SCHOOL OF MATERIALS AND MINERAL RESOURCES ENGINEERING

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MECHANICAL PROPERTIES AND IN-VITRO CORROSION BEHAVIOUR OF Mg-6Zn/BIOACTIVE GLASS COMPOSITE

By

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DECLARATION

I hereby declare that I have conducted, completed the research work and written the dissertation entitled "**Mechanical Properties and In-Vitro Corrosion Behaviour of Mg-6Zn/Bioactive Glass Composite**". I also declare that it has not been previously submitted for the award of any degree or diploma or other similar title of this for any other examining body or university.

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TABLE OF CONTENTS

Contents **Page**

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ALP	Alkaline Phosphatase
BG	Bioactive glass
BPR	Ball to powder weight ratio
EDX	Energy Dispersive X-ray
FESEM	Field Emission Scanning Electron Microscopy
HA	Hydroxyapatite
HBSS	Hank’s balanced salt solution
ISO	International Organization for Standardization
MMC	Metal Matrix Composite
mpy	mm per year
OM	Optical microscope
PM	Powder Metallurgy
Rpm	Rotation per minutes
SBF	Stimulated Body Fluid
XRD	X-ray Diffraction

LIST OF SYMBOLS

Å	Angstrom
GPa	Gigapascal
HV	Vicker hardness
MPa	Megapascal
pH	Potential of hydrogen
Wt.%	Weight percent

SIFAT-SIFAT MEKANIKAL DAN KAKISAN IN-VITRO KOMPOSIT Mg-6Zn/KACA BIOAKTIF

ABSTRAK

Biodegradasi magnesium dan aloinya digunakan secara meluas sebagai bahan implan tulang ortopedik yang berpotensi disebabkan mereka memiliki biokeserasian yang baik dalam bio-alam sekitar. Untuk meningkatkan sifat-sifat mekanikal dan in-vitro kakisan biodegradasi magnesium, magnesium-zink yang diperkukuh dengan biokaca (45S5) dengan peratus berat yang berbeza (0, 5, 10, 15 wt.%) telah difabrikasikan melalui kaedah metalurgi serbuk. Komposit telah dipadatkan pada tekanan 300 MPa dan telah disinterkan pada suhu 350°C. Mikrostruktur komposit telah dilihat menggunakan mikroskop optik. Sifat-sifat fizikal telah ditentukan dengan menggunakan piknometer gas. Sifat-sifat mekanikal seperti kekerasan mikro dan kekuatan mampatan telah dikaji. Kadar kakisan telah dikaji melalui ujian rendaman. Nilai ketumpatan komposit (1.845 - 1.958 g/cm^3) adalah dekat dengan ketumpatan tulang asli (1.8 - 2.1 g/cm^3). Semua komposit menunjukkan peningkatan dalam kekerasan mikro dan kekuatan mampatan jika dibandingkan dengan aloi Mg-6Zn. Mg-6Zn/5BG menunjukkan nilai tertinggi bagi kekerasan (67.21 HV) dan kekuatan mampatan (169MPa). Aglomerasi zarah biokaca dilihat dalam mikrostruktur komposit yang mengandungi 10 wt.% dan 15 wt.% biokaca. Ujian kakisan in-vitro menunjukkan bahawa Mg-6Zn/5BG mempunyai kadar kakisan yang paling rendah iaitu 0.154 mm/tahun. Walau bagaimanapun, keliangan komposit yang lebih daripada 7.0% (Mg-6Zn/10BG dan Mg-6Zn/15BG) akan membawa kesan buruk ke atas rintangan kakisan. Penambahan biokaca dalam Mg-6Zn telah meningkatkan pembentukan lapisan Ca-P selepas merendam dalam larutan SBF.

MECHANICAL PROPERTIES AND IN-VITRO CORROSION BEHAVIOUR OF Mg-6Zn/BIOACTIVE GLASS COMPOSITE

ABSTRACT

Biodegradable magnesium and its alloys are widely used as potential orthopedic bone implant materials due to their good biocompatibility in the bio-environment. To improve the mechanical properties and in-vitro corrosion behaviour of biodegradable magnesium, magnesium-zinc matrix reinforced with different weight percentage (0, 5, 10, 15 wt.%) of bioglass (45S5) were fabricated using powder metallurgy technique in this research work. The composites were compacted under pressure 300 MPa and were sintered at 350°C. Microstructure of composites was observed using an optical microscope. Density was determined using a gas pycnometer. The mechanical properties such as microhardness and compressive strength were studied. Corrosion rate was investigated by immersion test. Density (1.845 - 1.958 g/cm^3) of sintered composites are close to the density value of natural bone (1.8 - 2.1 g/cm^3). All composites show improvement in microhardness and compressive strength if compared to the naked Mg-6Zn alloy. Mg-6Zn/5BG shows the highest microhardness value (67.21 HV) and compressive strength (169MPa). Agglomeration of bioglass particles has been seen on the microstructure of composites with 10 wt.% and 15 wt.% of bioglass content. In-vitro corrosion test shows that Mg-6Zn/5BG has the lowest corrosion rate which is 0.154 mm/year. However, composites that have porosity of more than 7.0% (Mg-6Zn/10BG and Mg-6Zn/15BG) will have adverse effect on corrosion resistance. The addition of bioglass to the Mg-6Zn has also improved the formation of apatite layer after soaking in SBF solution.

