ABSTRAK

Dalam kajian ini, serbuk kalsium karbonat dan kalsium hydrogen fosfat telah ditindak balas melalui keadaan tindak balas keadaan pepejal menghasilkan trikalsium fosfat berliang $(Ca_3\ (PO_4)_2$. Kemudian spesimen berbentuk pelet telah dihasilkan melalui kaedah penekanan pada tekanan 45Mpa selama 15 saat. Spesimen yang telah ditekan menjalani proses pengeringan pada suhu 100^0C menggunakan ketuhar pengeringan. Spesimen yang telah dikeringkan kemudian dibakar pada lima suhu yang berbeza, iaitu 1075^0C, 1125^0C, 1175^0C, 1225^0C dan 1250^0C selama 2jam pada kadar pembakaran 10^0C/min bagi menentukan suhu pembakaran optimum untuk menghasilkan trikalsium fosfat berliang. Selain itu, kesan suhu sinter ke atas jumlah keliangan yang terhasil dalam trikalsium fosfat berliang juga telah ditentukan. Spesimen tersinter telah diuji dengan teknik-teknik pencirian seperti X-Ray Diffraction (XRD), ujian keliangan dan ujian mampatan. Analisis morfologi telah dilakukan dengan menggunakan Scanning Electron Microscopy (SEM). Fasa β-TCP menunjukkan prestasi terbaik apabila mempunyai jumlah keliangan sebanyak 40%. Oleh itu, β-TCP seramik dengan jumlah keliangan sebanyak 43% telah dihasilkan pada suhu 1125^0C. Ianya terbukti bahawa, parameter yang digunakan dalam kajian ini, fasa β-TCP yang telah terhasil kekal stabil sehingga suhu 1175^0C dengan jumlah keliangan sebanyak 40%.

ABSTRACT

In this study, calcium carbonate and calcium hydrogen phosphate powders were reacted via a solid state reaction to produce a porous tricalcium phosphate ($Ca_3(PO_4)_2$) sample. Then specimens with pellet shape had been produce through a pressing process at 45Mpa at 15seconds. The pellet shape specimen then underwent a drying process at 100°C using a drying oven. The sample were sintered at five different temperatures, which were 1075°C, 1125°C, 1175°C, 1225°C and 1250°C for 2 hours at heating rate of 10°C/min to determine the optimum sintering temperature to produce porous tricalcium phosphate. Besides that, the effect of sintering temperature on the amount of porosity in the porous tricalcium phosphate had been decided. The sintered specimens had been analyzed by characterization techniques such as X-Ray Diffraction (XRD), porosity test and compression test. The morphological analysis was done by using Scanning Electron Microscopy (SEM). β-phase of TCP give it best performance when it has 40% of porosity. Therefore, β-TCP ceramics with porosity of 43% were obtained at 1125°C. It is proven that under parameters adopted in this work, the β-TCP phase formed remains thermally stable up to 1175°C with an accompanying porosity up to 40%.

DEDICATION

To my beloved family members, especially my father and mother, Wan Yusuf Bin Wan Abd Rahman and Ros Lani binti Jusoh @ Ngah, who always stands behind me. Thank you for all you did. This work is dedicated to them.

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TABLE OF CONTENT

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ASTM	-	American Society for Testing Materials
TCP	-	TriCalcium Phosphate
CaP	-	Calcium Phosphate
HA	-	Hydroxyapitate
XRD	-	Xray Diffraction
SEM	-	Scanning Electron Microscopy
PRF	-	Platelets Rich Fibrins
UTM	-	Universal Tensile Machine

LIST OF SYMBOLS

wt.% - Weight Percentage

ß - Beta

α - Alpha

°C - Degree Celsius

kN - Kilo Newton

F - Force

°C/min - Degree Celsius per min

CHAPTER 1

INTRODUCTION

1.1 Background of Research

In recent times, several synthetic materials have been utilized as either bone graft substitute, internal fixation devices or dental fillers. Many materials have been used for these purposes including metals, polymers and ceramics. Examples of metals include tantalum, platinum, stainless steel, and titanium, whilst examples for polymers, include polyethene, acrylic resins, and silicon rubber, and for ceramics includes calcium phosphate, alumina, silicon dioxide and etc (Saska et. al., 2015).

