MICROSTRUCTURES AND CORROSION BEHAVIOR OF BIODEGRADABLE Mg–Ca–*x*Bi AND Mg–Ca–Zn–*x*Bi ALLOYS FOR BIOMEDICAL IMPLANT APPLICATION

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Specially dedicated to
my beloved family and friends
for their support and inspiration

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ABSTRACT

Low density, biodegradable and non-toxicity magnesium (Mg) has received great attention as biodegradable medical implants as it does not require second surgical procedure to remove the implant. However, poor corrosion resistance, rapid degradation and hydrogen gas evolution in human body fluid have limited its clinical application. This research is aimed to investigate the effect of bismuth (Bi) on the microstructures and corrosion behavior of Mg based alloy. The first stage of the research was focused on the effect of Bi on the binary Mg-Ca alloy by the addition of Bi from 0.5 to 12wt.%. The same process was repeated in the second stage by replacing binary Mg–Ca alloy with ternary Mg–Ca–Zn alloy. Microstructural analysis was conducted by optical microscopy, X-ray diffractometry (XRD), scanning electron microscopy (SEM) and energy dispersive X-ray spectroscopy (EDS). The corrosion resistance was investigated by using in vitro immersion tests and electrochemical test in Kokubo simulated body fluid (SBF). The results show that the grain size decreased with addition of Bi contents in both Mg-Ca-*x*Bi and Mg-Ca-Zn-*x*Bi alloys. SEM micrograph shows that the amount of intermetallic phases increased with increasing of Bi content in both ternary and quaternary alloys. The addition of 0.5 wt.% Bi content was found to enhance the corrosion resistance of both Mg based alloys and produced the lowest dissolution rate. Further addition of Bi content up to 12wt.% have deteriorate the corrosion resistance. These results show that the Bi element would enhance the corrosion behavior of Mg based alloys when it is solutes inside the α-Mg matrix. The precipitation of the intermetallic phases was detrimental to the corrosion resistance. The overall results show that Mg–Ca–0.5Bi and Mg–Ca–Zn–0.5Bi alloys presented highest corrosion resistance hence it can be good candidates for biomedical implant applications.

ABSTRAK

Magnesium (Mg) mempunyai ketumpatan yang rendah, biodegradasi dan tidak beracun telah mendapat penumpuan sebagai bahan implan biodegradasi kerana tidak memerlukan pembedahan tambahan untuk menanggalkan implan. Namun begitu, rintangan kakisan yang rendah, kadar degradasi yang tinggi dan pembebasan gas hidrogen telah mengehadkan aplikasi klinikal aloi Mg. Kajian ini bertujuan untuk menyelidik kesan bismuth (Bi) atas struktur mikro dan rintangan kakisan aloi Mg. Peringkat pertama kajian ini memberi tumpuan kepada kesan Bi dalam aloi binari Mg–Ca dengan penambahan unsur Bi daripada 0.5 ke 12wt.%. Proses yang sama telah diulang pada peringkat kedua dengan menggantikan aloi binari Mg–Ca kepada aloi ternari Mg–Ca–Zn. Analisis stuktur mikro telah dijalankan dengan menggunakan teknik mikroskop optik, pembelauan sinar-x (XRD), mikroskopi elektron imbasan (SEM) dan spektrometer serakan tenaga (EDS). Rintangan kakisan telah dikaji dengan menggunakan ujian rendaman dan kajian elektrokimia dalam larutan Kokubo pada suhu bilik. Keputusan kajian menunjukkan bahawa saiz bijian menurun dengan penambahan kandungan Bi ke atas aloi Mg–Ca dan Mg–Ca–Zn. Mikrograf SEM pula menunjukkan bahawa fasa antara logam meningkat dengan penambahan kandungan Bi. Penambahan 0.5 wt.% Bi ke dalam aloi juga dikenalpasti dapat meningkatkan rintangan kakisan dalam kedua-dua aloi dan menghasilkan kadar keterlarutan yang paling rendah dan rintangan kakisan yang paling tinggi. Namun begitu, penambahan seterusnya hingga 12 wt.% Bi telah mengurangkan rintangan kakisan. Keputusan ini menunjukkan bahawa unsur Bi hanya meningkatkan rintangan kakisan aloi Mg apabila unsur tersebut terlarut di dalam matriks α-Mg. Mendakan fasa antara logam telah mengurangkan rintangan terhadap kakisan. Keputusan keseluruhan kajian ini menunjukkan aloi Mg–Ca–0.5Bi dan Mg–Ca–Zn–0.5Bi memberikan sifat rintangan kakisan tertinggi. Oleh itu, aloi ini boleh digunakan dalam aplikasi bahan implan bioperubatan.

