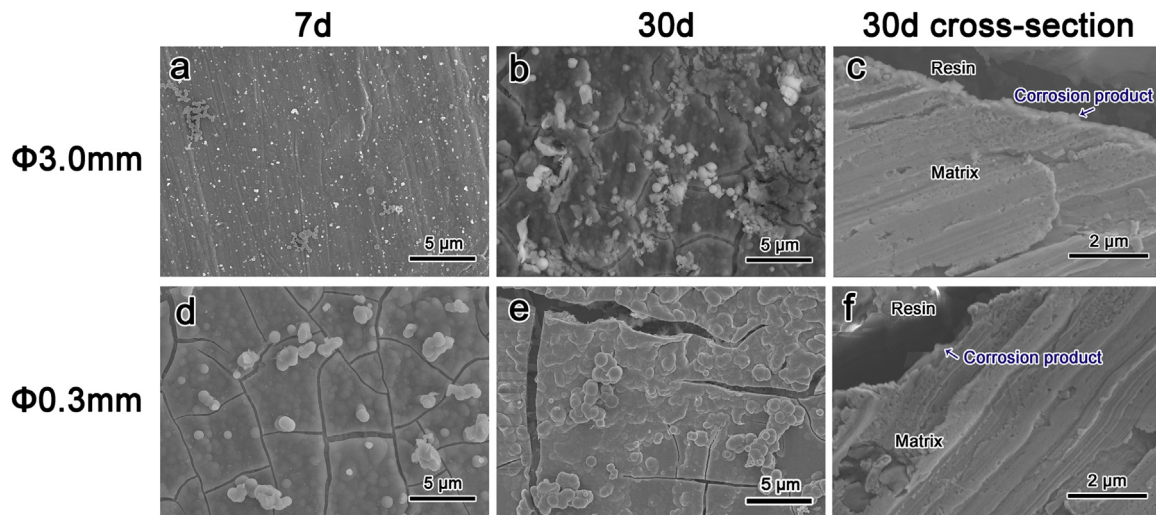


Fig. 5. Surface morphologies of (a–b) $\Phi 3.0$ mm and (d–e) $\Phi 0.3$ mm pure Zn wires after immersion for 7 d and 30 d, the thickness of corrosion product layers of (c) $\Phi 3.0$ mm and (f) $\Phi 0.3$ mm pure zinc wires at the cross-section.

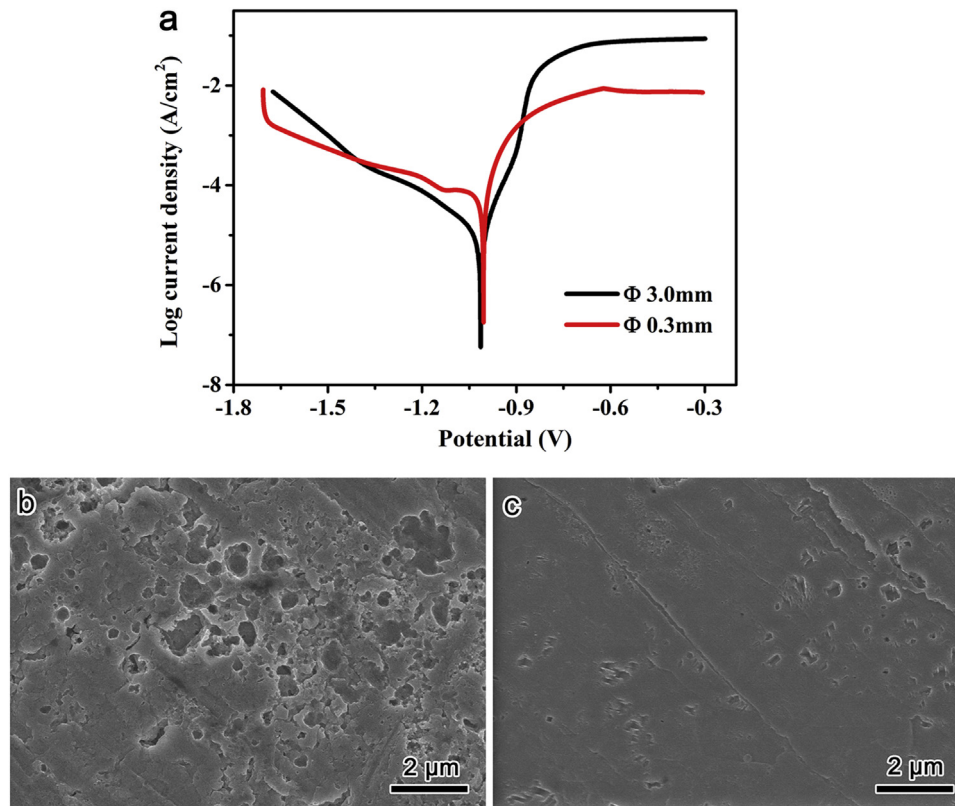


Fig. 6. (a) Potentiodynamic polarization curves, surface microstructures of (b) $\Phi 3.0$ mm and (c) $\Phi 0.3$ mm pure Zn wires after electrochemical test in Hank's solution.

