THE EFFECT OF GLASS-CERAMIC (GC) FILLED POLY(METHYL METHACRYLATE) BONE CEMENT COMPOSITES

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by

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DECLARATION

I hereby declare that the thesis entitles “The Effect of Glass-Ceramic (GC) Filled Poly (Methyl Methacrylate) Bone Cement Composites” submitted for the Master of Science degree at the Universiti Sains Malaysia is my original work, except where otherwise stated. It also has not been previously submitted by me at another University for any degree.

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LIST OF ABBREVIATIONS

AW-GC	: Apatite-wollastonite glass-ceramic
BPO	: Benzoyl peroxide
DMA	: Dynamical mechanical analysis
DMPT	: N, N-dimethyl-4-toluidine
DSC	: Differential scanning calorimetry
EDX	: Energy dispersive x-Ray
FTIR	: Fourier transform infrared
GCBC	: Glass-ceramic-filled bone cement
HA	: Hydroxyapatite
HABC	: Hydroxyapatite-filled bone cement
HCA	: Hydroxycarbonate apatite
HQ	: Hydroquinone
L/P	: Liquid to powder
MMA	: Methyl methacrylate
MMT	: Montmorillonite
MPS	: α-methacryloxypropyltrimethoxysilane
MWCNT	: Multi walled carbon nanotube
NIH	: National Institutes of Health
PC	: Polycarbonate
PE	: Polyethylene
PFF	: Poly (propylene fumarate)
PGA	: Poly (glycolic acid)
PLA	: Poly (lactic acid)
PMMA	: Poly(methyl methacrylate)
PP	: Polypropylene

PS	: Polystyrene
PVC	: Polyvinyl chloride
P/L	: Powder to liquid
SBF	: Simulated body fluid
SEM	: Scanning electron microscopy
SEN-B	: Single edge notch bending test
SG-P	: Silica glass powder
SI	: Standard International
SiC	: Silicon carbide
TCP	: Tricalcium phosphate
TF-XRD	: Thin film x-ray diffraction
XRD	: X-ray diffraction
XRF	: X-ray fluorescence

LIST OF SYMBOLS

%	Percent
μm	Micrometer
g	Gram
g/cm^3	Gram per centimeter cubic
GPa	Gigapascal
h	Hour
Hz	Hertz
inHg	Inches of mercury
kcal	Kilo calorie
kJ	Kilo joule
kmol/ml	Kilomole per milliliter
kV	Kilovolt
L	Litre
M	Molarity
mA	Milliampere
mg	Milligram
min	Minutes
ml	Milliliter
mm	Millimeter
mM	Millimolar
mm/min	Millimeter per minute
mm^2	Millimetre square
mol %	Mol percent
MPa	Megapascal
$MPa.m^{1/2}$	Megapascal meter square

N	Newton
nm	Nanometer
Nm	Newton meter
^{o}C	Degree celcius
$^{o}C/min$	Degree per minute
ppm	Parts per million
psi	Pound per square inch
T	Temperature
T	Time
t_{amb}	Ambient temperature
t_{d}	Dough time
T_{p}	Peak temperature
t_{set}	Setting time
wt%	Weight percent
θ	Theta

KESAN SERAMIK KACA (GC) TERISI KOMPOSIT POLIMETIL METAKRILAT (PMMA) SIMEN TULANG

ABSTRAK

Dalam kajian ini, komposisi seramik kaca telah dihasilkan berdasarkan kepada sistem kaca Na_2O-CaO-SiO_2 dan ia telah digunakan sebagai pengisi di dalam komersil simen tulang PMMA (PALACOS LV®). Dalam penghasilan serbuk seramik kaca, pertamanya serbuk kaca yang terhasil di analisa menggunakan DSC/TGA dan XRF, kemudian ia dipadatkan dan dirawat haba pada suhu antara 850 hingga 1000 ^oC. Keputusan XRD bagi seramik kaca yang dirawat haba pada suhu 950 ^oC telah menunjukkan sifat kristal wollastonite ($CaSiO_3$) dan sodium kalsium silikat ($Na_2Ca_3Si_6O_{16}$) yang tinggi. Ia juga menunjukkan kebioaktifan yang tinggi, yang mana ia menghasilkan lapisan apatit selepas direndam di dalam SBF selama 7 hari. Kemudian, seramik kaca yang dirawat haba pada suhu 950^oC digunakan sebagai pengisi di dalam simen tulang PMMA dengan 0, 4, 8, 12 dan 16 % berat pengisi dan keputusannya dibandingkan dengan komposit simen tulang terisi HA. Kesan pengisi terhadap sifat pengesetan, mekanikal dan terma telah dikaji. Didapati, suhu puncak dan masa doh simen tulang semasa pempolimeran menurun dengan meningkatnya peratus berat pengisi. Walaubagaimanapun, masa pengesetan tidak memberikan sebarang kesan dengan peningkatan peratus berat pengisi. Keputusan menunjukkan kekuatan lenturan dan keliatan patah menurun, manakala modulus lenturan meningkat dengan meningkatnya peratus berat pengisi. Selain itu, kestabilan terma, T_g dan modulus penyimpanan komposit simen meningkat dengan peningkatan bahan pengisi. Kajian morfologi ke atas bioaktiviti simen komposit menunjukkan pertumbuhan apatit di atas permukaan sampel GCBC4 dan GCBC8.

