In vitro degradation and biocompatibility of Fe–Pd and Fe–Pt composites fabricated by spark plasma sintering

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A B S T R A C T

In order to obtain biodegradable Fe-based materials with similar mechanical properties as 316L stainless steel and faster degradation rate than pure iron, Fe–5 wt.%Pd and Fe–5 wt.%Pt composites were prepared by spark plasma sintering with powders of pure Fe and Pd/Pt, respectively. The grain size of Fe–5 wt.%Pd and Fe–5 wt.%Pt composites was much smaller than that of as-cast pure iron. The metallic elements Pd and Pt were uniformly distributed in the matrix and the mechanical properties of these materials were improved. Uniform corrosion of Fe–Pd and Fe–Pt composites was observed in both electrochemical tests and immersion tests, and the degradation rates of Fe–Pd and Fe–Pt composites were much faster than that of pure iron. It was found that viabilities of mouse fibroblast L-929 cells and human umbilical vein endothelial cells (ECV304) cultured in extraction mediums of Fe–Pd and Fe–Pt composites were close to that of pure iron. After 4 days’ culture, the viabilities of L-929 and ECV304 cells in extraction medium of experimental materials were about 80%. The result of direct contact cytotoxicity also indicated that experimental materials exhibited no inhibition on vascular endothelial process. Meanwhile, iron ions released from experimental materials could inhibit proliferation of vascular smooth muscle cells (VSMC), which may be beneficial for hindering vascular restenosis. Furthermore, compared with that of as-cast pure iron, the hemolysis rates of Fe–Pd and Fe–Pt composites were slightly higher, but still within the range of 5%, which is the criteria for good blood compatibility. The numbers of platelet adhered on the surface of Fe–Pd and Fe–Pt composites were lower than that of pure iron, and the morphology of platelets kept spherical. To sum up, the Fe–5wt.%Pd and Fe–5wt.%Pt composites exhibited good mechanical properties and degradation behavior, closely approaching the requirements for biodegradable metallic stents.

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1. Introduction

Biodegradable stents are currently considered as ideal stents. They are expected to effectively avoid the late stent thrombosis which is often caused by permanent stents. The material for biodegradable stents is required to have good biocompatibility and it should be kept intact for several months before completion of vascular healing [1]. Two typical classes of metallic materials including Mg-based [2–9] and Fe-based [10–18] alloys have been researched for this application. Compared with Mg-based metals, Fe-based metals possess more attractive mechanical properties [10]. Iron is an essential nutrient element in human body and plays an important role in vital biochemical activities, such as oxygen sensing and transport, electron transfer and catalysis [19]. Pure iron also has good mechanical property [10], biocompatibility and hemocompatibility [20,21] close to 316L stainless steel, which serves as the golden standard for stent material. Animal experiments demonstrated that degradable iron stents can be safely implanted without significant vascular restenosis caused by inflammation, neointimal proliferation or thrombotic events, and there was no evidence for local or systemic toxicity [20,22–24]. A clinical outcome also showed that there was no association between iron status and the incidence of major adverse cardiac events or coronary restenosis in human body [25]. Therefore, iron-based materials are considered as suitable materials for further development of novel biodegradable coronary artery stent. However, a faster degradation rate of iron is desired to apply to stents [20,22].

To obtain iron-based materials with appropriate properties for clinical applications, researchers have focused on the development of new kinds of Fe-based materials by modifying the chemical composition and microstructure. Hermawan et al. [10,26] were the first to study the effect of alloying elements on the performance of biodegradable iron-based materials. They found that alloying with Mn increased the strength and degradation rate of pure iron. Liu et al. [27] discovered that the addition of 6 wt.% of Si in Fe–30 wt.%Mn alloy established the shape memory effect. Xu et al. [28] reported that Fe–30Mn–1C alloy showed lower magnetic susceptibility and better mechanical properties than Fe–30Mn alloy. Schinhammer et al. [29] added 1 wt.% of Pd into Fe–10Mn alloy that sped up the degradation rate ten times faster than that

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of low carbon steel. They also did a research for Fe–Mn–C–(Pd) alloys. The Fe–Mn–C–Pd alloys were characterized by an increased degradation rate compared to pure iron [16]. The effects of alloying elements (Mn, Co, Al, W, Sn, B, C, and S) on the in vitro degradation behavior and biocompatibility of pure iron were also investigated by Liu and Zheng [30]. The results showed that the addition of all alloying elements except for Sn improved the mechanical properties of iron after rolling.