0.2–0.3 μm after immersion for 30 days, while the $\Phi 0.3$ mm pure Zn wire displayed a very thin corrosion layer with less than 0.2 μm after 30 days immersion.

3.3.2. Corrosion behaviors for electrochemical measurement

Potentiodynamic polarization curves of two kinds of experimental pure Zn wires examined in Hank's solution are shown in Fig. 6(a). Typical parameters acquired from the test have been listed in Table 1. The corrosion potential (E_{corr}) between the two were comparable, with the value -1.016V and -1.009V , respectively. However, the corrosion current density of the $\Phi 3.0$ mm

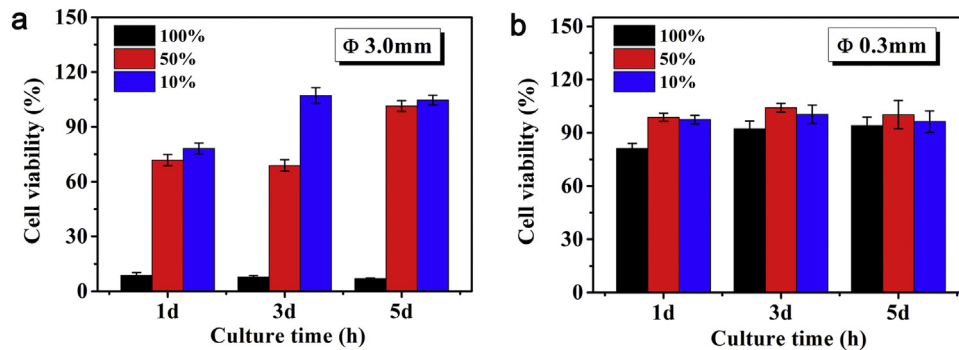
pure Zn wire was apparently higher than that of the $\Phi 0.3$ mm pure Zn wire. And the corrosion rate of the $\Phi 3.0$ mm pure Zn wire (0.90 ± 0.150 mm/year) was almost twice faster than the $\Phi 0.3$ mm pure Zn wire (0.421 ± 0.075 mm/year).

Fig. 6(b–c) shows typical surface microstructures of the two kinds of pure Zn specimens after electrochemical tests. Localized attacks with pits around 0.5–1.0 μm distributed on the surface of both specimens, while those on the $\Phi 0.3$ mm pure Zn wire were much smaller. At the bottom of pits, lamellar structures can be observed clearly.

Table 1

Typical electrochemical parameters of the pure Zn wires in Hank's solution.

Pure Zn wire	Open circuit potential (V_{SCE})	E_{corr} (V_{SCE})	I_{corr} ($\mu A \cdot cm^{-2}$)	Corrosion rate ($mm \cdot y^{-1}$)
$\phi 3.0$ mm	-1.018 ± 0.016	-1.016 ± 0.005	30.361 ± 5.002	0.909 ± 0.150
$\phi 0.3$ mm	-0.952 ± 0.019	-1.009 ± 0.006	14.045 ± 2.499	0.421 ± 0.075

**Fig. 7.** HUVECs cytocompatibility evaluation on (a) $\phi 3.0$ mm and (b) $\phi 0.3$ mm pure Zn wires.

The immersion test and electrochemical measurement are the two typical methods utilized to assess the corrosion behavior. In this experiment, the corrosion behaviors of the two kinds of pure Zn specimens applying electrochemical measurement were not completely consistent with the immersion test results. The electrochemical measurement is a transient test, and represents only a snapshot of the corrosion behavior at that time by itself [27]. When the potential applied, the protective layer formed naturally on the surface of the pure zinc might be destroyed, so severe corrosion occurred, with the higher current density and relatively fast corrosion rate. While as to the immersion test, it provides a simple benchmark for determining the actual amount of cumulative corrosion that has occurred for the materials *in vitro* [27]. During the immersion, the protective layers formed naturally on the surface of the two kinds of pure Zn specimens are relatively static and stable, so it took time to destroy the protective layer, and then the corrosion layer (mainly composed of Ca, P elements) began to form and then accumulate, preventing the further corrosion.

