SYNTHESIS AND CHARACTERIZATION OF HYDROXYAPATITE (HA) AND SILICON SUBSTITUTED HYDROXYAPATITE (Si-HA) PRODUCED BY A PRECIPITATION METHOD

by

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LIST OF ABBREVIATION

HA	:	Hydroxyapatite
Si-HA	:	Silicon-substituted hydroxyapatite
BET	:	Brunauer, Emmet and Teller
H_3PO_4	:	Phosphoric acid
$Si(OCOCH_3)_4$	:	Silicon tetra acetate
CaO	:	Calcium oxide
CaP	:	Calcium Phosphate
ICDD	:	International Centre for Diffraction Data
PO_4	:	Phosphate
SEM	:	Scanning Electron Microscope
TEM	:	Transmission Electron Microscopy
XRD	:	X-Ray Diffraction
β-TCP	:	Beta Tri-Calcium Phosphate
α-TCP	:	Alpha Tri-calcium Phosphate
$Ca(OH)_2$	:	Calcium hydroxyde
TEOs	:	Tetraethyl orthosilicate [$Si(OCH_2CH_3)_4$]
β-TCP	:	Beta Tri-Calcium Phosphate
α-TCP	:	Alpha Tri-calcium Phosphate
OH	:	Hydroxide
P	:	Phosphorus
SSA	:	Specific Surface Area
DTS	:	Diametral Tensile Strength

LIST OF PUBLICATIONS

1. Le Thi Bang, Radzali Othman, Kunio Ishikawa. (2008) *Effect of concentration on morphology of hydroxyapatite produced by precipitation method*. Proceeding of the "17th Electron Microscopy Society Malaysia (EMSM) Scientific Conference". Holiday Inn Glenmarie, Luala Lumpur, Malaysia, 18-20 December.

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SINTESIS DAN PENCIRIAN HIDROKSIAPATIT (HA)

DAN HIDROKSIAPATIT DITUKARGANTI SILIKON (Si-HA)

YANG DIHASILKAN MENERUSI KAEDAH MENDAK

ABSTRAK

Pemendakan adalah suatu kaedah yang berjaya untuk menghasilkan hidroksiapatit (HA) dan hidroksiapatit ditukarganti silikon (Si-HA) berketulenan tinggi pada suhu rendah. Dalam kajian ini, kalsium hidroksida [$(Ca(OH)_2$] dan asid fosforik (H_3PO_4) telah dipilih sebagai bahan mula untuk menghasilkan HA. Sewaktu sintesis, tindakbalas telah dilakukan secara pengadukan laju pada beberapa parameter berlainan. Serbuk HA yang terhasil telah dikalsin pada suhu 700, 850, 1000, dan 1200^oC selama 1 jam. Keputusan menunjukkan HA berketulenan tinggi dan stabil sehingga 1200^oC telah berjaya dihasilkan bila tempoh penuaan dipanjangkan ke 24 jam. Bahan mula yang berlainan kepekatan, yakni 0.5, 1.0, 1.5 dan 2.0 M telah juga dikaji. Keputusan menunjukkan bahawa zarah HA bersaiz nano berjaya diperolehi pada semua kepekatan manakala HA stoikiometri tulen dengan kestabilan terma sehingga 1200 ^oC diperolehi pada kepekatan 0.5 dan 1.0 M.

Berasaskan keadaan optimum yang diperolehi dalam sintesis HA, kaedah mendak turut digunakan untuk menghasilkan HA yang ditukarganti silikon pada paras 0.4, 0.8 dan 1.6 % berat silikon menggunakan silikon asetat [$Si(OCOCH_3)_4$] sebagai sumber Si. Serbuk/pelet HA dan Si-HA yang dihasilkan telah dikalsin pada suhu kalsin berlainan, iaitu 1150, 1200 dan 1250^oC. Keputusan menunjukkan bahawa Si-HA tulen telah berjaya dihasilkan pada ketiga-tiga paras silikon. Si-HA tulen pada paras 0.4 dan 1.6 % berat Si telah diperolehi pada semua suhu kalsin manakala Si-

