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Full Length Article

Enhanced performance of magnesium alloy for drug-eluting vascular scaffold application

Hongzhou Dong, Daikun Li, Daoyong Mao, Ningning Bai, Yashi Chen, Qing Li*

School of Chemistry and Chemical Engineering, Southwest University, Chongqing 400715, PR China

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ABSTRACT

Bio-absorbable magnesium alloys drug-eluting vascular scaffold was developed to resolve the defect of permanent metal and drug-eluting stents, most notably a chronic vessel wall inflammation and the risk of stent thrombosis. Nevertheless, violent chemical reaction and rapid degradation under physiological conditions limits their application. Furthermore, multifunctional drug-eluting stents which could reduce the formation of thrombus and repair the damaged vessels need more attention to fundamentally cure the coronary artery disease. Herein, a drug delivery system (Mg/MgO/PLA-FA) which can realize sustainable release of ferulaic acid was designed via anodic oxidation process and dip coating process. Electrochemical tests and immersion experiments showed that the superior anticorrosion behavior, it is due to the dense MgO-PLA composite layer. The released ferulaic acid can effectively decrease platelets adhesion and aggregation during the early stage of implantation. Besides, hemolysis tests showed that the composite coatings endowed the Mg alloy with a low hemolysis ratio. The Mg/MgO/PLA-FA composite materials may be appropriate for applications on biodegradable Mg alloys drug-eluting stents.

1. Introduction

Cardiovascular disease and stroke produce immense health and economic burdens globally [1–3]. Deploying stents in stenosed arteries is an effective way to expand the blocked vessel by overcoming the responses of acute elastic recoil and minimizing vascular trauma after transluminal angioplasty. The first generation of stents was introduced in 1980s by bare-metal, in order to reduce the restenosis rates caused by nondegradable metal, the drug-eluting were applied in 2000 and are the current tacit approval equipment for percutaneous coronary intervention [4,5]. Nevertheless, drug-eluting stents has its own limitations, for instance, the formation of thrombosis, delaying the healing of vessel, and expedited the form of neo-atherosclerosis. Besides, the permanent metal stents restrict the vasomotion and remodeling. Consequently, degradable metal scaffolds has become a hotspot in the research field of vascular disease.

Magnesium alloys have attracted more and more attention due to their biodegradability. Magnesium ion (Mg^{2+}) is the main degradation product in physiological medium, which is essential for human metabolism [6]. Its antiarrhythmic properties as well as the ability to prevent endothelin-induced vasoconstriction make magnesium alloy be advantageous in coronary vascular intervention [7,8]. In addition, as a calcium antagonist, magnesium ions could prevent the injure of calcium ions overload which were caused by ischemia [9]. Nevertheless, rapid corrosion rate of magnesium alloys in physiological medium environment result in the incapacitation of their mechanical properties during the period service. At the same time, local alkalization around the interface of magnesium alloys and tissue is adverse. Therefore, it is necessary to improve the corrosion resistance of magnesium alloys, and the surface modification is a kind of effective measures.

Anodization is an effective surface modification method to improve the corrosion resistance and bioactivity [10–12]. In order to further improve the corrosion resistance, anodization film is usually used to form a composite film with polymer. Poly(l-lactic acid) (PLA) is a good alternative to composite anodization film to form MgO/PLA compound coatings. As a biodegradable polymer, PLA has been approved for human clinical uses in cardiovascular scaffolds [13–15]. It undergoes a degradation process by the simple hydrolysis of an ester bond, and the final products are water and carbon dioxide. A fatal weakness of PLA is that its degradation generates acidic products that lower the local pH value, accelerating further degradation and triggering inflammatory and foreign body reactions [16–18].

* Corresponding author.
E-mail address: liqingswu@163.com (Q. Li).