New fabricating methods were also tried by researchers, such as powder metallurgy [31], electroforming [32–34], equal channel angular pressing (ECAP) technique [35] and SPS sintering [36]. Although the predecessors made a lot of efforts for the improvement of Fe-based materials, the corrosion rate of Fe-based materials still could not meet the clinical application demand.

Palladium is a common alloying element in dental alloys. It has relatively low price and density when compared to gold and platinum. Palladium possesses a good range of solubility in several metals and could improve the mechanical properties of the matrix metals, too [37]. There have also been reports of using Pd-based organometallic compounds as antineoplastic agents [38]. Platinum has good mechanical property, low corrosivity and high biocompatibility [39,40]. It is used as essential components for many medical devices including implantable defibrillators, catheters, stents, pacemakers, neuromodulation device and upper-lid implant [41,42]. So palladium and platinum themselves are both excellent biomedical materials with good biocompatibility. 

In addition, the standard electrode potential of palladium and platinum (Pd is about 0.126 V, Pt is about 1.2 V) is higher than that of iron (about −0.44 V) [43], and galvanic corrosion may occur in the place where two kinds of metals contact, then accelerating the degradation of pure iron. Dispersion of platinum and palladium into pure iron matrix may also make the corrosion of pure iron more uniform. Furthermore, the effect of dispersion strengthening caused by the addition of platinum and palladium was expected to improve the mechanical properties of pure iron. The objective of the present work is to investigate the feasibility of adding palladium and platinum to pure iron for the preparation of biodegradable iron-based composites.

2. Materials and methods

2.1. Material preparation

Pure iron powder (99.0%, −300 mesh), pure palladium powder (99.99%, −200 mesh) and pure platinum powder (99.99%, −150 mesh), which were provided by China Metal Materials Technology Company, were used as raw materials. Iron powder mixed with 5 wt.% of palladium and platinum powder were prepared, respectively. Then the mixed powders were put into a 20-mm diameter graphite die and sintered under vacuum by SPS–1050 system (Sumitomo Coal Mining Company, Ltd.) with sintering temperature of 1000 °C and holding time of 5 min. Pure iron (99.9%) prepared by casting served as control.

The as-sintered Fe–Pd and Fe–Pt composite specimens (∅20 × 7 mm) and as-cast pure iron were cut into square pieces (10 × 10 × 1.5 mm³) and cylinders (∅12 × 5 mm), respectively. Square pieces were used for density measurements, microstructure characterization and series tests of microhardness, electrochemical properties, corrosion behavior, cytotoxicity, hemocompatibility and platelet adhesiveness. Each sample was mechanically polished to 2000 grit, then ultrasonically cleaned in anhydrous ethanol and dried in the open air. Before cytotoxicity test, the samples were sterilized with ultraviolet radiation for at least 2 h. Cylinder specimens were used for compressive test.

2.2. Microstructure characterization

Specimens were polished by 0.15 μm diamond paste, further ultrasonically cleaned in anhydrous ethanol and dried in the open air. Optical microscope (Olympus BX51 M) was used to observe the metallographic structure after the specimens were etched with a 4% HNO₃/alcohol solution. X-ray diffractometer (XRD, Rigaku DMAX 2400) using CuKα radiation was adopted to identify the constituent phases of Fe–Pd and Fe–Pt composites with scanning range from 10° to 100° and scan rate of 6°/min. Energy dispersive spectrometer (EDS) was used for the analysis of chemical composition.

2.3. Mechanical test

The mechanical properties of experimental composites and pure iron were determined by microhardness test and compressive test. Micro-hardness tests were carried out by a microhardness tester (SHIMADZU HMV-2t) measuring Vickers hardness with loading force of 0.2 kg and dwell time of 10 s. Center point and other four points uniformly distributed around the center point on the surface of each sample were selected for microhardness test. An average of five measurements was taken for each material. Instron 5969 universal test machine was used for compressive tests according to ASTM E9-89a [44]. The specimens were in the form of cylinder 2.5 mm in diameter and 5 mm in length. Compression strain rate was 2 × 10⁻³/s. An average of at least three measurements was taken for each group.