HA pada paras 0.8 % berat Si telah mengurai kepada α-TCP pada suhu 1250^{o}C. Kesan silikon ke atas HA adalah dengan mengaruh peningkatan kecil parameter kekisi struktur apatit secara anjakan kecil corak XRD sampel Si-HA. Selain itu, silikon di dalam hidroksiapatit mengekang penumpatan pada suhu rendah (1150^{o}C) dan kesan ini menjadi semakin ketara bila paras penukargantian silikon meningkat. Ketumpatan hampir sempurna (> 90 %) telah diperolehi bagi HA tulen pada 1200^{o}C manakala sampel Si-HA mencecah ketumpatan ini pada 1250^{o}C. Pemerhatian SEM jelas menunjukkan penukargantian silikon juga merencat pertumbuhan butir pada suhu-suhu tinggi (1200 dan 1250^{o}C). Perencatan tumbesaran butir meningkat bila kandungan silikon meningkat. Pada ketumpatan hampir sempurna, nilai kekerasan sampel Si-HA mencecah nilai setanding dengan sampel HA. Walau bagaimanapun, kekuatan lebih tinggi diperolehi bagi sampel Si-HA dan ini mencapai nilai tertinggi 15.93 MPa pada suhu 1250^{o}C bagi sampel yang mengandungi 1.6 % silikon.

SYNTHESIS AND CHARACTERIZATION OF HYDROXYAPATITE (HA) AND SILICON SUBSTITUTED HYDROXYAPATITE (Si-HA) PRODUCED BY A PRECIPITATION METHOD

ABSTRACT

The precipitation method is a successful route to synthesize high purity hydroxyapatite (HA) and silicon-substituted hydroxyapatite (Si-HA) at low temperatures. In this research, calcium hydroxide ($Ca(OH)_2$) and phosphoric acid (H_3PO_4) were chosen as starting materials to synthesize HA. During synthesis, the reaction was carried out under vigorous stirring at various parameters. As-prepared HA powders were calcined at different temperatures of 700, 850, 1000 and 1200^oC for 1 hour. The results indicated that high purity HA was obtained and is stable up to 1200^oC when the aging time is prolonged to 24 hours. Different concentrations of reactants, viz. 0.5, 1.0, 1.5 and 2.0 M were also studied. The results indicated that nano-size HA particles were obtained at all the concentrations whereas pure stoichiometric HA with high thermal stability of up to 1200^oC was obtained at concentration of 0.5 and 1.0 M.

Based on the optimum conditions which were investigated in the synthesis of HA, the precipitation method was again employed to synthesize silicon-substituted HA with silicon contents of 0.4, 0.8 and 1.6% by weight using silicon acetate [$Si(OCOCH_3)_4$] as the Si source. The as-prepared HA and Si-HA powders/pellets were calcined at different calcination temperatures of 1150, 1200 and 1250^oC. The results showed that pure Si-HA samples were successfully prepared at all three silicon contents. At all the calcination temperatures, pure Si-HA at silicon content of

0.4 and 1.6 wt% was obtained whilst Si-HA at silicon content of 0.8 wt% decomposed into α-TCP at 1250^{o}C. The effect of silicon in HA induced a slight increase in lattice parameters of apatite structure resulting in slight shifting of XRD pattern of Si-HA samples. In addition, the silicon in hydroxyapatite inhibited densification at low temperature (1150^{o}C) and this effect being more significant as the level of silicon substitution increased. A near-full density (>90%) was achieved in pure HA at 1200^{o}C whilst the Si-HA sample reached this density at 1250^{o}C. SEM observation clearly showed that silicon substitution also inhibited grain growth at high temperatures (1200 and 1250^{o}C). The inhibition of grain growth increased as the silicon content increased. At a nearly full density, the hardness value of Si-HA sample reached the comparable value with HA sample. However, higher strength was achieved in Si-HA samples, and this reached a highest value of 15.93 MPa at 1250^{o}C for sample prepared at 1.6 % of silicon.