THE EFFECT OF GLASS-CERAMIC (GC) FILLED

POLY(METHYL METHACRYLATE) BONE CEMENT COMPOSITES

ABSTRACT

In this study, a composition of glass-ceramic was fabricated based on the Na_2O-CaO-SiO_2 glass system and was used as filler in commercial PMMA bone cement (PALACOS LV®). In producing the glass-ceramic powder, firstly the glass powders were analyzed using DSC/TGA and XRF, then it was compacted and heat treated at temperatures between 850 to 1000°C. XRD result of glass-ceramic heat treated at 950°C shows high crystallization of wollastonite ($CaSiO_3$) and sodium calcium silicate, ($Na_2Ca_3Si_6O_{16}$) in the glass composition. It also exhibits a high bioactivity which formed apatite after soaking in SBF for 7 days. Next, glass-ceramic heat treated at 950°C were used as a filler in the PMMA bone cement with filler loading of 0, 4, 8, 12, or 16 wt% and compared with HA composites. The effect of filler loadings on the setting, mechanical, and thermal properties were evaluated. It is found that the peak temperature and dough time during the polymerization of bone cement decreased with increasing filler loading. However, setting time did not show any significant trend. Result shows the flexural strength and fracture toughness decreased, and the flexural modulus increased as the filler loading increased. Besides, the thermal stability, T_g and storage modulus of cement composite increased with increasing filler loading. Morphological studies of the bioactivity of cement composite revealed the growth of apatite deposited on the GCBC4 and GCBC8 surface sample.

CHAPTER 1

INTRODUCTION

1.1 Background Study and Problem Statement

Self-curing polymethylmethacrylate (PMMA) bone cements have been in the market for more than 50 years since their introduction by Sir John Charnley in 1958 (Charnley, 1960). It was first used in dental applications followed by the use in orthopaedic surgery for the fixation of total joint replacement such as for hip and knee prosthesis. In orthopaedics surgery, PMMA bone cement functions to transfer body weight and service loads from the prosthesis to the bone. PMMA bone cement has also been used to increase the load carrying capacity of the prosthesis-bone cement-bone system (Lewis, 1997; Kuehn et al., 2005a). Commercial bone cements are prepared by mixing powder and liquid components with proportion of powder to liquid (P/L) equal to 2. The powder component consists of PMMA or PMMA-based copolymers, and a polymerization initiator, usually benzoyl peroxide (BPO). The liquid component consists of methyl methacrylate (MMA) monomer, accelerator (usually N-N-dimethyl-p-toluidine (DMPT)) and hydroquinone (HQ) as an inhibitor (Lewis, 1997; Hasenwinkel, 2004; Kuehn et al., 2005a). In the operation theatre, the powder and liquid parts are mixed for 2-3 minutes until a dough mixture is obtained and then applied to the desired bone cavity. Due to a rapid polymerization reaction, bone cement hardens in the ensuing 3-5 minutes (Serbetci et al., 2002).

The main adverse effect of bone cement application is a strongly exothermic reaction at the bone and cement interface during the setting period. Maximum

temperatures in the range of 80 ^{o}C to 124 ^{o}C have been reported and these values could damage living tissue (Pascual et al., 1996). In addition, bone-PMMA bone cement interface is known as one of the weak-link zones in the prosthesis-bone cement-bone construct because it does not bind or adhere to bone and has poor mechanical properties. The lack of ability to bind to bone sometimes results in the widening of the intervening fibrous tissue layer between bone and PMMA cement, causing aseptic loosening of the cement (Shinzato et al., 2000; Kamimura et al., 2002). On the other hand, PMMA has been demonstrated to be biocompatible and easy to shape *in vivo*, allowing its use as a bone substitute in reconstructive surgery of the knee and in vertebroplasty. However, high shrinkage during curing, and the release of monomer to the surrounding tissue and again, the ability to bond directly to bone, pose several potential risks that lead to prosthesis loosening with time due to tissue necrosis, interfacial failure, and cement failure (Goto et al., 2005).

Therefore, in an effort to improve their mechanical, thermal, handling and biocompatibility properties, investigations have been carried out on many different types of bone cements. Various approaches have been proposed and reported in the literature and one of them is bioactivation of PMMA bone cement by the incorporation of bioactive fillers in bone cement. The introduction of a bioactive phase in the PMMA matrix was suggested in order to enhance the quality of the bone-cement interface and to improve the setting and mechanical properties of the cement (Gilbert et al., 1995; Dalby et al., 2002). The *in vivo* studies of Kwon et al. (1997) found that there is new bone formation adjacent to the interface between the implant and surrounding bone as the amount of hydroxyapatite (HA) particles is increased. They also found that the

interfacial shear strength of the implanted specimens has a significant increase compared with the cement without HA.

Goto et al. (2008) reported that when using titania as filler in PMMA bone cement, lower peak temperature than for the unfilled cement were obtained. Besides HA and titania, Fujita et al. (1998) evaluated the bonding strength of the bioactive bone cements with higher percentage of apatite-wollastonite glass-ceramic powder. They found that bioactive bone cement had a higher bonding strength after surgery. The rationale for incorporating bioactive filler into PMMA cement had been also reported by Vallo (2000), and Dalby et al. (2002). From the literature, the cements showed good mechanical properties and excellent osteoconductivity by forming a biologically active bone-like apatite layer on their surfaces. However, trials using various fillers in bone cement produced unsatisfactory result due to deterioration of the mechanical properties after adding large weight percent (wt%) of the bioactive particles that caused difficulty in handling of the bone cement. The lack of bioactivity of the composite cement was also affected when the wt% of added bioactive particles is too small (Mousa et al., 2000).

In this study, a glass-ceramic composition ($55SiO_2$, 35CaO, $10Na_2O$ and $3P_2O_5$ (wt%)) was developed and characterized. Trials to incorporate this glass-ceramic particle as filler into commercial PMMA bone cement (PALACOS® LV) that possesses favorable physical, mechanical, thermal and bioactivity properties was carried out. Different weight percent (wt%) of the fillers were used and as compared, incorporation of commercially HA filler into PMMA bone cement also being investigated in this study.

1.2 Objectives

The objectives of project are listed as below:

1) To evaluate bioactivity of glass-ceramic filler in PMMA bone cement.
2) To study the effect of the incorporation different weight percent of glass-ceramic and HA fillers on the setting, mechanical, thermal and bioactivity properties of PMMA bone cement composites.