2.4. Electrochemical measurements

Electrochemical measurements were performed using three-electrode system at an electrochemical work station (CHI660C, China). The specimen, a platinum electrode and a saturated calomel electrode (SCE) were set as the working electrode, auxiliary electrode and the reference electrode, respectively. All the measurements were carried out at a temperature of 37 ± 0.5 °C in Hank’s solution. The area of working electrode exposed to the solution was 1 cm². The open circuit potential (OCP) measurement was set for 7200 s. Electrochemical impedance spectroscopy (EIS) was measured from 100 kHz to 10 mHz at OCP value after 2 h immersion in Hank’s solution. The potentiodynamic polarization curves were carried out from −1000 mV (vs. SCE) to 0 mV (vs. SCE) at a scanning rate of 0.33 mMVs⁻¹.

2.5. Static immersion test

In vitro static immersion test was performed in Hank’s solution, 50 ml for each sample following ASTM-G31-72 [45] at 37 °C in water bath. After 3, 10 and 30 days, the samples were removed from the soaking solution, gently rinsed with distilled water and quickly dried in case of oxidation. Changes on the surface morphologies of the specimens after immersion were characterized by ESEM (Quanta 200FE), equipped with an EDS attachment. Then, weighing after the corrosion products on the surface of samples dissolved in the 10 mol/l NaOH solution, an average of three measurements was taken for each group. The degradation rate was calculated based on the formula:

\[ CR = \frac{m}{St} \]

where CR (mg·cm⁻²·day⁻¹) is the corrosion rate, m (mg) is the mass loss, S (cm²) is the surface area of the specimen and t (day) is the time.

2.6. Dynamic immersion test

Dynamic immersion test was carried out using a dynamic corrosion test bench which was built in our previous research work [11]. Dissolved oxygen is an important factor that influences degradation of iron in a neutral medium, so the dissolved oxygen concentration in Hank’s solution was regulated to better simulate the blood environment. In this bench the wall shear stress (0.68 Pa), temperature (36.0–37.1 °C), pH value (7.35–7.45), and dissolved oxygen (2.8–3.2 mg·L⁻¹) were controlled to approach the common values in the
human coronary artery. Plate specimens were mounted in paraffin and then placed in a specimen holder. All specimens were exposed to the dynamic fluid flow (Hank’s solution) for 30 days (considering the generally bare metallic coronary stents would be covered by endothelial cells after 30 days in vivo implantation and no longer contact with blood directly) [11]. After the test, the samples were taken out, then the macroscopic surface morphology was characterized using a 2.5 dimensional precision image measuring instrument (HLEO, VACD-1010, China). After that the specimens were cleaned by deionized water and ethanol in turn, they were dried in the air. Changes on the surface morphology were characterized by ESEM (Quanta 200FEG), equipped with an EDS attachment. The corrosion rate was calculated based on the weight loss of specimens. Corrosion layers on the surface of samples were peeled off at first. The residual corrosion products were dissolved by 10 mol/l NaOH and rinsed by deionized water and alcohol in turn, then samples were weighed after they were dried in the open air. Corrosion rates were calculated by the same formula in static immersion test.

2.7. Contact angle measurement

Water contact angle of iron-based materials was measured by a contact angle analyzer (Kino SL200B); for each sample the measurements were carried out three times.