CHAPTER 1

INTRODUCTION

1.1 Introduction

Many millennia ago, the discovery by human kind that fire would irreversibly transform clay into ceramic pottery led eventually to an agricultural society and an enormous improvement in the quality and length of life. Within the last four decades another revolution has occurred in the use of ceramics to improve the quality of life. This revolution is the innovative use of specially designed ceramics for the repair and reconstruction of diseased or damaged parts of the body. Ceramics used for this purpose are termed bioceramics, which may be bioinert (e.g., alumina and zirconia), resorbable (e.g., tricalcium phosphate), bioactive (e.g., hydroxyapatite, bioactive glassed, and glass ceramics) or porous for tissue ingrowth (e.g., hydroxyapatite-coated metals). Applications of bioceramics include replacement for hips, knees, teeth, tendons and ligaments, as well as repair for periodontal disease, maxillofacial reconstruction, augmentation and stabilization of the jaw bone, spinal fusion and bone repair after tumor surgery (Hench, 1998).

Calcium phosphate-based bioceramics have been in use in medicine and dentistry for nearly 20 years (Hench et al., 1998). Among the different calcium phosphates, hydroxyapatite (HA), $Ca_{10}(PO_4)_6(OH)_2$, is the most important bioceramic used in dentistry and orthopedic surgery. Crystalline hydroxyapatite is a synthetic material analogous to calcium phosphate found in bone and teeth and a highly compatible material that has been considered for coating on metallic implants, as a porous ceramic that facilitates bone ingrowths, an inorganic component in a

ceramic-polymer composite, a granulate to fill small bone defects and for tissue engineering scaffolds (Maria and Daniel, 2005). Over the last two decades, numerous efforts have been made to prepare hydroxyapatite for bone tissue applications due to its excellent biocompatibility and bioactivity (Kothapalli et al., 2004).

1.2 Problem statement

The resorption property of calcium phosphates depends on Ca/P ratio, degree of crystallinity and crystal structure. A remarkable property of the synthetic HA is its bioactivity, in particular the ability to form chemical bonding with surrounding hard tissues after implantation (Fathi et al., 2008). However, most synthetic apatites are formed via high temperature processes (e.g. sintering), resulting in a well-crystallized structure, which has little or no activity toward bioresoption.

To produce synthetic HA powders with the desired properties, wet-chemical methods (precipitation, hydrothermal technique, and hydrolysis of other calcium phosphate) and dry processes (solid-state reaction) can be used. Other methods for the preparation of HA powders have also been reported: sol-gel (Feng et al., 2005), microwave irradiation (Meejoo et al., 2006), emulsion processing (Koumoulidis et al, 2003), and mechanochemical treatment. Depending upon the technique, materials with various morphology, stoichiometry and level of crystallinity can be obtained. The solid state reaction usually give a stoichiometric and well-crystallized product but they require relatively high temperatures and long duration of heat-treatment (Mobasherpour et al., 2007) whilst the sol-gel method involved molecular mixing of the calcium and phosphorous resulting in chemical homogeneity, but has drawbacks such as the possible hydrolysis of the phosphates and the high cost of raw materials.

Also, the HA prepared by this method resulted in relatively inferior crystallinity and thermal stability (Kothapalli et al., 2004).

In general, the wet-chemical methods allow the production of materials with good crystallinity, physiological stability and with the morphological characteristics of the hard tissue, but some of the physical, chemical and mechanical properties of the final products usually depend on the specific method used in the synthesis. (Donadel et al., 2005). The choice of precipitation method to produce HA in this research work can result in calcium phosphate material produced with a low-cost technique, simple and versatile using low temperature under atmosphere condition. Separately, during the reactions, the reaction media involves no foreign elements except water, the only by product. For these reasons, it is of great importance to develop inexpensive HA synthesis methods focused on the precise control of particle size, morphology and chemical composition (Binnaz et al., 2009).

