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Surface Modification on Biodegradable Magnesium Alloys as Orthopedic Implant Materials to Improve the Bio-adaptability: A Review

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Magnesium (Mg) and its alloys as a novel kind of biodegradable material have attracted much fundamental research and valuable exploration to develop its clinical application. Mg alloys degrade too fast at the early stage after implantation, thus commonly leading to some problems such as osteolysis, early fast mechanical loss, hydric bubble aggregation, gap formation between the implants and the tissue. Surface modification is one of the effective methods to control the degradation property of Mg alloys to adapt to the need of organism. Some coatings with bioactive elements have been developed, especially for the micro-arc oxidation coating, which has high adhesion strength and can be added with Ca, P, and Sr elements. Chemical deposition coating including bio-mimetic deposition coating, electro-deposition coating and chemical conversion coating can provide good anticorrosion property as well as better bioactivity with higher Ca and P content in the coating. From the biodegradation study, it can be seen that surface coating protected the Mg alloys at the early stage providing the Mg alloy substrate with lower degradation rate. The biocompatibility study showed that the surface modification could provide the cell and tissue stable and weak alkaline surface micro-environment adapting to the cell adhesion and tissue growth. The surface modification also decreased the mechanical loss at the early stage adapting to the load-bearing requirement at this stage. From the interface strength between Mg alloys implants and the surrounding tissue study, it can be seen that the surface modification improved the bio-adhesion of Mg alloys with the surrounding tissue, which is believed to be contributed to the tissue adaptability of the surface modification. Therefore, the surface modification adapts the biodegradable magnesium alloys to the need of biodegradation, biocompatibility and mechanical loss property. For the different clinical application, different surface modification methods can be provided to adapt to the clinical requirements for the Mg alloy implants.

1. Introduction

Metallic materials play an important role as biomaterials to assist with the repair or replacement of bone tissue that has become diseased or damaged due to their combination of high mechanical strength and fracture toughness, which are more suitable for load-bearing applications compared with ceramics or polymeric materials[1]. However, the limitations of current metallic biomaterials are the unmatched elastic moduli with that of natural bone tissue and possible release of toxic metallic ions and/or particles through corrosion or wear processes[2,3]. Moreover metallic biomaterials remain as permanent fixtures, which must be removed by a second surgical procedure after healing[4].

Magnesium-based metals can readily dissolve or corrode in aqueous solutions, which inspire the biomaterial researchers to develop a new concept of degradable implants. Over the last decade, research interest is rapidly growing in fundamental research and valuable exploration to develop its clinical application. The rapid degradation of magnesium however is a double edged sword, and after implantation it will lead to some problems such as osteolysis, early fast mechanical loss, hydric bubble aggregation, and gap formation between the implants and the tissue[5]. Thus it is necessary to control the corrosion rate of the materials to satisfy their clinical demands. In response, surface modification has been suggested as the effective methods to control the degradation of Mg alloys.

Moreover, there is a need for this new generation of biodegradable implants, which should be able to stimulate the healing responses of injured tissues at the molecular level. For example in bone graft strategies, it should provide osteoinductivity,

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osteoconductivity, suitable degradation/resorption and replacement by new bone tissue[6]. Moreover, it is also expected to be avoided from infection by bacterial invasion.

There are lots of technologies available for coating magnesium and its alloys. These include the micro-arc oxidation coating, chemical conversion coating, electrodeposition coating, bio-mimetic deposition coating, etc.[7–11]. Each of these will be described in detail in the following sections. Considering the demands of various clinical applications, especially in orthopedics, different modification methods are applied in view of their specific performances. The focus of this review concerns the development of biocompatible and biodegradable coatings for Mg and its alloys, with the intent of improving the bio-adaptability among degradation, mechanical integrity and biocompatibility for orthopedic application.

2. Current Coating Technologies

2.1. Micro-arc oxidation coating

Micro-arc oxidation (MAO) treatment, also known as plasma electrolytic oxidation, is a common technique for corrosion protection of magnesium alloys in the industrial sector. In micro-arc oxidation, higher potentials are applied, which locally exceeds the dielectric breakdown potential of the growing oxide film, and discharges occur. These discharges result in localized plasma reactions, with conditions of high temperature and pressure, which modify the growing oxide. Processes include melting, melt-flow, re-solidification, sintering and densification of the growing oxide[12]. By the MAO process a relatively thick, dense and hard oxide coating can be produced on the surface of magnesium alloys[13]. The coating is a chemical conversion of the substrate metal into its oxide, and grows both inward and outward from the original metal surface, which has excellent adhesion to the substrate and offers protection against wear and corrosion.

2.2. Chemical conversion coating

Conversion coatings arise in a complex interaction of metal dissolution and precipitation, usually during treatments in aqueous solutions. The chemical conversion layers are obtained by immersion of substrates in a bath and show, besides magnesium oxide and magnesium hydroxide, mixtures of other metal oxides and hydroxides, which arise from the dissolved ions in the bath[5]. Such conversion coatings represent an effective way to increase the corrosion resistance of magnesium alloys or, as a pre-treatment, to improve the adhesion of a final deposited coating[14].