TABLE OF CONTENTS

3 RESEARCH METHODOLOGY

4 RESULT AND DISCCUSION

5 CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE WORK

LIST OF TABLES

LIST OF FIGURES

LIST OF SYMBOL/ ABBREVIATIONS

ASTM	-	American Society For Testing And Materials
DNA	-	Deoxyribonucleic acid
RNA	-	Ribonucleic acid
ISO	-	The International Standards Organization
MEM	-	Minimum Essential Medium
PBR	-	Pilling-Bedworth Ratio
SBF	-	Simulated Body Fluid

LIST OF APPENDICES

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Nowadays, metallic biomaterials have become the trend to produce biomedical implants. According to M. Niinomi *et al.* [1] metallic biomaterials acquire remarkable effect for reconstruction of failed tissue, especially hard tissue. It can help to improve the quality of life of the patient. Its excellent mechanical strength and fracture toughness have made it become the most common implant materials [1]. The demand of these implants increased rapidly since the world population is getting older and it can help to improve the movement of these elderly people. However, degradation products that formed during the corrosion process of metallic biomaterials might generate some unexpected metallic ion when in contact with the biological environment which may be toxic [2]. The studies on the toxicity potential and inflammatory effect on the release of degradation products to the surrounding tissues of metallic biomaterials have become fundamental issues. All of this is related to the biodegradable and corrosion behavior of the biomaterials. Thus, the studies on these prospective are essential in order to find potential alloys for biomaterials.

Biodegradable implants are getting substantial attention in biomedical applications especially when impermanent orthopedic placement is required. By using these implants, the need for secondary surgery to eliminate them is unnecessary [3]. This kind of implant will dissolve and subsequently excreted through the urine at a certain pace [4]. The implant aimed to provide the strength required during healing process and eventually will absorb by the body [3-5]. No implant removal or secondary surgery that might be fatal to the patient especially elderly people is required. In contrast, the use of representative practical metallic biomaterials such as stainless steels, titanium (Ti) and cobalt-chromium-based (Co-Cr) alloys can cause allergies and sensitization in the human body [4]. According to Y. Shi *et al.* [5] the permanent presence of this metallic implant in human body could be a trouble since the implant might cause osteoporosis due to mismatch in mechanical properties with human bones. Therefore, metals based on physiological trace element like magnesium (Mg) and calcium (Ca) seem to be promising as an alternative to current implant materials in cardiovascular and musculoskeletal applications [5].

Recently, biodegradable polymers have become the primary materials for tissue engineering applications and bone repair implant [6]. Basically, there are two types of biodegradable polymer which are natural-based materials (proteins) and synthetic polymers (polylactic acid) [6]. Biodegradable polymer have been demonstrated to be biocompatible and degraded in vivo into non-toxic components with controllable degradation rates by Tan *et al.* [6]. However, biodegradable polymers have relatively low mechanical strength, X-ray transparency and the non-specificity foreign body reaction, thus their application are normally limited to low load-bearing application [6,7]. Metal based biodegradable materials are attracting much attention for biomedical applications as the alternative of biodegradable polymers owing to their higher load-bearing capacity [7].

Mg–based metals, including pure magnesium and its alloys show great potential in biomedical application owing to their easy corrosion in body environment [6]. It can be taken as characteristics of biodegradation since most of the Mg–based metals only release biosafety absorbed or excreted degradation product [5-8]. Mg-based metals have been used as one of the most suitable bone substitute materials since it have similar mechanical properties with natural bones with excellent biocompatibility and biodegradability [8]. Mg is a lightweight metal with density of 1.74 g/cm^3. Its density is very similar to those human bones which are 1.8 g/cm^3 [8, 9]. Besides, human body usually contains magnesium approximately 35 g per 70kg body weight and the demand for magnesium is about 375mg [9]. An excess of Mg^{2+} is not harmful since it will excretes through urine [8]. Mg has been considered as bio-safe material that is suitable for body implant due to its high daily requirement.

