POTENTIAL USE OF Mg-Ca ALLOYS FOR ORTHOPEDIC APPLICATIONS

Ana-Iulia BITA[1], Iulian ANTONIAC[2], Ion CIUCA[3]

The potential of magnesium alloys show great interest to replace existing materials used in orthopedic applications.

The ability to use magnesium implants both as scaffolds where new bone can grow and as a fixtures to keep the bone together as needed for natural healing to occur is increasing lately. Its biocompatibility and elasticity modulus with values very close to those of the bone make magnesium and its alloys to be extraordinarily desirable for this type of applications. Another feature of great interest to use magnesium for implants is represented by its ability for in situ degradation. That means there is no need for another surgery for the implant removal.

This paper presents a review of potential magnesium alloys that can be used as materials for orthopedic applications.

Keywords: magnesium alloys, orthopedic implant, degradation, medical applications, biocompatibility

1. Introduction

Biodegradable metals have an increasing interest in the last few years. The main interest to develop biodegradable metals is their degradation abillity in the physiological environment. The perception on metallic biomaterials is changing lately because the implants made out from this class of metals may completely disappear after the clinical function of implants is achieved. The main advantage of biodegradable implants is the elimination of the follow-up surgery to remove the implant after the healing process [1,2]. Consequently, there is a reduction of lifelong problems caused by permanent implants [3]. Even the biodegradable polymers, bioceramics and biocomposites are now dominant biomaterials for biodegradable implants on the medical market, some biodegradable metals like Mg-based [4], Fe-based [5,6] and Zn-based alloys [7] being proposed as better biodegradable materials for medical applications due to their superior mechanical properties.

[1] Faculty of Materials Science and Engineering, Univeristy POLITEHNICA of Bucharest, Romania, e-mail: anaiulia.bita@gmail.com
[2] Faculty of Materials Science and Engineering, Univeristy POLITEHNICA of Bucharest, Romania, e-mail: antoniac.iulian@gmail.com
[3] Faculty of Materials Science and Engineering, Univeristy POLITEHNICA of Bucharest, Romania, e-mail: ion.ciuca11@gmail.com

Based on the literature analysis, we can consider that magnesium based alloys have remarkable advantages over Fe-based and Zn-based ones. The elements like magnesium, iron and zinc are all essential nutritional elements for the human body. The recommended daily intake of magnesium in the adults case (240 - 420 mg day–1) is up to 52.5 times more than that of iron (8 - 18 mg/day) and zinc (8 - 11 mg/day) [8]. Also, the elastic modulus of magnesium (41 - 45 GPa) is closer to that of natural bone (3 - 20 GPa) than that of iron (211.4 GPa) or zinc (90 GPa) [1,9]. The biomedical incompatibility related to the difference in elastic modulus can result in critical clinical issues, such as early implant loosening, and chronic inflammation [10,11]. Pure magnesium has been reported to possess good biocompatibility in the human body, show no signs of toxicity and stimulate the formation of new bone [1,12].

Early clinical investigations on magnesium alloys for medical applications found that it was too brittle, had limited mechanical properties and also degraded too quickly. As a result, the application of magnesium alloys in medicine had nearly ceased. But with the technological advances in developing new high-purity magnesium alloys with superior mechanical and corrosion performance, renewed the interest in medical applications of magnesium based alloys marked by the studies of Heublein et al. [13] in 2000 - 2003.

Starting from this point, some magnesium based implants are already in clinical use. As is shown in Fig. 1, absorbable metal stents AMS (Fig. 1a) from WE43 and modified Mg-based alloys, and the MAGNEZIX screw (Fig. 1b) are currently used in medical applications [14, 15].

a) b)

Fig. 1. Commercial implants made by magnesium based alloys: (a) cardiovascular stent - AMS®, Biotronik, U.S.A.; (b) compression screw MAGNEZIX®, Syntellix AG, Germania.