1.3 Outline of Thesis Structure

Chapter 1:

Introduction of PMMA bone cement and problem statement has been briefly explained in this chapter. The objectives of the study also have been stated.

Chapter 2:

This chapter reviews the literature on biomaterials and bioceramics field. In addition, literature on PMMA bone cement as polymer biomaterials and highlights on various studies and published works on incorporation of bioactive fillers into PMMA bone cement has been summarized in this chapter.

Chapter 3:

This chapter describes the detail of raw materials, chemicals and equipments that have been used to synthesize glass-ceramic and PMMA bone cement composites. Experimental and characterization methods have been explained in this chapter.

Chapter 4:

Chapter 4 consists of results from the experiments and presented in charts, tables and micrographs. The results obtained from the experiments have been evaluated and discussed thoroughly.

Chapter 5:

Several conclusions of the present study are discussed in this chapter and a few suggestions and recommendations are proposed for future studies.

CHAPTER 2

LITERATURE REVIEW

2.1 Biomaterials

2.1.1 Introduction

According to Black (1992) biomaterials can be defined as a material used in a medical device, intended to interact with biological systems. Over the years, various definitions of biomaterials have been proposed. For example, a biomaterial can be simply defined as a synthetic material used to replace part of a living system or to function in intimate contact with living tissue (Park & Bronzino, 2002). The other definition most commonly accepted is from the National Institutes of Health (NIH) which describes a biomaterial as:

"*any substance (other than a drug) or combination of substances, synthetic or natural in origin, which can be used for any period of time, as a whole or as part of a system which treats, augments, or replaces any tissues, organ, or functions of the body*" (Williams, 1987).

A material that can be used for medical application must possess a lot of specific characteristics, of which the first and foremost requirement is biocompatibility. Biocompatibility is the ability of a material to perform with an appropriate biological host response in a specific application (Williams, 1987). It means that, it should be non-toxic and non-carcinogenic, cause little or no foreign-body reaction, and be chemically stable and corrosion resistant. The biomaterial also should possess adequate physical and mechanical properties to serve as augmentation or replacement of body tissues. For

practical use, a biomaterial should be able to formed or machined into different shapes, relatively cheap, and be readily available.

Biomaterials have been widely used in application such as (Davis, 2003):

(1) orthopaedics – total joint replacements (hip, knee), bone cements, bone void fillers, fracture fixation plates, and artificial tendons and ligaments;

(2) cardiovascular applications - heart valves, pacemakers, artificial heart and ventricular assist device components, stents, and blood substitutes;

(3) ophtalmics – contact lenses, corneal implants and artificial corneas, and intraocular lenses;

(4) other applications- dental implants, cochlear implants, tissue screws and tacks, burn and wound dressings and artificial skin, tissue adhesives and scalants, drug-delivery systems, and sutures.

In general, biomaterials can be broadly categorized into the following categories: metals, ceramics, polymers, and composites. Table 2.1 illustrates some of the biomaterials types and their applications for these four groups of synthetic materials used for implantation.

Table 2.1: Classification of biomaterials types in medical devices and dental applications (Binyamin et al., 2006; Davis, 2003)

Classification	Biomaterial	Examples of applications
Metal	316L stainless steel	Surgical instruments, orthopedic fixation devices, stents
	Ti and Ti-containing alloys	Fracture fixation, pacemaker encapsulation, joint replacement
	Nickel-Titanium Alloy (Nitinol)	Stents, orthondotic wires, bone plates
	Platinum and platinum-containing alloys	Electrodes
Polymer	Polytetrafluoroethylene (Teflon, Gore-Tex)	Vascular grafts, catheters, introduces
	Poly(ethylene terephthalate) (polyester, Ethibond, Dacron)	Vascular graft, drug delivery, non-resorbable sutures
	PMMA	Bone cement, intraocular lenses, dental restorations
	Polyurethane	Cathethers, tubing, wound dressing, heart valves, artificial hearts
	Silicone rubber (polydimethylsiloxane)	Cathethers, feeding tubes, drainage tubes, introduces tips, flexible sheaths, gas exchange membranes
	Polycarbonate	Major component in renal dialysis cartridge, heart-lung machine,trocars, tubing interconnectors
	Hydrogels (poly(ethylene oxide)), poly(ethylene glycol), poly(vinyl alcohol), etc.)	Drug delivery, wound healing, hemostasis, adhesion prevention, contact lenses, extracellular matrices, reconstruction
	Polyamides (nylon)	Non-resorbable sutures
	Polypropylene (i.e., prolene)	Non-resorbable sutures, herni mesh
Ceramic and glasses	Alumina	Joint replacement, dental implants, orthopaedic prostheses
	Carbon	Heart valves, biocompatible coatings, electrodes, dental implants
	Hydroxyapatite	Implant coatings, bone filler
	Bioglass	Metal prosthesis coating, dental composites, bone cement fillers
	Porcelain	Dental restorations
Composites	BIS-GMA-quartz/silica filler	Dental restorations
	PMMA-glass filler	Dental restorations (dental cements)

2.1.2 Classification of Biomaterials: Based on Types of Biomaterials

2.1.2.1 Metallic Biomaterials

Metals are inorganic materials that have unique atomic arrangements and bonding characteristics leading to enhanced mechanical, thermal and electrical properties. Their excellent electrical and thermal conductivity, fair biocompatibility and mechanical properties like high stiffness, high ductility and good wear resistance make them very ideal for a variety of medical applications especially for load bearing properties (Binyamin et al., 2006). One of the advantages of using metals as biomaterials is their availability and relative ease of processing from raw ore to finished products. Although they have excellent mechanical properties, metallic materials can have serious corrosion problems in an *in vivo* environment. The consequences of corrosion are the disintegration of the implant material per se, which result in releasing toxic metal ions to the body and also weakening the implants. Thus, corrosion resistance is a primary criterion in selecting metals for biomedical implants (Desai et al., 2008; Donglu, 2006).