Despite various benefits of Mg and its alloy, there are some limitations that restrict the development of it as orthopedic materials. Firstly, the mechanical properties of Mg–based alloys are much lower than those commonly used Ti alloy and stainless steel for load bearing bone [6]. The elastic modulus of Mg–based alloy is 41-45 GPa which is lower than Ti alloy (110-117 GPa) and stainless steel (189-205 GPa) [8]. However, the mechanical properties like elastic modulus of Mg–based alloys (40GPa) are similar to human bones. Therefore, Mg–based alloys have more potential to fabricate as low load bearing implant. Secondly, the applications of Mg–based alloys are also restricted due to their relatively low corrosion resistance as well as the release of hydrogen gas when exposed to human body fluid [1, 2, 6-10]. These phenomena may cause the hemolysis, osteolysis and fast decreases of mechanical strength when implant inside human body [6]. According to Gu *et al.* [12], it takes three to four months from fracture callus formation to new bone formation and eventually solid bone healing restoring most bone original strength. However, due to the high degradation rate of Mg-based alloy inside human body plasma, most Mg–based alloy cannot provide sufficient mechanical strength more than three months. It might result in the second fracture occurrence on the patients [11, 12]. Thus, various researches have been conducted to enhance the corrosion resistance of Mg–based alloys and the main focus was alloying [1, 2, 10].

Nowadays, most of the researches on the biodegradable Mg–based alloy for biomedical application are focus on the alloying element such as aluminum (Al), zirconium (Zr), manganese (Mn) or rare earth like cerium (Ce) and neodymium (Nd).

However the release of these metallic elements inside human body might induce toxic effect. Firstly, Al ions are found to be harmful to the nerve of human body [10] and might induce dementia since these can bind to inorganic phosphate causing a lack of phosphate in the body [2, 7]. Excess Mn also has been testified to cause neurotoxicity that can cause Parkinsonism [2, 13]. Furthermore, the presence of Zr has been reported by Song [7] to cause liver cancer, breast cancer, lung cancer, and nasopharyngeal cancer. Some RE elements exhibit anti-cancerogenic properties [13] which possess certain potential toxicity to human body [10]. The biosafety and biodegradability of Mg–based alloys became the main focus of current research.

Calcium (Ca) is one of the alkaline metal elements that can be tolerated in human body [7]. It is a main component of human bone. Besides, the release of Ca^{2+} will also improve the bone healing process [6, 9, 10, 14]. Besides, as Mg, Ca also has a low density 1.55 g/cm^3 which similar to the density of the bones (1.8 – 2.1 g/cm^3) [6]. Previous research from Kirkland *et al.* [14] has shown the effect of Ca inside the Mg alloy which greatly improved the corrosion resistance of Mg–based alloys. Researches on binary Mg–based alloys indicate that binary Mg–Ca alloys with 0.6-1.5 wt.% Ca provide good mechanical properties and corrosion resistance [10, 14, 15]. Another essential element in the human body, Zinc (Zn) also can be used to strengthen the Mg–based alloy [6, 14]. The addition of Zn to Mg alloy result in enhanced the mechanical strength significantly due to the refinement of grain [14]. The results have been promising, since some Mg–Ca–Zn reported to show better corrosion resistance and mechanical properties [10, 14, 15]. Integrating two of the most biocompatible elements diminishes any possibility of toxicity-related problems when placed in human body [14].

The development of Mg–Ca and Mg–Ca–Zn alloy has currently reached a saturated form. However, further improvement is still necessary especially in improving the corrosion resistance of the alloy. Adding another alloying element was one of the best options where heavy metal element, bismuth (Bi) might be a good choice of it. According to Yang *et al.* [6], Bi compound are almost non-toxic, and it is significantly less toxic than arsenic and antimony which are in the same group with Bi in the periodic table. It is not bio-accumulative [3] and purified Bi metal can be used in the preparation of various pharmaceutical products and it has long been used in medicine [16-18]. Moreover, Bi is neither essential nor stimulatory in human and its biological half-life for whole body retention is five days [19]. However, if patients were treated extensively with bismuth compound, it might damage their kidney and liver [3, 18, 19]. The toxicity of bismuth is depended on the rate at which soluble bismuth is available intravenously, whereas slow admiration is well tolerated [3]. Addition of Bi to magnesium alloy has also been reported to improve the tensile strength and creep resistance significantly [16, 17].