A remarkable progress was made on the development of magnesium based alloys for medical applications over the last years, a number of fundamental challenges waiting to be solved. The range of applications of Mg-based alloys is still inhibited by their high degradation rates and the rapid formation of hydrogen gas bubbles, usually within the first week after surgery [16, 17].

This paper aims to review the recent advances of Mg-Ca alloys for biodegradable orthopedic implants, with emphasis on the alloy development strategy and the performances of currently developed Mg-Ca alloys, as well as to provide a perspective of current challenges and future trends.

2. Biodegradable magnesium alloys

Biodegradable materials are designed to assure temporary support during the healing process of a damaged tissue and to degrade thereafter [17]. This concept supposes that the implants will provide appropriate mechanical properties for the intended use, suitable resistance, and acceptable biocompatibility [18].

It is clear that the specific design and selection criteria of biodegradable metals depend on the intended applications. Screws, pins, plates and other load-bearing orthopedic applications are implanted in the bone to maintain mechanical integrity while the bone tissue heals [1]. Thus dedicated magnesium based alloys should combine both high strength and a low modulus close to that of bone to avoid ‘‘stress shielding’’ [18].

Pure magnesium in the as-cast state has a very low strength, at just less than 30 MPa, and a very fast corrosion rate of 2.89 mm year^{-1} in 0.9% NaCl solution [19]. Generally, alloying elements can directly strengthen the mechanical properties by solid solution strengthening, precipitation hardening and grain-refinement strengthening mechanisms [20]. Alloying elements introduced to strengthen the matrix must have high and temperature-dependent solubility in magnesium. Mostly investigated biodegradable Mg-based alloys, such as Mg–Zn-based, Mg–Al-based, and Mg–rare earth (RE)-based alloys, have obvious precipitation hardening due to high solubility of the secondary element in magnesium. The methods of grain refinement during solidification have recently been reviewed by StJohn et al. [21,22].

Extensive studies have proven that Ca, Zr, Si, etc. have excellent grain refinement efficiency in magnesium. In addition to alloying-element-induced grain refinement, plastic deformation appears to be the most efficient ways to refine the grain size [22].

There are a few considerations for element selection in developing biodegradable magnesium alloys. The first are related to the toxicity of the elements from the alloy chemical composition. The degradation products of the magnesium alloys should be non-toxic and absorbable by the surrounding tissues. From this point of view, elements can be classified into the following groups [23]:

- toxic elements: Be, Ba, Pb, Cd, Th;
- elements that are likely to cause toxicity or allergic problems: Al, V, Cr, Co, Ni, Cu, La, Ce, Pr;
- nutrient elements found in the human body: Ca, Mn, Zn, Sn, Si;
- nutrient elements found in plants and animals: Al, Bi, Li, Ag, Sr, Zr.

The second consideration is the ability of the elements to improve the mechanical properties, and four groups can be identified [24]:

- impurities: Fe, Ni, Cu, Co;

- elements that can improve all the mechanical properties: Al, Zn, Ca, Ag, Ce, Ni, Cu, Th
- elements that can only improve ductility:Cd, Tl, Li;
- elements that increase the strength of magnesium: Sn, Pb, Bi, Sb.