3.4. In vitro cytocompatibility evaluation

The viabilities of HUVECs cultured in extraction mediums of the two kind samples for 1, 3 and 5 days are shown in Fig. 7. For the $\phi 3.0$ mm pure Zn wire group, the cell viability was expectedly most reduced with 100% extract concentration, and increased as the extract percentage decreased. After 3 days of culture with extracts, no cytotoxicity was observed for 10% extract concentration as non-significant decrease in cell viability was observed. After 5 days of culture, cell viabilities were both high at 50% and 10% extract concentrations. On the contrary, the cell viabilities were all relatively high with 100%, 50% and 10% extract concentrations of $\phi 0.3$ mm pure Zn wire group, while the highest one was displayed with 50% extract concentration.

Cell morphologies of HUVECs cultured in the two kind extracts for 24 h are shown in Fig. 8. For the $\phi 3.0$ mm pure Zn wire group, cell density cultured with the 100% extract concentration were apparently lower compared with the control group. Cells were sparse and displayed shrunken shapes, which indicated the high cytotoxicity of the wire. As for the $\phi 0.3$ mm pure Zn wire group, no significant difference in cell morphology was observed among experimental and control groups. Cells showed benign response to the wire, with good spreading morphologies to numerous directions, as well as good cell-to-cell connection and visible stained

cytoplasmic filament. And the cell densities were high among the groups, demonstrating the good biocompatibility of the $\phi 0.3$ mm pure Zn wire. Zinc has been reported to exhibit noncytotoxic performance within released concentration lower than $3 \mu g/ml$ (3 ppm) in the cell culture medium [29,30] but induce cytotoxicity at high concentrations [31,32]. Shearier et al. [33] also found the different LD_{50} values of Zn^{2+} concentration for three types of vascular cells, with $50 \mu M$ for hDF (human dermal fibroblasts), $70 \mu M$ for AoSMC (human aortic smooth muscle cells), and $265 \mu M$ for HAEC (human endothelial cells). In our experiments, the released zinc ions were measured by ICP-OES, and the Zn^{2+} concentrations of the $\phi 3.0$ mm and $\phi 0.3$ mm pure Zn wires after 1 day DMEM immersion were $31.17 \mu g/ml$ and $2.56 \mu g/ml$ respectively, which was in good agreement with the above mentioned researches and experiment results. The current study proved the acceptable *in vitro* biosafety of the $\phi 0.3$ mm pure Zn wire.

3.5. In vitro antibacterial property

During the process of the wound closure or post-operation, infection is one of the key point the surgeon care about [34]. Since the *S. aureus* is one of the most common bacterium (Gram-positive bacteria) causing infections, the antibacterial effects of the two pure Zn wires were determined using the *S. aureus*. The bacteria suspensions around the samples after immersion for 24 h were re-cultivated on agar according to the bacteria counting method, as shown in Fig. 9. It could be seen that the percentage reduction of *S. aureus* colonies on the $\phi 3.0$ mm and $\phi 0.3$ mm pure Zn wires were $79.95 \pm 4.26\%$ and $71.72 \pm 3.23\%$, respectively compared with that on the blank control group. We also investigated the antibacterial effects of the wires against *E. coli* (Gram-negative bacteria), another common bacteria appeared in surgical site infections. As we can see in Fig. 9(e–h), there is no obvious difference of the percentage reduction of *E. coli* colonies on the $\phi 3.0$ mm and $\phi 0.3$ mm pure Zn wires, with high values of $92.61 \pm 4.36\%$ and $90.91 \pm 4.21\%$, respectively. The result demonstrates that both wires present partly antibacterial effect on *S. aureus* and *E. coli*, with no significant differences between them. Moreover, some previous works have reported that zinc ion seems to be only bacteriostatic, rather than be bacteriocidal [30,35].