Researches on the properties of Mg–Ca and Mg–Ca–Zn alloys as well as the corrosion and degradation mechanism of the alloys had been conducted by other researcher previously [6-8]. However, the study on the relationship between these properties and the microstructure of the alloys had received little attentions. It is obvious that comprehensive studies on this area are essential to increase the usage of these alloys for biomedical applications. Therefore, the main approach of this research is to investigate the effect of alloying element such as Bi on microstructure and corrosion behavior of binary Mg–Ca and ternary Mg–Ca–Zn alloys and whether these Mg-based alloys are potential to be used as biomedical implant.

1.2 Problem Statement

Magnesium has many advantages over traditional metallic materials, ceramics and biodegradable polymers. However, the poor corrosion resistance of pure magnesium inside human body plasma has hindered its biomedical applications. Besides, clinical application of magnesium is also limited by the release of hydrogen gas when exposed to human body fluid. These characteristics deteriorate the mechanical properties of pure magnesium before the new tissues healed properly. Therefore, it is necessary to improve the biodegradable and corrosion behavior of Mg–based alloys by addition of alloying element. Many researches on the binary Mg–Ca and ternary Mg–Ca–Zn alloys have shown its excellent properties and biocompatibility. Ca is a major component of human bone and can accelerate the bone growth. Additional of Zn element can enhance the tensile strength and corrosion resistance of Mg-based alloy. However, most of the Mg-based alloys still have not reach the sufficient corrosion behavior for orthopedic application. Thus, the additional of another alloying element to binary Mg–Ca and ternary Mg–Ca–Zn alloys is expected to further improve the corrosion behavior of it. It has been reported that bismuth. Bi has been use in many pharmaceuticals like anticancer and anti-inflammation products for many years and Bi can help to enhance the corrosion effect as alloying element. Consequently, Bi was a potential candidate to further improve the corrosion behavior of Mg-based alloy.

1.3 Objectives of the Study

The aim of the research is to investigate the effect of bismuth in various magnesium alloys for biomedical implant. Specific objectives are:

i. To fabricate the ternary Mg-Ca–*x*Bi and quaternary Mg–Ca–Zn–*x*Bi alloys.
ii. To identify the surface morphology, microstructures and phases of ternary Mg–Ca–*x*Bi and quaternary Mg–Ca–Zn–*x*Bi alloys before and after corrosion test.
iii. To investigate the corrosion behavior of ternary Mg–Ca–*x*Bi and quaternary Mg–Ca–Zn–*x*Bi alloys.

1.4 Scopes of the Research

The scopes of the research cover the followings:

i. Mg–based alloys namely Mg–Ca and Mg–Ca–Zn were used as the main materials. They were produced by casting.
ii. Bismuth was used as the main alloying element to improve the properties of the magnesium alloys. The additions to the alloy were limited to between 0.5 to 12 wt.%.
iii. The responses on the effect of bismuth addition are limited to the microstructure analysis, corrosion rate and corrosion properties of Mg–Ca–*x*Bi and Mg–Ca–Zn–*x*Bi.
iv. The specimens were subjected to microstructural characterization using optical microscopy, X-ray diffractometry, Fourier-transformed infrared spectroscopy, scanning electron microscopy and energy dispersive X–ray spectroscopy.
v. The corrosion resistance was examined in-vitro by electrochemical test and immersion test in Kokubo stimulated body fluid (SBF) solutions at room temperature.

REFERENCES

1. Niinomi, M., Nakai, M., & Hieda, J. (2012). Development of new metallic alloys for biomedical applications. Acta Biomaterialia, 8(11), 3888-3903
2. Purnama, A., Hermawan, H., Couet, J., & Mantovani, D. (2010). Assessing the biocompatibility of degradable metallic materials: State-of-the-art and focus on the potential of genetic regulation. Acta Biomaterialia, 6(5), 1800-1807.
3. Remennik, S., Bartsch, I., Willbold, E., Witte, F., & Shechtman, D. (2011). New, fast corroding high ductility Mg–Bi–Ca and Mg–Bi–Si alloys, with no clinically observable gas formation in bone implants. Materials Science and Engineering: B, 176(20), 1653-1659.
4. Witte, F., Kaese, V., Haferkamp, H., Switzer, E., Meyer-Lindenberg, A., Wirth, C. J., & Windhagen, H. (2005). In vivo corrosion of four magnesium alloys and the associated bone response.
5. Shi, Y., Qi, M., Chen, Y., & Shi, P. (2011). MAO-DCPD composite coating on Mg alloy for degradable implant applications. Materials Letters, 65(14), 2201-2204.
6. Tan, L., Yu, X., Wan, P., & Yang, K. (2013). Biodegradable Materials for Bone Repairs: A Review. Journal of Materials Science & Technology, 29(6), 503-513.
7. Song, G. (2007). Control of biodegradation of biocompatable magnesium alloys. Corrosion Science, 49(4), 1696-1701.
8. Staiger, M. P., Pietak, A. M., Huadmai, J., & Dias, G. (2006). Magnesium and its alloys as orthopedic biomaterials: A review. Biomaterials, 27(9), 1728-1734.
9. Li, N., & Zheng, Y. (2013). Novel Magnesium Alloys Developed for Biomedical Application: A Review. Journal of Materials Science & Technology, 29(6), 489-502.