2.3. Electrophoretic deposition coating

Electrophoretic deposition (EPD) is a term for a broad range of processes, which include cathodic electrodeposition, anodic electrodeposition, and electrophoretic coating. A characteristic feature of this process is that colloidal particles suspended in a liquid medium migrate under the influence of an electric field (electrophoresis) and are deposited onto an electrode. Fig. 1 presents a schematic illustration of the two electrophoretic deposition processes[15]. This method mainly concerns the deposition of inorganic phases. The relevant literature reveals that cathodic electrodeposition leads to better results in the production of HA layers than chemical conversion layers. However, careful adjustment of the parameters is necessary. Sometimes there are traces of the substrate mixed into the coating forming new phases, such that the coating is not purely by deposition but also to some extent by conversion at the interface.

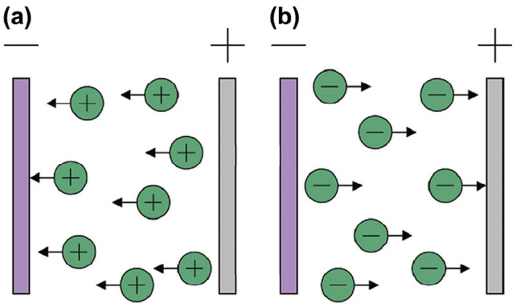

Fig. 1. Schematic illustration of electrophoretic deposition process: (a) Cathodic EPD and (b) anodic EPD[15].

3. Adaption to the Need of Biodegradation Property of Biodegradable Magnesium Alloys by Surface Modification

The idea of biodegradable Mg implants was discarded a century ago because of their rapid degradation. Recent advances in the design and processing of metal alloys have revived interest in Mg-based materials and devices. Most researches have focused on decreasing Mg degradation through alloying and surface treatment. However, the potential long-term toxicity induced by addition of alloying elements (e.g., rare earth elements) is a concern[16]. Coating is proved to be an effective method to make Mg degradation tunable and biocompatible. It can be seen that surface coating protected the Mg alloys at the early stage providing the Mg alloy substrate with lower degradation rate[5]. From the viewpoint of corrosion resistance, different coatings showed varied degradation behaviors, which is dependent on the formation mechanism. Chemical conversion including MAO can provide better corrosion resistant coating by the chemical reaction or plasma discharging oxidation.

The degradation behavior of MAO-coated Mg alloys in simulated body fluids solution was widely studied by Lin et al.[17], Xu et al.[18] and Wan et al.[19]. In all studies MAO showed a lower corrosion current density in polarization studies than uncoated samples. Lin et al.[17] fabricated a forsterite-containing MAO coating on ZK60 magnesium alloy and demonstrated the voltage influence on the morphology and subsequent degradation property of the MAO layer. The corrosion resistance of MAO coating was increased with the elevation of the preparation voltage. Besides, the effect of various electrolytes on the electrochemical corrosion behavior of MAO coating has previously been studied[20]. Liang et al.[21] also reported the influence of pH on the deterioration of MAO coated AM50 alloy in NaCl solutions. Moreover, it is known that the coating with typical porous structures is featured by MAO technique, where the solution could penetrate at the pore places and corrode the matrix. Thus the composite coating was fabricated outside the MAO coating to improve the corrosion resistance[22]. In particular, a MAO coating with self-sealing structure was reported by Gan et al.[23]. The Ca—P compounds can be simultaneous deposited in the pore during MAO process (as shown in Fig. 2). Wang et al.[24] studied the *in vitro* and *in vivo* degradation of this MAO coating with self-sealing structure. The results (Fig. 3) showed that the coating significantly retarded the *in vivo* corrosion after implantation for 12 weeks compared with the uncoated sample.

Fig. 4 summarized the percentage reduction on the corrosion rates of magnesium alloys with different coatings reported in the literature compared with uncoated alloys. It can be seen that polymer coatings (chitosan coatings[25], polycaprolactone and dichloromethane coatings[26]), electrodeposition coatings (dicyclopentadiene (DCPD), hydroxyapatite (HA) and fluoridated hydroxyapatite (FHA) coatings[27]), alkaline heat treatment[28] and fluoride treatment[29] can