Most of the implants in orthopaedics surgery are made of biocompatible homogenous materials such as metals. The materials used for orthopaedic implants are normally dense and have no pores. However use of the metals may cause bone fracture to occur during healing due to a stress protection phenomenon and patient need to do a second operation to remove the implant. This happens because of metals have high stiffness. Furthermore, metal sensitization may occur and lead to mutagenicity of the implants. This disadvantageous condition led to a searching for alternative materials. However, it can be overcomed if the implants were to be replaced with bone graft substitute which no longer need a second operation.

The success of bone graft substitute can be determined by various factors, for example design considerations such as interconnection, porosity and amount of pores which play significant roles in determining graft performance. Torres et al., (2000), also stated that the biological properties of the bone substitute materials are also influenced by their porosity, surface chemistry and surface geometry. Porosity is an important characteristic of a bone graft substitute materials. The pores act as vascularisation because they allow the migration of osteoblasts. Migration of osteoblast are necessary for bone tissue formation. Higher porosity is expected to enhance osteogenesis. This hypothesis has been verified by numerous studies and the results due to the larger surface area that resulted in higher ion exchange and bone-inducing factor adsorption. High amount and size of pores enhance bone ingrowth of the implant after surgery.

Torres et. al., (2000) stated that from 1980's until nowadays, interest in the studies of bone substitute has arisen. This is the result from the fact that about 10-20% of the patients that need treatments with dental implants, required bone regeneration procedures before implant placement. In daily clinical practice, there are many cases that bone volume is insufficient for patient to do an ideal dental implant placement. Bone regeneration can provide the structural support necessary in these cases to make sure the bone volumes is sufficient to do an implant.

Today, the use of dental implants is an important component and has become a significant clinical challenge in modern dentistry to provide support for replacement of missing teeth. In the past few years, the use of materials and techniques in dental implants has increased dramatically from a result of advances in research in implant design. This phenomenon is expected to expand further in the future. There are many types of implants that are available for applications to different clinical cases including calcium phosphate.

Calcium phosphate, CaP is one of the special form of ceramics which can be used in biomedical application. It belongs to the bioactive synthetic materials group and those frequently used are hyroxyapitate (HA) which is 'nonresorable' and the tricalcium phosphate (TCP) which is 'resorbability' (Madfa et. al., 2013). CaP has similar properties to the osteoconductive, bioactive properties and composition to the bone. It can exist in different form, such as cements, composites and coating. All of these forms are used in many dental and medical applications. CaP is useful for inducing hard tissue formation as it has biocompatible properties. Applications of CaP includes repair of augmentation of alveolar bone, periodontal defects, replacement of tooth and sinus lifts.

Calcium phosphate ceramic preparation has been widely researched throughout the world. A few unique methods have been created for preparation of this type of ceramic. These techniques include solid state reaction, wet chemical method, hydrothermal synthesis, sol-gel procedures, mechanochemical synthesis, electrochemical deposition, microwave irradiation and combustion synthesis (Anwar, 2016).

In 1920, tricalcium phosphate, TCP, was used as bone graft substitute for the first time. TCP is less crystalline and more soluble. Implants that contains TCP are biocompatible and osteoconductive. Osteocondutivity describes a graft that supports the attachment of new osteoblast cells onto a structure with an interconnected pore system that allows these cells and others, to migrate (Greenwald et. al., 2003). Madfa et. al., 2013 reported that the first dental application was used in 1972. Then, after years, synthetic porous material that was obtained by sintering a tricalcium phosphate reagent is used.

In this study, porous tricalcium phosphate will be produced direct from a solid state reaction of calcium carbonate ($CaCO_3$) and calcium hydrogen phosphate ($CaHPO_4$). Calcium carbonate is formed by three main elements that are calcium, carbon and oxygen. Calcium hydrogen phosphate is also known as dibasic calcium phosphate or calcium monohydrogen phosphate. Its chemical formula is $CaHPO_4$. This experiment will focus about the processing, porosity and compatibility of porous tricalcium phosphate in dentistry application.

1.2 Problem Statement

The use of metal or other type of materials in orthopedics surgery may cause bone fracture and lead to the need of a second surgery, but, with the use of tricalcium phosphate as a bone graft substitute, second surgery can be avoided. TCP is a resorbable phase calcium phosphate and shows some good properties such as osteoconductive. It is one of the bioactive materials that show osteoconductive properties that can independently stimulate bone regeneration.