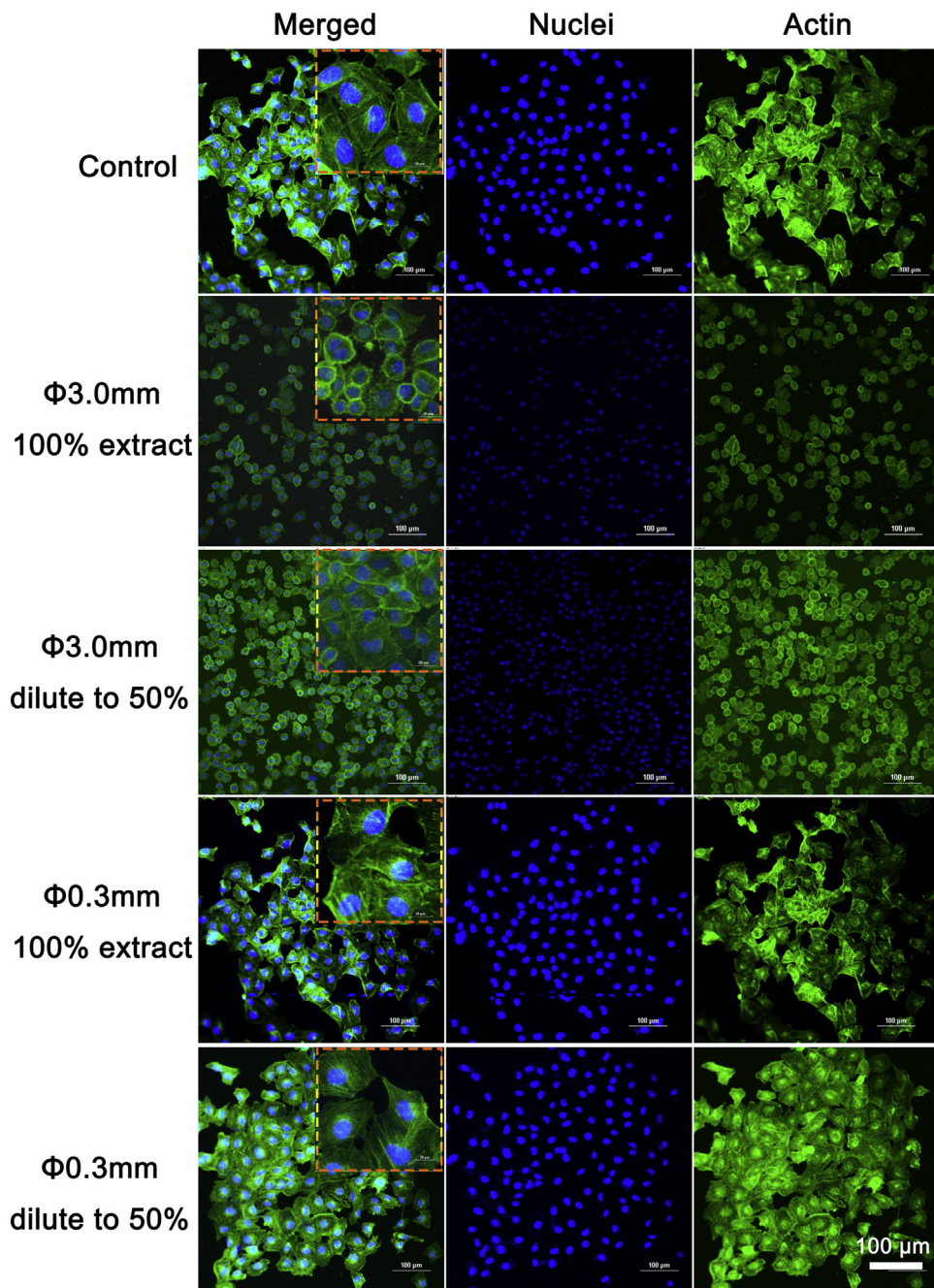


Fig. 8. Fluorescent morphologies of HUVECs cultured in the extracts of $\phi 3.0$ mm and $\phi 0.3$ mm pure Zn wires.

4. Discussion

4.1. Corrosion mechanism of the pure zinc wires

As for the $\phi 0.3$ mm pure Zn wire, the grain size decreased and the number of grain boundaries increased after drawing process compared to the $\phi 3.0$ mm pure Zn wire. The tiny hairline cracks existing on the surface of $\phi 0.3$ mm wire would also accelerate the corrosion tendency. Therefore, the $\phi 0.3$ mm pure Zn wire is more liable to corrode when immersed in Hank's solution. The corrosion process can be described as follows [36]: the anodic reaction is the dissolution of zinc, and the corresponding cathodic reaction is mainly oxygen reduction according to Eqs. (1) and (2), respectively.

Then the generated zinc ions react with the hydroxyl ion (OH^-) to form hydroxide precipitation following Eq. (3).