However, even if the biocompatibility of HA is excellent, the bioactive process in HA shows some drawbacks when compared with other bioactive materials. For instance, the bioactivity reactions in silica based glasses occur in a few minutes, whereas those in HA take several days. It is believed that the bioactive behavior of HA can be improved by introducing some substitutions in the structure (Palard et al., 2008). The apatite structure can incorporate a wide variety of ions, which affect both its cationic and anionic sublattices (Maria and Daniel, 2005). The most common example of this is the substitution of carbonate ions into the HA structure (Gibson et al., 2001; Lafon et al., 2007) such that the product contains 3 to 8 wt% carbonate, which is similar to the levels detected in bone mineral. Other ions,

which are found in bone mineral, have been substituted into the HA structure, such as magnesium (Yasukawa et al., 1996), fluorine (Jha et al., 1997) and sodium, although their role on the biological performance of HA has not been clearly established (Gibson et al., 2002).

It was found that, silicon in small quantities has a significant effect on the development and growth of hard tissue of living bodies (Best et al., 2001). Particularly, synthetic calcium phosphate-based materials including 0.1% to 5% by weight of Si clearly demonstrate improved biological performances in terms of enhanced bone apposition, bone ingrowth and cell-mediated degradation. It has been suggested that, despite comparable dislocation density, Si-HA ceramics undergo faster dissolution, occurring preferentially around grain boundaries and triple junctions (Bianco et al., 2009). Thus, the sintering of ceramics made of substituted HA incorporating silicate (SiO_4^{4-}) was investigated. There are not so many researches up to date that have been done on the synthesis of silicon-substituted hydroxyapatite (Si-HA). Most of the researches focused on the synthesis of carbonated hydroxyapatite or K, Na substituted hydroxyapatite. Moreover, the synthesis of pure Si-HA powders has always been a difficulty. Not so many researchers succeeded in preparing pure silicated hydroxyapatite using different processes. In addition, the calcination behavior of Si-HA as well as its mechanical properties were rarely considered.

The synthesis of HA by a precipitation method in present study based on the study of Lazic et al., (2001), Afshar et al., (2003), Saeri et al., (2003) and Mostafa et

al., (2005), using $Ca(OH)_2/H_3PO_4$ system. The optimum process parameters was used to further synthesized Si-HA with $Si(OCOCH_3)_4$ as a silicon source.

1.3 Objective of research

The aim of this research is to synthesize single phase hydroxyapatite (HA) and silicon substituted hydroxyapatite (Si-HA) powders with high thermal stability by a precipitation process and comparing the physical and mechanical properties of HA and Si-HA obtained. With this main object, the following studies were conducted:

1. Synthesis of HA and Si-HA by a precipitation method and characterizing the physical and mechanical properties.
2. Investigation on the effect of silicon on the formation of HA.

1.4 Research scope

In general, the research work is divided into two parts which will be described in details in chapter 3. The first part is the synthesis and characterization of HA using a wet precipitation method with $Ca(OH)_2$ and H_3PO_4 as starting materials. The precipitation process parameters such as stirring speed, reaction temperature, aging time and concentration of reactants were investigated. Based on these optimum process parameters, the second part is the synthesis of silicon substituted HA with $Ca(OH)_2$, H_3PO_4 and $Si(OCOCH_3)_4$ as precursors. The characterization technique includes XRD, SEM, FTIR, TEM, TG/DSC. The density and specific surface area were measured. The mechanical properties of HA and Si-HA pellets were

determined by using Vickers hardness test and diametral tensile strength. Figure 1.1 and Figure 1.2 illustrate generally the methodology in this research.

