The potential application of Mg alloys as bioabsorbable/biodegradable implants has attracted much recent attention in China. Advances in the design and biocompatibility evaluation of bio-Mg alloys in China are reviewed in this paper. Bio-Mg alloys have been developed by alloying with the trace elements existing in human body, such as Mg-Ca, Mg-Zn and Mg-Si based systems. Additionally, novel structured Mg alloys such as porous, composites, nanocrystalline and bulk metallic glass alloys were tried. To control the biocorrosion rate of bio-Mg implant to match the self-healing/regeneration rate of the surrounding tissue in vivo, surface modification layers were coated with physical and chemical methods.

**INTRODUCTION**

The concept of biodegradable implant materials is not new, yet the development of biodegradable metals became a key research focus in the past 5–10 years due to their good combination of mechanical property and biocompatibility.1,2 Magnesium alloys would be degraded into Mg ions in biofluid environment which can be further absorbed/excreted by human body.1,2 The degradation/corrosion of Mg alloys is promising for orthopedic and cardiovascular applications, since there is no need for a removal surgery. The previous studies on biomedical Mg alloys focused mainly on two aspects: the corrosion and biocompatibility evaluation of commercial Mg alloys (Mg-Al3–6 and Mg-RE4,7,8 alloy systems), and the new Mg alloy system containing nontoxic or low-toxicity alloying elements. Many novel composition designs were investigated for biomedical application.

Besides the pioneering works at NSF Engineering Research Center for Revolutionizing Metallic Biomaterials, and MagIC-Magnesium Innovation Centre, GKSS Forschungszentrum Geesthacht GmbH, much research on biodegradable Mg alloys has been done in China, and will be summarized in this article.

**NEW ALLOY SYSTEMS OF BIOMEDICAL MAGNESIUM**

**Mg-Ca**

Li et al.9 explored the effect of nutrient element Ca on the mechanical and corrosion properties of binary Mg-xCa (x=1~3 wt.%) alloys. The second phase Mg-Ca precipitated along the grain boundary with increasing Ca content, which weakened the mechanical and corrosion properties of the Mg-Ca alloys. The ultimate tensile strength and elongation of the as-cast Mg-1Ca alloy (71.38±3.01MPa and 1.87±0.14%) were largely improved after hot rolling (166.7±3.01MPa and 3±0.78%) and hot extrusion (239.63±7.21MPa and 10.63±0.64%). During the in vivo implantation period, the Mg-1Ca alloy pins gradually degraded within 90 days in rabbit femoral shafts and well aligned osteocytes as well as newly formed bone with an appropriate inflammatory host response were observed 3 month post-surgery. No significant difference (p>0.05) of serum magnesium was detected at different degradation stages. A mixture of Mg(OH)2 and hydroxyapatite corrosion product layer were formed on the surface of Mg-1Ca alloy during the in vitro/vivo corrosion. A possible biocorrosion mechanism was proposed (Figure 1). Du et al.10 indicated that the 2% Zn addition showed 22% improvement in ultimate tensile strength and the eutectic (Mg+Mg2Ca+Ca3Mg2Zn4) phase contributed to the corrosion resistance.
of Mg-3Ca alloys.

**Mg-Zn**

Zinc is essential for human body and contributes to strength and corrosion resistance due to solid solution strengthening and elevated corrosion potential. An Mg-6wt.% Zn alloy was designed and fabricated for implant application, exhibiting the tensile strength and elongation of approximately 279.5 MPa and 18.8% after solid solution treatment and hot working. The Mg-Zn rods were implanted into the femoral shaft of rabbits and gradually absorbed in vivo at about 2.32 mm/yr degradation rate with newly formed bone surrounding the implant. The histology examination (containing heart, liver, kidney, and spleen tissues) and the biochemical measurements [including serum magnesium, serum creatinine, blood urea nitrogen, glutamic-pyruvic transaminase and creatine kinase] proved that the degradation of Mg-Zn did not harm the important organs. However, Zhang et al. found that the increasing Zn content would deteriorate the mechanical properties and corrosion resistance of the Mg alloy. Further modification on low Zn content Mg-Zn alloy was proposed by adding Mn, Ca and Zn to refine and modify the morphology of Mg2Si. The results showed that Ca addition slightly refined the grain size and Mg2Si phase morphology, however, not contributed to mechanical property. In contrast, Zn addition obviously modified Mg2Si phase morphology from coarse eutectic structure to a small dot or short bar shape. As a result, mechanical properties (especially the elongation improved by 115.7%) and bio-corrosion resistance were improved significantly. Gu et al. reported that the addition of Sn could increase the strength, but reduce the corrosion resistance of pure Mg. In addition, binary Mg-1wt.%Sn alloy indicated no toxicity to fibroblasts (L-929 and NIH3T3 cells) and osteoblasts (MC3T3 cell line). A patented Mg-Sn-Mn alloy (Sn 1.0–3.0% and Mn 0.15–1.0%) was proposed for stent application. Moreover, binary Mg-RE alloy systems were also designed, including Mg-Y, Mg-Ce, Mg-Nd, Mg-La, for biomedical application and Mg-Nd alloy indicated a much slower corrosion rate than the others.