Metallic biomaterials have been used mainly for the fabrication of medical devices for the replacement of hard tissue such as total hip and knee prostheses and for fracture healing aids such as bone plates and screws, pins and spinal fixation devices. Besides orthopaedic, there are other markets for metallic implants and devices, including oral and maxillofacial surgery and dental implants (Niinomi, 2008). Some metals have also been used for repairing soft tissues as part of cardiovascular surgery as vascular stents, as pacemaker leads, and catheter guide wires. Besides that, surgical instruments, dental instruments, needles, staples, and implantable drug pump housings are also made from metallic materials (Davis, 2003).

Metallic biomaterials have the longest history among the various biomaterials. The main material groups that dominate biomedical metals are stainless steel, cobalt-based alloy, titanium alloys, and shape memory alloys such as nickel-titanium alloy known as nitinol (Pelton et al., 2000; Niinomi, 2002; Bartel et al., 2006; Frosch & Sturmer, 2006). Generally, these materials are popular primarily because of their ability to bear significant loads, withstand fatigue loading, and undergo plastic deformation prior to failure. They also exhibit good biocompatibility, which does not cause serious toxic reactions in the human body.

2.1.2.2 Polymer Biomaterials

Polymers are the most widely used materials in biomedical applications. They have addressed neurological, cardiovascular, ophthalmic, and reconstructive pathologies with implantable devices designed to sustain or enhance human life. They have also been found useful in temporary therapies such as hemodialysis and coronary angioplasty. In addition, polymers are also used extensively in dentistry as composite (resin-ceramic), implants, dental cements, and denture bases and teeth (Davis, 2003). The advantage of using polymers as biomaterials, is their manufacturability. Polymers are easy to fabricate into various sizes and shapes (rod, film, fiber, sheet, etc) compared to metals and ceramics. They are also light in weight and have a wide range of mechanical properties for different applications. The range of polymer biomaterials applications can be classed into types; synthetic and natural polymers (Donglu, 2006).

Synthetic polymers are the majority of the polymer biomaterials that have been widely used in making various medical devices, such as disposable supplies, implants,

drug delivery systems and tissue engineering scaffolds. Synthetic polymers, then can be divided into two types: synthetic non-biodegradable polymers and synthetic biodegradable polymers. Although most synthetic non-biodegradable polymers were originally developed for non-biomedical uses, they are widely used as biomaterials mainly because of the necessary physical-mechanical properties they have. There are still no newly engineered biomaterials that can replace those non-degradable polymers. A good example is PMMA bone cement which has been used for fixation of artificial joint since 1943 and is still being widely used clinically nowadays (Kuehn, 2005). Example of others non-biodegradable polymers include polyvinyl chloride (PVC), polyethylene (PE), polypropylene (PP), polystyrene (PS), polycarbonate (PC), polyesters, polyamides (nylon), polyurethanes, and polysiloxanes (silicone) (Donglu, 2006).

Synthetic biodegradable polymers have attracted much attention in the last decade because they offer the advantage of being able to be eliminated from the body after fulfilling its intended use. Therefore, the second surgery can be avoided. This polymer is becoming more and more important in biomaterials and for the regeneration of tissues and organs. Example of this kind polymers include polyamino acid, poly (propylene fumarate) (PFF) and aliphatic polyester, such as poly (glycolic acid) (PGA), and poly (lactic acid) (PLA) (Donglu, 2006).

Commonly encountered natural polymers are proteins, collagen, chitin and chitosan, hyaluronic acid, heparin and DNA. These materials are used as biomaterials largely because their structures are similar to the human tissue they intend to replace. These are important classes of biomaterials because of their biodegradation

characteristics and they are easily to find abundantly. However, the use of naturally occurring polymers often has some problem that provokes immune reaction of the host tissue. Therefore, many of them have to be chemically modified before being used as biomaterials.

2.1.2.3 Ceramic Biomaterials

Ceramics are non-metallic, refractory, polycrystalline compounds and usually inorganic material, which have some typical properties which are extremely hard, chemically stable, good wear resistance, and high durability that make them good materials as inert materials and useful for medical applications. But, ceramics are limited by their relative brittleness, high melting temperature and low electrical and thermal conductivity. Examples of ceramics include silicates, metallic oxides, carbides, sulfides, refractory hydrides, selenides and carbon structures such as diamond, graphite and pyrolized carbons. They are produced under a high temperature heat treatment process called firing**.** Ceramics used for the body are called bioceramics. Bioceramics used in fabricating implants typically can be classified as inert, bioactive and biodegradable or resorbable (Billotte, 2003; Binyamin et al., 2006; Navarro et al., 2008). The details of these bioceramics materials will be discussed in Section 2.2

2.1.2.4 Composite Biomaterials

Composite materials are combinations of two or more distinct constituent materials or phases on a macroscopic scale and in which mechanical properties are significantly altered in comparison with the homogenous constituents (Lakes, 1993). Composite materials offer some advantages which include control over material bulk

properties and improvements in surface properties. The bulk properties of composite materials depend upon the volume fraction and the shape of the heterogenities. The principal inclusion shape categorized as the particle, fiber, and lamina. Particles and fiber reinforcements have been used to improve properties of biomaterials. For example, rubber used in catheters, where rubber gloves are usually reinforced with very fine particles of silica to make the rubber stronger and tougher. In dental composite materials, glasses or ceramic particles are blended in a polymeric organic resin matrix with interfacing silane coupling agents. Composite such as graphite fibers in epoxy resin can be as strong as steel when loaded in the fiber direction but much lighter. However, this material is compliant when loaded transversely to the fibers (Bhat, 2005).

