Fabrication, Properties and in Vitro Study Of Magnesium/Zinc/Bioglass Composite Fabricated by Powder Metallurgy Method

By

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TABLE OF CONTENTS

CHAPTER 3: METHODOLOGY

CHAPTER 4: RESULTS AND DISCUSSION

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

ACP	Amorphous Calcium Phosphate
A.D	Anno Domini
Al	Aluminium
ASTM	American Society for Testing and Materials
A-W	Apatite-Wollastonite
Ca	Calcium
Ca^{2+}	Calcium ion
$Ca_{10}(PO4)_6(OH)_2$	Hydroxyapatite
Cl^-	Chloride ion
CaO	Calcium oxide
$CaO\text{-}P_2O_5$	Calcium oxide phosphate
CaP	Calcium phosphate
CMS	Calcium Magnesium Silicate
CO_3^{2-}	Carbonate ion
Co-Cr	Cobalt-Chromium
Co-Cr-Mo	Cobalt-chromium-molybdenum
Cu	Copper
ECAP	Equal channel angular pressing
FA	Fluoroapatite
Fe	Ferum
H_2	Hydrogen gas
HAP	Hydroxyapatite

H_3O^+	Hydronium
HCl	Hydrochloric acid
HCO_3^-	Hydrogen carbonate ion
HPO_4^{2-}	Hydrogen phosphate ion
Mg	Magnesium
Mg^{2+}	Magnesium ion
$MgCl_2$	Magnesium Chloride
Mg-Gd-Y	Magnesium-Gadolinum-Yttrium
$Mg(OH)_2$	Magneisum hydroxide
MgO	Magnesium oxide
MWCNTs	Multi Wall Carbon Nano Tubes
Na_2O	Natrium oxide
O	Oxygen
OH^-	Hydroxide ion
P	Phosphorus
P_2O_5	Phosphate
PBS	Phosphate buffered saline
PMMA	Polymethyl methacrylate
PLA	Poly(lactide)
PGA	Poly(glycolide)
PLGA	Poly(lactide-co-glycolide
RNA	Ribonucleic acid
SBF	Simulated body fluid
Si	Silicon

SiC	Silicon carbide
SiO_2	Silica
Si-OH	Silicon oxide
Sr	Ceria
THR	Total hip replacement
Ti	Titanium
UCS	Ultimate compressive stress
Zn	Zinc
ZnO	Zinc oxide

LIST OF SYMBOLS

%	Percent
°C	Degree Celsius
μm	Micrometre
ρ	Density
Å	Angstrom
A	Exposed specimen area,cm^2
g	Gram
g/cm^3	Gram per centimetre cube
$mg/cm^2/h$	Milligram per centimetre square per hour
mM	Millimolar
mm	Millimetre
MPa	Mega Pascal
mm/year	Millimetre per year
rpm	Rotation per minute
wt. %	Weight percentage

Fabrikasi, sifat-sifat dan kajian in vitro magnesium/zink/biokaca komposit difabrikasi menggunakan kaedah metalurgi serbuk