CHAPTER 1

INTRODUCTION

1.1 Background

The human's life expectancy has been lengthened recently and results in an increase worldwide in the average age of the human population. As the body ages, the load-bearing joints in the body would be prone to illness. Therefore, there is a big demand for biomaterials to be developed for implantation (Nag and Banerjee, 2012).

Metallic biomaterials such as stainless steel, cobalt-chromium alloys, titanium alloys and magnesium alloys, have high mechanical property and they are easy to process, therefore, they are widely utilized in load-bearing bio-medical applications (Saini et al., 2015). However, they are some concerns remains in metallic biomaterials such as the toxicity, long term health problems and cytotoxicity (Rao et al., 1996). To select a metallic biomaterial, non-toxic implant materials with a good combination of excellent mechanical properties, favorable corrosion resistance and improved biocompatibility are desired.

Magnesium alloys have gained great attention as potential orthopedic bone implant materials due to their biodegradability and biocompatibility in the human body. Another benefit is their exceptionally lightweight. The most significant property is that elastic modulus (41-45 GPa) of the magnesium alloys are similar to that of the cortical bone (3-20 GPa) which can reduce the stress shielding effect effectively (Staiger et al., 2006; Zeng et al., 2008).

Corrosion properties are also of the main concern for various implant applications. Biodegradable material is beneficial as it could degrade naturally and reduce the number of surgeries. However, it must not decompose too early before the fixation can normally function. There are two methods to improve corrosion resistance which are through alloying (Peng et al., 2010) or coating (Gray-Munro et al., 2009). Both methods have shown encouraging results in improving the corrosion resistance.

Zinc can be used as an alloying element for biomedical magnesium materials. The results of biochemical and histological investigations show that the degradation of the Mg-Zn based alloy would not injure the organ of organism (Li and Zheng, 2013). Zhang et al. (2010) have also done an investigation on an extruded Mg–6Zn alloy as a biodegradable material. The results of the research showed that Mg–6Zn alloy is believed to be suitable for implant applications. Mg-6Zn alloy had higher tensile and compression strength than Mg-Ca alloy. As reported, the Mg–6Zn alloy exhibits good biocompatibility in vitro (Zhang et al., 2009a; Zhang et al., 2010).

The bioactivity of the biomaterials is also another important consideration. The ability for bond formation surrounding bone tissue after implantation is essential but not always concerned and studied. Several studies have shown good bone attachment to magnesium implants after 9 to 18 weeks of post-implantation as there is no inflammation interference. This indicates magnesium alloy has good biocompatibility in vivo (Xu et al., 2007). However, Zhang et al. (2010) found that there is a gap between the implant and bone tissue after 14-weeks post-operation due to the fast degradation rate and elevated ambient pH. To improve the surface bioactivity, Ca-P coating is done on the Mg-based alloys as it enhances the cell adhesion and growth (Xu et al., 2009).

Apart from Ca-P coating, another study suggested that inducing the deposition of Ca–P compounds from simulated body fluid into a metal matrix is an effective way to improve the bioactivity of the matrix material by addition of the bioactive particles to form a metal matrix composite (Ye et al., 2010). For instances, Ti/hydroxyapatite (HAP) biocomposite is able to induce apatite nucleation and growth on its surface in simulated body fluid (Ning and Zhou, 2002). Abdullah et al. (2013) have done a modification on the Mg/HAP composite by using cold spray deposition to form HAP-coated magnesium-based alloy. The results showed the HAP-coated samples improved the biodegradability of Mg alloy. However, it has been reported that HAP coating on magnesium alloys are loose flake-like morphology and poor crystallization (Song et al., 2008; Zhang et al., 2009a), indicating that complications of the coating process and the need of improving it.

There are many studies have proved that bioactive glass shows the best bioactivity behavior among all the bioactive materials. The results obtained from in vivo implantation studies demonstrated that certain compositions of bioactive glasses containing CaO, SiO_2, and P_2O_5 did not cause any local or systemic toxicity, inflammation, and foreign-body response (Sepulveda et al., 2002).The bioactive glasses with specific compositions show degradation gradually but also bone bonding after implantation (Martin et al., 2001). Its bioactive behavior accompanied by the release of ionic products that stimulated the proliferation of bone-related cells (Xynos et al., 2000). These advantageous properties make the bioactive glass a potential material as the secondary phase to be added to Mg-based composite for the improvement of bioactivity.

In the study of Martin et al. (2001), bioglass particles of compositions 45S5, 52S and 55S were used as implants in the distal femoral epiphysis of rabbits. All materials are degradable and show bone bonding. 45S5 shows the highest bone bonding kinetics

and the highest degradation rates (Martin et al., 2001). The effect of bioglass (45S5) addition on corrosion resistance and physical properties of Mg-5Zn matrix composite has been investigated in the study of Zaludin et al. (2014). Hence, in the present study, bioglass 45S5 has been chosen to be the secondary phase in Mg-Zn matrix.

There are two methods for metal matrix composite fabrication. In a composite ingot made by the semi-solid casting method, porosity may arise from gas entrapment during mixing, hydrogen evolution, and shrinkage during solidification (Hashim et al., 1999). Study of Huan et al. (2010), found that when bioactive glass particles were added to magnesium alloy through a semi-solid high-pressure casting process, the porosity in stir-cast composites increased almost linearly with particle content (Huan et al., 2010). Zaludin et al. (2014) proved that Mg-5Zn/BG composite has been successfully fabricated by powder metallurgy, but it is also observed that the increased amount of BG hindered the densification of the Mg-5Zn matrix. The increase corrosion rate of the samples with an amount greater than 15 wt% may be subjected to the porosity of the composites (Zaludin et al., 2014). Hence, bioglass 45S5 with the composition of less than 15% is suggested to be added as the secondary phase in magnesium-based composite through powder metallurgy method for further investigation.