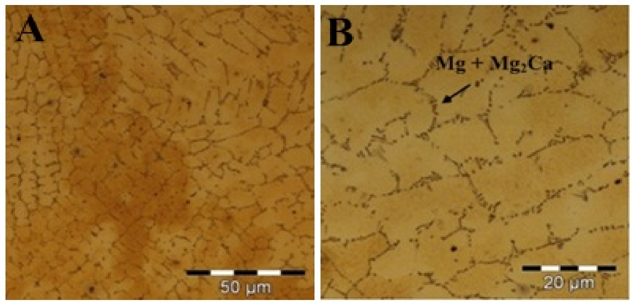
Many magnesium based alloys were investigated as a new class of implant material, especially starting with the commercial magnesium based alloys because they have well-known properties in engineering applications. Pure magnesium, AZ31, AZ61, AZ91, AM60, ZK30, ZK60 and WE43 [25] have been extensively investigated. The weakest point in all these cases it that in designing magnesium alloys for engineering applications, the toxicity and biocompatibility in biological environments was not considered. For example, because aluminum is a well-known neurotoxic element all magnesium alloys containing Al are not suitable for medical applications. Starting with this consideration, many magnesium binary alloys like Mg–Ca [6], Mg–Zn [4], Mg–Si, Mg–Gd, Mg–Zr, Mg–Sr and Mg–Y were developed and studied. Mg-Ca alloys appear to be one of the most studied binary magnesium alloy for medical applications [26].

3. Microstructural aspects of Mg-Ca Alloys

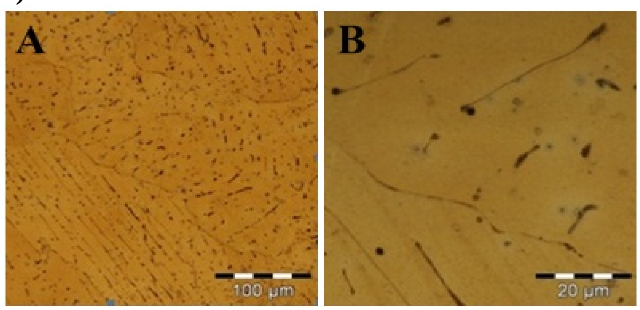
Magnesium alloys from the Mg-Ca binary system potentially used as biomaterials have attracted attention of many research groups in the last years. On the magnesium rich side of Mg-Ca system, the maximum solubility of calcium in the magnesium lattice is 0.8 wt %, at room temperature. The Mg-Ca alloy solidifies in eutectic composition at a calcium concentration of 16.2 wt %. The low alloyed Mg-Ca systems, from the microstructural point of view, present an α-phase solid solution (interstitial calcium in magnesium matrix) and an eutectic (α-phase + Mg_2Ca). Mg_2Ca has the identical crystal structure as Mg [27]. Ca is a unique alloying addition element to magnesium in the context of biodegradability. It's important to mention that the addition of a small amount of Ca has two effects on Mg-Ca alloys: increases the corrosion resistance and minimizes the grain growth (leads to smaller grains in cast state). Relevant microstructural aspects are presented in Fig. 2, that show the results of optical microscopy investigations for two experimental Mg-Ca alloys.

Rad et al. [28] studied the effect of calcium content on the microstructure in the case of different Mg-Ca alloys containing 0.5, 1.25, 2.5, 5.0, and 10.0 wt % Ca. The grain size and dendritic cell size decrease when higher amounts of Ca are added, while more Mg_2Ca phase appears at the grain boundaries, for higher Ca content, according to this study. Also, the microstructural aspects influence the mechanical behavior, which is determined by the metallurgical history [29]. A fine grain structure possesses the lowest ductility and with the increase of the grain size its ductility increases.

From the plastic deformation point of view, previous studies showed that the extruded Mg-Ca alloys have an inhomogeneous distribution of grain size but in non-extruded state the grain size distribution is more homogeneous.



a) *500x* *1000x*



b) *500x* *1000x*

Fig. 2. Optical microscopy images show relevant microstructural aspects for Mg-Ca alloys: a) Mg0.8Ca; cast stage; reagent: Nital 5 %; b) Mg1.8Ca; cast stage; reagent: Nital 5 %.