ABSTRAK

Pembangunan biobahan logam menjadi aktiviti kajian yang utama sebagai implan dalam aplikasi ortopedik. Pada masa kini, titanium tulen secara komersial dan aloi, aloi berasaskan kobalt dan keluli tahan karat adalah bahan-bahan logam yang biasa digunakan sebagai implan dan mereka dikategori sebagai bahan biolengai. Salah satu topik utama penyelidikan terpenting dalam pembangunan biobahan adalah bagaimana untuk menggabungkan bioaktif, biodegradasi dan bahan-bahan biolengai. Kajian ini bertujuan untuk memfabrikasi bio-komposit yang mempunyai ketahanan kakisan yang tinggi, tindak balas bio-aktiviti yang tinggi dan kekuatan mampatan menghampiri tulang semulajadi untuk aplikasi bioperubatan. Tujuh komposisi komposit yang berbeza telah difabrikasi menggunakan serbuk Mg, Zn dan biokaca. Peratus berat biokaca di variasi dari 0, 5, 10, 15, 20, 25 dan 30. Bahan-bahan mentah diadun menggunakan mesin putaran selama 1 jam pada 140 rpm. Komposit-komposit ditekan menggunakan mesin tekan tangan hidraulik pada 500 MPa. Proses pensinteran dilakukan selama 3 jam pada 450°C dan 550°C menggunakan relau tiub di dalam persekitaran gas argon. Mikrostruktur komposit dicirikan menggunakan mikroskop optik dan mikroskop imbasan elektron. Fasa yang terbentuk di dalam komposit ditentukan menggunakan pembelauan sinar x-ray (XRD). Sifat-sifat fizikal seperti keliangan, ketumpatan sebenar dan ketumpatan pukal ditentukan menggunakan pycnometer. Sifat mekanikal ditentukan menggunakan ujian mampatan. Kelakuan perambatan retak selepas ujian mampatan dikenalpasti menggunakan mikroskop optik. Untuk ujian kakisan in vitro, semua sampel di rendam di dalam bendalir badan tersimulasi (SBF), fosfat berpenimbal salin (PBS) dan larutan Ringers selama 72 jam dan perubahan pH dipantau menggunakan meter pH. Produk kakisan diperiksa meggunakan XRD dan mikroskop optik. Kajian bioaktiviti in vitro dijalankan dengan merujuk kepada garis panduan Kokubo dan Takadama. Semua sampel direndam dalam SBS dan PBS selama 24 jam pada 36.5°C. Pembentukan lapisan apatit diperhatikan menggunakan SEM bersama EDS. Mikrostruktur komposit menunjukkan liang berhampiran sempadan butir dan biokaca bergugus dengan pertambahan kandungan biokaca. Ketumpatan sebenar komposit meningkat dengan peningkatan kandungan biokaca dan nilai keliangan paling tinggi ditunjukkan oleh komposit dengan 30% bt. biokaca. Sampel dengan penambahan biokaca 5% bt. disinter pada 550°C menunjukkan nilai kekuatan mampatan paling tinggi iaitu 117.43 MPa. Secara umumnya, perambatan retak boleh dilihat condong 45° daripada beban kenaan kecuali sampel dengan 30% bt. biokaca. Bagi ujian kakisan in vitro, sampel direndam dalam larutan Ringers menunjukkan kadar kakisan paling rendah diikuti sampel direndam dalam PBS dan SBF. Keputusan ini menunjukkan kehadiran fosfat yang tinggi di dalam PBS merencat kadar kakisan Mg/3Zn/BG komposit. XRD menunjukkan kehadiran $Mg(OH)_2$ sebagai produk kakisan utama untuk semua sampel di dalam semua larutan. Secara umumnya, kadar kakisan menurun dengan penambahan biokaca. Untuk ujian in vitro bio-aktiviti, pembentukan apatit sfera dengan nisbah Ca/P antara 0.83 hingga 2.12 diperhatikan. Semakin tinggi kandungan biokaca, semakin tinggi nisbah Ca/P. Tiada pembentukan apatit dilihat pada sampel direndam dalam larutan PBS. Secara keseluruhannya, sampel yang disinter pada suhu 550°C menunjukkan sifat yang lebih baik berbanding sampel yang disinter pada suhu 450°C dengan sampel

Mg/3Zn/5BG, Mg/3Zn/10BG dan Mg/3Zn/15BG masing-masing menunjukkan kekuatan mampatan, sifat kakisan dan sifat bio-aktiviti paling baik di antara semua sampel yang diuji.

Fabrication, properties and in vitro study of magnesium/zinc/bioglass composite fabricated by powder metallurgy method