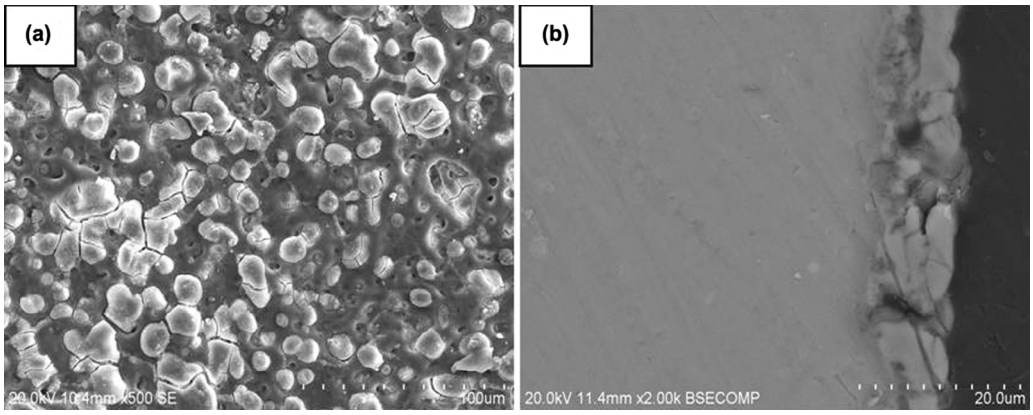

Fig. 2. Morphologies of MAO coatings with self-sealing structure[23].

reduce the corrosion rate of the magnesium alloy substrate by approximately 50%–80%. In comparison, a more than 90% reduction in corrosion rate can be obtained for the MAO coatings[30]. Overall, the MAO coating is very stable, hard and corrosion resistant. For orthopedic implants, MAO coating could be supposed to desired coating, which can effectively slow down the corrosion rate and also supply better adhesion and abrasion resistance.

4. Adaption to the Need of Biocompatibility Property of Biodegradable Magnesium Alloys by Surface Modification

For biomedical applications coatings should possess, besides corrosion protection, other functions, such as an enhancement of biocompatibility or osseointegration in the case of orthopedic applications, bioactivity, antibiotic ability, or local drug delivery ability. As for orthopedic applications, bioactive coatings such as calcium phosphate and fluoride-containing layers are the most interesting in this category. Fig. 5 shows the model explaining the improvements due to the presence of bioactive calcium orthophosphate coatings on Mg and its alloys[31].

One approach to obtain calcium phosphate-containing coatings is immersion in simulated body fluids (SBF); this process is often termed bio-mimetic if carried out at 37 °C and a pH of 7.4. Various compositions of surface layers depending on the bath solution were reported by Rettig and Virtanen[32], including amorphous carbonated calcium/magnesium phosphate layers, which formed after immersion in SBF solution for 5 days. Moreover the adjustment of the phases during processing is the most important requirement. The layers are often mainly amorphous, but they contain some crystallized HA and also other calcium phosphate phases[5]. Chen et al.[33] used a calculated equilibrium diagram to obtain a stable HA coating using a calcium nitrate and sodium phosphate solution. Nevertheless, a post-treatment in alkaline solution was necessary to develop an HA component within the coating. Wang et al.[34] obtained a Ca—P coating in the AZ31 alloys (as shown in Fig. 6) and assessed the biocompatibility via *in vitro* and *in vivo* tests. The results showed that the coating could significantly decrease the happening of the hemolysis and showed better osseointegration after implantation.

Electrodeposition (ED) has been suggested as another means of depositing CaP coatings on Mg based on the extensive research and application of ED on clinical titanium implants. Previous investigations reported ED as a successful means of establishing single crystalline phases such as HA[27], brushite[35] or octacalcium[36]. Most authors described the obtained CaP coatings as porous or microporous, whereas high-temperature sintering/annealing was mentioned and shown to create a more dense and uniform CaP coating post-ED[37], with greater adhesion properties[38]. The electrophoresis process has also been modified to include pulse currents as opposed to a constant current in recent protocols. Adjustment of pulse current parameters and electrolyte solution has been suggested as an effective means of controlling the coating structure deposited on the substrate[35]. Qiu et al. fabricated a Si doped Ca—P coating by pulse ED and found that the double layer structure was formed due to pulse parameters[39]. The coating with composition of DCPD showed excellent biocompatibility for the orthopedic application. Moreover, to improve the bioactivity and biofunction, many nutrient elements in the human body were doped into the HA coating with formation of Si—HA, Sr—HA, FHA and Ag—HA[40–43]. The biocompatibility study showed that the coating could provide the cell and tissue stable and weak alkaline surface micro-environment that adapts to the cell adhesion and tissue growth.

On the other hand, the rapid degradations of magnesium alloys could induce some problems such as inflammation and hydrogen evolution of Mg implants[43], which will affect their future clinical applications. The *in vivo* corrosion study by Witte et al.[44] shows that all magnesium implants exhibited clinically and radiographically visible subcutaneous gas bubbles, which appeared within one week after surgery. Song [45] studied and compared the corrosion rate of different Mg alloys and postulated hydrogen evolution rate of 0.01 mL/cm^2/day as a tolerated level in the human body. Thus, the harm effects by hydrogen gas accumulation could be avoided, if a favorable magnesium alloy with a suitable coating is applied as an implant material.