1.2 Problem statement

Commercial pure magnesium and magnesium alloys can corrode too quickly under the high chloride conditions of the physiological environment. Rapid corrosion of magnesium alloys in chloride-conditioning solutions including human body fluids and blood plasma limits the orthopedics applications due to a too high degradation rate leads

to a faster release of hydrogen from the implant and to early deterioration of biomechanical properties (Staiger et al., 2006; Song, 2007). Efforts have done to overcome this problem such as incorporate the magnesium-based alloys with secondary phase.

On the other hand, bioactive glasses have excellent bioactivity, the ability to deliver cells, and controllable biodegradability. These advantages make bioactive glasses promising reinforcement particle in magnesium-zinc alloy to improve bioactivity of magnesium-zinc alloy in the human body.

Not many papers related to Mg-Zn/bioglass composite have been well established and the results of corrosion properties are varied. Huan et al. (2012) discovered that the surface morphologies and compositions of 10 wt.% bioglass in ZK30 samples showed the highest corrosion resistance among the other samples (5 wt.% and 15 wt.%) (Huan et al., 2012). On the other hand, Zaludin et al. (2014) found that additions of 15 wt.% of bioglass in Mg-5Zn showed the greatest corrosion resistance compared to other samples (5, 10, 20, 25 and 30 wt. %) and the increase corrosion rate of the samples with an amount greater than 15 wt.% may cause porosity in the composites (Zaludin et al., 2014). In present study, addition of different compositions (0, 5, 10, and 15 wt.%) of bioglass in Mg-6Zn alloy was done to study the optimal composition of Mg-6Zn/BG for orthopedic bone implants application with high corrosion resistance and good bioactivity meanwhile retain the excellent mechanical properties of magnesium-zinc.

1.3 Objective

1. To fabricate Mg-6Zn/bioglass composite by powder metallurgy technique.
2. To study the effect of different weight fraction of bioglass on microstructure, physical properties and mechanical properties of Mg-6Zn/bioglass composite.
3. To study the corrosion resistance and to investigate the formation of deposition layer of Mg-6Zn/bioglass composite.

1.4 Scope of research work

This project aimed at investigating mechanical properties and corrosion properties of magnesium-biodegradable glass composite (Mg-Zn/BG) and confirming the good surface bioactivity of the composites. Bioactive glass (BG) 45S5 (45 wt % SiO_2, 24.5 wt. % Na_2O, 24.5 wt. % CaO, 6 wt. % P_2O_5) was chosen as the reinforcement phase while magnesium alloy Mg-6Zn (6 wt % zinc) as the matrix phase. Mg-6Zn/BG composites with different weight percentage of bioglass were synthesized by powder metallurgy method. The microstructures of the composites of bioactive particles in the matrix as well as their physical and mechanical properties were then investigated. Compressive test and hardness test were carried out to determine the strength and hardness of the composites. The surface bioactivity of the composites was evaluated by characterizing the corrosion layer on samples soaked in a simulated body fluid and comparing it with that of the Mg-6Zn matrix sample.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

This chapter presents a review on existing knowledge and research of the topics related to introduction of biomaterials, development of implant biomaterials, modification and improvement of magnesium alloy in biomedical field, important parameters of magnesium alloy, bioactive glass as reinforcement phase and fabrication methods for metal matrix composite.

2.2 Biomaterials

Biomaterials is a material that planned to incorporate with biological systems to evaluate, treat or replace any tissue, organ, part or function in the body (Ali, 2013). There are different common classification types of biomaterials implanted with human biological systems as shown in Figure 2.1. The first category is based on natural biomaterials, while the second category of biomaterials is based on synthetic engineering biomaterials. With the advanced technology of engineering biomaterials tissues, a new third category is created, called combined of biomaterials. Biomaterials classifications are necessary for suitable use in medical industries according to reference standards (Ali et al., 2013).

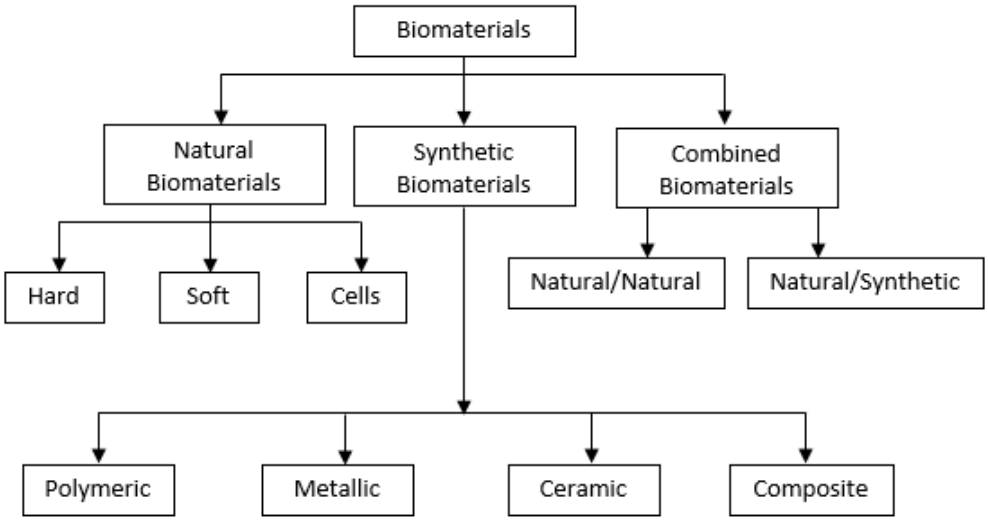

Figure 2.1: Classification of biomaterials (Ali et al., 2013)

2.2.1 Natural biomaterials

Human natural biomaterials are materials that contain similar architectures to the native tissue they are replacing with donor natural elements needed for proper tissue reconstruction. Natural biomaterials in the human biological system are classified into soft, hard and cells (Ali et al., 2013).