ABSTRACT

The development of metallic biomaterials becomes a major research activity especially for load bearing implants in the orthopaedic applications. Currently, commercially pure titanium and its alloy, cobalt-based alloys and stainless steel are common metallic materials used as implants and they are grouped as bio-inert materials. One of the main important research topics in development of biomaterials is how to combine bioactive, biodegradable and bio-inert materials. The aim of this research is to fabricate high corrosion resistance of biocomposite, high bioactivity response and compressive strength close to the natural bone for biomedical application. Seven different compositions of composites were fabricated using Mg, Zn and bioglass powders. Bioglass weight percentage was varied from 0, 5, 10, 15, 20, 25 and 30wt. %. The raw materials were mixed for 1 hour using a roll mill machine at 140 rpm. The composites were compacted using a hydraulic hand press machine at 500 MPa. Sintering process was done for 3 hours at 450 ˚C and 550 ˚C using a tube furnace under argon gas environment. Microstructure of the composites was characterised using optical and scanning electron microscope (SEM). The phases developed in the sintered samples were determined using x-ray diffraction (XRD). Physical properties such porosity, true density and bulk density were measured by pycnometer. Mechanical property of the samples was determined by compression test. Crack propagation behaviour after compression test was identified using optical microscope. For in vitro corrosion test, all samples were immersed in simulated body fluid (SBF), phosphate buffered saline (PBS) and Ringers solution for 72 hours and pH changes was monitored using pH meter. The corrosion products were examined by XRD and optical microscope. In vitro bioactivity study was performed by referring to Kokubo & Takadama procedure guideline. All samples were immersed in SBF and PBS for 24 hours at 36.5 °C. The formation of apatite layer was observed by SEM with EDS. The microstructure of the composite showed that the pore segregated near the grain boundaries and bioglass clustering was observed with increasing content of bioglass. The true density of the composites increased with the increasing content of bioglass and the highest value of porosity was indicated by the composites with 30 wt. % of bioglass. Compressive strength value shows the increasing trend with the increasing sintering temperature. Sample with 5 wt. % bioglass addition sintered at 550 °C shows the highest compressive strength with 117.43 MPa. Generally, crack propagation can be seen slanted 45° from the applied load except for sample with 30 wt. % bioglass addition. For in vitro corrosion test, samples immersed in the Ringers solution shows the lowest corrosion rate followed by the samples immersed in PBS and SBF. The results indicated that the existence of high phosphate ions in PBS has retarded the corrosion rate of composite Mg/Zn/BG. XRD showed the presence of $Mg(OH)_2$ as the major corrosion product for samples immersed in all solutions. In general, the corrosion rate of samples decreased with the addition of bioglass. For in vitro bioactivity test, spherical apatite formation with Ca/P ratio ranging from 0.83 to 2.12 was observed precipitated on the sample surface. Higher bioglass content lead to higher Ca/P ratio. However, no apatite formation observed on sample immersed in PBS. Generally, sample sintered at 550°C shows better properties compare

CHAPTER 1

INTRODUCTION

1.1 Research Background

Today, biomaterials represent a significant portion of the healthcare industry with an estimated market size of over $ 9 billion per year in the United States. The industry expert predict that implantable device market will grow more than 8% per year in the United State to top $50 billion in 2015 (Carter et al., 2011). Over 500,000 artificial joint replacements, such as the knee or hip, are implanted yearly in the United States. Through the years the increasing numbers of injuries due to road accidents, sports, war and etc. lead to the increasing numbers of implant demand (Sargeant & Goswami, 2006; Paital & Dahotre, 2009). The life expectancy is increasing for every century. The average age is around 80 years at the end of 20^{th} century compare to 40 years in the early of 20^{th} century. The ageing of population risking to several health problem for example osteoporosis which is not so generic in the earlier century (Vallet-regí, 2010). Furthermore the worldwide population of people younger than 40 years of age receive hip implant is expected to be 80 million by 2030 which is likely to create a need for implant that last longer in vitro (Krishna et al., 2008). The increasing demand in the U.S market indicates that this biomedical industry is also increasing worldwide.

Biomaterial is considered as a relatively young field however its origins date back thousands of years. Archaeologists have discovered of humans containing metal dental implants from as early as 200 A.D., and it is known that linen was used as a suture material by the Egyptians. However, the development of the biomaterials field significantly increased after the World War II (Temenoff & Mikos, 2008).

There are three different generations of biomaterials which are bioinert materials (first generation), bioactive and biodegradable materials (second generation) and materials that can stimulate specific cellular response (third generation). Starting in the 1960s-1970s, the first generation of biomaterial was designed to be inert, or inactive with the body, thus decreasing the potential for negative immune response to the implant (Navarro et al., 2008). Several examples of bioinert materials are stainless steel, cobalt-chrome based alloys, titanium based alloys and zirconia. Stainless steel and cobalt-chrome based alloys were the first metallic materials successfully used during the twentieth century. Stainless steel was the first used in orthopaedic surgery in 1926. Besides used as implant materials, stainless steels were also used to manufacture surgical and dental instrument. However the usage of stainless steel can bring adverse effect to the patient due to release of nickel and cobalt ions (Paital & Dahotre, 2009; Chen & Thouas, 2015). Ceramic materials in the first generation biomaterials commonly consist of alumina, zirconia and several porous ceramics (Ratner et al., 2004).

The second generation of biomaterial appeared between 1980 and 2000. The second generation can be defined as the development of bioactive materials. Bioactivity can be defined as the property of the material to develop a direct, adherent, and strong bonding with the bone tissue. The most common ceramics that can be classified in this category are bioglass, glass ceramic and calcium phosphate (CaPs) (Park et al., 2006; Ionita et al., 2007).