It was known that the processing and deformation will influence the corrosion of magnesium alloys. Thus the degradation was not only dependent on the coating protection, but also relevant to the processing status of the Mg alloy substrate. Carboneras et al.[46] studied the *in vitro* performance of magnesium processed by different routes. It is found that the metallurgical route used to produce magnesium has more significant consequences on biodegradation and biocompatibility than the effects of the surface coating. Han et al.[47] studied the degradation behavior of different processing status and also biological response of Mg—Sr alloy for bone substitutes. The results showed that the as-cast Mg—Sr alloy exhibited a rapid degradation rate compared to the as-extruded alloy due to the intergranular distribution of second phase and micro-galvanic corrosion. However, the initial degradation could be tailored by the coating protection, which was proved to be cytocompatible and also suitable for bone repair observed by *in vivo* implantation. The integrated fracture calluses were formed and bridged the fracture gap without gas bubble accumulation (Fig. 7) as the substitutes simultaneously degraded[47]. Thereby, it is potential to obtain the tailored degradation according to the clinical demands by regulation of microstructure of Mg alloys and combined appropriate coating.

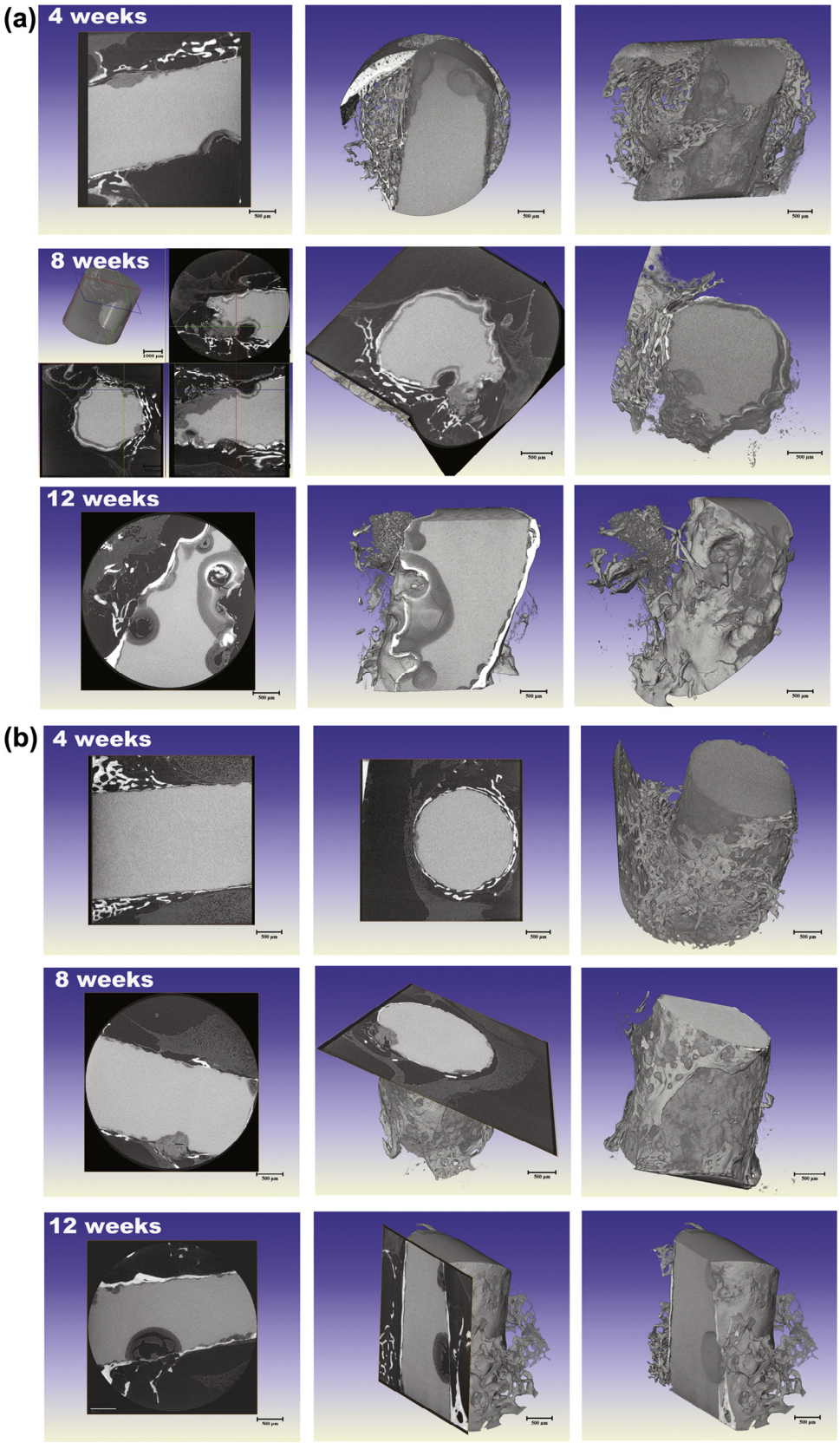

Fig. 3. 2D slice and 3D reconstruction morphologies of (a) the uncoated and (b) coated samples at implantation periods of 4, 8, and 12 weeks by HRTXRT[24].