2.8. Cytotoxicity test

The cytotoxicity test was performed by an indirect contact method. Murine fibroblast cells (L-929), human vascular smooth muscle cells (VSMC) and umbilical vein endothelial cells (ECV304) were used to evaluate the cytotoxicity of experimental Fe–Pd and Fe–Pt composites. At first, all the cell lines were cultured in the Dulbecco’s modified Eagle’s medium (DMEM) with 10% fetal bovine serum (FBS), 100U·ml⁻¹ penicillin and 100 μg·ml⁻¹ streptomycin at 37 °C in a humidified atmosphere of 5% CO₂. According to ISO 10993-12 [46], extraction medium was prepared using DMEM with a surface area/extraction medium ratio of 1.25 cm²·ml⁻¹ in a humidified atmosphere with 5% CO₂ at 37 °C for 72 h. After the extracts were centrifuged, the supernatant fluid was withdrawn and stored at 4 °C before cytotoxicity test. The control groups involved DMEM medium as the negative control and DMEM including 10% dimethyl sulfoxide (DMSO) as the positive control. The metallic concentrations of ions in the extraction medium were measured by inductively coupled plasma atomic emission spectrometry (ICP-AES) (Leeman, Profile). Cells were incubated in the 96-well plates at the density of approximately 5 × 10⁴ cells per 100 μl medium in each well and incubated for 24 h to allow attachment. DMEM was then sucked out and replaced by extraction medium. Then 10 μl serum was...
added to each well. After 1, 2 and 4 days' incubation in the incubator respectively, the 96-well plates were observed under an optical microscope. Thereafter, 10 \( \mu l \) of MTT was added to each well. The cells were incubated with MTT for 4 h. Then 100 \( \mu l \) of formazan solubilization solution (10% sodium dodecyl sulfate in 0.01 M HCl) was added to each well and incubated for 10 h. The absorbance of each well was tested by a microplate reader (Bio-RAD680) at 570 nm with a reference wavelength of

### Table 1

<table>
<thead>
<tr>
<th>Materials</th>
<th>Density (g/cm³)</th>
<th>Relative density</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure iron</td>
<td>7.83 (0.03)</td>
<td>100%</td>
</tr>
<tr>
<td>Fe–Pd</td>
<td>7.15 (0.09)</td>
<td>88.3%</td>
</tr>
<tr>
<td>Fe–Pt</td>
<td>7.04 (0.02)</td>
<td>86.3%</td>
</tr>
</tbody>
</table>

*a Number in the brackets represents the standard deviation.

**Fig. 3.** SEM images of surface morphology and energy spectrum analysis of (a) Fe–Pd and (b) Fe–Pt composites.

**Fig. 4.** Compressive stress–strain curves of pure iron and Fe–Pd and Fe–Pt composites.
Here $\text{OD}_1$ is the mean absorbance of the experimental sample group and $\text{OD}_2$ is the mean absorbance of the negative control group.

Direct contact cytotoxicity of ECV304 cells was also carried out according to ISO 10993-5 [47]. 600 µl cell suspension was respectively added to each sterilized sample at a cell density of $6 \times 10^3$/ml. After being cultured in the incubator for 24 h, the medium was removed. Then the samples were gently washed by phosphate buffered saline (PBS); cells on the samples were fixed with 2.5% glutaraldehyde solution at room temperature for 1 h, then dewatered with gradient alcohol solution (50%, 60%, 70%, 80%, 90%, 95% and 100%) for 10 min, and finally freeze-dried for 2 days. The morphology of cells adhered on the specimens was observed by ESEM (Quanta 200FEG).

2.9 Hemolysis test and platelet adhesion

Healthy human blood (anticoagulant was 3.8 wt.% citric acid sodium) extracted from volunteers was diluted by physiological saline according to volume ratio 4:5. Pure iron and Fe–Pd and Fe–Pt composites were installed in centrifugal tubes with 10 ml physiological saline. Temperature was kept at 37 °C for 30 min. Then 0.2 ml diluted blood was added to each tube and incubated at 37 °C for 60 min, 10 ml deionized water with 0.2 ml diluted blood as the positive control and 10 ml physiological saline with 0.2 ml diluted blood as the negative control. Upon completion of the above operations, samples were removed, and then these tubes were centrifuged at 800 g for 5 min. Supernatant was transferred to 96-well multiplates, the absorbance ($\text{OD}$) was determined by a microplate reader (Bio-RAD680) at a wavelength of 545 nm. Hemolysis of samples was calculated by the formula:

$$\text{Hemolysis} = \frac{\text{OD}(\text{test}) - \text{OD}(\text{negative control})}{\text{OD}(\text{positive control}) - \text{OD}(\text{negative control})} \times 100\%.$$  

For platelet adhesion, whole blood from healthy human body was centrifuged at 1000 r/min for 10 min. Platelet rich plasma (PRP) was obtained from the upper fluid. Samples after ultraviolet disinfection were moved to 24-well multiplates and 0.2 ml PRP was added to each well, incubated at 37 °C for 1 h. After gently flushed by phosphate buffered saline (PBS), platelets on samples were fixed with 2.5% glutaraldehyde solution at room temperature for 1 h, then dewatered with gradient alcohol solution (50%, 60%, 70%, 80%, 90%, 95% and 100%) for 10 min, and finally freeze-dried for 2 days. The morphology of platelet adhered on the specimens was observed by ESEM (Quanta 200FEG).