The third generation biomaterials are meant to be new materials that are able to stimulate specific cellular responses at the molecular level. In this generation, bioactive and biodegradable properties are combined. Tissue engineering scaffold appeared approximately at the same time as the third generation biomaterials. Tissue engineering scaffold are three dimensional structures that assist in the tissue engineering process by providing a site for cell to attach, proliferate, differentiate and secrete an extra cellular matrix, eventually leading to tissue formation (Edwards et al., 2004).

Recently, magnesium can be classified as biodegradable materials because of its ability to degrade in human body. Magnesium and its alloys are popular materials used for implant research nowadays due to their excellent mechanical and physical properties, non-toxicity and also biodegradability in bioenvironment. Magnesium is actually needed by the human body for bone strength and growth in substantial amount (Xu et al., 2009; Xue et. al, 2012). Magnesium is the fourth abundant cation in the human body and it can stabilize DNA and RNA structure (Staiger et al., 2006).

None of the metallic materials used in orthopaedics is bioactive. In order to improve the bioactivity of the alloys, various attempts have been made such as anodisation, coating, ion implantation and chemical etching (Ye et al., 2009). Besides that, there is also the application of metal matrix composites to enhance the bioactivity properties. The adding of bioactive materials to metal matrix such as fluoroapatite, hydroxyapatite, bioglass and others are being made to make the implant bond well to the living bone (Razavi et al., 2010; Huan et al., 2011; Wan et al., 2016). Research using bioglass in metal matrix composites is still lower in number.

In 1972, Hench discovered that some glasses system which is bioglass can spontaneously bond to the living bones without having the fibrous tissue (Hench, 2006). Bioglass are fabricated usually with composition of 45% SiO_2, 24.5% CaO, 24.5%Na_2O and 6% P_2O_2. The essential requirement for a material to bond to living bones is formation of apatite layer on the implant surface after implanted to the living bone. This formation allowed bonding to the living bone. The ability to form apatite is reported to increase in the order hydroxyapatite < apatite-wollastonite < bioglass. The degree of ability to form apatite on the implant surface can predict the in vivo bioactivity of the materials as long as the materials does not contain any substance that can induce toxicity (Kokubo & Takadama, 2006). Most of the current work focused on bioglass alone on how to improve the bioactivity of bioglass by incorporating with ZnO and MgO (Balamurugan et al., 2007; Majhi et al., 2011; Saboori et al., 2009; Yu et al., 2015; Shankhwar & Srinivasan, 2016) and also to combine the bioinert materials such as Co-Cr-Mo and Ti alloys with bioactive materials (Oksiuta et al., 2009; Jurczyk et al., 2011; Martínez et al., 2013; Doni et al., 2015).

In this research powder metallurgy method is being used to fabricate Mg/3Zn/bioglass composite. Addition of bioglass as bioactive materials to magnesium will combine the biodegradable properties of magnesium and bioactive properties of bioglass, thus increasing the corrosion resistance of magnesium alloys. This combination is expecting to bring longevity to implant condition lifespan without the need for second surgery procedure.

1.2 Problem Statement

- Cobalt alloys, titanium alloys and stainless steel are the most common implant used nowadays. However the mechanical and physical properties are found to differ with natural human bone. These differences in properties led to stress shielding due to incompatibility of elasticity modulus (Chen & Thouas, 2015). Stress shielding occurs when the load which was originally carried by bones alone was shared by implants and bones. Bones will naturally reduce their mass under lower load or stress. This will lead to the formation of weaker bones (Ridzwan et al., 2007). Cobalt alloys, titanium alloys and stainless steel also usually need second surgery procedure due to the loosening affected by wears and also to remove the implant after the affected tissue healed. Furthermore the demand for more advanced materials to produce implant that can sustain longer in human body, lesser toxicity effect and also by any chance can eliminate the second surgery procedure led to further research on new materials for biomedical application (Staiger et al., 2006; Akca & Erarslan, 2012).
- An implant or artificial material implanted into human bones defects generally encapsulated by fibrous tissue, leading to their isolation from surrounding bones. This problem commonly occurs in nowadays used cobalt alloys, titanium alloys and stainless steel implant. One of the important research focuses is to combine the biodegradable and bioactive materials. There are several fabrication methods in combining biodegradable and bioactive materials and the two major methods are coating and casting. Coating method by thermal spray often occur flake off due to poor ceramic metal interface bonding while thin film methods are expensive (Khalid et al., 2016; Sola et al., 2011). Fabrication via powder