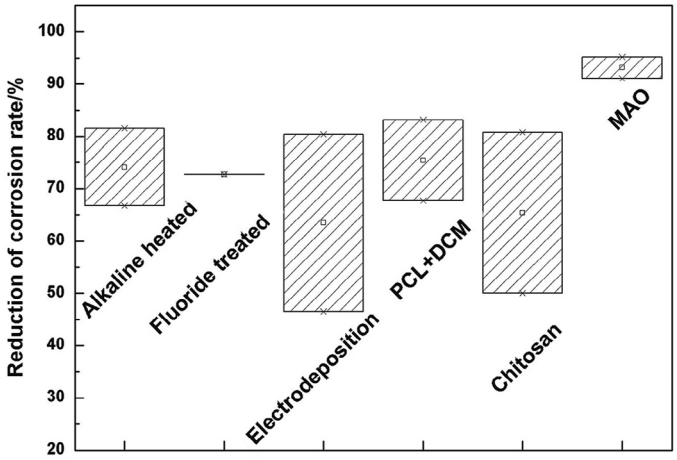

Fig. 4. Reduction in corrosion rate for magnesium alloys with different coatings deduced from the literature[25–30].

5. Adaption to the Need of Mechanical Integrity of Biodegradable Magnesium Alloys by Surface Modification

Basically, the magnesium-based implants are expected to be used with a temporary function, such as bone fixation and bone substitute. The implants should provide a mechanical supporting especially in the load-bearing sites and promote bone healing[48]. Thus an ideal implant for orthopedic application should be able to compromise its degradation and mechanical integrity during implantation, as illustrated in Fig. 8. Theoretically, degradation occurs in initial with a very slow rate to maintain enough mechanical strength for the vessel forming and bone remodeling. After a period of 3–6 months, the bone reconstruction is expected to be completed[49].

Bakhsheshi-Rada et al.[50] developed a new surface treatment for the Mg—Ca—Bi alloy, combining physical vapor deposition (PVD) and dip coating techniques. The results showed that this coating has significantly higher compressive strength, thus can sufficiently protect the alloy and enhance the mechanical properties. Shen et al.[51] designed a bio-glass coated magnesium alloy with a combination of suitable mechanical strength and adjustable corrosion resistance. This coating combined with mild interfacial stress could improve the cohesion/adhesion strength.

Tan et al.[52] studied the loss of mechanical properties *in vivo* and bone-implant interface strength of AZ31B magnesium alloy screws with Si-containing coating. The interface strength was evaluated in terms of the extraction torque required to back out the screws. The loss of mechanical properties over time was indicated by one-point bending load loss of the screws after these were extracted at different times. The results showed that the extraction torque of coated AZ31B increased with implantation time, and was higher than that of poly-L-lactic-acid (PLLA) after 4 weeks of implantation (as shown in Fig. 9). The bending loads of non-coated AZ31B and PLLA screws degraded sharply after implantation, and that of coated AZ31B degraded more slowly (as shown in Fig. 10).

From the interface strength between Mg alloys implants and the surrounding tissue study, it can be seen that the surface modification improved the bio-adhesion of Mg alloys with the surrounding tissue which is believed to be contributed to the tissue adaptability of the surface modification.

The valid periods of the coating is significant to ensure good corrosion resistance and the mechanical integrity of magnesium alloy