However, tri-calcium phosphate is difficult to sinter (Madfa et al., 2013) and it is cannot be precipitated directly from the aqueous solution method. There are many techniques to synthesize porous TCP. These techniques include solid state reaction, sponge method, wet chemical method, hydrothermal synthesis, sol-gel procedures, mechanochemical synthesis, electrochemical deposition, microwave irradiation and combustion synthesis. Most of these techniques require high amount of cost. Thus, developing more feasible synthesizing methods for TCP is required. It involves very long and many stages when it comes to common technique, that is sponge method in producing porous tricalcium phosphate. This method takes time to finish all the process. However, by using direct solid state process in producing porous tricalcium phosphate, the steps and time taken can be reduced.

1.3 Objectives

I. To study a simpler and faster way to produce porous tri-calcium phosphate directly by using a solid state reaction process.

II. To investigate the effect of different sintering temperatures on the amount of porosity in the tricalcium phosphate produced.

III. To study the correlation between amount of pores and its strength.

1.4 Scope of Study

The main focus in this study is to produce porous tri-calcium phosphate using solid state reaction which is simpler, faster and cheaper compared to conventional method that need many steps and time consuming to finish the process. Raw materials such as calcium carbonate and calcium hydrogen phosphate will be used to fabricate tri-calcium phosphate.

In this experiment, samples with different sintering temperature and different soaking time will be prepared. The main purpose of using different sintering temperatures is to get different size of pores in the fabricated tri-calcium phosphate samples. Different size of pores of the porous tri-calcium phosphate will promote different applications. The data collected will be used to measure which parameters are the best in producing porous tri-calcium phosphate that is compatible with dentistry applications.

The mixing process of calcium carbonate and calcium hydrogen phosphate will be calculates to get the right composition to fabricate tri-calcium phosphate when the two materials were mixed together. The right molar ratio of calcium to phosphate must be 1.5.

The fabrication process of tricalcium phosphate involves the forming of green ceramic specimen. Green refers to the unfired ceramic body. The dry mixture of calcium carbonate and calcium hydrogen phosphate is homogenized in a ball mill at 32rpm of speed to get fine powder which will then be pressed into pellet with a hydraulic press under uniaxial pressure using 45MPa pressure for 15second. After the shaping process, the ceramic pellets will be direct before being sintered. Sintering process is a process of applying a heat-treatment to a compact powder in order to impart strength. The green ceramic pellets will be sintered at different temperatures of 1075°C, 1125°C, 1175°C, 1225°C and 1250°C for 2 hours at a heating rate of 10°C/min. It has been stated that the ß–TCP is stable below 1180ºC, α–TCP between 1180ºC and 1400ºC (Ryu et. al., 2002).

Finally, all of the samples will then be subjected to physical analysis and characterization analysis using Scanning Electron Microscopy (SEM) and X-Ray Diffraction (XRD). The microstructure analysis of the fractured surface of the produced ceramic will be conducted using a scanning electron microscope (SEM). X -ray diffraction (XRD) analysis will be used to analysis the phases present in the sintered samples. The samples will be tested for the amount and size of porosity, strength and density.

1.5 Project Significance

There are some potential benefits that can be gained by the community especially for medical and dentistry fields after the completion of this study. There is no need for second surgery with the use of tricalcium phosphate as a bone graft substitute. This experiment will be conducted to study a simpler and faster way to produce tricalcium phosphate by using a solid state process. This simpler, faster and cheaper processing is needed because there is considerable demand for bone augmentation and bone substitutes materials in the medical and dental fields. Besides, this works also aims to investigate the effect of changes in temperature and different soaking time on the size and amount of porosity in the compacted tricalcium phosphate.

1.6 Organization of Report

There are the five chapters in this report.

I. Chapter 1 is the introduction of the research. This chapter consists of the background of research, problem statement, objectives of the work, scope of study and conclusion of this chapter.

II. Chapter 2 is the literature review. This chapter represents the published literature that is relevant to a particular topic of this research, demonstrating the information of any previous work, facts and discussion.

III. Chapter 3 is the methodology employed in this work. This chapter will discuss about the raw materials, method carried out and testing that were used in this research in order to produce the desired product.