4. Mechanical Properties and Corrosion Aspects of Mg-Ca Alloys

Mechanical properties are very important, especially in the case of magnesium alloys for biodegradable implants. Many studies were made in order to obtain Mg-Ca alloys with low amounts of calcium, ranging from 1 to 4.0 wt % [27, 30]. Some of those demonstrate that the tensile strength and the 0.2% elastic limit increases with the increase of calcium concentration. For higher concentration of Ca, the difference between tensile strength and elastic limit decreases and no significant increase in the tensile strength was observed above 2.0 wt % of calcium. On the other hand, the workability decreases and extrusion force increases significantly for higher amounts of calcium in the case of direct extrusion. More than that, the processing of alloys containing more than 4.0 wt % calcium can only be done by the indirect extrusion due to its low workability and we can conclude that this type of Mg-Ca alloys is not suitable for biomedical applications [27].

Some explanation for these mechanical properties can be made based on microstructural characteristics. Precipitation of the brittle Mg_2Ca phase at the grain boundaries and within the grains is responsible for poor ductility above 1.5 wt % Ca concentration. In these respect, the machining of these brittle magnesium alloys with conventional methods are very limited.

Table 1 [27]

Mechanical and corrosion properties of binary Mg-based alloys for biodegradable implants

Alloy	Condition	YS (MPa)	UTS (MPa)	Elongation	In vitro corrosion rate (mm year^{-1})	
					Weight loss	Electrochemical test (solution)
Mg-1Ca	As-cast	40	71.38	1.87	-	12.56 (SBF)
Mg-1Al	As-cast	40	160	16.5	-	2.07 (SBF)
Mg-1Ag	As-cast	23.5	116.2	13.2	-	8.12 (SBS)
Mg-1Mn	As-cast	28.5	86.3	7.5	-	2.46 (SBF)
Mg-1Zn	As-cast	25.5	134	18.2	-	1.52 (SBF)
Mg-1Zr	As-cast	67.5	172	27	-	2.20 (SBF)
Mg-2Sr	As-rolled	147.3	213.3	3.15	0.37 (Hanks')	0.87 (Hanks')
Mg-6Zn	As-extruded	169.5	279.5	18.8	0.07 (SBF)	0.16 (SBF)

From the corrosion point of view, the surface of magnesium alloys passivates when exposed to air and forms a thin grey magnesium oxide layer. But magnesium alloys is significantly affected in saline media such as human body environment is. Magnesium can be absorbed within the human body like other resorbable biomaterials but give the great advantage of presenting higher mechanical strength as opposed to biodegradable ceramics or biopolymers. Dissolution of magnesium in chloride containing media like human body happens through the following reaction (1) [27]:

$$Mg_{(s)} + 2H_2O_{(aq)} \rightarrow Mg(OH)_{2(s)} + H_{2(g)} \quad (1)$$

Magnesium reacts with water, major component in body fluid, and produces hydroxide and hydrogen. A schematic representation of this process is shown in Fig. 3.

In high pH environments, magnesium hydroxide can act as a stable and protective layer on the surface for magnesium alloys, but a lower pH will increase the corrosion of magnesium alloys in aqueous solution . Since the local pH at the implant-bone interface is around the value of 7.4 due to metabolic post-surgery processes [31], the magnesium hydroxide layer will not cover the entire surface that will induce an accelerated corrosion on the magnesium alloys surface in the case of *in vivo* experiments.

Hydrogen gas is produced during magnesium alloys dissolution. For this reason, the rate of hydrogen evolution of magnesium alloys in simulated aqueous medium is used as a measure of corrosion rate. Eudiometry of hydrogen has been used as a tool to study long term degradation behavior of Mg-Ca implants *in vitro* and corrosion of one gram magnesium results in production of 1.081 liter hydrogen gas [27, 31].