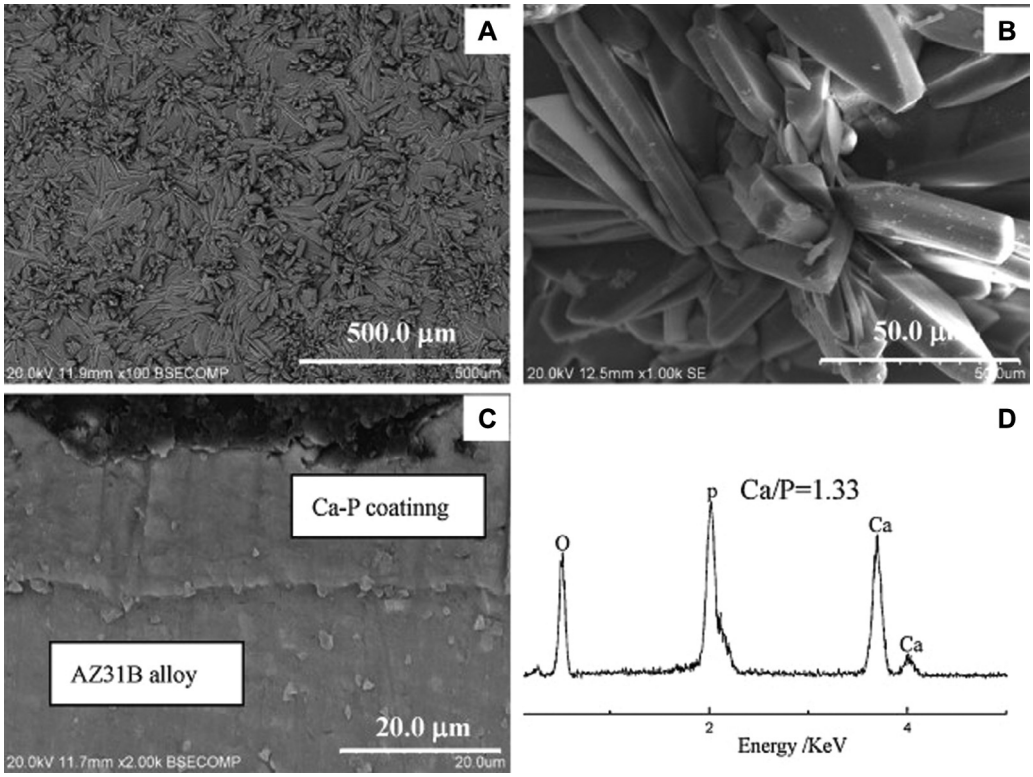

Fig. 5. A model explaining the improvements due to the presence of bioactive calcium orthophosphate coatings on Mg and its alloys. (A) A relatively rapid degradation rate of Mg might lead to formation of gaps at the interface. (B) A typical tetracycline label taken 14 weeks post-operation. (C) Protective calcium orthophosphate coatings can reduce the degradation rate and simultaneously ameliorate biocompatibility. (D) Corrosion-protective effects of calcium orthophosphate coatings measured via the H_2 release rate and the change in pH value[31].

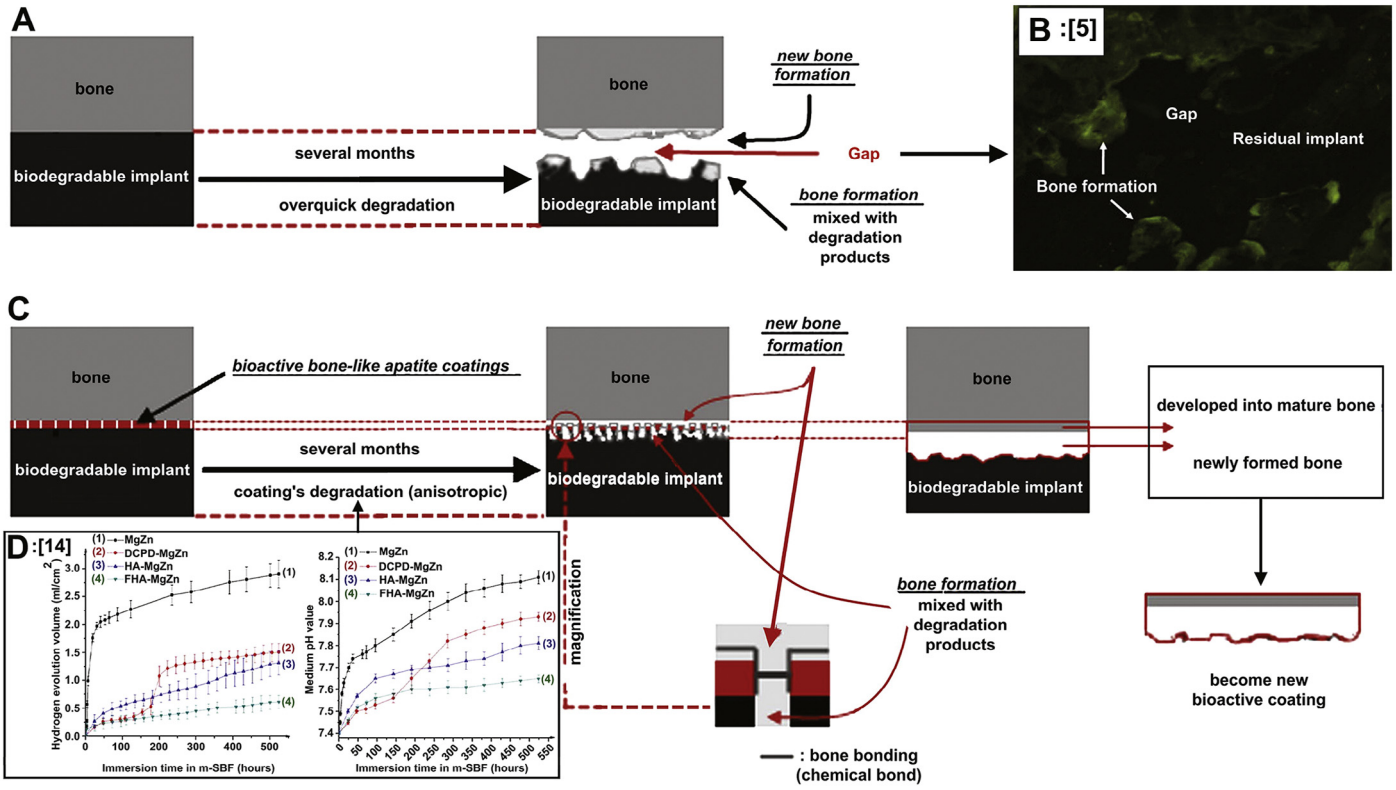

Fig. 6. Morphology of Ca–P coating fabricated in AZ31B alloy by conversion method[34].