IV. Chapter 4 is the result and discussion. This chapter shows and discusses the results from all testing and characterization work gained from this experiment.

V. Chapter 5 is the conclusion and recommendation. This chapter is to conclude the experiment that has been conducted and suggest the recommendation that can improve this experiment in the future.

1.7 Conclusion

This chapter approaches the most current bone substitute materials used in implant dentistry, as in research as in clinical application, for alveolar ridge augmentation and guided bone regeneration. In addition, concepts of tissue engineering used for the development of the new materials and techniques for implant dentistry were approached. Many alternatives for the replacement of autografts, allografts and xenografts are emerging. Clinical studies are necessary to confirm the cost effectiveness of these approaches over traditional bone grafts methods with benefits of technological advancement exceeding risks to the patient and costs of implantation.

CHAPTER 2

LITERATURE REVIEW

2.1 Biomaterial

Biomaterials are known as any synthetic material that has biocompatible properties to the host tissue and to the body during implantation. In other words, biomaterial is a material of man-made or natural origin that was used to replace the functions of living tissues of the human body. It can be metals, polymers, ceramics and composites (Hussain *& Santos,* 2010). Biocompatibility can also be defined as the ability of a material to perform well to the host response in a specific application (Guelcher et. al., 2006).

Material's biocompability can be influence by numerous factors (refer Figure 2.1) and the importance of these factors is primarily influenced by the anatomical site, materials-tissue response, contact duration and functional properties. These factors requirements are also dependent upon the application (Bourg & Lisle, 2010).

For materials to be biocompatible, it must:

- Meet the functional demands of its application e.g. be capable of maintaining a load over a few months if it is used as a bone plate to immobilise a fracture.

Elicit an appropriate host response. The reaction tissue to the implant is called host response, which controls the performance of physiological by the patient after placement of the implant (Bourg & Lisle, 2010).

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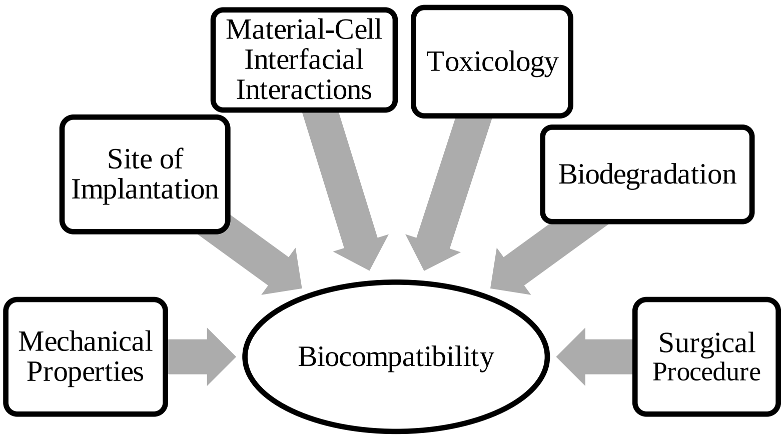

Figure 2.1: Diagram representing factors that influence the functional biocompatibility of an implantable device (Bourg & Lisle, 2010).

Over the last 50 years, biomaterial has been steadily developed. Nowadays, it has become so much important to the world including in medicine, chemistry, biology, and materials science. Today, the ability to remain in contact with tissues of the human body make biomaterial can stands out. Biomaterials have been used for several applications, such as artificial tissue, blood vessel prostheses, bone cement, bone plates, joint replacements, and tendons and tooth fixation for dental implant. Figure 2.2 shows further information about the applications of biomaterials.