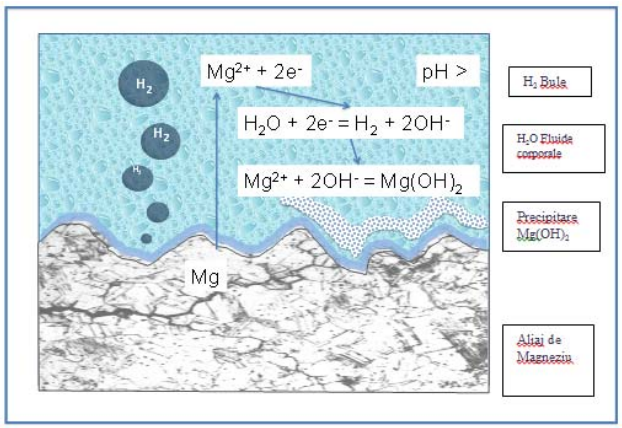


Fig. 3. Schematic representation of the corrosion process in aqueous medium for magnesium alloys

Unfortunately, the accelerated corrosion rate will lead to early loss of mechanical integrity. Also, if the hydrogen release is higher and appears too fast for the human body to deal with will result in the formation of subcutaneous gas bubbles [31]. Magnesium alloys present different degradation rates depending on the alloying element.

The influence of Ca amount and chloride concentration within the corroding media, on corrosion behavior for Mg-Ca alloys was studied by Hassel et al. [27]. They observed that the magnitude of the corrosion current density (i_{corr}) changed with the Ca content and the higher the Ca content was, the larger the current density became. The eudiometric investigations revealed that Mg-Ca alloys corrode slower than pure magnesium. Also, hydrogen evolution rate and corrosion rate depends strongly on electrolyte concentration. Most important it was that the same trend was observed for other Ca amounts in Mg-Ca binary alloys. Rad et al. [28] studied the effect of Ca content on corrosion behavior of Mg-Ca alloys with varying Ca content ranging from 0.5 to 10.0 wt. %. Corrosion rate for experimental Mg-Ca alloys increased significantly with higher amounts of Ca in the alloys.

Another important aspect are the influence of increasing calcium (Ca) content in binary Mg-Ca alloys along with the composition of the bio-fluid on in vitro degradation rate. Kirkland et al. [29] investigated during a very complex study the Mg-Ca alloys with different Ca contents (0.4, 0.8, 1.34, 5.0, 10.0, 16.2, and 28.0 wt %) from this point of view. Three different fluids that simulate human body environment were used: first fluid was the classical simulated body fluid (SBF), the second fluid was obtained by adding amino acids and vitamins to SBF, and the third fluid was obtained by adding proteins (the third bio-fluid) to SBF. All three fluids were buffered and the pH and temperature values were kept constant. It was observed that the corrosion rate increased with increasing Ca content and the corrosion potential became more negative. As the experimental fluids mimicked the human body environment more closely, the corrosion rate decrease and corrosion potential became more positive. Liu et al. [32] investigated the effect of albumin adsorption on the magnesium alloys surface during in vitro degradation behavior of Mg-Ca1.5 alloy. The albumin adsorption conduct to decreased hydrogen release rates and corrosion.

This means that using more physiologically relevant test environments are necessary to effectively study the in vitro biodegradation behavior of Mg-Ca alloys.

The corrosion mechanism is very important, particularly with regard to the mechanical properties during biodegradation process. Magnesium alloys tend to pitting corrosion, especially in the presence of chloride ions in aqueous media. But the carbonate ions are able to suppress pitting corrosion and for this reason, the addition of Ca to magnesium based alloys enhances their general and pitting corrosion resistance. A homogenous texture and a uniformly distributed corrosion was observed in the case of Mg-Ca alloys with up to 1 wt % Ca, but higher percent of calcium lead to irregular and widespread corrosion [6].

An important contribution to understand the corrosion mechanism for biodegradable magnesium alloys could be given by different microscopically techniques used for surface analysis like scanning electron microscopy and atomic force microscopy. Fig. 4 presents an example of scanning electron microscopy analysis made on the experimental Mg0.8Ca alloy surface after the corrosion evaluation using immersion test in simulated body fluid (SBF) at different times.