2.2 Bioceramics

2.2.1 Introduction

Park (2008) stated that bioceramics are ceramic materials that are used to make devices for the replacement, repair and reconstruction of diseased, damaged or "worn out" parts of living systems or to function in intimate contact with living tissues. In general, bioceramics show better biocompatibility with tissue response compared to polymer or metal biomaterials (Bilotte, 2003). Other than biocompatibility, ceramic materials have the following excellent properties: (a) non-toxic, (b) non-carcinogenic, (c) non-allergic, (d) non-imflammatory, and (e) biofunctional for its lifetime in the host. However, despite the excellent biocompatibility of bioceramics, the problems that occur in conventional ceramics also exist in bioceramics. The primary drawbacks of bioceramics are their brittleness, low strength, and inferior workability. Consequently,

bioceramics are very sensitive to notches or microcracks because they do not deform plastically (Bilotte, 2003).

2.2.2 Classification of Bioceramics

In general, bioceramics can be classified into three types based on their tissue response in the body. These are bioinert, bioactive, and bioresorbable (Thamaraiselvi & Rajeswari, 2004). The implant – tissue response are listed in Table 2.2.

Table 2.2: Consequences of implant-tissue interactions (Hench & Wilson, 1993)

Implant-tissue Reaction	Consequence	Example
Bioinert	Tissue forms a non-adherent fibrous capsule around the implant	Alumina, Zirconia and Carbon
Bioactive	Tissue forms an interfacial bond with the implant	Hydroxyapatite (HA), Bioactive glass Bioactive glass-ceramics
Bioresorbable	Tissue replace implant	β-tricalcium phosphate (β-TCP), carbonated hydroxyapatite, calcium carbonate

2.2.2.1 Bioinert Ceramics

Bioinert ceramics are biocompatible materials that maintain their mechanical and physical properties after implantation. This bioinert material undergoes little or no chemical reactivity, even after long term of exposure to the physiological condition and therefore, shows minimal interfacial bonds with the living tissues (Bhat, 2005). Examples of this type of materials include alumina (Al_2O_3), zirconia (ZrO_2), pyrolitic carbon, and silicon nitrides. Bioinert ceramics are very popular in orthopaedics and commonly used for structural support applications. They are also known to have

excellent wear properties and are therefore useful for gliding functions (Binyamin et al., 2006; Li & Hastings, 1998).

2.2.2.2 Bioresorbable Ceramics

Bioresorbable ceramics refer to materials that, upon placement within the human body, would start to dissolve and slowly be replaced by advancing tissues. In other words, resorbable implants are designed to degrade gradually with time and be replaced with natural tissues (Bilotte, 2003). It leads to tissue regeneration instead of replacement. The rate of degradation varies from one material to another. The advantage of this type of implant is that it will be replaced by normal functional bone, thus eliminating any long term biocompatibility problems. However, during the remodeling process, the load bearing capacity of the implant could possibly be weakened and resulted in mechanical failure. Therefore, the resorption rates of the material should be matched with the repair rates of body tissues (Hench & Wilson, 1993).

2.2.2.3 Bioactive Ceramics

Hench and Anderson (1993) define bioactive materials as a material that elicits a specific biological response at the interface of the material which results in the formation of a bond between the tissues and the material. When a bioactive material is implanted into the human body, it will interact to some extent with the surrounding bone or other tissue. An ion-exchange reaction between the bioactive implant and surrounding body fluids results in the formation of a bone-like apatite layer on the implant that is chemically and crystallographically equivalent to the mineral phase in the bone, which promotes the bonding between the natural tissues and the material (Liu et al., 2008).

Typical examples of conventional bioactive ceramics used in orthopaedic surgery are synthetic HA, Bioglass®, Ceravital®, and A-W Glass-ceramic (Hench, 1998; Ratner et al., 2007).

The ability for the formation of this apatite layer on the implanted substrate in the body environment is essential for the direct bonding to living bone. An estimate of the potential for apatite layer formation on a ceramic material is carried out by *in vitro* testing. Kokubo and his colleagues developed a simulated body fluid (SBF) similar with regard to inorganic ions to the human body plasma (Kokubo et al., 1990; Kokubo & Takadama, 2006). Materials that form apatite in SBF are expected to form apatite in the body and bond to living bone; therefore, SBF has been widely used to estimate the *in vivo* bone bioactivity of various types of bioactive materials (Kamitakahara et al., 2009).

2.2.3 Applications of Bioceramics

Bioceramics are produced in a variety of forms and phases, and serve many different functions in the repair of the human body, which are summarized in Table 2.2. Most applications of bioceramics relate to the repair of the skeletal system, composed of bones, joints, and teeth, and to augment both hard and soft tissues. These repairs become necessary when the existing part becomes diseased, damaged, or just simply worn out. There are many other applications of bioceramics including pyrolotic carbon coatings for heart valves and special radioactive glass formulations for the treatment of certain tumors (Carter & Norton, 2008). In other situations, bioceramics are used as reinforcing components in a composite, combining the characteristics of both components into a

new material with enhanced mechanical and biochemical properties. Figure 2.3 shows a number of clinical uses of bioceramics (Hench & Wilson, 1993; Ishikawa et al., 2003).

Ceramics are also widely used in denstistry as restorative materials, gold porcelain crowns, glass-filled ionomer cements, endodontic treatments, dentures, and so forth and the materials used in these applications are called dental ceramics. Ceramics and glasses have been used for a long time outside the body for a variety of applications in the health care industry. Eye glasses, diagnostic instruments, chemical ware, thermometers, tissue culture flasks, chromatography columns, lasers and fibre optics for endoscopy are commonplace products in the industry (Hench & Wilson, 1993).

