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REVIEW ARTICLE

A review on magnesium alloys as biodegradable materials

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Abstract Magnesium alloys attracted great attention as a new kind of degradable biomaterials. One research direction of biomedical magnesium alloys is based on the industrial magnesium alloys system, and another is the self-designed biomedical magnesium alloys from the viewpoint of biomaterials. The mechanical, biocorrosion properties and biocompatibilities of currently reported Mg alloys were summarized in the present paper, with the mechanical properties of bone tissue, the healing period postsurgery, the pathophysiology and toxicology of the alloying elements being discussed. The strategy in the future development of biomedical Mg alloys was proposed.

Keywords biomaterials, magnesium alloys, degradation, corrosion

1 Introduction

Magnesium alloys, as a new kind of degradable biomaterials, have attracted great attention recently. The major advantages of magnesium alloys as temporary biomaterials are their good mechanical properties, biocompatibilities: (i) Magnesium and magnesium alloys are exceptionally lightweight metals with density ranging from 1.74 to 2.0 g/cm^3, which is much less than that of the biomedical Ti alloy (4.4–4.5 g/cm^3) and close to that of the bone (1.8–2.1 g/cm^3) [1]. (ii) The fracture toughness of magnesium is greater than ceramic biomaterials, while the elastic modulus (41–45 GPa) is close to that of the bone that avoids the stress shielding effect. (iii) Magnesium is essential to human metabolism and is the fourth most abundant cation in the human body, with estimated 25 g magnesium stored in human body and approximately half of the total content stored in bone tissue. Magnesium is a cofactor for many enzymes and stabilized the structures of DNA and RNA [1,2]. (iv) Magnesium has standard electrode potential of −2.37 V, and bare magnesium metal exhibits even poorer corrosion resistance in Cl^- containing physiologic environment. Therefore, magnesium alloys could be developed as a new biodegradable metal, taking advantage of their fast corrosion rate in the physiologic environment.

The previous studies on biomedical magnesium alloys focused mainly on two aspects. On the one hand, the biomaterials researchers have devoted themselves to the corrosion and biocompatibility evaluations of commercial magnesium alloys. Most commercial magnesium alloys contain Al and rare earth, whereas Al is a neurotoxicant [3], and severe hepatotoxicity was detected after the administration of rare earth [4]. Therefore, another research highlight is the exploration of the new magnesium alloy system containing nontoxic or low toxic element. However, it lacks the uniform criterion to evaluate the biomedical properties of magnesium alloys.

Generally, degradable biomaterials should have sufficient strength, matching degradation rate with tissue healing rate and good biocompatibilities. This paper will review and compare the mechanical properties, corrosion properties, and biocompatibilities of current researched magnesium alloys with those of the human tissues, such as bone and blood vessels.

2 Mechanical property

The implantation of biomaterials, such as bone plates and stents, is used to substitute for the human tissue, which means they should match the mechanical property of tissue. Table 1 summarizes the mechanical properties of current researched magnesium alloys and the traditional biomaterials, in comparison with that of human tissue. It can be seen that magnesium alloys indicate much close elastic modulus to the cortical bone compared with the traditional Ti6Al4V, better ductility than the synthetic HA, and higher strength than DL-PLA. For the synthesis, magnesium alloy is as dominant as newly developed biomaterials.

Magnesium alloys have a large range of ultimate tensile

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Table 1 Mechanical properties of different tissues compared with current biomedical magnesium alloys and traditional biomaterials [5–9]

tissue/material	density/(g·cm^{-3})	compressive yield strength/MPa	ultimate tensile strength/MPa	elastic modulus/GPa	yield strength/MPa	elongation/%
cortical bone	1.8–2.0	164–240	35–283	5–23	104.9–114.3	1.07–2.10
cancellous bone	1.0–1.4	–	1.5–38	10–1570 (MPa)	–	–
arterial wall	–	–	0.50–1.72	1 (MPa)	–	–
Ti6Al4V	4.43	–	830–1025	114	760–880	12
synthetic HA	3.05–3.15	100–900	40–200	70–120	–	–
DL-PLA	–	–	29–35	1.9–2.4	–	–
Mg-cast	1.74	–	86.8±2.5	41	20.9±2.3	13±1.4
AZ91D-die cast	1.81	160	230	45	150	3
AZ31-extruded	1.78	60–70	235	45	125–135	7
LAE442	–	–	247	–	148	18
WE43-extruded T5	1.84		280	44	195	10
AM60B-die cast	1.78	130	220	45	–	6–8
Mg-Zn-Mn-extruded	–	–	280.3±0.9	–	246.5±4.5	21.8±0.6
Mg-1Ca-extruded	–	–	239.6±7.2	–	135.6±5.4	10.6±0.6

strength and elongation, from 86.8 to 280 MPa and from 3% to 21.8%, respectively. Given the fast loss of strength during the early degradation stage [10] *in vivo*, the intrinsic strength of magnesium alloy is still not high enough. However, internal fixation does not need the highest strength or stiffness, since it only provides temporary support but permanent substitute of bone [11]. Furthermore, the mechanical property of magnesium alloy can be improved by the alloying and processing history. Our previous work showed that the addition of Al, Ag, In, Si, Sn, Zn, and Zr could improve both the strength and elongation of magnesium alloys [7]. Moreover, hot rolling, hot extruding, and ECAP also contribute to the strength of magnesium alloys, whereas these sometimes deteriorate their ductility [7,9,12]. Therefore, it is possible to obtain satisfying strength for magnesium alloy through the alloying, processing, etc.