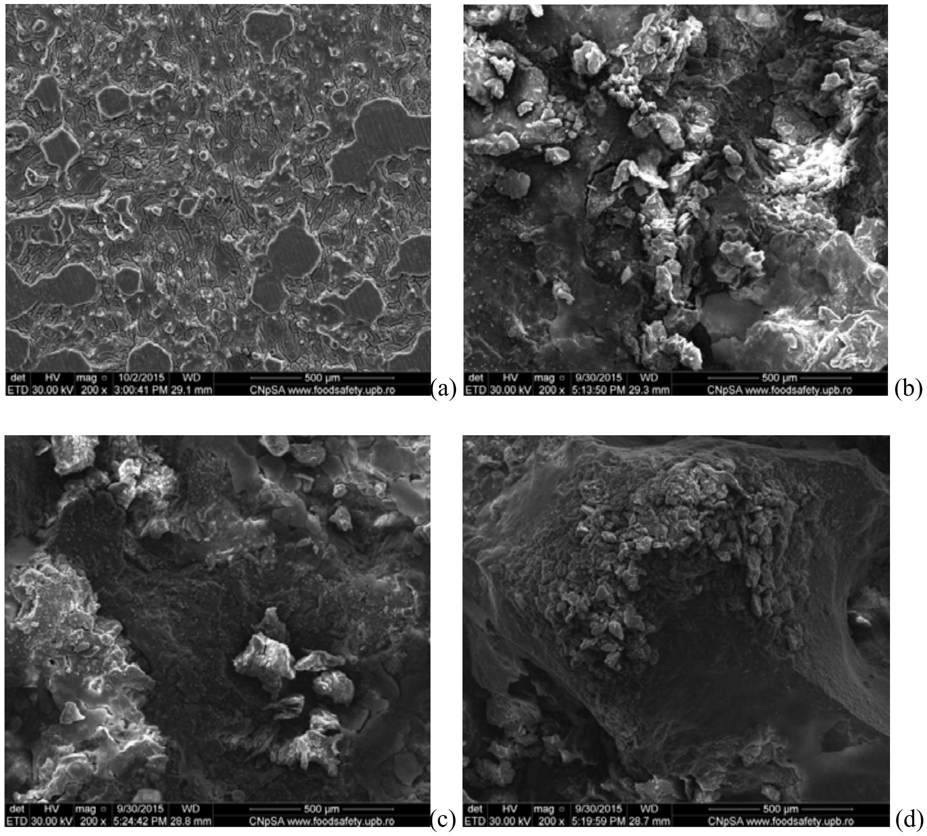


Fig. 4. SEM images on the Mg0.8Ca alloy surface after corrosion evaluation using immersion test in simulated body fluid (SBF) during different time: a) 1 day; b) 3 days; c) 7 days; d) 10 days. (*Magnification 200x*)

5. Conclusion and future trends

The present review shows that significant progress has been made in the development of Mg-Ca alloys and their characterization of *in vitro* and *in vivo* performances. The next-generation biodegradable metallic implants require the metallic alloys to provide appropriate mechanical properties, suitable corrosion and excellent biocompatibility in the human body. Mechanical properties and corrosion resistance strongly depend on the microstructure of the alloys, which result from alloy design, element selection, and processing history.

Magnesium-calcium (Mg-Ca) alloys have shown to be very promising in development of biodegradable orthopedic implants. The microstructure, the mechanical properties, electrochemical behavior, and the degradation kinetics of Mg-Ca implants are all affected by the amount of the alloying elements.

Although, there have been made studies on Mg-Ca orthopedic products very recently, there is a lot left to be done in order to successfully produce Mg-Ca alloys as degradable orthopedic material in medical device manufacturing.

Exact simulation of the physiology, surrounding a bone trauma in the human body, should be a major concern in future studies. There is still need to explore how the surface integrity relates to the performance in human body of Mg-Ca alloys. Surface properties like roughness, microhardness, and microstructure appear to be the main factor that influence the degradation kinetics of Mg-Ca implants.