3. Results and discussion

3.1. Microstructures

Fig. 1 shows the metallographs of pure iron and Fe–Pd and Fe–Pt composites and the corresponding grain size distribution measured from metallographs. The average grain sizes of these two kinds of experimental composites are quite close, both around $20 \pm 8 \mu m$, which are much smaller than that of as-cast pure iron ($180 \pm 90 \mu m$). It may be caused by the different preparation methods. For spark plasma sintering, lower temperature and shorter holding time could sinter powders to crystal with little grain growth [48]. The second phase particles inhibiting grain growth should also be taken into consideration. The decrease of the grain size could contribute to the improvement of mechanical properties.

Fig. 2 displays XRD patterns of experimental composites, as-cast pure iron as control. It can be found that the Fe-5wt.%Pd and Fe-5wt.%Pt composites both consist of α-Fe phase and FeO phase, but pure Pd or Pt phase was not found. PDF CARDS recorded that the peaks of Fe9.7Pd0.3 and Fe9.7Pt0.3 phases almost overlap with that of α-Fe phase in X-ray diffraction spectrum. As the contents of both Pd and Pt in experimental composites are less than 3 at.%, there might be quite a part of Pd and Pt solute in the surrounding pure iron matrix forming Fe9.7Pd0.3 and Fe9.7Pt0.3 phases in the sintering process, so the content of Pd or Pt phase was too low to be detected by X-ray diffraction. Fig. 3 showed that Pd and Pt were uniformly distributed in the iron matrix. The dark areas mainly consisted of Fe and O, which

![Fig. 5. Electrochemical test results of pure iron and Fe–Pd and Fe–Pt composites in Hank's solution: (a) Potentiodynamic polarization curve, (b) Nyquist plots.](image-url)
Fig. 6. Macrographs of surface morphology of experimental materials static immersed in Hank’s solution for 10 and 30 days.

Fig. 7. SEM images of samples’ surface morphology after statically immersed in Hank’s solution for different periods and the corresponding X-ray diffraction patterns of corrosion products on the surface of pure iron.
should be FeO phase, as revealed by the XRD results. Table 1 shows the density of Fe–Pd and Fe–Pt composites with as-cast pure iron as control at room temperature. Relative density of both Fe–Pd and Fe–Pt composites were less than 90%, which was probably due to the relatively low sintering temperature and pressure, as well as the existence of FeO in the composites.

3.2. Mechanical properties

Fig. 4 shows the compression stress–strain curves of Fe–Pd and Fe–Pt composites, with pure iron as control. The yield strengths (YS) of Fe–Pd and Fe–Pt composites were both about three times as that of pure iron. The ultimate compressive strength (UCS) of Fe–Pt composite was slightly higher than that of Fe–Pd composite. The rigidity of Fe–Pd and Fe–Pt composites was also much larger than that of pure iron. According to the binary phase diagram of Fe–Pd [49] and Fe–Pt [50] alloys, a small quantity of Pd and Pt could dissolve into iron matrix. However, the atomic radii of Fe (1.40 Å), Pd (1.40 Å) and Pt (1.35 Å) are very close [51], so the lattice distortion of α-Fe was negligible. Then the solution strengthening effect in these composites could not be significant. Therefore, the strength enhancement of the composites should be mainly attributed to the second phase strengthening effects. Moreover, the decrease of the grain size could make considerable contributions to the strength improvement of these composites [52]. However, the Fe–Pd and Fe–Pt composites exhibited low ductility, which can be explained mainly by the relatively low density (Table 1) [53].