10. Du, H., Wei, Z., Liu, X., & Zhang, E. (2011). Effects of Zn on the microstructure, mechanical property and bio-corrosion property of Mg–3Ca alloys for biomedical application. Materials Chemistry and Physics, 125(3), 568-575.
11. Mordike, B. L., & Ebert, T. (2001). Magnesium: Properties — applications — potential. Materials Science and Engineering: A, 302(1), 37-45.
12. Gu, X.N., Zheng, Y.F. (2010). A review on magnesium alloys as biodegradable materials. Front. Mater. Sci. China, 4, 111–115.
13. Witte, F., Hort, N., Vogt, C., Cohen, S., Kainer, K. U., Willumeit, R., & Feyerabend, F. (2008). Degradable biomaterials based on magnesium corrosion. Current Opinion in Solid State and Materials Science, 12(5–6), 63-72.
14. Kirkland, N., Staiger, M., Nisbet, D., Davies, C. J., & Birbilis, N. (2011). Performance-driven design of Biocompatible Mg alloys. JOM, 63(6), 28-34.
15. Rad, H. R. B., Idris, M. H. (2011). Characterization and Corrosion Behavior of Biodegradable Mg-Ca and Mg-Ca-Zn Implant Alloys. Applied Mechanics and Materials, 121-126, 568.
16. Guangyin, Y., Yangshan, S., & Wenjiang, D. (2001). Effects of bismuth and antimony additions on the microstructure and mechanical properties of AZ91 magnesium alloy. Materials Science and Engineering: A, 308(1–2), 38-44.
17. Zhou, W., Aung, N. N., & Sun, Y. (2009). Effect of antimony, bismuth and calcium addition on corrosion and electrochemical behaviour of AZ91 magnesium alloy. Corrosion Science, 51(2), 403-408.
18. Yang, N., & Sun, H. (2007). Biocoordination chemistry of bismuth: Recent advances. Coordination Chemistry Reviews, 251(17–20), 2354-2366.
19. Fowler, B. A., & Sexton, M. J. (2007). Chapter 22 - Bismuth. In G. F. Nordberg, B. A. Fowler, M. Nordberg & L. T. Friberg (Eds.), Handbook on the Toxicology of Metals (Third Edition) (pp. 433-443). Burlington: Academic Press.
20. Manivasagam G., Dhinasekaran D., and Rajamanickam A.(2010). Biomedical Implants: Corrosion and its Prevention - A Review. Recent Patents on Corrosion Science. 2: 40-54.