Future work should focus on the development of controllable properties in Mg-Ca alloys using various strategies, including surface processing and coatings, as well as to reveal the biological degradation at the interface between biodegradable Mg-Ca implants and the surrounding tissues.

Acknowledgement

The work has been funded by the Sectoral Operational Programme Human Resources Development 2007-2013 of the Ministry of European Funds through the Financial Agreement POSDRU/159/1.5/S/132397.

R E F E R E N C E S

[1] *M.P. Staiger, A.M. Pietak, J. Huadmai, G. Dias*: Magnesium and its alloys as orthopedic biomaterials: a review, Biomaterials, (2006) 27:1728–34.
[2] *S. Fare, Q.A. Ge, M. Vedani, G. Vimercati, D. Gastaldi, F. Migliavacca et al.*: Evaluation of material l properties and design requirements for biodegradable magnesium stents, Materia-Brazil, (2010) 15:103–12.
[3] *M. Moravej, D. Mantovani*: Biodegradable metals for cardiovascular stent application: interests and new opportunities, Int. J. Mol. Sci., (2011) 12:4250–70.
[4] *Z.J. Li, X.N. Gu, S.Q. Lou, Y.F. Zheng*: The development of binary Mg–Ca alloys for use as biodegradable materials within bone, Biomaterials, (2008) 29:1329–44.
[5] *Q.M. Feng, D.Y. Zhang, C.H. Xin, X.D. Liu, W.J. Lin, W.Q. Zhang et al.*: Characterization and in vivo evaluation of a bio-corrodible nitrided iron stent, J. Mater. Sci.: Mater. Med., (2013) 24:713–24.
[6] *M. Schinhammer, A.C. Hanzi, J.F. Loffler, P.J. Uggowitzer*, Design strategy for biodegradable Fe-based alloys for medical applications, Acta Biomater. (2010) 6:1705–13.
[7] *P.K. Bowen, J. Drelich, J. Goldman*: Zinc exhibits ideal physiological corrosion behavior for bioabsorbable stents, Adv. Mater., (2013) 25:2577–82.
[8] *P. Trumbo, S. Schlicker, A.A. Yates, M. Poos*: Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids, J Am Diet Assoc (2002) 102:1621–30.
[9] *A. Purnama, H. Hermawan, J. Couet, D. Mantovani*: Assessing the biocompatibility of degradable metallic materials: state-of-the-art and focus on the potential of genetic regulation, Acta Biomater., (2010) 6:1800–7.

[10] *M. Salahshoor, Y.B.Guo*: Biodegradable orthopedic magnesium–calcium (MgCa) alloys, processing, and corrosion performance. Materials (2012) 5:135–55.

[11] *F. Witte, J. Fischer, J. Nellesen, H.A. Crostack, V. Kaese, A. Pisch, et al.*: In vitro and in vivo corrosion measurements of magnesium alloys. Biomaterials (2006) 27:1013–8.

[12] *F. Witte*: The history of biodegradable magnesium implants: a review. Acta Biomater (2010) 6:1680–92.

[13] B. Heublein, R. Rohde, V. Kaese, M. Niemeyer, W. Hartung, A. Haverich: Biocorrosion of magnesium alloys: a new principle in cardiovascular implant technology? Heart (2003) 89:651–6.

[14] http://www.syntellix.com/produkte

[15] *M.B. Kannan, R.K.S. Raman:* In vitro degradation and mechanical integrity of calcium-containing magnesium alloys in modified-simulated body fluid, Biomaterials (2008) 29:2306–14.

[16] *G.E.J. Poinern, S. Brundavanam, D. Fawcett*, Biomedical magnesium alloys: a review of material properties, surface modifications and potential as a biodegradable orthopaedic implant, Am J Biomed Eng (2012) 2:218–40.

[17] *H. Hermawan*, Biodegradable metals: state of the art, Berlin: Springer; (2012). p. 13–22.