Afterwards, aggressive ions like Cl^- from Hank's solution will attack the protective film on Zn substrate and cause the dissolution of $\text{Zn}(\text{OH})_2$ following Eq. (4). Subsequently, the HPO_4^{2-} ions from Hank's solution can react with dissolved zinc ions to form insoluble phosphate such as $\text{Zn}_3(\text{PO}_4)_2 \cdot 4\text{H}_2\text{O}$.



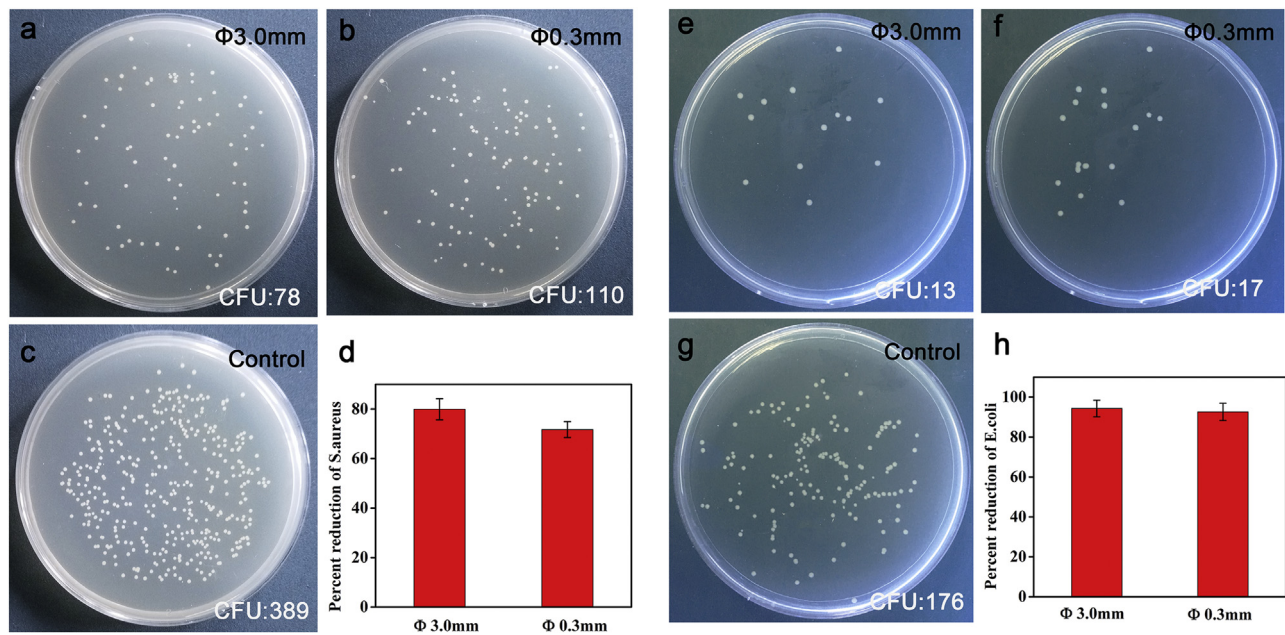
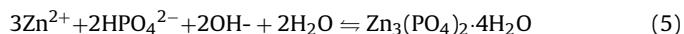


Fig. 9. Antibacterial assay results. The *S. aureus* colonies re-cultured on agar after incubating around the (a) $\phi 3.0$ mm and (b) $\phi 0.3$ mm pure Zn wires for 24 h, (d) percentage reductions of *S. aureus* colonies on the two kinds of experimental pure Zn wires compared to (c) control group. The *E. coli* colonies re-cultured on agar after incubating around the (e) $\phi 3.0$ mm and (f) $\phi 0.3$ mm pure Zn wires for 24 h, (h) percentage reductions of *E. coli* colonies on the two kinds of experimental pure Zn wires compared to (g) control group.

Table 2

Comparison of biodegradable polymers sutures in current clinical application and experimentally fabricated magnesium alloy sutures.