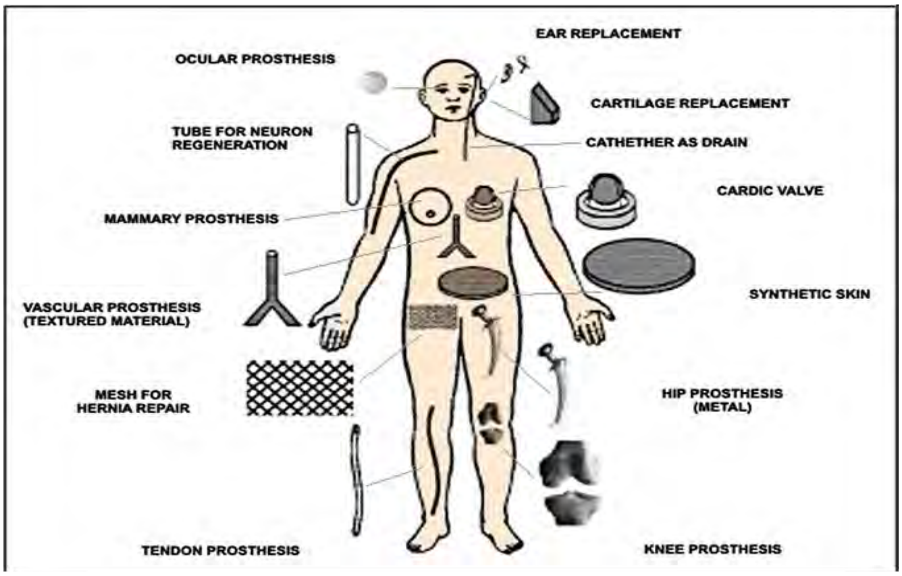

Figure 2.2: Examples of biomedical materials.

2.1.1 Biomaterial in orthopaedic

Bone, joint damage and inflammatory problems are international issues and affect many of people around the world. They accounted for half of every single endless disease in individuals more than 50 years old. Likewise, it is anticipated that the rate of persons more than 50 years old influenced by bone infections will rise twofold by 2020 (Navaro et. al., 2008). Subsequently, orthopedic biomaterials are suitable to be embedded in the human body as constituents of gadgets that are meant to complete a couple of natural capacities by supplanting or repairing tissues, for example, bone, ligament, tendons.

There are typically three materials that are used in orthopedics which are metals, polymer and ceramics. Metals are known as inorganic materials that have non-directional metallic bonds with exceedingly versatile electrons. Table 2.1 shows a list of metals and alloys that are commonly used in biomedical applications. Metals are solid and generally simple to form into complex shapes. This makes metals suitable materials for orthopedics substitutions, dental filling and for cardiovascular applications, for example, stents and pacemaker leads.

Table 2.1: Types of metal used in biomedical applications

Metal	Applications
Cobalt-chromium alloys	Dental prosthesis, artificial heart valves, orthopedic fixation plates and components of artificial joint.
Gold and platinum	Dental filling.
Silver-tin-copper alloys	Dental amalgams.
Stainless steel	Dental prostheses, orthopaedics fixation plates, vascular stents.
Titanium alloys	Artificial heart valves, dental implants, artificial joint components, orthopedic screws, peacemaker cases and vascular stents.

Polymers have long chains held together by covalent bonds. Polymers are helpful in orthopedic application because of their light weight, low flexibility and simple to shape. Despite the fact that characteristic polymers support bone cell connection and biomedical reaction in particular circumstances, there are concerns with respect to antigenicity and immunogenicity, potential sickness transmissions, sourcing, poor mechanical properties and the absence of controlled biodegradability. When contrasted with characteristic polymers, engineered polymers can be custom-made to control their properties, for example, mechanical quality and degradation rate (Zhou *et al*., 2012). They can be effortlessly handled into composite frameworks with attractive morphological elements helpful for tissue development. As of late, biodegradable polymers, particularly poly(lactic-co-glycolic acid), poly(lactic acid), and poly(glycolic acid) have been utilized essentially as part of the biomedical and pharmaceutical application.

Ceramics may contain crystal structure or amorphous glasses. Ceramics are hard and may oppose numerous environmental attract compared to metals. Calcium phosphate is one type of ceramic materials that are used in orthopaedics applications. The application of calcium phosphate materials as bone substitutes begin around the 1970s (Navarro *et. al*., 2008) and have been majorly utilized as bone defect fillers.

There is a scope of fitting Calcium Phosphate (amorphous CaP (ACP), β-TCP, α-TCP, OCP, HA, CDHA, TTCP and periodically FA) that can be used as CaP bonds (CPCs). These materials are injectable, solidify inside the harm bone tissue and produce low heat exchange that the unexpected passing of neighboring cells. It is also possible to form composite materials to improve surface properties of biomaterials. The composites are often created to optimize mechanical properties of biomaterials. Composites are materials consisting of two or more chemically different components and usually one of them is often a polymer because of their radio transparency and non-magnetic particle.