**NOVEL STRUCTURED Mg ALLOYS**

**Porous**

A magnesium-alloy-based scaffold was fabricated for bone tissue application by different methods, including the traditional powder metallurgy (P/M), laser perforation technique, and metal/gas eutectic unidirectional solidification method (GASAR process). The open-cellular pure Mg (porosities: 36–55%; pore sizes: 200–400 \( \mu m \)) were prepared by the P/M process using carbamide \((\text{CO(NH}_2\text{)}_2)\) as space holder particles. Zhuang et al. indicated that the porous Mg specimens showed changeable mechanical properties and in vitro degradation rate. The compressive strength and flexure strength of the specimen (36%–55% porosity) were 15–31 MPa and 14.1–27 MPa. After 144 h immersion in 0.9% NaCl, the specimen with 36% porosity lost 15% weight while the specimen with 55% porosity lost 60% weight.

Tan et al. designed three-dimensional honeycomb-structured magnesium scaffolds with interconnected pores of accurately controlled pore size and porosity by laser perforation technique, as shown in Figure 2. It was found that its compressive strength mainly depended on the pore arrangement. Elastic modulus and compressive strength similar to human bones could be obtained for the porous Mg with porosity of 42.6%–51%. Moreover, this porous magnesium coated with \( \beta \)-tricalcium phosphate showed improved biocompatibility with the human osteosarcoma cells (UMR106) well adhered and proliferated on the surface, meaning that the \( \beta \)-TCP coated porous Mg was promising as a bone tissue engineering scaffold material.

The lotus-type porous pure magnesium was prepared using a metal/gas eutectic unidirectional solidification method (GASAR process; Figure 2b). The compressive yield strength of compact and porous pure magnesium was \((110.3\pm8.5)\)MPa and \((23.9\pm4.9)\) MPa before immersion test, and porous pure Mg exhibited slower decay in compressive yield strength than that of a compact one with the extending of immersion period in SBF. The indirect cytotoxicity result indicated the Grade I RGR value to L-929 cell.

**Composite**

To improve biocompatibility, most investigations on magnesium metal matrix composite (MMC) adopted a P/M technique with bioceramic particles as reinforcement. The investigation of Mg/HA and ZK60A/CPP P/M composite indicated that the strength and ductility of the composites were reduced by HA or CPP addition and the properties further decreased...
with increasing reinforcement content. The corrosion resistance of these composites, however, was enhanced over that of the matrix due to the accelerated precipitation of calcium phosphate compounds on the surface of composite which improved the protection effect of corrosion product layer.\textsuperscript{26,27} Liu et al.\textsuperscript{28} also reported improved corrosion resistance of Mg-Zn/HA MMC in SBF over the matrix. Gu et al.\textsuperscript{29} proposed the novel Mg/Ca P/M composite by mixing Mg and Ca powders. Compared to the extruded Mg-1Ca alloy, Mg/1wt.%Ca and Mg/5wt.%Ca composite showed significantly improved yield tensile strength and appropriate ultimate tensile strength and elongation. The corrosion resistance of the composite decreased with increasing Ca content.

Besides the conventional P/M technique, Ye et al.\textsuperscript{30} added 1 wt.% nanosized gelatin coated HA particles into Mg-Zn-Zr alloy matrix using the stirring cast method and the MMC showed improved corrosion resistance and cyto-compatibility. Gu et al.\textsuperscript{31} proposed a novel Mg-Ca alloy based composite by melt infiltration method using the HA/TCP scaffold as porous preform. The result indicated that HA/TCP-MgCa composite showed 200-fold improved compressive strength than that of the HA/TCP scaffold whereas half of the strength of Mg-Ca master alloy. Moreover, the corrosion rate of the composite in Hank’s solution was 0.029 mL/cm\textsuperscript{2}, slower than that of the master alloy.

**Nanocrystalline and Glassy**

In general, the low corrosion resistance of Mg alloys is caused by the internal galvanic attack due to impurities and/or alloying elements,\textsuperscript{32} which can be improved by microstructure refinement. Rapid solidification processing was adopted to refine both the matrix grains and intermetallic particles as well as improve chemical homogeneity of Mg-3Ca alloy.\textsuperscript{33} With extreme fine grain size (200–500 nm), RS alloy ribbon showed largely decreased corrosion rate (0.36–1.4 mm/yr) and uniform corrosion morphology over the cast one (21 mm/yr).\textsuperscript{33}

A magnesium-based bulk metallic glass was also proposed due to its single-phase and chemically homogeneity, eliminating the galvanic corrosion caused by second phase.\textsuperscript{34} The result indicated that Mg66Zn30Ca4 exhibited decreased corrosion rate, uniform corrosion morphology and improved cytocompatibility, with MG63 cell well adhered and growth on its surface.\textsuperscript{35}