21. Wu G., Ibrahim J.M., and Chu P.K., Surface design of biodegradable magnesium alloys - A review. Surface & Coatings Technology, 2012. doi.org/10.1016/j.surfcoat.2012.10.009.
22. Zheng, Y. F., Gu, X. N., & Witte, F. (2014). Biodegradable metals. Materials Science and Engineering: R: Reports, 77(0), 1-34.
23. Witte, F. (2010). The history of biodegradable magnesium implants: A review. Acta Biomaterialia, 6(5), 1680-1692.
24. Witte. F, Elizer. A, and Cohen. S. (2010). The history, challenges and the future of biodegradable metal implants. Advanced Materials Research, 95, 3.
25. Maguire, M., & Cowan, J. (2002). Magnesium chemistry and biochemistry. Biometals, 15(3), 203-210.
26. K.W.Guo. (2010). A review of magnesium/magnesium alloys corrosion and its protection. Recent Patents on Corrosion Science, Volume 2, Pages 13-21.
27. Li, Q.-F., Weng, H.-R., Suo, Z.-Y., Ren, Y.-L., Yuan, X.-G., & Qiu, K.-Q. (2008). Microstructure and mechanical properties of bulk Mg–Zn–Ca amorphous alloys and amorphous matrix composites. *Materials Science and Engineering: A*, *487*(1–2), 301-308.
28. Gu X., Zheng Y., and Cheng Y., In vitro corrosion and biocompatibility of binary magnesium alloys. Biomaterials, 2009. 30: 484-498.
29. Bornapour, M., Celikin, M., Cerruti, M., & Pekguleryuz, M. (2014). Magnesium implant alloy with low levels of strontium and calcium: The third element effect and phase selection improve bio-corrosion resistance and mechanical performance. *Materials Science and Engineering: C, 35*(0), 267-282.
30. Angrisani, N., Reifenrath, J., Seitz, J.-M., & Meyer-Lindenberg, A. (2012). *Rare Earth Metals as Alloying Components in Magnesium Implants for Orthopaedic Applications*.
31. Rad, H. R. B., Idris, M. H., Kadir, M. R. A., & Farahany, S. (2012). Microstructure analysis and corrosion behavior of biodegradable Mg–Ca implant alloys. *Materials & Design, 33*(0), 88-97.
32. Hagihara, K., Fujii, K., Matsugaki, A., & Nakano, T. (2013). Possibility of Mg- and Ca-based intermetallic compounds as new biodegradable implant materials. *Materials Science and Engineering: C, 33*(7), 4101-4111.

33. Kim, W.-C., Kim, J.-G., Lee, J.-Y., & Seok, H.-K. (2008). Influence of Ca on the corrosion properties of magnesium for biomaterials. *Materials Letters, 62*(25), 4146-4148.
34. Wan, Y., Xiong, G., Luo, H., He, F., Huang, Y., & Zhou, X. (2008). Preparation and characterization of a new biomedical magnesium–calcium alloy. *Materials & Design, 29*(10), 2034-2037.
35. Nayeb-Hashemi A.A. and Clark J.B. (1988), Phase diagrams of binary magnesium alloy. ASM International.
36. Li, Z., Gu, X., Lou, S., & Zheng, Y. (2008). The development of binary Mg–Ca alloys for use as biodegradable materials within bone.
37. Zhang, S., Zhang, X., Zhao, C., Li, J., Song, Y., Xie, C., Bian, Y. (2010). Research on an Mg–Zn alloy as a degradable biomaterial. *Acta Biomaterialia, 6*(2), 626-640.
38. Song, Y., Han, E.-H., Shan, D., Yim, C. D., & You, B. S. (2012). The effect of Zn concentration on the corrosion behavior of Mg–xZn alloys. *Corrosion Science, 65*(0), 322-330.
39. Takei T. (1929). The equilibrium diagram of the system magnesium–zinc. Kinzokuno Kenkyu, Japan Institute of Metals. 6: 177-183.
40. Zhang, B., Hou, Y., Wang, X., Wang, Y., & Geng, L. (2011). Mechanical properties, degradation performance and cytotoxicity of Mg–Zn–Ca biomedical alloys with different compositions. *Materials Science and Engineering: C, 31*(8), 1667-1673.
41. Geng, L., Zhang, B. P., Li, A. B., & Dong, C. C. (2009). Microstructure and mechanical properties of Mg–4.0Zn–0.5Ca alloy. *Materials Letters*, *63*(5), 557-559.
42. Kirkland, N. T., Birbilis, N., & Staiger, M. P. (2012). Assessing the corrosion of biodegradable magnesium implants: A critical review of current methodologies and their limitations. *Acta Biomaterialia*, *8*(3), 925-936.Nayeb-Hashemi, A. A., & Clark, J. B. (1985). The Bi-Mg (Bismuth-Magnesium) system. *Bulletin of Alloy Phase Diagrams*, *6*(6), 528-533.
43. Okamoto, H. (1992). Bi-Mg (Bismuth-Magnesium). *Journal of Phase Equilibria*, *13*(6), 672-673.
44. Kainer K.U., Srinivasan P.B., Blawert C., and Dietzel W. (2010). Corrosion of Magnesium and its alloys. Shreir's Corrosion, 2011-2041.