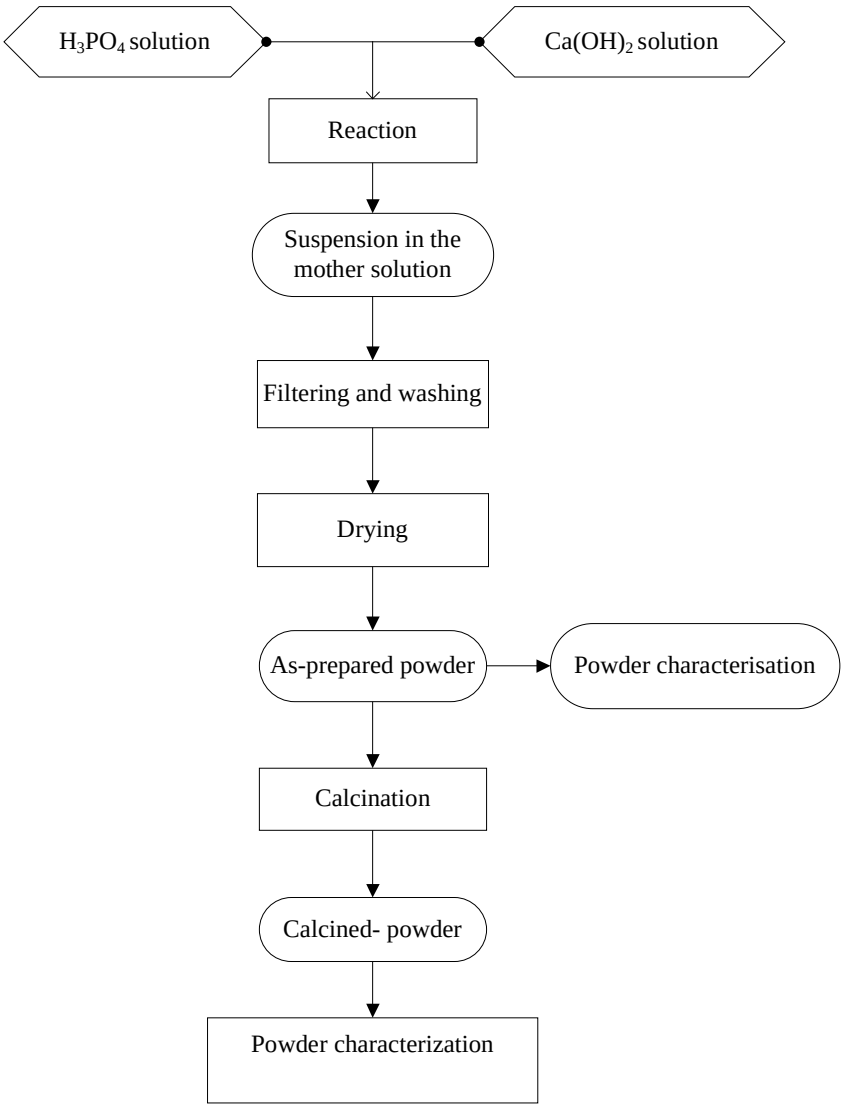

Figure 1.1 Flow chart for the synthesis of hydroxyapatite

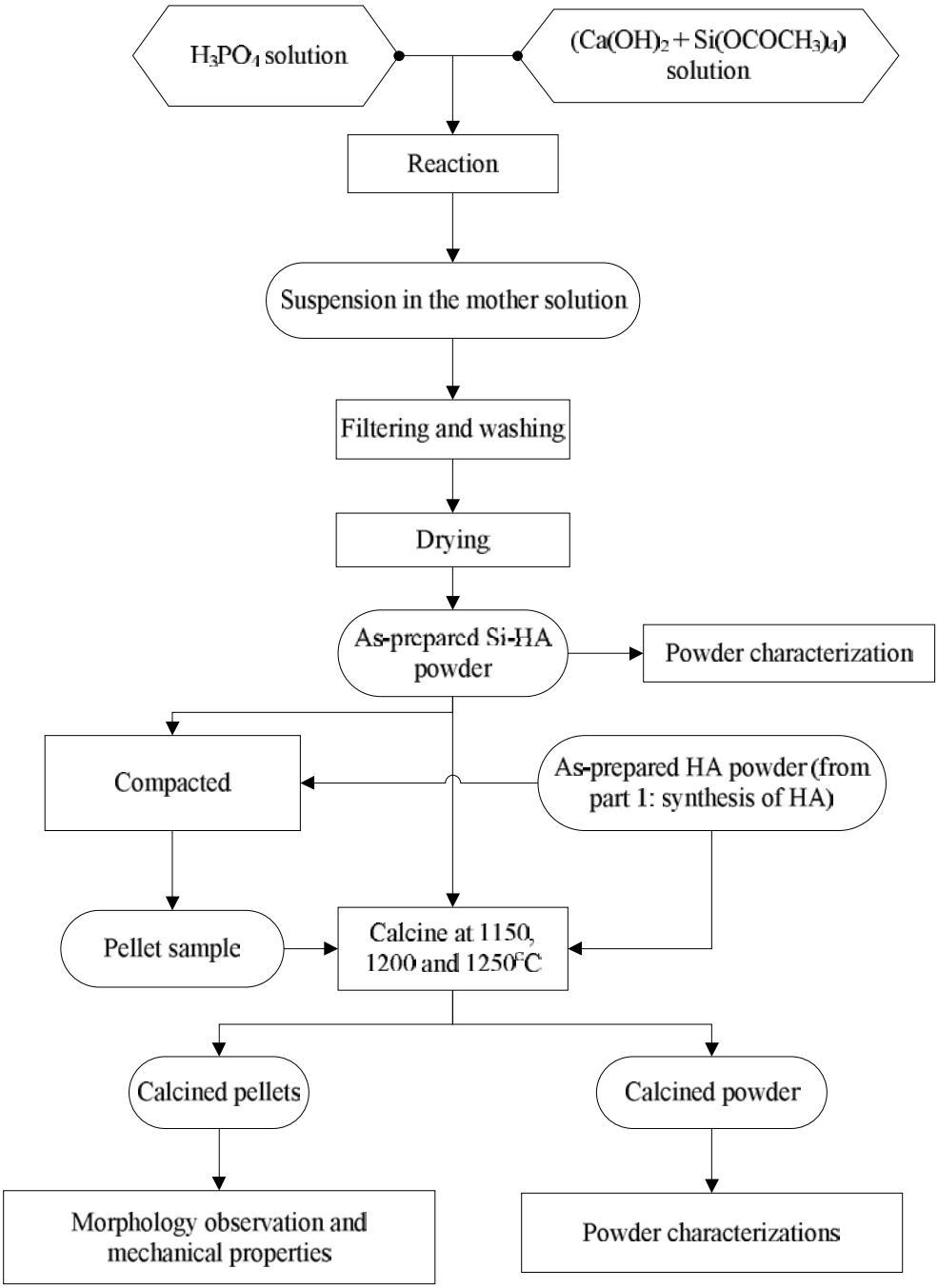

Figure 1.2 Flow chart for the synthesis of Si-HA and properties comparison between HA and Si-HA

CHAPTER 2

LITERATURE REVIEW

2.0 Introduction

The use of bone substitutes in human surgery has dramatically increased over the last few decades. These materials have been used to guide and expand the bone healing tissue, to become intergrated within it and then subjected to the same remodeling process as the natural bone (Frayssinet, 1998). However, the available amount of proper bones substitution is generally limited and the implantation requires a second operation which is very painful (Neumann, 2006). Therefore, there is high demand for the synthetic bone substitution material.

In recent years, synthetic hydroxyapatite has been extensively used as the synthetic bone substitution material due to its excellent biocompatibility and its similar characteristics with biological bone. However, the bioactivity behavior of hydroxyapatite can be improve by introducing Si ions to produce Si-HA which resembles bone tissue composition. Consequently, a number of studies have been focused on the production of synthetic HA and Si-HA ceramic for bone substitutes.