Table 2.3: Form, phase and function of bioceramics (Hench & Wilson, 1993)

Form	Phase	Function
Powder	Polycrystalline Glass	Space filling, therapeutic treatment, regeneration of tissues
Coating	Polycrystalline Glass Glass-ceramic	Tissue bonding, thromboresistance, corrosion protection
Bulk	Single crystal Polycrystalline Glass Glass-ceramic Composite (multi-phase)	Replacement and augmentation of tissue, replace functioning parts

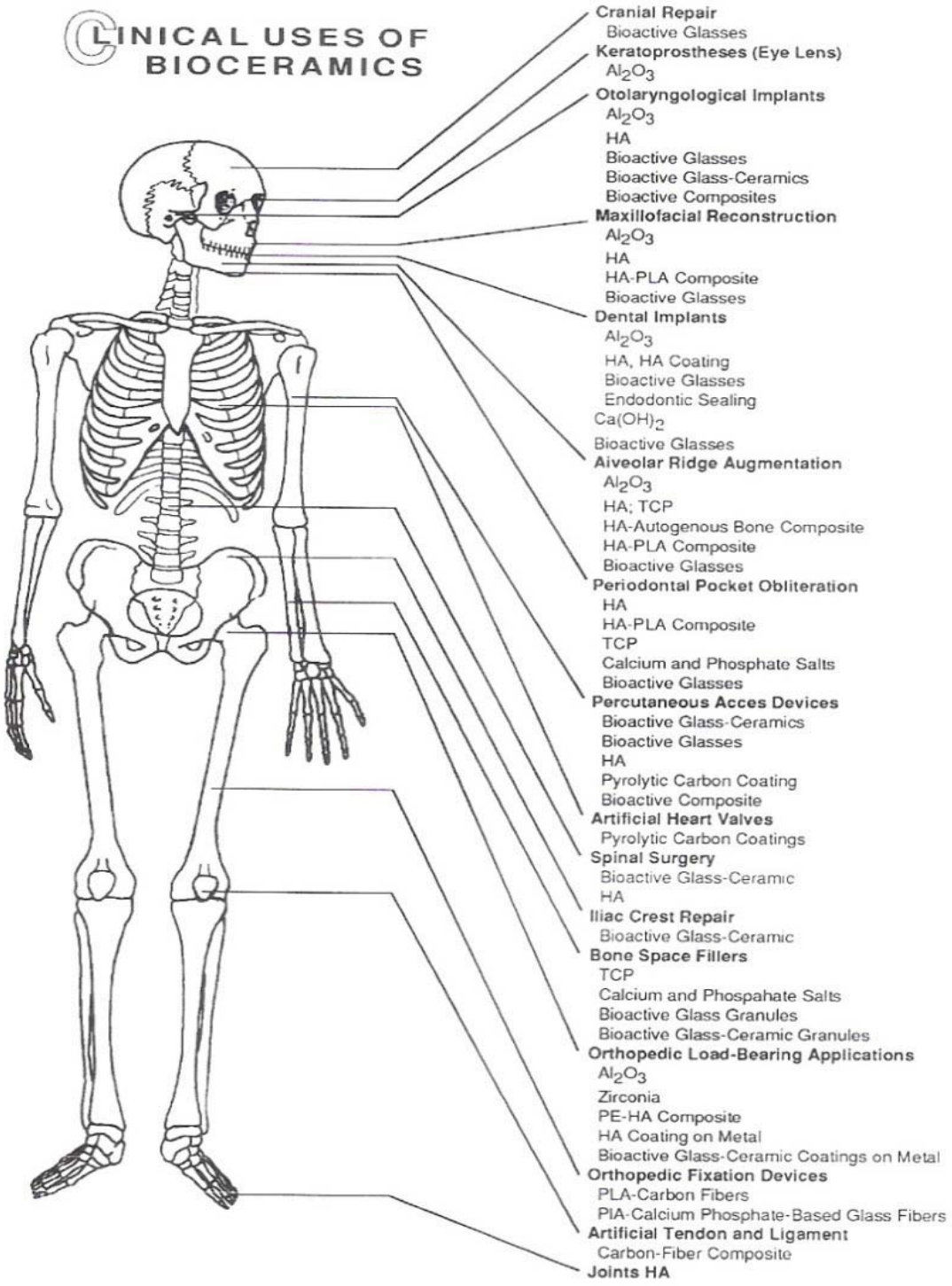

Figure 2.1: Clinical uses of bioceramics (Hench & Wilson, 1993)

2.3 Bioactive Glasses and Glass-ceramics

2.3.1 Bioactive Glasses

The first and most thoroughly studied bioactive glass is known as Bioglass® 455S (Hench, 1991). Bioglass® 45S5 is a multicomponent oxide glass where the main composition SiO_2, Na_2O, CaO and P_2O_5. The majority of bioactive glasses and glass-ceramics are based on these four components and all current bioactive glasses are silicates. There are three key compositional features to these bioactive glasses that distinguished them from traditional soda-lime-silica glasses: a) less than 60 wt% SiO_2, b) high Na_2O and CaO contents, and c) high CaO/P_2O_5 ratio. These compositional features make their surface highly reactive when exposed to an aqueous medium such as the body fluids (Davis, 2003). The 45S5 composition and several typical bioactive glasses are given in Table 2.4.

Table 2.4: Composition (wt%) and mechanical properties of bioactive glasses (Cao & Hench, 1996)

Component	**45S5 Bioglass®**	**45S5.4F Bioglass®**	**45B15S Bioglass®**	**52S4.6 Bioglass®**	**55S4.3 Bioglass®**
SiO_2	45	45	30	52	55
P_2O_5	6	6	6	6	6
CaO	24.5	14.7	24.5	21	19.5
Na_2O	24.5	24.5	24.5	21	19.5
CaF_2		9.8			
B_2O_3			15		
Structure	Glass and Glass-ceramic	Glass	Glass	Glass	Glass

This work is studied by Hench and co-workers and summarized in the ternary SiO_2-Na_2O-CaO diagram as shown in Figure 2.2. It illustrates the compositional dependence of bone bonding and soft tissue bonding for the SiO_2-Na_2O-CaO glasses.