45. Ghali, E., Dietzel, W., & Kainer, K.-U. (2004). General and localized corrosion of magnesium alloys: A critical review. *Journal of Materials Engineering and Performance, 13*(1), 7-23.
46. Liu, L. J., & Schlesinger, M. (2009). Corrosion of magnesium and its alloys. *Corrosion Science, 51*(8), 1733-1737.
47. Atrens, A., Liu, M., & Zainal Abidin, N. I. (2011). Corrosion mechanism applicable to biodegradable magnesium implants. *Materials Science and Engineering: B, 176*(20), 1609-1636.
48. Xin Y., Hub T., and Chu P. K. (2011). In vitro studies of biomedical magnesium alloys in a simulated physiological environment: A review. Acta Biomaterialia, 7: 1452-1459.
49. Dieter, L. (2007). Localized Corrosion Phenomena *Corrosion and Surface Chemistry of Metals* (pp. 275-329): EFPL Press.
50. Vander Voort, G. F. (2013). Metallography of Magnesium and its Alloys. Bel-Ray Specialty Lubricant: Tech-Notes (vol 4, issue 2).
51. Kokubo, T., & Takadama, H. (2006). How useful is SBF in predicting in vivo bone bioactivity? *Biomaterials, 27*(15), 2907-2915.
52. ASTM G3-72. (2004) Standard practice for laboratory immersion corrosion testing of metals [S]. West Conshohocken, PA: American Society of Testing and Materials, 3.
53. Zhang, E., & Yang, L. (2008). Microstructure, mechanical properties and bio-corrosion properties of Mg–Zn–Mn–Ca alloy for biomedical application. *Materials Science and Engineering: A, 497*(1–2), 111-118.
54. L. Lu, A.K. Dahle, J.A. Taylor, et al. (2005). Theoretical and practical considerations of grain refinement of Mg–Al alloys, *Mater. Sci. Forum*, 488–489 299–302.
55. Sedighi, M., Arghavani Nia, B., Zarringhalam, H., & Moradian, R. (2013). Density functional theory study of the structural and electronic properties of Mg3Bi2 in hexagonal and cubic phases. *The European Physical Journal - Applied Physics, 61*(01), null-null.
56. Shi, Z., Liu, M., & Atrens, A. (2010). Measurement of the corrosion rate of magnesium alloys using Tafel extrapolation. *Corrosion Science, 52*(2), 579-588.

57. Zhang, E., Yin, D., Xu, L., Yang, L., & Yang, K. (2009). Microstructure, mechanical and corrosion properties and biocompatibility of Mg–Zn–Mn alloys for biomedical application. *Materials Science and Engineering: C, 29*(3), 987-993.
58. Bakhsheshi-Rad HR, Abdul-Kadir MR, Idris MH, Farahany S. (2012). Relationship between the corrosion behavior and the thermal characteristics and microstructure of Mg–0.5Ca–xZn alloys. *Corrosion Science. 64(0):184-97.*
59. H.R. Bakhsheshi-Rad, M.H. Idris, M.R. Abdul-Kadir, A. Ourdjini, M. Medraj, M. Daroonparvar, E. Hamzah. (2014). Mechanical and bio-corrosion properties of quaternary Mg–Ca–Mn–Zn alloys compared with binary Mg–Ca alloys. *Materials and Design 53, 283-292.*
60. Zhu Li, Yao Meiyi, Sun Guocheng et al. (2013). Effect of bi addition on the corrosion resistance of zr-1nb alloy in deionized water at 360 ℃ and 18.6 MPa. Acta Metall Sin, 49(1): 051.
61. Yao, M. Y., Zhou, B. X., Li, Q., Zhang, W. P., Zhu, L., Zou, L. H., . Peng, J. C. (2013). Effect of Bi Addition on the Corrosion Behavior of Zirconium Alloys. *Volume 1*, V001T002A014.
62. Bamberger M., Levi G., and Sande J.B. (2006) Precipitation Hardening in Mg-Ca-Zn Alloys. Metallurgical and Materials Transactions A, 37: 481-488.
63. Lisitsyn, V., Ben-Hamu, G., Eliezer, D., & Shin, K. S. (2010). Some particularities of the corrosion behaviour of Mg–Zn–Mn–Si–Ca alloys in alkaline chloride solutions. *Corrosion Science, 52*(7), 2280-2290.