The main advantage of natural biomaterials over synthetic biomaterials is that they provide mechanical and shape compatibility compared to synthetic scaffolds. However, a major issue is immunological reaction as immune system in the body recognizes foreign material and tries to destroy it. Natural biomaterials require a high natural variability. Also, they are structurally more complex than traditional materials. Technological manipulation is more elaborate (Ige et al., 2012).

2.2.2 Synthetic biomaterials

There is a big demand for biomaterials to assist; replace organ or function for improving quality of life. Synthetic biomaterials are artificial engineered materials that utilized to replace function to a body tissue and continuously directly or indirectly in contact with body fluid conditions. One of the main reasons of development of synthetic biomaterials is to physically replace hard or soft tissues that have become damaged or destroyed through some pathological process (Davis, 2003). Synthetic engineered biomaterials can be classified into four main types: metallic biomaterials, ceramic biomaterials, polymeric biomaterials and composite biomaterials (Ali et al., 2013).

2.3 Development of implant biomaterials

The life expectancy has been expanded over last few decades and this has increased in the average age of the world's population. As the human body grow older, the load-bearing joints would be more susceptible to illness and weakness. This has, in turn, resulted in a globally increasing number of surgical procedures including prosthetic bone implantation per year. Hence, there is a critical demand for advanced biomaterials and developed processing technologies for implant fixation, more so for orthopedic and dental applications (Nag and Banerjee, 2012).

An implant material with modulus of elasticity that comparable to natural bone must be selected to ensure more uniform distribution of stress at implant and to minimize the relative movement at implant bone interface. High compressive strength and hardness are important factors as they decrease the wear, prevent fractures and improve functional stability of the implants (Saini et al., 2015). Biocompatibility is the

prime requisite in orthopedic implants and it depends on the corrosion characteristics and cytoxicity of corrosion products. Implant biomaterial should be corrosion resistant. Corrosion can result in roughening of the surface, weakening of the restoration, release of metal elements, toxic reactions. Surrounding tissues may affected and cause allergic reactions in patients (Saini et al., 2015).

Proper selection for the biomaterial play an important role in successful of long term implant fixation. Material selection and appropriate design are the key factors for the surgical implants' performance like mechanical properties, corrosion behaviors, bioactivity, and biocompatibility (Simon and Fabry, 1991). There are three categories of materials presently used in orthopedic bone implant: metals, polymers, and ceramics. These materials have been developed with the advancements in technology for various biomaterial applications.

2.3.1 Polymeric implants

The most popular polymer used in orthopedics is ultra-high molecular weight polyethylene (UHMWP) and high density polyethylene (HDPE) (Simon and Fabry, 1991). Polymers were chosen for their physical properties can be altered based on their use as their composition may be changed easily. They can be modified into more porous or softer form and also show fibrous connective tissue attachment. Nevertheless, they have some disadvantages that could not be ignored: poor inferior mechanical properties; lack of adhesion to tissues; and adverse immunologic reactions (Hodosh et al., 1969). These properties will affect the in vivo applications. Wear of polyethylene may be caused a contact of debris particles with the surface of bone and in turn, leaded to prosthetic loosening (Simon and Fabry, 1991).

2.3.2 Ceramic implants

The ceramics used in orthopedic implants include aluminum oxide and calcium phosphates. These materials can bear with high compressive stress, but weak under tension and shear, and it is highly brittle (Geesink et al., 1988). Apart from that, ceramics were used for surgical implant devices because of their inert behavior and physical properties such as minimum thermal and electrical conductivity.

Alumina has excellent corrosion and wear resistance and high strength. In fact, the coefficient of friction of the alumina-alumina surface is better than that of metal-polyethylene surfaces (Ratner et al., 2004). It also has excellent biocompatibility that enables fixation of implants. Despite these advantages, the primary drawback of using alumina ball-and-socket joints is the relatively high elastic modulus of alumina (>300 GPa), which is responsible for stress shielding effects (Nag and Banerjee, 2012).

2.3.3 Metallic implants

Since metallic biomaterials possess a good combination of high mechanical property and fracture toughness, they are widely being used in load-bearing bio-medical applications. Besides these properties metals are also easy to process and have good finish. Metallic implants can be sterilized by the common sterilization procedure which makes them easy to use (Saini et al., 2015). Stainless steel, cobalt-chromium alloys, titanium and its alloys have been utilized in orthopedic implants but their applications were confined due to their clinical limitations.

Stainless steel is not appropriate for a long term implant due to its low fatigue strength, poor corrosion resistance and liability to undergo plastic deformation

(Crowninshield, 1988). Although cobalt-based alloys like cobalt-chromium alloys have good corrosion resistance, ion release in-vivo is still of some concern. Also, chromium is known carcinogen while cobalt is suspected carcinogen which will cause cancer if the patient exposed to these metals for a long time period (Simon and Fabry, 1991). Titanium used in prosthetic implants involves pure commercial titanium and titanium alloys such as Ti-6Al-4V and Ti-6Al-7Nb because they are highly biocompatible. However, there are some concerns remains as effect of vanadium is known to be cytotoxic while aluminum ions may cause a long term health problems like osteomalacia and Alzheimer diseases (Rao et al., 1996; Walker et al., 1989). Hence, non-toxic implant materials which have excellent mechanical properties, favorable corrosion resistance and improved biocompatibility are desired.