The microhardness of Fe–Pd (184 ± 10 HV0.2/10) and Fe–Pt (309 ± 8 HV0.2/10) composites was much higher than that of pure iron (119 ± 3 HV0.2/10), especially for Fe–Pt composite, which was nearly three times as that of pure iron. Obviously, the addition of Pd or Pt greatly enhanced the strength of iron matrix.

3.3. Corrosion properties of Fe–Pd and Fe–Pt Composites

3.3.1. Electrochemical measurements

Fig. 5 shows the potentiodynamic polarization curves (Fig. 5(a)) and Nyquist plots (Fig. 5(b)) of Fe–Pd and Fe–Pt composites immersed in Hank’s solution, with as-cast pure iron as the control. The average electrochemical parameters were listed in Table 2. It was found that the corrosion potential was largely decreased and the corrosion current densities were increased after adding Pd and Pt into the iron matrix. As the Nyquist plots shown, plotted the variation in the excitation frequency impedance imaginary part (z") as a function of the impedance real part (z''), which obtained a series of semicircles. The diameters of semicircles obtained from Fe–Pd and Fe–Pt composites were smaller than that of pure iron, revealing their worse corrosion resistance. Since the diameter of high frequency capacitive loop can be considered as the charge transfer resistance and smaller charge transfer resistance corresponds to faster corrosion rate [54].

3.3.2. Static immersion corrosion behavior

Samples after 3 days’ immersion in Hank’s solution exhibited no conspicuous change on the surface. After 10 days’ immersion, localized corrosion mainly happened at the edge of pure iron sample, and the products were reddish brown. However, uniform corrosion could be observed on the surfaces of Fe–Pd and Fe–Pt composites, with claybank corrosion products (Fig. 6). When the samples were immersed in Hank’s solution for 30 days, most of corrosion products fell off, as shown in Fig. 6. Different orientations of the grains showed different colors.

Fig. 9. SEM images of samples’ surface morphology after dynamically immersed in Hank’s solution for 30 days: (a) pure iron and (b) Fe–Pd and (c) Fe–Pt composites. SEM images of these samples’ surface morphology after removed corrosion products: (d) pure iron and (e) Fe–Pd and (f) Fe–Pt composites.
Local distribution of black etch pits could also be found on the surface of pure iron, indicating localized corrosion feature of pure iron. However, a large number of corrosion pits were distributed uniformly on the surface of Fe–Pd and Fe–Pt composites, representing their macroscopically uniform corrosion behavior. Fig. 7 shows the SEM images of surface morphology of experimental samples, as can be seen from the figure:

(1) After 3 days' immersion, all the samples' surfaces almost kept intact.
(2) After 10 days' immersion, most area on the surface of pure iron remained intact, and only several corrosion pits were locally distributed on the surface. The surface of Fe–Pd composite was covered by a thin corrosion layer, and this layer didn't closely adhere to the matrix. Fe–Pt composites corroded most severely and a lot of deep corrosion pits were uniformly distributed on the surface.
(3) After 30 days' immersion, because the most of the corrosion products fell off from the surface of samples, grain boundary obviously presented on the surface of pure iron. Fe–Pd and Fe–Pt composites corroded much more seriously than pure iron. The iron substrate surrounded Pd- and Pt-rich areas corroded more seriously. This should be attributed to the galvanic corrosion occurred at the contact place of Fe and Pd or Pt. Pd- and Pt-rich areas that have relatively high corrosion potential as cathode.

Fig. 10. Water contact angles of (a) pure iron and (b) Fe–Pd and (c) Fe–Pt composites.

Fig. 11. (a) Ion concentration in extraction mediums of experimental materials and cell viability after cultured in extraction mediums and positive control for 1, 2 and 4 days; (b) L-929, (c) ECV304 and (d) VSMC.
sites, iron as anode sites, then formed a lot of tiny galvanic cells in the composites when immersed in Hank’s solution, so as to accelerate the corrosion rate of iron.

(4) The XRD spectrum of corrosion products on the surface of as-cast pure iron which had immersed in Hank’s solution for 10 days indicated that the corrosion products were mainly the Fe + 3O(OH) and Fe(OH)3. Corrosion products on the surface of Fe–Pd and Fe–Pt composites were the same as that on pure iron.