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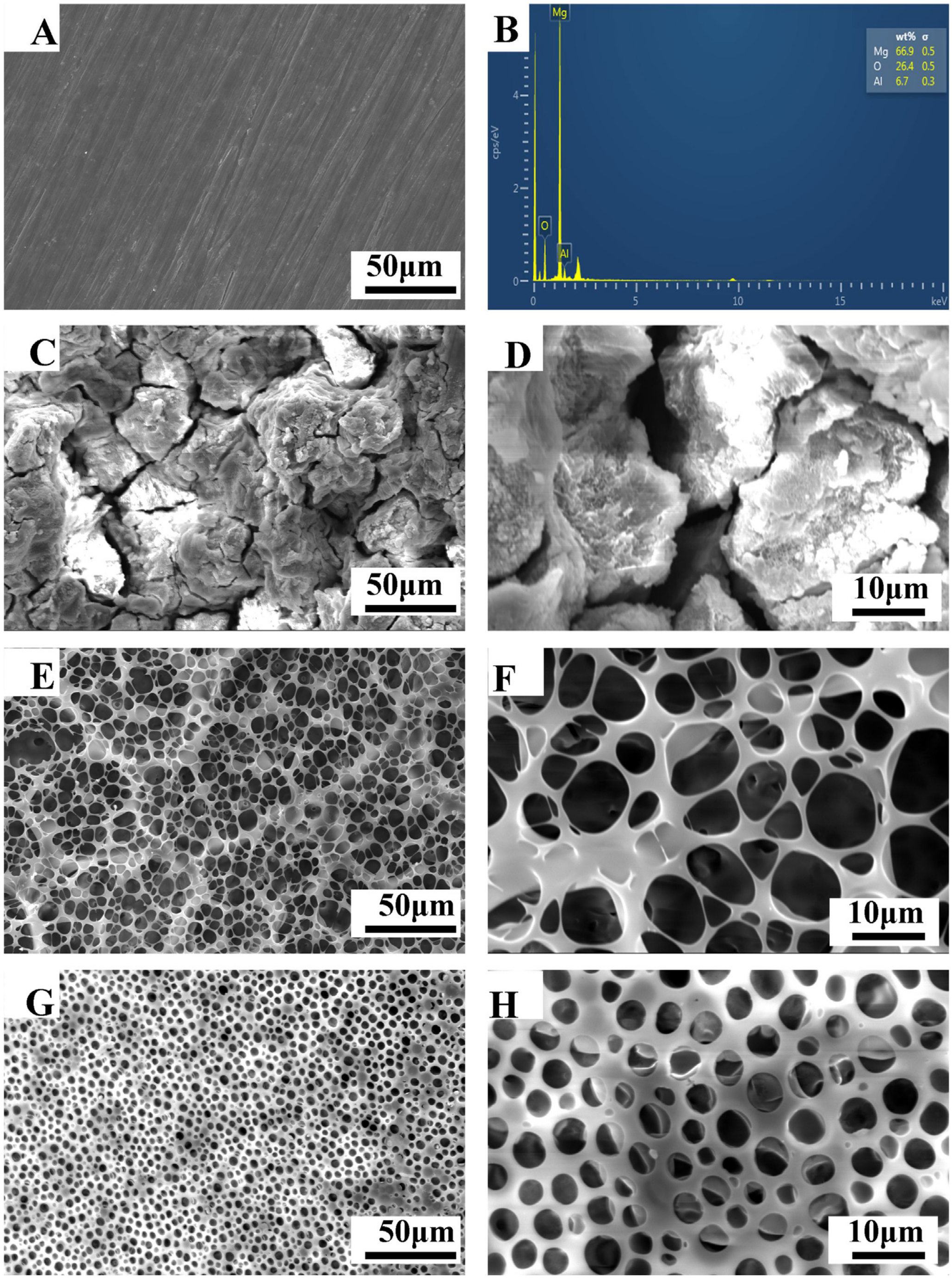

Fig. 1. The SEM images and EDS of the samples, (a) AZ31, (b) EDS of C, (C and D) Mg/MgO (E and F) Mg/ MgO/PLA, (G and H) Mg/ MgO/PLA-FA MIX.

Various fruits and vegetables containing ferulic acid, and it is the main effective components in angelicae sinensis [19,20]. FA exhibits many physiological functions, for instance, anti-adhesive, antioxidant, antiapoptotic, and neuroprotective properties [21–23]. Besides, it is reported that FA could eliminate superoxide anions [24], bring about hypotensive effect [25]. Furthermore, FA also inhibits vascular smooth muscle cell proliferation [26].

In light of this, MgO/PLA-FA compound coating was manufactured on AZ31 magnesium alloy by anodizing treatment and dip coating. The anodization film act as an intermediate layer and furnish sufficient adhesion strength to AZ31. FA was decorated onto the compound film to reduce inflammation, restrain platelet adhesion and promote the healing of vessels. The properties of drug release stents was detected by tape test, corrosion resistance measurement, immersion test, and hemocompatibility tests. Release property of FA was investigated to insight into the mechanisms that control the release of drug from compound film.

2. Experimental

2.1. Materials

A commercial AZ31 magnesium alloy (Chongqing Boao Mg-Al Manufacturing Co., Ltd., China) was used as the substrate material. The elements composition of AZ31 are listed in Table1. Poly-