2.4 Magnesium and its alloys for biomedical application

Biodegradable magnesium and its alloys have gained great attention as potential orthopedic bone implant materials due to their biocompatibility in the bio-environment. Magnesium materials have been proven to successfully achieve enhanced bone response, excellent interfacial strength and improved implant stability when orthopedic implanted (Castellani et al., 2011). Magnesium-based materials have also been used for various types of fixation devices for orthopedic and trauma surgery, for instance screws, fasteners and plates (Witte et al., 2005; Guangdao et al., 2007). Study of Zhang et al. (2010) has also shown that the implantation of a magnesium device shows minimal changes to blood composition within a 6 month post-implantation without bringing about harm to organs.

2.4.1 Alloying elements for magnesium biomaterials

There have been several types of alloying elements added to magnesium based materials to monitor their mechanical properties and corrosion behaviors. Alloying elements for example, Mn, Cu, Al and Zn have been explored and investigated for their feasibilities for implantation of biomaterials.

Manganese is primarily added to magnesium alloys to improve their corrosion resistance. In humans, excessive amounts of Mn have been shown to induce "Manganism" which is a neurological disorder similar to Parkinson's disease (Culotta et al., 2005). The addition of copper has been shown to increase the strength of magnesium casts, but also accelerate magnesium alloy corrosion rate in a NaCl electrolyte. Excessive copper amounts in the body have been linked to neurodegenerative diseases like Alzheimer's, Menkes, and Wilson disease (Strausak et al., 2001). Alloys containing aluminum generally possess a high quality combination of mechanical properties, corrosion resistance, and die-castability. In high doses, aluminum has been shown to cause neurotoxicity, with altered functions of the blood-brain-barrier (Banks and Kastin, 1989).

Zinc is commonly used as an alloying element for magnesium alloys, and the yield strength of magnesium alloys increase with its mass fraction in magnesium. Corrosion resistance and mechanical properties of pure magnesium can be improved with the addition of zinc through alloying process. Although a gap between the implant and surrounding bone tissue occurred during animal implant experiments due to a rapid degradation, the newly formed trabeculae and osteoblasts were still observed. Meanwhile, no disorders of the heart, kidney, liver and spleen existed because of the release of Zn ions (Zhang et al., 2010). Hence, it indicates that Zn element is safe to be

considered as an important potential biomedical materials. As an alloying element in a biomedical implant, the dissolution of Zn from the bulk material due to corrosion when placed in-vivo would be less detrimental than other elements like Mn, and Al. This is because Zn is readily absorbable by biological functions within the cell (Zhang et al., 2010).

Hydrogen evolution reveals that in alloys with less content of Zn result in strong H_2 gas evolution during degradation in simulated body fluids, whereas Zn-rich alloys form less hydrogen gas (Zberg et al., 2009). Zinc ions in solution around the bulk material are removed from solution. The zinc ions that are in solution further compete with the Mg^{2+} ions in solution for binding with free OH^- to form $Zn(OH)_2$, which ultimately decrease the amounts of H_2.

However, excessive amounts of Zn have the potential to be corrosive in nature if consumed. When Zn^{2+} ions react with hydrochloric acid (HCl), Zn-Cl products are formed which has been shown to damage parietal cells lining the stomach.

2.5 Important parameters of magnesium alloy

2.5.1 Mechanical properties

To meet the requirements of orthopedic implants, the maintenance of mechanical integrity is widely regarded as an important parameter. This requirement is met by magnesium quite well as shown in Table 2.1. Excellent mechanical strength and fracture toughness of magnesium alloy make them suitable for load-bearing application. Furthermore, the uncommonly lightweight of magnesium alloys is also the reason of being important biomaterials. The most compelling property is that mechanical

properties of the magnesium alloys, particularly elastic modulus (41-45 GPa) are close to that of the natural bone (3-20 GPa) in the human body and hence it decreases the stress shielding effect adequately (Staiger et al., 2006; Zeng et al., 2008). In contrast to the used of titanium or steel implants, magnesium get rid of the need of second surgery for removing implants (Staiger et al., 2006).

Table 2.1: Physical and mechanical properties of various implant biomaterials in comparison to natural bone (DeGarmo, 1979; Choi et al., 1998; Gibson and Ashby, 1999)

Properties	Natural bone	Magnesium	Ti alloy	Co-Cr alloy	Stainless steel	Synthetic hydroxyapatite
Density (g/cm^3)	1.8-2.1	1.74-2.0	4.4-4.5	8.3-9.2	7.9-8.1	3.1
Elastic modulus (GPa)	3-20	41-45	110-117	230	189-205	73-117
Compressive yield strength (MPa)	130-180	65-100	758-1117	450-1000	170-310	600
Fracture toughness ($MPam^{1/2}$)	3-6	15-40	55-115	N/A	50-200	0.7

2.5.2 Corrosion properties

Apart from the mechanical properties, corrosion properties are also required for a wide variety of the implant applications. Magnesium alloys degrade in aqueous solutions by several oxidation-reduction reactions which are affected by different types alloying elements. Generally, the degradation of magnesium in water will produce magnesium-hydroxide and hydrogen gas evolution. The following net reaction (Pollock, 2010) from half-cell reactions are given below:

$$Mg(s)+2H_2O(aq)\rightarrow Mg(OH)_2(s)+H_2(g) \quad \text{(Equation 2.1)}$$

The half-cell reactions are:

$Mg(s) \rightarrow Mg^{2+}(aq)+2e^-$ (Oxidation) (Equation 2.2)

$2H_2O(aq)+2e^- \rightarrow H_2(g)+2OH^-(aq)$ (Reduction) (Equation 2.3)

$Mg^{2+}(aq)+2OH^-(aq) \rightarrow Mg(OH)_2(s)$ (By-product formation) (Equation 2.4)

Magnesium has the ability to biodegrade, which means it is able to decompose and be absorbed into a human body. The main benefit of biodegradable implants is that reducing the number of surgeries. Biodegradable materials must fulfil many requirements, for example, they must not release toxic doses of metallic ions and both the products of the corrosion reactions and the original biomaterial must not cause any allergic reaction of the organism. Therefore, the appropriate corrosion rates should be reached. However, it must be noted that the implant must not decompose too early, for instance, a screw fixation of broken bones should function for at least 12–16 weeks (Zlitine et al., 2016).

The methods of corrosion properties improvement include through alloying process (Peng et al., 2010) and coating process (Gray-Munro et al., 2009). Both methods have shown encouraging results in improving the corrosion resistance.

2.5.3 Biological performance

Another crucial consideration of these degradable biomedical materials is concerning the biological performance of the metal alloys. Biological behaviour of cells after modifications include its biocompatibility and bioactivity. The effects on the cell tissues, for instances, forming bond surrounding bone tissue after implantation and the compatibility with living tissue are as essential as the corrosion issue.

Table 2.2 summarizes the cell viability of several cell lines cultured in magnesium alloy extracts. According to ISO 10993-5:2009, the reduction of cell viability by more than 30% is considered to have an undesired cytotoxic effect. Cytotoxic effect is the effect of being toxic to cells. Based on the Table 2.2, only as-casted pure Mg and Mg-3Ca alloy have a cytotoxic effect on L929 cells. Most of magnesium alloys are badly hemolytic (more than 5 % of hemolysis), that will damage the red blood cell in the body. However, it is found that hemolysis rate of Mg-6Zn, Mg-1Si and WE43 alloys is less than 5 % as shown in Figure 2.2.

Table 2.2: Cell viability of several cell lines cultured in magnesium and its alloys extracts (Li and Zheng, 2013; Gu et al., 2009; Li et al., 2008; Gu et al., 2010; Zhang et al., 2010; Zhang and Yang, 2008; Zhang et al., 2011)

Materials	Working history	Cell line	Culture time (d)	Cell viability (%)	Reference
Pure Mg	As-cast	L929	4	65.7	Gu et al., 2009
	As-cast	NIH3T3	7	90.6	
	As-cast	MC3T3-E1	7	87.5	
	As-cast	ECV304	7	76.8	
	As-cast	VSMC	7	93.6	
Mg–1Ca	As-cast	L929	4	81.8	Li et al., 2008
Mg–3Ca	As-cast	L929	4	~55	Gu et al., 2010
	RS15	L929	4	~90	
	RS30	L929	4	~100	
	RS45	L929	4	~105	
Mg–1Zn	As-cast	L929	4	111.8	Gu et al., 2009
	As-cast	NIH3T3	7	114.1	
	As-cast	MC3T3-E1	7	112.7	
	As-cast	ECV304	7	98.9	
	As-cast	VSMC	7	110.6	
Mg–6Zn	As-extruded	L929	4	~100	Zhang et al., 2010
Mg–1Zn–Mn	As-extruded	L929	3	100	(Zhang and Yang, 2008) Zhang and Yang, 2008
Mg–1Zn–1Ca	As-cast	L929	7	~75	Zhang et al., 2011
Mg–2Zn–1Ca	As-cast	L929	7	~70	Zhang et al., 2011

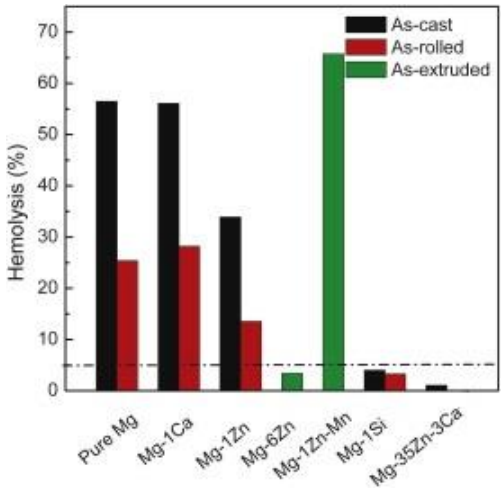

Figure 2.2: Hemolysis rate of several kinds of magnesium alloys (Gu et al., 2009; Li et al., 2008; Zhang et al., 2010; Zhang et al., 2011; Brar et al., 2012)

According to the study of Xu et al. (2007), bone attachment to magnesium implants in rats after 9 to 18 weeks of post-operation have shown good result because it is 100% implants were fixed and there was no inflammation interference. This indicate magnesium alloy has good biocompatibility in vivo (Xu et al., 2007).

Several possibilities exist to tailor the corrosion rate of magnesium by using alloying elements and protective coatings processes and meanwhile properties of magnesium had to be retained. Properties of non-toxic and biologically compatible is a minimum requirement.