**SURFACE MODIFICATION OF BIOMEDICAL Mg ALLOYS**

In studies of the in vivo corrosion of bare Mg-Ca,\textsuperscript{9} Mg-Zn,\textsuperscript{12} LAE442,\textsuperscript{4} etc., Mg alloys exhibited rapid corrosion rate, inducing the mismatch of bone healing rate and gas cavity between the implant and tissue. These problems may induce the early loosening/disintegration of Mg alloy implants and thus fail due to a second fracture. The healing or regeneration process of bone generally proceeds in three phases\textsuperscript{36} an inflammatory phase lasting from 3 to 7 days, a reparative phase for strong healing union lasting about 3–4 months, and a remodeling phase that can require months to years.\textsuperscript{36} It is desirable to have the implanted fixation present for at least 12 weeks.\textsuperscript{1} However the currently developed bare magnesium alloys degrade earlier than the actual period of the bone healing process. Therefore, there is a high demand to reduce the corrosion rate for better synchronization between the implant biodegradation and new bone formation by various surface treatment techniques.

Li et al.\textsuperscript{37} and Gu et al.\textsuperscript{38} reported that alkaline heat treatment could effectively improve the corrosion resistance of Mg substrate indicating no cytotoxicity. Gu et al.\textsuperscript{38} showed that the alkaline heat treated coatings was mainly composed of MgO and the effectiveness of coating was related to the thickness and defects inside the coating. Chiu et al.\textsuperscript{39} synthesized a 1.5 μm thick MgF\textsubscript{2} coating on Mg providing corrosion resistance 40 times stronger than the uncoated one.

For orthopedic applications, the calcium phosphate coating prepared through different methods was widely investigated. Xu et al.\textsuperscript{40} prepared the brushite (CaHPO\textsubscript{4}·2H\textsubscript{2}O) coating by a traditional phosphating process which could improve both the corrosion resistance and surface bioactivity of Mg-Mn-Zn alloy, promoting early
bone formation at the interface. Wang et al. immersed Mg in the Ca and P containing solution (6.2 g Na₂HPO₄ and 15.9 g Ca(NO₃)₂ into 300 mL de-ionized water and the resulting pH was 3.5) and got a dicalcium phosphate dihydrate (DCPD) coating showing its effectiveness within 21 days. Song et al. prepared three kinds of coating (DCPD, HA and FHA) by electrodeposition and concluded that the chitosan coating was long-term stable and remained intact even after 1 month immersion in m-SBF. However, Wang et al. reported that the coating derived by the traditional cathodic electrodeposition was loose, porous, and low adhesive due to the applied static potential. Thus, Wang et al. adopted a pulse reversed current process for Ca-deficient HA coating preparation and the coated Mg-Zn-Ca alloy exhibited increased ultimate tensile strength (5.6%) and time of fracture (16.6%) in SBF, suggesting a longer support period for the fracture bone. Yao et al. introduced Ca and P into the ceramic MAO coating on AZ91D alloy and indicated the coating reduced the corrosion current density by two orders of magnitude. Additionally, the corrosion resistance and bioactivity of MAO-treated Mg-Ca alloys was reported to be related to the different applied voltage. 360 V-treated Mg-Ca alloy indicated a good combination of corrosion resistance and cytocompatibility with MG63 cells well adhered, proliferated and differentiated on the MAO coating.

Due to the complete biodegradability of the Mg alloy substrate, the surface coating was desired to be degradable and thus some degradable polymers coatings were used. Gu et al. investigated the influence of chitosan molecular weight and layer numbers of coating on the corrosion resistance of Mg-Ca alloy and concluded that the chitosan coating prepared by 2.7x10⁵ chitosan for six layers had a smooth and intact surface morphology suggesting the slowest corrosion rate of Mg-Ca alloy in SBF. Wong et al. adopted a controllable polymeric membrane coating fabricated by polycaprolactone and dichloromethane onto AZ91 alloy and the in vivo test indicated higher volumes of new bone without hydrogen gas accumulation around the polymer coated samples (Figure 3). This polymer coated AZ91 maintained compressive strength at approximately 170 MPa after 60 days immersion whereas the strength of the uncoated one dropped to 111 MPa. Li et al. adopted a PLGA coating on the top of the Mg-6Zn alloy and the result showed that the PLGA coating would not deteriorate the mechanical properties of the substrate and showed improved corrosion resistance and enhanced cell attachment.

Furthermore, other surface coatings (including calcium phosphate, hydroxapatite and collagen) prepared by ion-beam assisted deposition, magnetron sputtering deposition, and chemical reaction could also provide corrosion protection of the Mg alloy substrate by different levels.

**CONCLUSIONS**

Magnesium alloys are promising candidates for orthopedic and stent application, given the appropriate mechanical properties and biocompatibility. However, the investigation of biodegradable/bioabsorbable magnesium alloys is still a fundamental research highlight in China. More effort and systematic study is needed to answer some scientific questions, such as potential or long-term toxicity of the alloying element, degeneration of mechanical properties during degradation, stress corrosion or corrosion fatigue behavior, and the elimination of hydrogen gas, etc.

**References**

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