Materials	Diameter (mm)	Tensile strength (MPa)	Elongation (%)	Total tensile strength loss (days)
Polymers [38,42]				
Polyglactin 910 (Vicryl)	0.189 (0.010)	1377 (127)	52.8 (2.6)	28
Polyglycomer 631 (Biosyn)	0.287 (0.003)	868 (35)	102.4 (8.8)	28
Polydioxane (PDS II)	0.299 (0.002)	558 (16)	144.2 (8.2)	90
Plain surgical gut	0.299 (0.009)	413 (58)	55.4 (3.4)	14–21
Chromic surgical gut	0.302 (0.005)	410 (56)	52.0 (2.8)	14–21
Polyglyconate (Maxon)	0.301 (0.007)	726 (35)	93.6 (6.6)	56
Mg alloys [43,44]				
ZEK100	0.274	458(2)	10.6(1.1)	N/A
MgCa0.8	0.274	235(18)	9.4(4.2)	N/A
AL36	0.274	206(1)	14.4(2.0)	N/A
AZ31B	0.300	300(4)	14.9(3.1)	14–21



While as for incubating in DMEM, the different corrosion behaviors of the two pure zinc wires were largely ascribed to the diverse immersion medium and measuring methods. For the wires incubated in DMEM for 1 day, the corrosion courses of the samples are in the initial stage following Eqs. (1)–(3), so the insoluble hydroxides form and may offer the protective effect to the substrate to some extent. Due to the influences of protective corrosion products and protein in culture medium on the $\phi 0.3$ mm pure zinc wire, the corrosion rate decreased, and the free zinc ions released in the extracts, which were prepared by collecting the supernatants of culture medium, are relatively low. Thus, the zinc ions concentration of $\phi 0.3$ mm pure Zn wire measured by ICP-OES is lower than that of $\phi 3.0$ mm pure Zn wire. The different corrosion performance and released zinc ions concentration of the two wires result in the diverse behaviors in biocompatibility and antibacterial effect.

4.2. Potential application for biodegradable suture materials

Sutures are some of the most widely utilized medical devices for decades [37], which are used to facilitate closure and healing process of trauma or surgical-induced wounds [38]. In general,

an ideal suture should be easy to handle, form secure knots [39], possess adequate strength, have good ductility and elasticity to accommodate wound tissue and edema [40], have appropriate biocompatibility [37] and antibacterial effect in some extent [41]. Furthermore, sutures should be visible, easily sterilized, and inexpensive.

In current clinical fields, the most common utilized biodegradable sutures are composed of natural and synthetic polymers, for instance, collagen, chitosan, polyactic acid (PLA), polyglycolic acid (PGA) and Polyactic glycolic acid (PLGA), as shown in Table 2. However, the adverse inflammatory responses and severe local tissue reaction are reported in postoperative recovery. As for the biodegradable metal, they have been widely investigated for the application as cardiovascular and orthopedic implants, exhibiting adequate mechanical properties, favorable biocompatibilities and corrosion rates, which indicates the immense application potential in biodegradable sutures. In recent years, some studies have been focusing on the manufacture of magnesium alloy wires and the feasibility as biodegradable metal sutures (Table 2). The tensile strength manufactured are around 200–400 MPa, with more than 10% elongation to failure.

Since the strength of sutures should be no more than the tissue to be sewn, it indicated that the relatively lower strength was

not the obstacle for the pure Zn wire in suture application. Moreover, different strength value and degradation rate are required with various type of tissues. Hence, from the standpoint of biocompatibility, the $\phi 0.3$ mm pure Zn wire could satisfy the requirement for suture application, which exhibits favorable cytotoxicity and a certain degree of antibacterial effect, as well as moderate mechanical strength. One thing needs to be noted is that the pure Zn wire displayed a relatively low corrosion rate, which is too slow to meet the degradation time requirement, i.e., around 90 days at most. Further works should towards fabricating zinc-based alloy wires with smaller diameter and accelerated corrosion rate, as well as surface modification technique to endow specific biological and medical functional properties to the wires. For instance, they can be knitted into stents, as well as be fabricated into surgical clips and staples, applying to various body regions with diverse conditions, and they can also exert the anti-inflammation, anti-hyperplasia or anti-tumor effects during the service period.

5. Conclusion

In this study, the $\phi 0.3$ mm pure Zn wire had been prepared via drawing process and investigated for the feasibility as a potential biodegradable suture material, and the $\phi 3.0$ mm extruded wire was used as a comparison. On the one hand, the mechanical properties and corrosion resistance of the $\phi 0.3$ mm wire were significantly improved compared with the $\phi 3.0$ mm one. On the other hand, the $\phi 0.3$ mm pure Zn wire presented benign cytocompatibility even in 100% concentration extract, whereas the $\phi 3.0$ mm pure Zn wire exhibited higher cytotoxicity in 100% concentration extract and improved cytocompatibility after diluting its 100% concentration extract. Furthermore, both wires showed partly antibacterial effect on *S. aureus* and *E. coli* to avoid potential infection.

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