[18] *M. Erinc, W.H. Sillekens, R. Mannens, R.J. Werkhoven*: Applicability of existing magnesium alloys as biomedical implant materials. PA: Minerals, Metals and Materials Scociety; (2009) p. 209–14.

[19] *Y. Chen, Z. Xu, C. Smith, J. Sankar:* Recent advances on the development of magnesium alloys for biodegradable implants Acta Biomaterialia (2014) 11:4561–4573.

[20] *M. Bamberger, G. Dehm*: Trends in the development of new Mg alloys. Annu Rev Mater Res (2008) 38:505–33.

[21] *D.H. StJohn, M. Qian, M.A. Easton, P. Cao, Z. Hildebrand*: Grain refinement of magnesium alloys. Metall Mater Trans A (2005) 36A:1669–79.

[22] *Y.C. Lee, A.K. Dahle, D.H. StJohn*: The role of solute in grain refinement of magnesium. Metall Mater Trans A (2000) 31:2895–906.

[23] *Y. Nakamura, Y. Tsumura, Y. Tonogai, T. Shibata, Y. Ito*: Differences in behavior among the chlorides of seven rare earth elements administered intravenously to rats, Fundam Appl Toxicol (1997) 37:106–16.

[24] *Z. Yang, J.P. Li, J.X. Zhang, G.W. Lorimer, J. Robson*: Review on research and development of magnesium alloys. Acta Metall Sin (English Lett) (2008) 21:313–28.

[25] *C.H. Ye, Y.F. Zheng, S.Q. Wang, T.F. Xi, Y.D. Li*: In vitro corrosion and biocompatibility study of phytic acid modified WE43 magnesium alloy, Appl Surf Sci (2012) 258:3420–7.

[26] *T. Hassel, F.W. Bach*: Production and properties of small tubes made from mgca0.8 for application as stent in biomedical science. In Proceedings of the 7th International Conference on Magnesium Alloys and Their Applications, Kainer, K.U., Ed.; Wiley-VCH Verlag GmbH & Co.: Hoboken, NJ, USA, (2007) pp. 432–437.

[27] *N.T. Kirkland, N. Birbilis, J. Walker, T. Woodfield, G.J. Dias, M.P. Staiger*: In vitro dissolution of magnesium-calcium binary alloys: Clarifying the unique role of calcium additions in bioresorbable magnesium implant alloys. J. Biomed. Mater. Res. B (2010), 95, 91–100.

[28] *H.R.B. Rad, M.H. Idris, M.R.A. Kadir, S. Farahany*: Microstructure analysis and corrosion behavior of biodegradable Mg-Ca implant alloys. Mater. Des. (2012) 33, 88–97.

[29] *K.U. Kainer, E. Lach*: Deformation behavior of AZ alloys at high strain rates. In Magnesium Alloys and Their Applications; Mordike, B.L., Kainer, K.U., Eds.; Werkstoff-Informationsgesellschaft: Frankfurt, Germany, (1998) pp. 369–374.

[30] *A. Drynda, T. Hassel, R. Hoehn, A. Perz, F.W. Bach, M. Peuster*: Development and biocompatibility of a novel corrodible fluoride-coated magnesium-calcium alloy with

improved degradation kinetics and adequate mechanical properties for cardiovascular applications, J. Biomed. Mater. Res. A (2010) 93, 763–775.

[31] *F. Witte, V. Kaese, H. Haferkamp, E. Switzer, A. Meyer-Lindenberg, C.J. Wirth, H. Windhagen*: In vivo corrosion of four magnesium alloys and the associated bone response. Biomaterials (2005) 26, 3557–3563.

[32] *C.L. Liu, Y.J. Wang, R.C. Zeng, X.M. Zhang, W.J. Huang, P.K. Chu*: In vitro corrosion degradation behavior of Mg-Ca alloy in the presence of albumin. Corros. Sci. (2010) 52, 3341–3347.