3 Corrosion property

Another vital performance for degradable biomaterial is the degradation rate, i.e., the corrosion rate for magnesium alloy. It not only matters to the tissue healing period but also influences the loss of mechanical properties of biomaterials during degradation.

One promising application of magnesium alloy is absorbable stent. Zartner et al. [13] implanted the absorbable metal stent (AMS; Biotronik, Bülach, Switzerland) in a preterm baby with inadvertent ligation of the left pulmonary artery. Reperfusion of the left lung was established and persisted throughout the 4-month follow-up period during which the gradual degradation process of the stent completed [13]. The AMS stent was also evaluated in a multicenter and nonrandomized study of 63 patients at nine clinical sites with a single de novo native coronary lesion. The results showed that 71 stents, 10–15 mm in length, 3.0–3.5 mm in diameter, and about 3 mg in weight, could achieve an immediate angiographic result similar to the result of other metal stents and can safely degraded after 4 months [14].

For orthopedic biomaterials, it needs 3–4 months from fracture callus formation to new bone formation and eventually solid bone healing restoring most of the bone's original strength [11]. That is, magnesium alloy should maintain its mechanical property for at least 3 months as orthopedic implants to avoid the second fracture occurrence resulting from the fast degradation of magnesium alloy implant. Table 2 shows the *in vitro* corrosion rate in different physiological solutions and *in vivo* corrosion rate of currently researched magnesium alloys. It can be seen that the LAE442 [15] and Mg-Mn-Zn [8] alloys show the slowest corrosion rate, with about 30% and 54% degradation percentage after 18 weeks *in vivo* implantation, yet unfortunately, the residue magnesium implants might not provide good enough mechanical property for fracture fixation. Therefore, the current researched magnesium alloy exhibits too fast corrosion rate and further improvement of corrosion resistance, for example, surface modification is strongly needed.

4 Biocompatibility

The biosafety and biocompatibility of absorbable biomaterials should be considered since all the element of magnesium alloy will enter into the human body. Table 3 summarizes the pathophysiology and toxicology of Mg and the alloying element used in current researched magnesium alloys. In Table 2, the cast Mg-1Ca alloy

Table 2 The *in vitro* and *in vivo* corrosion rates of different magnesium alloys [7–9,12,15–23]

material	*in vitro* electrochemical corrosion rate /(μA·cm^{-2})				*in vitro* immersion corrosion rate /(mg·cm^{-2}·h^{-1})				*in vivo* corrosion rate /(mg·mm^{-2}·yr^{-1})
	0.9% NaCl	Hank's solution	SBF	m-SBF	0.9% NaCl	Hank's solution	SBF	m-SBF	
pure Mg (99.95%)	–	15.98	86.06	–	–	0.011	0.038	–	–
AZ31	34.10	31.60	–	–	–	0.0065	–	–	1.17
AZ91	22.56	–	–	65.70	–	0.0028	–	–	1.38
WE43	27.30	30.60	16.03	–	–	–	0.085	–	1.56
ZE41	–	–	–	–	–	0.0626	–	–	–
LAE442	–	–	–	–	–	–	–	–	0.39
AZ91Ca	–	–	–	17.80	–	–	–	–	–
AZ61Ca	–	–	–	36.50	–	–	–	–	–
cast Mg-Mn-Zn	–	1.45–1.60	–	–	–	0.003–0.010	–	–	–
extruded Mg-Mn-Zn	–	–	79.17	–	–	–	0.05	–	0.92
extruded Mg-Zn-Y	–	1.88–4.47	–	–	–	–	0.015–0.04	–	–
cast Mg-1Ca	–	–	546.09	–	–	–	0.136	–	2.28
extruded Mg-1Ca	–	–	75.65	–	–	–	0.040	–	–

