Development and degradation behavior of magnesium scaffolds coated with polycaprolactone for bone tissue engineering

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ABSTRACT

Rapid degradation of magnesium (Mg) alloys is the major drawback preventing these materials from being applicable as tissue engineering scaffolds. In order to resolve this issue, in this paper, porous Mg scaffolds coated by polycaprolactone (PCL) were synthesized and their material properties and *in vitro* biodegradation were fully examined. The results indicated that PCL coating can significantly enhance the compressive strength and degradation resistance of Mg scaffolds. We showed that while the uncoated Mg scaffold degrades completely (100% weight loss) after 72 h, the degradation (weight loss) of the Mg scaffolds coated by 3% and 6% PCL is only 36% and 23%, respectively. Thus PCL-coated Mg scaffolds, as a biodegradable metal scaffold, can potentially have a promising application in bone tissue engineering.

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1. Introduction

Designing appropriate scaffolds is one of the main challenges in tissue engineering (TE) [1–4]. TE scaffolds are mostly made by ceramics, polymers and hydrogels [2,3,5]. However, lack of mechanical strength in these materials is the main concern in the applicability of the produced scaffolds especially for bone TE [6,7]. Scientists have tailored several materials as both nanoparticles and bulk materials for various biomedical applications [8]. Metals are among the most appropriate materials, in terms of mechanical strength for biomedical scaffolds and implants [9]. Since usual metallic biomaterials are not biodegradable, producing new biodegradable metallic alloys becomes an appreciated research objective [10,11]. Among biodegradable metals, Mg alloys are of particular interest as they have mechanical properties close to bone, are bioactive and encourage bone growth [12,13].

However, current synthesized Mg scaffolds have a high degradation rate, resulting in early weakening of their mechanical strength [14–16]. It is well-known that surface modification can effectively enhance the properties of metals, especially for biomedical applications [17–20]. Coating of Mg alloys seems to be necessary to improve their degradation resistance [21,22]. Polymeric materials are used extensively in biomedical applications, and PCL is one of the most popular FDA approved ones [23]. Some investigations exist on the PCL coating on bulk Mg alloys and the influence of PCL on the degradation rate of non-porous bulk Mg [24–26]. However, to the best of our knowledge, there is no study on employing PCL to coat Mg porous scaffolds. In this paper, we demonstrated that PCL can be a promising candidate as a coating material for Mg scaffold as it can control the degradation rate and may maintain the temporal mechanical strength of the scaffold.

2. Materials and methods

For production of Mg scaffolds, pure Mg powder was purchased from Sigma-Aldrich with the following quality: purity > 99%, semi-spherical morphology, particle size: 150–300 μm. Carbonate hydrogen ammonium powder was employed as the space-holder with particle size in the range of 150–300 μm. The space-holder was added to the Mg powder with the volume contents of 35%. This value of volume contents was selected based on the previous report in which this amount was introduced as the most appropriate carbonate hydrogen ammonium particles amount in Mg scaffolds that resulted in the best mechanical properties of scaffolds [14]. The mixed powders were pressed at a pressure of 200 MPa.

The green compacts were then heat treated to burn out the space holder particles in an oven under vacuum and to sinter the porous samples separately in a furnace under vacuum. For the heat treatment process, the samples were first heated up to 175 °C and

stayed at this temperature for 2 h in an oven. In order to sweep away the decomposition products of ammonium carbonate, after 2 h, the door was opened slightly and the vacuum was closed. The samples were cooled in oven and then heated up to 600 °C and kept at the final temperature for 2 h in a furnace. After that, the produced scaffolds were coated with PCL. The PCL solution was prepared by mixing PCL with the average molecular weight 80,000 g/mol and dichloromethane (DCM). Two different concentrations of coating material, 3% (w/v) PCL or 6% (w/v) PCL, in solvent were applied.

The coating process parameters were optimized in order to have a complete coating on the inner surfaces of the Mg scaffolds. For this purpose, the viscosity of PCL coating solution was decreased to penetrate easily into the inner surface. The viscosity of the 3% PCL and 6% PCL solutions were adjusted to about 60 and 120 cP (centipoises), respectively. The coating was performed by immersing the samples into the PCL solution for 1 h. The immersed samples were kept in desiccators connected to a vacuum pump. Vacuum facilitated pulling the PCL solution inside the pores for coating purpose. The vacuum pressure was increased gradually, but always kept below 0.7 atm. Above this pressure, some bubbles were observed in the solution which had an adverse effect on the deposition of the PCL solution on the substrate. The solution was repressurized several times to have a complete coating on the inner surfaces.