2.1.1.1 Bone structure

Bone is a composite of collagen, mineral, non-collagenous proteins, water and other organic. Bone is one of a set of vertebrate mineralised tissues which uses some version of calcium phosphate as their mineral (Kokubo, 2008). Later (Hussain & Santos, 2010) state that, in general, bone is composed of approximately 70% of minerals and 30% of proteins. Bone also enriched with few trace elements such as sodium, carbonate, citrate, magnesium, chloride, fluoride, iron and potassium for various metabolic functions. In 2014, Kobayashi *et al*., (2014) state that bone is an enormous and dynamic configuration of extracellular proteins and minerals that held an important role in calcium and phosphate homeostasis, blood, circular component formation and structural support against gravity. Toughness and rigidity of the bone is providing by the element of mineral, while tensile strength and flexibility providing by the element of collagen. Composition of the bone is found in Table 2.2;

Table 2.2: Bone tissue compositions

Inorganic phase (wt.%)	**Organic phase (wt.%)**
Hydroxyapitate ~ 60	Collagen ~ 20
Carbonate ~ 4	Water ~ 9
Citrate ~ 0.9	Non-collagenouse proteins ~ 3
Sodium ~ 0.7	(osteonectin, osteocalcin, thrombospondin,
Magnesium ~ 0.5	osteopontin, morphogenetic proteins, serum
Other traces:	proteins, sialoprotein,)
Cl^{-}, F^{-}, Sr^{2+}, K^{2+}, Pb^{2+}, Fe^{2+}, Zn^{2+}, Cu^{2+}	Others:
	Cytokines, lipids and Polysaccharides.
	Primary none cells:
	Osteoblasts, ostosclast, osteocytes.

Osteoblast, osteocytes and osteoclasts is a several different type of cell associated with the bone tissue with regard to their functions (Hussain & Santos, 2010):

- Osteoblast: Formation of new bone tissue is responsible by the osteoblast cell.

- Osteocytes: Known as matured cells that derived from the osteoblast and provides maintenance of the bone tissue. It also function as an agents in transporting minerals between bone and blood .

- Osteoclasts: It is known as the large cells found at the surface of the bone mineral next to the resorbing bone and responsible for the resorbtion of the bone tissue.

Bone is organized with a multi-level pores, macro to nano, for the establishment of multiple functions, including transportation of nutrient, oxygen and body fluids. At the macrostuctural level, the matured bone can be distinguished into two types, namely, spongy bone and compact bone. These two type of bone structure are radically different in density. There are about 20% of the total bone are occupied by the spongy bone and also called as cancellous bone. It has high number of pores, higher concentration of blood vessels and less dense compared to the compact bone. Sponge bone is a more permeable, lightweight kind of bone with an irregular arrangement of tissue which allows high strength. For biomedical applications, treatment that used cancellous bone for the bone defects is known as a bone graft.

On the other hand, compact bone is known as dense bone or cortical and it is much dense compared to spongy bone. Dense bone has less porosity and less concentration of blood vessels. This is because dense bone occupies about 80% of the total bone. The spongy bone functions mainly in compression while compact bone functions mechanically in tension, torsion, and compression.

2.1.2 Biomaterial in dentistry

The market for the development of Dentistry materials has been arise in recent years. Spending on Dentistry is rapidly increasing in the United States of America, resulting in the need for new biomaterials. In 2008, it was reported by American Dental Association (ADA) that concerned about the rising costs of dental treatment has been aware by 94% of the U.S. population. Recently, there is pressure both from government agencies and from patient, which require materials that cause less environmental impact and demand for more esthetics. Dental materials should be easy to use, not toxic and also should not be corrosive or irritating. The biomaterials used in Dentistry includes metals (silver amalgam, gold and titanium), ceramics (feldspar, zirconia and alumina) and composites.

2.1.2.1 Alveolar ridge preservation

Successful dental implant is to presence of sufficient volume of healthy bone at the recipient. Recipient site must have sufficient height and width of bone for the insertion of implant of appropriate length. After a tooth extraction, original width and height of bone is expected to be lost in an average of 40% to 60% (refer Figure 2.3). The greater loss of bone will occur within the first year after the extraction. Clinical studies have shown that