Table 3 The summary of the pathophysiology and toxicology of Mg and some alloying elements [5,24,25]

element		blood serum level	pathophysiology	toxicology	daily allowance
essential element	Mg	0.9 mmol/L	activator of many enzymes; coregulator of protein synthesis and muscle contraction; stabilizer of DNA and RNA	almost no evidence indicates toxicity of magnesium	0.7 g
	Ca	1.3 mmol/L	most abundant mineral and mainly stored in bone and teeth; participation blood clotting; activator or stabilizer of enzymes	calcium metabolism disorder; kidney stones	0.8 g
	Zn	46 μmol/L	essential trace element; appears in all enzyme classes	neurotoxic and hinder bone development at higher concentration	15 mg
	Mn	1 μmol/L	essential trace element; activator of enzyme; Mn deficiency is related to osteoporosis, diabetes mellitus, atherosclerosis	excessive Mn results in neurotoxic	4 mg
potential essential element	Si	–	cross linking agent of connective tissue base membrane structures; necessary for growth an bone calcification	excessive SiO_2 causes lung diseases	–
other element	Li	2–4 ng/g	used in the treatment of manic-depressive psychoses	reduced kidney function and central nervous system disorders	0.2–0.6 mg
	Al	2.1–4.8 μg	–	neurotoxic and accumulation in bone	total amount in human < 300 mg
	Zr	total < 250 mg	–	high concentration in liver and gall bladder	3.5 mg
	Y& RE	< 47 μg	compound of drugs for treatment of cancer	accumulation in bone and liver	–

indicates the highest corrosion rate (0.136 mg·cm^{-2}·h^{-1}) among other magnesium alloys, whereas the daily releasing amount of Mg is still at milligram level, which is far below the daily allowance of Mg. It means that the releasing of Mg during the degradation process is safe to human. The result of the *in vivo* implantation also indicated that the cast Mg-1Ca alloy showed good biocompatibility, and no significant difference for serum magnesium was observed before and 1–3 months after implantation [9].

In the design of degradable biomaterials, elements with

potential toxicological problems should be ideally avoided if possible, and these elements should be only used in minima and in acceptable amounts if they cannot be excluded from the design. Since Ca, Zn, and Mn are essential for human; these three elements should be the first choice as alloying element for biomedical magnesium alloy. For magnesium alloy, the addition of Ca and Zn should not be higher than 2 wt.% and 6 wt.% [26], respectively, under the consideration of the corrosion properties of magnesium alloy. Thus, even if the corrosion rate of magnesium alloy is estimated as 0.2 $mg \cdot cm^{-2} \cdot h^{-1}$ (referred to the highest corrosion rate 0.136 $mg \cdot cm^{-2} \cdot h^{-1}$ in Table 2), the releasing amount (0.096 and 0.288 $mg \cdot cm^{-2}$) of Ca and Zn per day is expected, which is below the daily allowance. It was reported that magnesium alloy, alloying with 1.5 wt.% Mn, showed good corrosion resistance and mechanical property [26], and the daily releasing of Mn is about 0.072 $mg \cdot cm^{-2}$, which is safe to human. In addition, Si is possible essential to human, and its toxicity is mainly caused by the SiO_2 powder [25]. The micro-alloying with Si may also be a good choice because alloying with Si can improve the strength of magnesium alloy, however even the addition of 1 wt.% Si can result in poor corrosion resistance [7].

The second choice of the alloying element should be those important for the property of magnesium alloy, including elements Li, Al, and Zr. The *in vivo* experiments of LAE442 and AZ91 alloys showed that these two magnesium alloys had good biocompatibility [15,16]. However, given the severe toxicity of Li and Al, the addition of these two elements should be done in a cautious manner, especially with compositions the added amount. Zr is considered to be a micro-alloying element, the content of which is not higher than 0.8 wt.% [26]. Thus, Zr can be used to refine grain and improve mechanical and corrosion properties, since no obvious toxicity is found.

So far, the toxicology and metabolic pathway of the Y and rare earth are still unclear, even their compound of drugs is used for treatment of cancer. The AMS stent showed good biocompatibility for both animal tests and clinical trials [14], with the compositions of Zr, Y, and rare earth (10 wt.%). Moreover, Y and rare earth are very important for improving the mechanical property and corrosion resistance of magnesium alloy, and the utility and dosage of Y and rare earth need further investigation.

5 Concluding remark

The practical usage of biodegradable magnesium alloys faces the challenge that their corrosion/degradation rates under physiological environment are too fast. One of the useful procedures to slow down the corrosion rate of magnesium alloys is the surface modification, including alkaline heat treatment [27,28], microarc oxidation [29], phosphating treatment [30], electrodeposition [31], and polymer coating [32]. Another effective method to improve the corrosion resistance of magnesium alloys is the exploration of the biomedical magnesium based alloy with new structure, for example, bulk metallic glass (BMG). Our recent study showed that Mg-Zn-Ca BMG had improved corrosion resistance and indicated much more uniform corrosion microstructure than the crystalline magnesium alloys [33]. Zberg et al. [34] indicated that Mg-Zn-Ca BMG showed great reduction in hydrogen evolution *in vivo* and good tissue compatibility.

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