The uncoated Mg scaffold, PCL-coated Mg scaffold with 3% (w/v) PCL, and PCL-coated Mg scaffold with 6% (w/v) PCL were labeled as Mg scaffold, Mg scaffold/3% PCL and Mg scaffold/6% PCL, respectively. Microstructural studies were conducted using scanning electron microscopy (SEM: Hitachi UHR FE S-4800). Fourier transform infrared spectroscopy (FTIR, Agilent 680 IR) was utilized to identify the functional group of samples. For FTIR analysis, the outer surface of samples was examined.

Total porosity (Π) of the porous scaffolds was measured according to the following equation [14]:

$$\Pi = (1 - \rho/\rho_s) \times 100\% \tag{1}$$

in which ρ_s is the density of the Mg scaffolds evaluated via the immersion method and ρ is the apparent density of the sample, which can be measured by the weight-to-volume ratio of the scaffold.

The contact angle experiment was conducted using the measurement of the wetting degree between the water and the surface of massive nonporous samples. For this purpose, an optical microscope was used to take the images of 0.2 μl water droplet on the surface of different samples. The coating procedure on Mg massive samples was similar to the coating of porous sample.

The samples were immersed in a physiological saline solution (PSS) with the pH value of 6.2 as a corrosive solution. Since the main aim of our work was improving the degradation properties of the Mg scaffolds specifically at the early stage of immersion, we accelerated the degradation process by employing the PSS solution with a low pH value (6.2). This approach allowed us to monitor the significant changes in degradation rates of samples at the short time. No buffer had been used during the degradation measurement.

Each sample was immersed in 25 ml PSS at 37 °C for 72 h, and the changes in pH value of the solution were monitored by a pH meter (Sartorius). The degradation products were removed from the surface by immersing the degraded samples in chromic acid solution with the concentration of 180 g/L. Chromic acid reacts with the degradation products and dissolves them in the solution, with no influence on the Mg substrate. The solution was stirred manually for 20 min and renewed one time during the immersion. Removal of the degradation product was assessed by visual observation of both outside and inside (cross-section) of the scaffolds. The scaffold containing degradation products was white while the color completely turned into dark gray after removal of the degradation products. The difference in weight before and after immersion in PSS indicated the amount of weight gain, and the difference in weight before and after chromic acid immersion for removing the corrosion products indicated the amount of weight loss.

The compression test was performed according to ASTM E9 standard [27] by a Shimadzu AGSX mechanical testing machine at
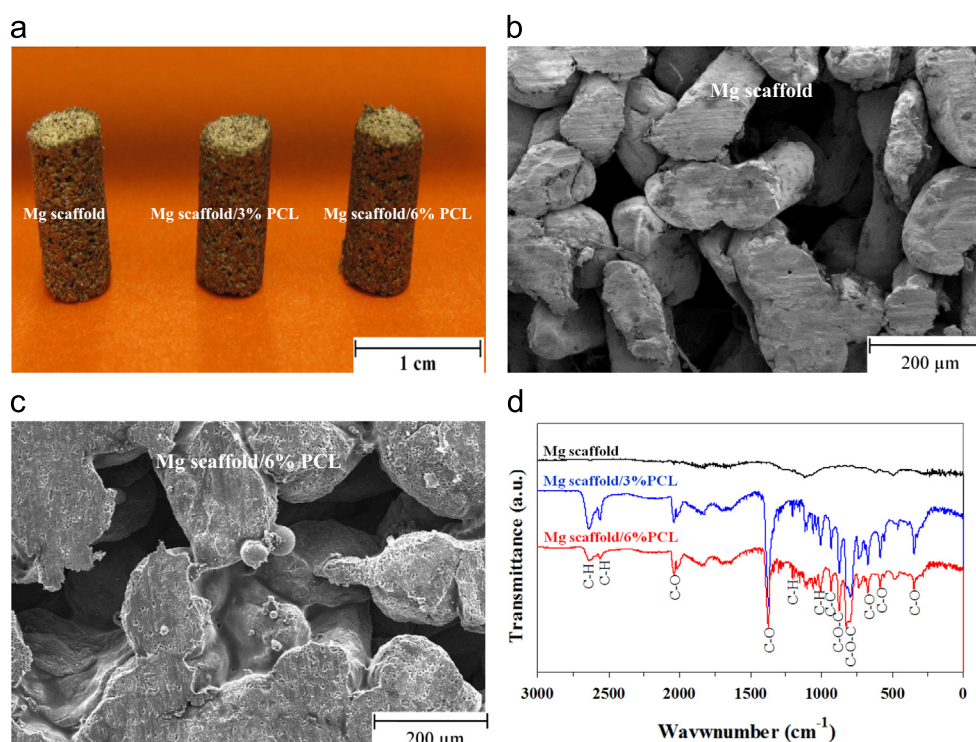

Fig. 1. Overall view of produced Mg scaffolds (a), SEM images of the uncoated (b) and coated (c) scaffolds and FTIR spectra from scaffolds (d).