2.6 Improvement of mechanical properties, corrosion properties and biological performance

2.6.1 Alloying

Magnesium alloys mostly have better mechanical properties than pure magnesium. Through alloying process, the improvement of the mechanical properties

particularly occurs by precipitation hardening or by strengthening of a solid solution. It is essential to note that an appropriate alloying composition can enhance the resistance to corrosion attack on magnesium alloys.

As mentioned before, zinc can be used as an alloying element which naturally occurs in body tissue. Various kinds of Mg–Zn based alloys were studied. The results of biochemical and histological investigations showed that the degradation of the Mg-Zn based alloy would not injure the organ of organism (Li and Zheng, 2013). The phase diagram of binary Mg-Zn alloy is shown schematically in Figure 2.3. Based on the diagram, the maximum solid solubility of Zn in Mg is approximately 6.2 wt% at 325˚C (Avedesian and Baker, 1999). In the study of Zhang et al. (2010) and Zhang et al. (2009a), a binary Mg-6Zn alloy was reported to exhibit suitable mechanical properties for implant application, a decreased of in-vitro degradation rate and also a good in-vivo biocompatibility.

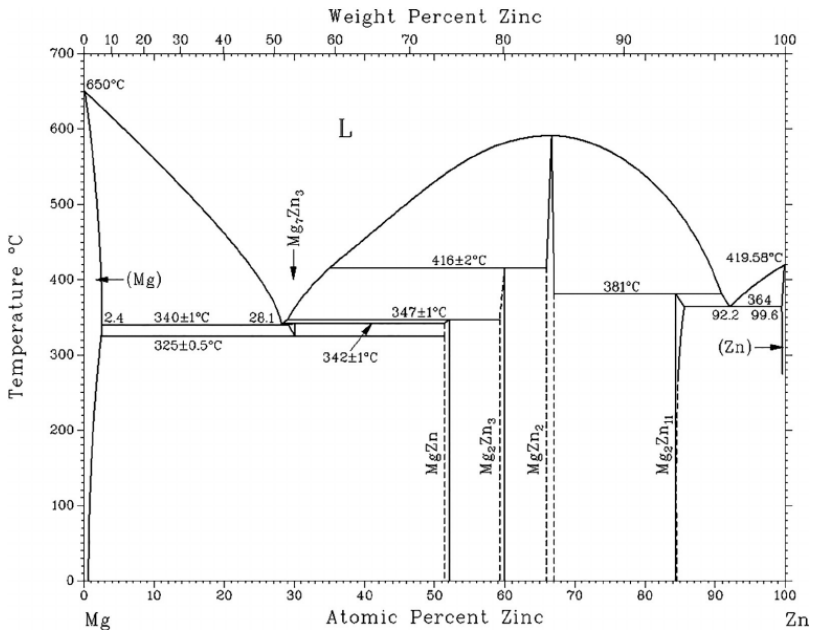

Figure 2.3: The Mg-Zn phase diagram (Ansara et al., 1998)

If zinc is used as in magnesium-zinc alloys, the corrosion reactions can be represented by the following equations:

$$Zn(s)+2H_2O(aq) \rightarrow Mg(OH)_2(s)+H_2(g) \quad \text{(Equation 2.5)}$$

$$Zn(s) \rightarrow Zn^{2+}(aq)+2e^- \text{ (Oxidation)} \quad \text{(Equation 2.6)}$$

Magnesium metal can also remove zinc ions from solution:

$$Mg(s)+Zn^{2+}(aq) \rightarrow Zn(s) + Mg^{2+}(aq) \quad \text{(Equation 2.7)}$$

As seen from these equations, magnesium reactions with aqueous solutions produce hydrogen gas. Hence, if the material is used in orthopedic applications, it will cause the formation of potentially harmful hydrogen pockets. Experimental result has shown that the addition of Zn has the ability to significantly decrease the amount of hydrogen gas evolved when measured by electrical corrosion testing (Witte et al., 2006).

Zhang et al. (2010) have done investigation on an extruded Mg–6Zn alloy as a biodegradable material. A uniform single phase is formed after solid solution treatment and hot working on Mg-6Zn alloy, thus it can prevent galvanic corrosion. The results of the research showed that Mg–6Zn alloy is believed to be suitable for implant applications. Mg-6Zn alloy had higher tensile and compression strength than Mg-Ca alloy. The in-vitro cytotoxicity of Mg–6Zn to L929 cells was found to be Grade 0–1 and the hemolysis rate is 3.4% (Zhang et al., 2009a; Zhang et al., 2010), indicating the Mg–6Zn alloy exhibits good biocompatibility in vitro. The Mg–6Zn alloy rods were implanted into the femoral shaft of rabbits and gradually absorbed in-vivo at degradation rate about 2.32 mpy with newly formed bone surrounding the implant (Zhang et al., 2010). The examination and the biochemical measurements proved that the degradation of Mg–Zn alloy did not cause any damage on the organs such as liver and kidney (Zhang et al., 2010; He et al., 2009).

However, there is research reported unstable results on magnesium bone implantation. (Zhang et al., 2010) found that there are large weight differences between original weight of Mg-6Zn alloy and its residual weight after 14 weeks of post-operation. The gap was also observed between the implant and bone tissue. The reasons are the degradation rate of Mg-Zn binary alloy is considered fast and the elevated ambient pH.