This review chapter provides an overview of biomaterials. The topic on bioceramic material, as a part of biomaterials, will be explained in more detail. As HA and Si-HA are the calcium phosphate based bioceramics, the properties of these bioceramics are presented in this chapter. This is followed with a review of previous synthesis of HA and Si-HA by other researchers.

2.1 Biomaterials

Biomaterials is a term used to indicate materials that constitute part of medical implants and disposables that have been utilized in medicine, surgery, dentistry and veterinary medicine as well as in every aspect of patient health care (Hench and Wilson, 1998). A biomaterial is a synthetic material used to replace part of a living system or to function in intimate contact with living tissue. The Clemson University Advisory Board for Biomaterials has formally defined a biomaterial to be "a systemically and pharmacologically inert substance designed for implantation within or incorporation with living systems" (Wong and Bronzino, 2007).

Biomaterials can broadly be classified as biological biomaterials (soft and hard tissue type) and synthetic biomaterials (metallic, polymeric, ceramic and composite biomaterials). Each type of synthetic biomaterial has advantages and disadvantages in properties as well as processibility and was exploited for different specific applications. Some examples of biomaterials are provided in Table 2.1.

Table 2.1: Materials for use in the body (Wong and Bronzino, 2007)

Material	Advantages	Disadvantages	Examples
Polymer (nylon, silicone rubber, polyester, polytetrafuoroethylene, etc.)	Resilient Easy to fabricate	Not strong Deform with time May degrade	Sutures, blood vessels, hip socket, ear, nose, other soft tissues, sutures
Metals (Ti and its alloys, Co-Cr alloys, stainless steels, Au, Ag, Pt, etc.)	Strong, tough, ductile	May corrode, dense, difficult to make	Joint replacements, bone plates and screws, dental root implants, pacer and suture wires
Ceramics (aluminum oxide, calcium phosphates including hydroxyapatite, carbon)	Very biocompatible, inert, strong in compression	Brittle, not resilient, difficult to make	Dental; femoral head of hip replacement, coating of dental and orthopedic implants
Composites (carbon-carbon, wire or fiber reinforced bone cement)	Strong, tailor-made	Difficult to fabricate	Joint implants, heart valves

2.2 Types of Synthetic Biomaterials

In general, synthetic biomaterial can be classified into three groups namely metallic biomaterials, ceramic biomaterials and polymer biomaterials. The details will be discussed in the following sections.

2.2.1 Metallic biomaterials

Metals have been used almost exclusively for load-bearing implants, such as hip and knee prostheses, fracture fixation wires, pins, screws and plates (Dee et al., 2002). Metals are also used as biomaterials due to their excellent electrical and thermal conductivity and mechanical properties. Since some electrons are independent in metals, they can quickly transfer an electric charge and thermal energy. The mobile free electrons act as the binding force to hold the positive metal

ions together. This attraction is strong, as evidenced by the closely packed atomic arrangement resulting in high specific gravity and high melting points of most metals (Wong and Bronzino, 2007).

The mechanical properties of materials are of great importance when designing load-bearing orthopedic and dental implants. Some mechanical properties of metallic biomaterials are listed in Table 2.2. With a few exceptions, the high ultimate tensile and fatigue strength of metals, compared to ceramic and polymers make them the materials of choice for implants that carry mechanical loads.

Table 2.2: Selected properties of metallic biomaterials (Dee et al., 2002)

Materials	**Young's modulus, E [GPa]**	**Yield strength, σ_y [MPa]**	**Tensile strength, σ_{UTS} [MPa]**	**Fatigue limit, σ_{end} [MPa]**
Stainless steel	190	221-1,213	586-1,351	241-820
Co-Cr alloys	210-253	448-1,606	655-1,896	207-950
Titanium	110	485	760	300
Ti-6Al-4V	116	896-1,034	965-1,103	620
Natural bone	15-30	30-70	70-150	-

The elastic moduli of the metals listed in Table 2.2 are at least seven times greater than that of natural bone. This mismatch of mechanical properties can cause "stress shielding", a condition characterized by bone resorption (loss of bone) in the vicinity of implants. This clinical complication arises because the preferential distribution of mechanical loading through the metallic prosthesis deprives bone of the mechanical stimulation needed to maintain homeostasis.