Composition in the middle of the diagram (region A) forms a bond with bone and is defined as bioactive bone bonding boundary. When the concentration of SiO_2 in the glass network exceeds 55% the rates of reaction decrease, and bonding to bone is very slow. Silicate glasses within region B behave as almost bioinert materials and elicit formation of a fibrous capsule at the implant-tissue interface. Glasses within region C are resorbable and disappear within 10-30 days of implantation. Compound of glasses within region D are not technically interesting and therefore, have not been tested as implants (Cao & Hench, 1996).

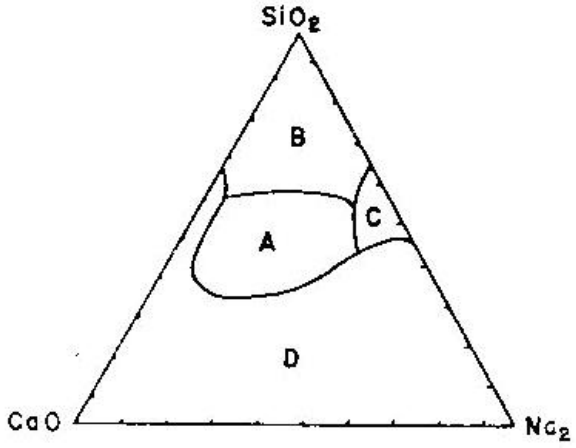

Figure 2.2: The SiO_2-CaO-Na_2O ternary phase diagram (Cao & Hench, 1996)

The main advantage of the bioactive glasses is the rapid surface reaction that brings about fast connections for tissue bonding and their primary disadvantages are mechanical weakness and low fracture toughness due to an amorphous two-dimensional glass network. The bending-tensile strength of most composition of bioactive glass vary between 40-60MPa, which make them unsuitable for load-bearing applications and find use as coatings on metals, in low-loaded or compressively loaded devices, in the form of powders or as the bioactive phase in composites (Hench & Wilson, 1993).

Bioactive glasses may be produced in various forms depending on the repair function they will serve. One of the most successful uses of bioactive glass is as replacement for the ossicles (tiny bones) in the middle ear and to repair the bone that supports the eye. Cone-shaped plugs of bioactive glasses also have been used in oral surgery to fill the defect in the jaw created when a tooth is removed. In powder form, bioactive glasses are used in the treatment of periodontal disease and for the treatment of patients with paralysis of one of the vocal cords (Carter & Norton, 2007).

2.3.2 Bioactive Glass-ceramics

2.3.2.1 Glass-ceramic Processing

James, (1995) defined that glass-ceramics are materials obtained by controlled crystallization of certain glasses. Bioactive glass-ceramics have been developed to improve the mechanical performance of bioactive materials, or to introduce other interesting properties such as the machinable glass-ceramic Bioverit®. The formation of glass-ceramics is influenced by two important factors which are nucleation and growth of small crystal (< 1μm in diameter) and uniform size distribution. It is estimated that about 10^{12} to 10^{15} nuclei per cubic centimeter are required to achieve such small crystals. In addition to the metallic agents already mentioned, Pt groups, TiO_2, ZrO_2 and P_2O_5 are widely used as nucleating agents. The nucleation of glass is carried out at temperatures much lower than the melting or glass transition temperature, at which the melt viscosity is in the range of 10^{11} to 10^{12} Poise for at least 1 to 2 h. To obtain a more microcrystalline phase, the glass is further heated to an appropriate temperature for maximum crystal growth. In this process, deformation of the products, phase transformation within the crystalline phases, or re-dissolution of some of the phases

should be avoided. The crystallization is usually more than 90% complete when grain sizes are 0.1 to 1 μm, which are much smaller than in conventional ceramics. Figure 2.3 is a schematic representation of the temperature –time cycle for a glass-ceramic.

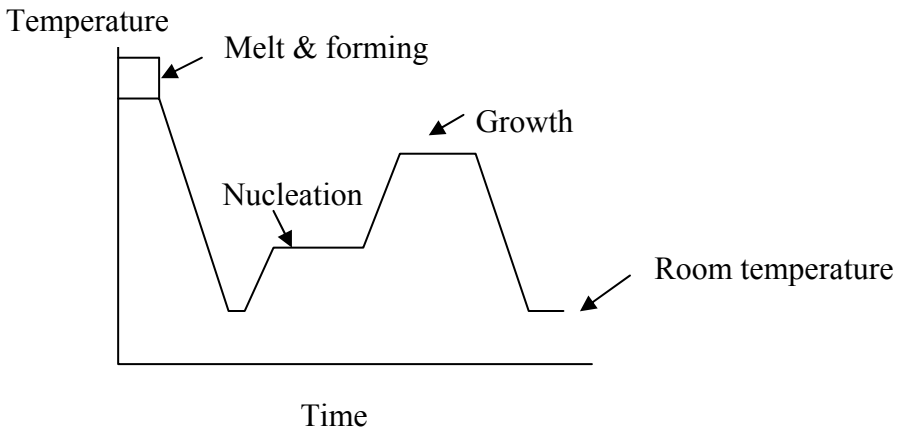

Figure 2.3: Temperature-time cycle for a glass-ceramic

2.3.2.2 Properties of Glass-ceramics

Glass-ceramics have several desirable properties compared with glasses and ceramics. The thermal coefficient of expansion is very low. Due to the controlled grain size and improved resistance to surface damage, glass-ceramics can have at least double the tensile strength (from 100 to 200 MPa). The resistance to scratching and abrasion of glass-ceramics is similar to that of sapphire. The modulus of elasticity is of the order of 100 GPa, and the compressive strength is about five times the tensile strength, as given in Table 2.5.