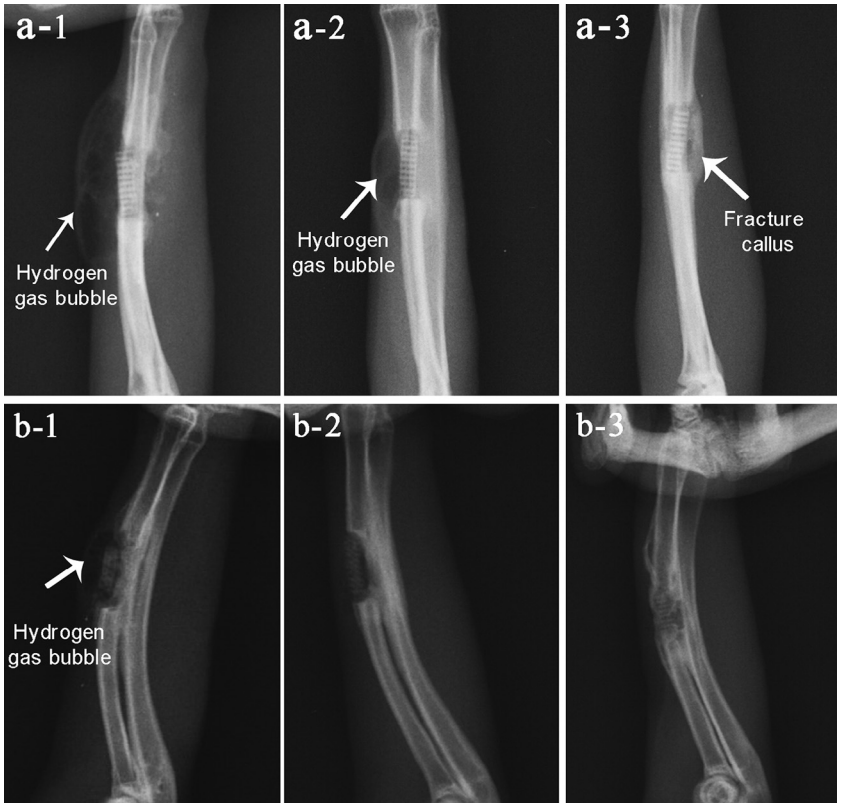

Fig. 7. Post-op X-ray images after implantation of (a) 4 and (b) 8 weeks for (1) as-cast alloy, (2) as-extruded alloy and (3) as-cast alloy with coating[47].

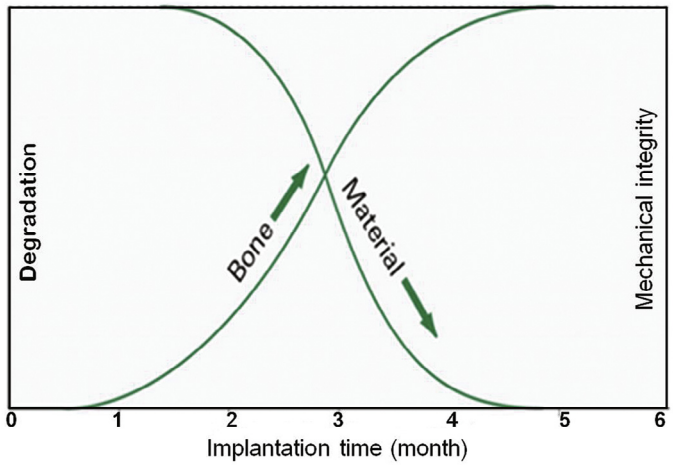

Fig. 8. Illustration of an ideal model between mechanical integrity and degradation for orthopedic application.

implants. It was reported that the *in vitro* degradation of MAO coating on Mg—Ca alloys is over 50 days[30], which is significantly greater than that of an alkaline heated and chitosan-coated sample, which showed 10 days validity[25,28]. The studies on the *in vivo* degradation of MAO coating showed that the implants could maintain most integrity at 12–18 weeks[53]. Comparatively, the failure periods of DCPD, HA and FHA coatings were about 1 week, 2–3 weeks and 4–6 weeks[27], respectively, whereas a MgF_2 coating was degraded within 4 weeks after implantation[54].