Fig. 8 shows the corrosion rates that were calculated from the weight loss after samples immersed in Hank’s solution for 30 days. The corrosion rates of both Fe–Pd and Fe–Pt composites were faster than that of as-cast pure iron. The corrosion rate of Fe–Pt composite was the fastest, about 2.73 times as that of as-cast pure iron. Compared to the corrosion rate of Fe-5wt.%W (about 1.15 times as that of as-cast pure iron) and Fe-0.5wt.%CNT composites (about 1.96 times as that of as-cast pure iron) [36], the addition of Pd and Pt increased the corrosion rate of pure iron much more significantly. In addition to the galvanic corrosion, FeO contained in Fe–Pd and Fe–Pt composites which could be easily oxidized to oxidation products was also an ignorable reason for increasing corrosion rate.

3.3.3. Dynamic immersion corrosion behavior

Fig. 9 panels (a)–(c) were SEM images showing surface morphology of experimental materials after corroding in dynamic environments. As can be seen from these figures, the numbers of corrosion products on the surface of Fe–Pd and Fe–Pt composites are much more than that on the surface of pure iron.

After the corrosion product layers were removed, surface morphologies of the substrates appeared, as shown in Fig. 9(d)–(f). Grain boundaries could be observed obviously on the surface of pure iron. The surface of Fe–Pd composite was much smoother. Fe–Pt composite corroded most seriously, with a lot of deep corrosion pits on the surface.

The corrosion rates calculated from weight loss of samples after dynamic immersion tests were also shown in Fig. 8. Compared with as-cast pure iron, both the Fe–Pd and Fe–Pt composites corroded much faster, and the Fe–Pt composite performed the fastest corrosion behavior. This result was in good consistence with the results from electrochemical tests and static immersion tests. Furthermore, corrosion rate of samples in dynamic immersion tests was much faster than that in static immersion tests. It was because in the dynamic immersion tests, 2.8–3.2 mg·l⁻¹ oxygen was dissolved in Hank’s solution to simulate blood environment, which was much higher than that in static immersion tests. In addition, continuous flow of Hank’s solution could impede deposition of ferrous ion and wash away part of the corrosion products, so the contact time of materials and Hank’s solution was prolonged.

3.4. Biocompatibility

3.4.1. Contact angle tests of Fe–Pd and Fe–Pt composites

The contact angles of Fe–Pd and Fe–Pt composites were shown in Fig. 10, with pure iron as control. The contact angles of pure iron and Fe–Pd and Fe–Pt composites were 51.73°, 64.74° and 51.83°, respectively. Generally, the smaller the contact angle is, the better the hydrophilicity will be and much easier the cell adhesion becomes. So, it could be a preliminary judgment that the biocompatibility of as-cast pure iron and Fe–Pt composite was superior to that of Fe–Pd composite.
3.4.2. Cytotoxicity tests of Fe–Pd and Fe–Pt composites

Fig. 11 illustrates the ion concentration in the extraction mediums (Fig. 11(a)) and the cell viabilities of L929, ECV304 and VSMC expressed as a percentage of the viability of cells cultured in the negative control after 1, 2, and 4 days' incubation in pure iron and Fe–Pd and Fe–Pt composite extraction mediums (Fig. 11(b) to (d)). It can be seen that the order of iron ion concentration in extraction mediums was: Fe–Pt composite > Fe–Pd composite > as-cast pure iron, which matched well with the results of in vitro corrosion tests. Pd and Pt ion concentrations were very low. Firstly, the contents of these two kinds of metals added to the composites were low. A more important reason was that these two kinds of metals have high chemical stability and were difficult to be corroded. Based on Fig. 11(b) to (d), the cell viability slightly decreased after being cultured with Fe–Pd and Fe–Pt composite extracts compared with pure iron group. This may be related to the concentration of leaching solution as higher iron ion concentration led to lower cell viability value. As for palladium and platinum ions, studies showed that palladium ion has a slight toxicity to eukaryotic cells and it is considered to be tolerated by human body [37,55], but Pt ion has high cytotoxicity [56]. However, the ion concentration of both palladium and platinum was extremely low, so their effects on cell reproduction should be very weak.