2.6.2 Surface treatments

In order to slow down the corrosion rate of magnesium alloys, as well as to maintain their mechanical integrity and to improve their biocompatibility, various surface modifications have been developed. Surface modification such as Al coating (Chiu et al., 2003; Chiu et al., 2005), Ti coating (Zhang et al., 2005) and heat treatment (Liu et al., 2007) have been applied to magnesium alloys and successfully improve the corrosion resistance. However, surface biocompatibility was not enhanced.

Among all types of surface coating, calcium phosphate coatings are the most widely studied coatings for biomedical magnesium alloys for orthopedic applications because of their excellent biocompatibility, nontoxicity, bioactivity, bone inductivity, and stability (Li and Zheng, 2013).

Xu et al. (2009) have also been demonstrated that calcium phosphate (Ca-P) coated on a magnesium alloy by phosphating process in order to enhance the surface bioactivity of Mg-based materials and provide a good cell adhesion and growth. Samples were treated in a phosphating bath for 6 min for Ca–P treatment after surface activation in order to obtain layer of Ca–P coating on the surface. There is a significant

increase ($p < 0.05$) in Ca–P coated Mg alloy in the cell number between day 1 and day 3 while there is no evident increase for pure magnesium, indicating that the Ca–P coated Mg alloy has a significantly better surface bioactivity than the Mg alloy. Also, compared with the Mg alloy, routine pathological examination analysis results reveal clearly that the Ca–P coated Mg alloy exhibits better surface biocompatibility than the alloy at the first 4 weeks post-operation. There is no inflammation occurred during week 1, thinner connective tissue and the formation of bone matrix at week 2, growing of bone matrix and interconnected bone trabecular at week 3, and more newborn bones at week 4 (Xu et al., 2009).

However, it has been reported that coating technique has its drawbacks. Some studies found that HA coating on magnesium alloys is loose flake-like morphology and poor crystallization, indicating that complications of coating process and the requisite of improving it (Song et al., 2008; Zhang et al., 2009b).

2.6.3 Metal matrix composites

In consideration of biocompatibility, reinforcements in magnesium metal matrix composites (MMCs) are usually hydroxyapatite (HA), fluorapatite (FA), calcium polyphosphate, calcium and many more. Generally, due to the physical properties of reinforcements in magnesium MMCs, which is usually hard and brittle, the MMCs exhibit improved compression strength but reduced tensile strength and elongation than the master alloys (Li and Zheng, 2013).

By adding the bioactive particles to produce metal matrix composite, the surface biocompatibility and bioactivity of the metal matrix can be improved (Ye et al., 2010).

One of the examples of bioactive particles is Ti/hydroxyapatite composite which can dissolve the Ca-O phase in SBF to promote apatite formation and growth on its surface (Ning and Zhou, 2002). Another study modified the Mg/HA composite by using cold spray deposition to form HAP-coated magnesium-based alloy as to improve the biodegradability and bioactivity of Mg alloy. Re-precipitation of apatite occurred because there are changes in pH as well as the influences of molar Ca/P and Mg/Ca ratios in SBF solution (Noorakma et al., 2013).

In the study of Witte et al. (2007), metal matrix composite which made of magnesium alloy AZ91D as matrix and HA particles as reinforcements was designed for investigating in vitro its mechanical, corrosive and cytocompatible properties. The results are encouraging, showing that magnesium alloy with 20 wt% HA composite is a cytocompatible biomaterial (Witte et al., 2007).

It is however reported that HA has a minimal degradability and its bioactivity still needs to be improved (So et al., 2006). Furthermore, it has been reported that the phagocytosis of damage debris from HA coating is likely responsible for the inflammation and disturbance in bone remodeling, leading to the local osteolytic process (Laquerriere et al., 2003). It is thus assumed that HA particles added to a magnesium alloy as reinforcing phase might only enhance the bioactivity to a limited extent.

2.7 Bioactive glasses

Bioactive glasses are used widely today as it fill defects and to promote and support the regeneration of bone tissue. Bioglass contains less silica and higher amounts of calcium and phosphorous if compared to soda-lime glass which is generally used in

windows or bottles. Mistry et al. (2012) have compared and evaluated the effect of bioactive glass, HA, and BG/HA composite bone graft particles in the treatment of infrabony defects. Bioglass and its composite was the better compared to HA for the reconstruction of infrabony defects. HA does not contain silicon, consequently an incubation period for the HA implant is necessary to accumulate biological hydroxyapatite on the implant, which would delay the deposition process of biological hydroxyapatite on the surface of the implant while soluble silicon in bioglass allows rapid bone formation (Schepers et al., 1991). This has suggested that bioglass has better bioactive behaviour than HA.

There are many papers have proved that bioactive glass which consists of a family of compositions shows the best bioactivity behavior among all the bioactive materials. For example, the results obtained from previous in vivo implantation studies demonstrated that certain compositions of bioactive glasses containing $CaO\text{-}SiO_2\text{-}P_2O_5$ have no local or systemic toxicity, no inflammation, and no foreign-body response (Sepulveda et al., 2002). The bioactive glasses with specific compositions show degradation gradually as well as bone bonding after implantation (Martin et al., 2001). Its bioactive behavior accompanied by the release of ionic products that stimulated the proliferation of bone-related cells (Xynos et al., 2000).

Bioactive glasses have excellent osteoconductivity and bioactivity (Wilson et al., 1981), ability to deliver cells (Gatti et al., 1994), and controllable biodegradability (Martin et al., 2001). These advantageous properties make the bioactive glass used as the secondary phase to be added to Mg-based composite.

Third generation biomaterials are having the combination of the properties of bioactive or resorbable, with the aim of the body heal itself after successfully implanted.