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Review article

Design of magnesium alloys with controllable degradation for biomedical implants: From bulk to surface

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A B S T R A C T

The combination of high strength, light weight, and natural biodegradability renders magnesium (Mg)-based alloys promising in orthopedic implants and cardiovascular stents. Being metallic materials, Mg and Mg alloys made for scaffolds provide the necessary mechanical support for tissue healing and cell growth in the early stage, while natural degradation and reabsorption by surrounding tissues in the later stage make an unnecessarily follow-up removal surgery. However, uncontrolled degradation may collapse the scaffolds resulting in premature implant failure, and there has been much research in controlling the degradation rates of Mg alloys. This paper reviews recent progress in the design of novel Mg alloys, surface modification and corrosion mechanisms under different conditions, and describes the effects of the structure, composition, and surface conditions on the degradation behavior *in vitro* and *in vivo*.

Statement of Significance

Owing to their unique mechanical properties, biodegradability, biocompatibility, Mg based biomaterials are becoming the most promising substitutes for tissue regeneration for impaired bone, vascular and other tissues because these scaffolds can provide not only ideal space for the growth and differentiation of seeded cells but also enough strength before the formation of normal tissues. The most important is that these scaffolds can be fully degraded after tissue regeneration, which can satisfy the increasing demand for better biomedical devices and functional tissue engineering biomaterials in the world. However, the rapid degradation rate of these scaffolds restricts the wide application in clinic.

This paper reviews recent progress on how to control the degrdation rate based on the relevant corrosion mechanisms through the design of porous structure, phase structure, grains, and amorphous structure as well as surface modification, which will be beneficial to the better understanding and functional design of Mg-based scaffolds for wide clinical applications in tissue reconstruction in near futures.

Contents

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1. Introduction

Since the mechanical strength and fracture toughness of stainless steels and titanium alloys are superior to those of polymers and ceramics [1], they are widely used in biomedical fields, especially orthopedic, dental, and cardiovascular implants in load-bearing situations. Meanwhile they can better maintain the mechanical integrity during tissue healing [1,2]. However, some metallic biomaterials such as nitinol release toxic ions during corrosion causing allergic reactions, local anaphylaxis, and inflammation [3]. Furthermore, the mechanical properties of common metallic biomaterials such as stainless steels, Ti and Ti-based alloys, CoCr-based alloys and so on do not match those of hard tissues. For example, mismatch of the Young's modulus can cause stress shielding effects under load bearing load potentially leading to bone resorption [4–6]. More importantly, these conventional biometals used as temporary implants are not degradable in the physiological environment, and may need to be removed by a follow-up surgery after healing. In practice, the demand for temporary implant materials like plates, screws or stents is booming, for example, the number of implanted drug-eluting coronary stents alone exceeded two million in 2004 [7]. Therefore, materials scientists and engineers have been researching novel biomaterials to replace conventional biometals. Owing to the excellent mechanical properties and biodegradability. Mg and Mg-based alloys are attracting much attention in the field of biomaterials [8–14].

1.1. Evolution of Mg alloys in biomedical applications

Although Mg wires were firstly used as ligatures to stop bleeding vessels of patients in as early as 1878 [15], rapid corrosion *in vitro* and *in vivo* presented insurmountable problems. Materials scientists and surgeons have shifted their interests to other metallic biomaterials such as stainless steels, pure Ti, and Ti6Al4V since the late 1940s [16]. Since Langer and Vacanti made a report in 1993 [17], tissue engineering has been attracting much attention because it provides the ideal therapy to repair or reconstruct damaged tissues [18–20]. Since biodegradable or bioresorbable scaffolds with sufficient strength are crucial, research of the suitable biodegradable metals such as Mg alloys has been increasing [21–27].

It is well known that biodegradable implants must meet several specific properties, including an adequate stability, a moderate and homogeneous degradation, full bone regeneration within 12–15 months and biocompatibility [8]. Mg-based metals are considered to well meet some requirements.

Currently, clinical trials or animal tests focus on the application of Mg-based metals to cardiovascular stents [24,25] and bone implants [26,27] made of Mg alloys such as Mg-Ca [28], Mg-Zn [29], Mg-Zr [30], Mg-Si [31], Mg-Sr [32], and Mg-RE [33] as well as the Mg-based hybrid materials [25,34]. The typical vascular stent made of AE21 containing 2% aluminium and 1% rare earth elements shown in Fig. 1T is used to prevent stenosis of the coronary artery and spur revascularization [24]. After implantation of the stent, the coronary artery (Fig. 1M(A)) shows open arterial lumen with no residual stenosis due to low elastic recoil (Fig. 1M (B)) and 4 months later, the angiogram displays an open vessel lumen with no sign of luminal narrowing or edge effect. In comparison with just after implantation (Fig. 1L(A)), the intracoronary ultrasound shows a vessel wall without stent struts after absorption but with small zones of high intensity corresponding to the previous stent strut position (Fig. 1L(B)) [24]. Furthermore, the overall target lesion revascularization rate among 63 patients is 45% after 1 year. No myocardial infarction, subacute, late thrombosis, or death occur [24]. As shown in Fig. 2, in patients with symptomatic hallux valgus, after osteosynthesis is fixed by either