Table 2.5: Mechanical properties of glass-ceramics (Park, 2008)

Properties	Bioglass®	Ceravital®	A-W Glass-ceramic®
Young's modulus (GPa)	35	100-159	118
Tensile strength (MPa)	200	400	-
Compressive strength (MPa)	42	500	1080
Bending strength (MPa)	160-190	130	215
Hardness (Vickers)	458	294	680
Fracture toughness ($MPa.m^{1/2}$)	2.0	4.6	3.34

A negative characteristic of the glass-ceramic is its brittleness. In addition, limitations on the compositions used for producing a biocompatible glass-ceramics hinder the production of glass-ceramic which has substantially higher mechanical strength. Thus, glass-ceramics cannot be used for making major load-bearing implants such as joint implants. However, they can be used as fillers for bone cement, dental restorative composites, and coating material (Billotte, 2003).

2.3.2.3 Commercial Bioactive Glass-ceramics

Several kinds of glass-ceramics compositions are bioactive and their behaviour in the body is very similar to that of bioactive glass which has an ability to form a strong interfacial bond with hard and soft tissues. There are three examples of well-known bioactive glass-ceramics that have been developed for implantation: machinable glass-ceramic (Bioverit® I), Ceravital® and A-W Glass-ceramic® (Carter & Norton, 2007). Table 2.6 shows compositions of some bioactive glass-ceramics.

Table 2.6: Compositions of some bioactive glass-ceramics (Cao & Hench, 1996; Park, 2008)

Type	**SiO_2**	**CaO**	**Na_2O**	**P_2O_5**	**MgO**	**K_2O**
A-W Glass-Ceramic®	34.2	44.9	-	16.3	4.6	
Ceravital®	40-50	30-35	5-10	10-15	2.5-5	0.5-3
Bioverit® I	29.5-50	13-28	-	8-18	6-28	-

All type of bioactive glass-ceramic composition in weight percent (wt%). In addition, Al_2O_3 (0-19.5), Na_2O/K_2O (5.5-9.5), F (2.5-7), Cl (0.01-0.6) and TiO_2 (additions) are present in Bioverit® I. A-W Glass-ceramic® has CaF_2 (0.5%).

A-W Glass-ceramic® is produced by crystallization of a glass of composition as can be seen in Table 2.6. The crystalline phases are oxyfluroapatite [$Ca_{10}(PO_4)6(OH_1F_2)$] and β-wollastonite ($CaO\text{-}SiO_2$) and also content a residual glassy matrix. A-W Glass-ceramic® has excellent mechanical properties and forms a bond with bone that has very high interfacial bond strength. This type of glass has been used successfully in hundreds of patients for replacing part of the pelvic bone and in vertebral surgery (Hench & Kokubo, 1998). Ceravital® has been successfully used clinically in middle ear surgery to replace damaged bone. In this application the mechanical properties of the material are sufficient to support the minimal applied loads. To control the dissolution rate, Al_2O_3, F, and Cl are added in Ceravital® glass-ceramic. Bioverit® I is a mica-apatite glass-ceramic and known as machinable bioactive glass-ceramic. The key to the development of Bioverit® I was to form a phase separated base glass consisting of three glassy phases and to control the nucleation and crystallization by heat treating the glass.

2.3.2.4 Mechanism of Bioactive Bonding

Bonding of bone to bioactive glasses and glass-ceramics involves 11 reaction stages summarized in Figure 2.4. The first five reaction stages that occur on the surface of bioactive glass and glass-ceramic do not depend on the presence of tissues. They occur in distilled water, tris-buffer solutions or SBF, and have been well studied using Fourier transform infrared (FTIR) spectroscopy, Auger electron spectroscopy, and electron microprobe analysis. These reactions result in a hydroxycarbonate apatite (HCA) crystal layer forming on the implant surface. Stages 6-11 are necessary for the implant to bond to tissues.

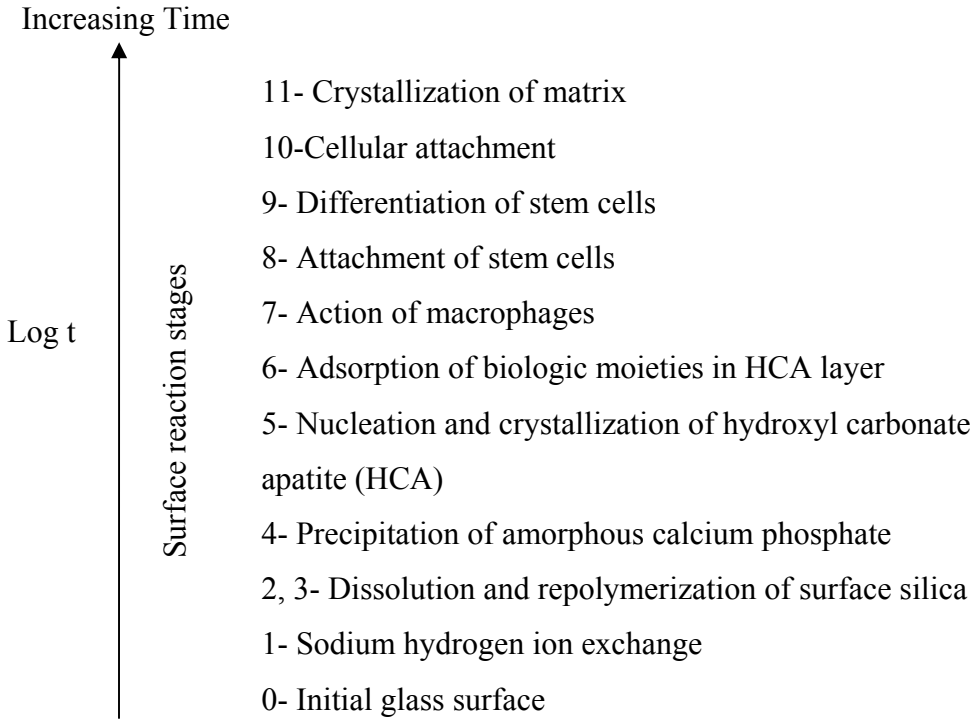

Figure 2.4: Sequence of interfacial reactions involved in forming a bond between bone and bioactive glasses (Cao & Hench, 1996)