Thus different coatings should be chosen according to the clinical application, such as bone fixation, bone grafting, ACL reconstruction, and varied for different tissues, e.g. 6–12 weeks for upper limbs[55] and 12–24 weeks for lower limbs[56]. In general, micro-arc oxidation (MAO) coating was preferentially used in bone fixation, like screw (as shown in Fig. 11(a)), which was attributed to its abrasive and corrosion resistance. Niu et al. developed DCPD coating on JDBM alloys for bone fixation application (Fig. 11(b))[57]. Also chemical conversion coating[34] was employed for plates and screws (provided by Trauson Holdings Company Ltd, as shown in Fig. 11(c, d)). Regarding bone substitutes, Han et al.[47] developed Sr, Ca, and

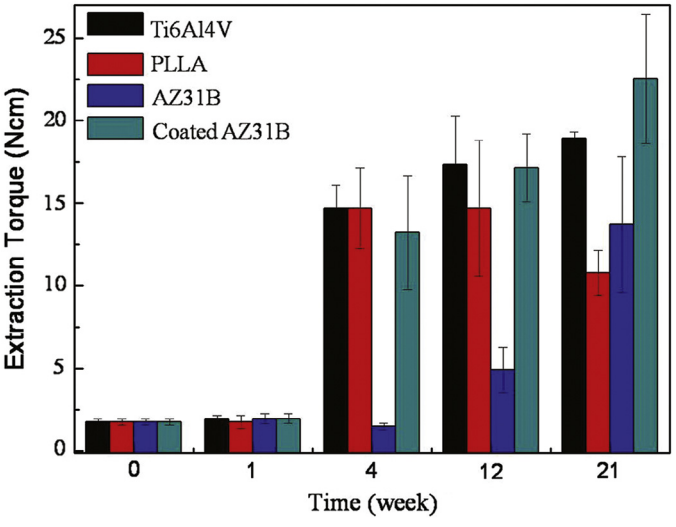

Fig. 9. Results of extraction torque measurements on non-coated AZ31B, coated AZ31B, PLLA and Ti6Al4V implanted *in vivo* for 1, 4, 12 and 21 weeks, respectively[52].

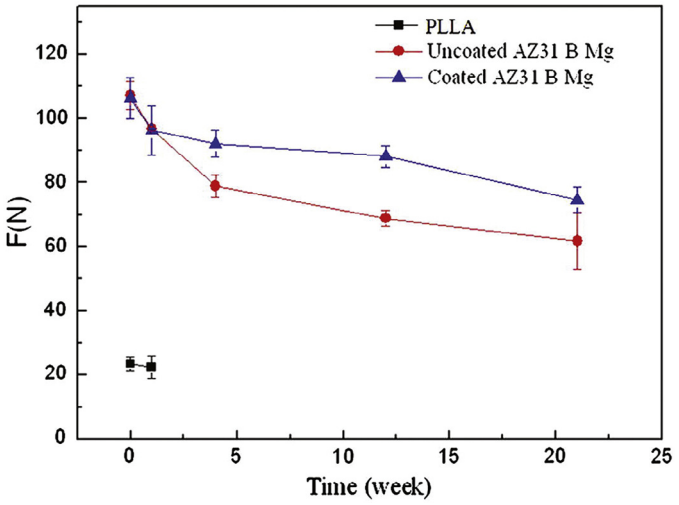

Fig. 10. Variations of the one-point bending loads of non-coated AZ31B, coated AZ31B and PLLA screws when extracted from the bones after 1, 4, 12 and 21 weeks of implantation[52].

P contained MAO coating to tailor degradation and biological response for bone repair and reconstruction.

Biodegradable magnesium-based metals are considered as the next generation of metallic biomaterials and their efficiency and efficacy are proved by more animal tests and clinical trials[58], which give us great confidence in the future development on Mg-based implants and devices. Accompanying more devices and products that are being developed and approved by CE and other drug regulation administration, coating will receive more attention and exert impacts to ensure bio-safety, clinical efficacy and bio-functions.

Fig. 11. The magnesium-based metallic devices with different coatings application, (a) MAO coating on pure magnesium screw (courtesy of EON Co., Ltd), (b) DCPD coating on JDBM alloys[57], (c) AZ31B screw with Si-containing coating[34], (d, e) chemical conversion coated screw and plate for animal test (courtesy of Trauson Holdings Company Ltd).

6. Conclusion

The previous literature has revealed that a wide range of coatings on Mg and Mg alloys can increase the corrosion resistance of these materials. More functions achieved by the coatings, besides increasing the corrosion resistance of the substrates, are controllable degradability, mechanical maintainability and improved osseointegration, as demonstrated by *in vitro* and *in vivo* testing. In this review, the relevant adaptability between these performances was discussed. From the above results, it can be concluded that the surface modification could adapt the biodegradable Mg alloys to the need of biodegradation, biocompatibility and mechanical loss property. For the different clinical application, different surface modification methods can be provided to adapt to the clinical requirements for the Mg alloy implants.

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