For L-929 and ECV304 cells, values of cell viability in experimental materials’ extracts were nearly 100% or more than 100% after cultured for 1 day. However, viabilities decreased to around 80% compared with that of negative control after 2 or 4 days' incubation. According to ISO 19003-5 [47], the cell viabilities of L-929 and ECV304 cells for experimental materials were both more than 70%, indicating Fe–Pd and Fe–Pt composites' slight cell toxicity to L929 and ECV304 cells. Zhu's work [57] also demonstrated that iron ions almost have no effect on metabolism of ECV304 cells. For VSMC, the cell viability in extracts of experimental materials was just about 60% compared with that of negative control after 4 days' incubation. According to Mueller's work [58], ferrous iron could reduce the proliferation rate of VSMC by influencing growth-related gene expression. The cell toxicity for VSMC was good for antagonizing restenosis in vivo [58].

Endothelial process is very important for stents. Thrombogenicity would decrease as the stent surface is covered by regrowth of endothelium [59]. So, direct contact cytotoxicity of ECV304 cells was also performed. The morphology of ECV304 cells after 24 h cultivation on the pure iron and Fe–Pd and Fe–Pt composites is shown in Fig. 12. ECV304 cells spread out on the surface of experimental materials in good condition, indicating that the experimental materials exhibited no inhibition on vascular endothelial process.

3.4.3. Hemocompatibility tests of Fe–Pd and Fe–Pt composites

The hemolysis rates of experimental materials were shown in Fig. 13(a). Hemolysis rates of Fe–Pd and Fe–Pt composites were slightly higher than that of pure iron. Nevertheless, the hemolysis rates of all materials were still below 5%, the judging criterion for excellent blood compatibility in ASTM F756-08 [60].

Fig. 13(b) illustrates the number of platelets per unit area adhered on the surface of samples. The number of platelets adhered to the Fe–Pd composite was the least, about 50% as that of pure iron. Platelets adhered to the Fe–Pt composite was slightly less than that to pure iron. Combined with the result of contact angle test, platelet adhesion might be associated with materials' hydrophilicity. Materials with poor hydrophilicity resist platelet adhesion. The morphologies of adhered human platelets on the experimental materials were shown in Fig. 14. Although a lot of corrosion products can be observed on the surfaces of Fe–Pd and Fe–Pt composites, the platelets adhered on these surfaces stayed round. However, the platelets adhered on the as-cast pure iron stretched a small amount of pseudopods. The generation of pseudopods is an obvious sign of platelet activation [61]. Therefore, compared to pure iron, the thrombosis of both Fe–Pd and Fe–Pt composites would decrease.

4. Conclusions

In order to meet the clinical application demands of biodegradable coronary stent, Fe-5wt.%Pd and Fe-5wt.%Pt composites were prepared by spark plasma sintering. The mechanical properties, corrosion behaviors and biocompatibility of these composites were systematically investigated by XRD, EDS, ESEM, ICP-AES and some other characterization techniques. The main conclusions were listed as follows:

1. Pd and Pt were uniformly distributed in iron matrix. The grain size of Fe-5wt.%Pd and Fe-5wt.%Pt composites was much smaller than that of as-cast pure iron. The addition of Pd or Pt improved the yield strength, rigidity and microhardness of pure iron.
2. Fe-5wt.%Pd and Fe-5wt.%Pt uniformly corrode in Hank’s solution. The addition of Pd or Pt greatly accelerates the degradation rate of pure iron, especially for the Fe–Pt composite.
3. Fe-5wt.%Pd and Fe-5wt.%Pt composites exhibited slight cytotoxicity to L-929 and ECV304 cells. At the same time, Fe–Pd and Fe–Pt composites indicate an inhibitory potential to VSMC, which is beneficial to prevent vascular restenosis.
4. The hemolysis of both Fe-5wt.%Pd and Fe-5wt.%Pt composites is slightly higher than that of as-cast pure iron, but still less than 5%. Furthermore, the number of platelets adhered to Fe–Pd and Fe–Pt composites is less than that of as-cast pure iron, and the platelets adhered on the specimens were round, without apparent induced thrombosis.

In summary, iron-based composites reinforced by Pd or Pt are promising biodegradable biomaterials for vascular stents with good combination of mechanical properties and biocompatibility as well as a proper degradation rate.