2.2.2 Ceramic and glass biomaterials

Ceramics are defined as the art and science of making and using solid articles that have as their essential component, inorganic nonmetallic materials (Kingery et al., 1976). Ceramic are refractory, polycrystalline compounds, usually inorganic, including silicates, metallic oxides, carbides and various refractory hydrides, sulfides, and selenides. Oxides such as Al_2O_3, MgO, SiO_2 and ZrO_2 contain metallic and nonmetallic elements and ionic salts, such as NaCl, CsCl, and ZnS. Exceptions to the preceding include covalently bonded ceramics such as diamond and carbonaceous structures like graphite and pyrolized carbons (Park and Lakes, 1992).

In recent years, humans have realized that ceramics and their composites can also be used to augment or replace various parts of the body, particularly bone. Thus, the ceramics used for the latter purposes are classified as bioceramics. Their relative inertness to the body fluids, high compressive strength, and aesthetically pleasing appearance led to the use of ceramics in dentistry as dental crowns.

Unlike metals and polymers, ceramics are difficult to shear plastically due to the ionic nature of the bonding and minimum number of slip systems. These characteristics make the ceramics brittle and are responsible for almost zero creep at room temperature. Consequently, ceramics are very susceptible to notches or microcracks because instead of undergoing plastic deformation, they will fracture elastically on initiation of a crack. At the crack tip the stress could be many times higher than the stress in the material away from the tip, resulting in a stress concentration which weakens the material considerably. The latter make it difficult to predict the tensile strength of the ceramic. This is also the reason ceramics have

low tensile strength compared to compressive strength. If a ceramic is flawless, it is very strong even when subjected to tension (Park and Lakes, 1992).

Ceramics are generally hard; in fact, the measurement of hardness is calibrated against ceramic materials. Diamond is the hardest, with a hardness index of 10 on Moh's scale, and talc ($Mg_3Si_3O_{10}COH$) is the softest ceramic, while ceramics such as alumina (Al_2O_3), quartz (SiO_2) and apatite ($Ca_5P_3O_{12}F$) are in the middle range. Other characteristic of ceramic materials are (1) their high melting temperature and (2) low conductivity of electricity and heat. These characteristics are due to the chemical bonding within ceramics (Wong and Bronzino, 2007).

The desired properties of implantable bioceramics are (Wong and Bronzino, 2007):

- Non-toxic
- Non-carcinogenic
- Non-allergic
- Non-inflammatory
- Biocompatible
- Biofunctional for its lifetime in the host

Ceramics used in fabricating implants can be classified as nonabsorbable (relatively inert), bioactive or surface reactive (semi-inert) and biodegradable or resorbable (non-inert). Alumina (Al_2O_3), zirconia (ZrO_2), silicon nitrides (Si_3N_4) and carbons are inert bioceramics. Certain glass ceramics and dense hydroxyapatites are

semi-inert (bioreactive) and calcium phosphates and calcium aluminates are resorbable ceramic (Wong and Bronzino, 2007).

Ceramics and glasses are used as components of hip implants, dental implant, middle ear implants, and heart valves. Overall, however, these biomaterials have been used less extensively than either metals or polymers. Some ceramics that have been used for biomedical application are listed in Table 2.3.

Table 2.3: Ceramics used in biomedical applications (Dee et al., 2002)

Ceramics	**Chemical formula**	**Remarks**
Alumina	Al_2O_3	Bio-inert
Zirconia	ZrO_2	Bio-inert
Pyrolytic carbon		Bio-inert
Bioglass	$Na_2O.CaO.P_2O_3$-SiO_2	Bioactive
Hydroxyapatite (sintered at high temperature)	$Ca_{10}(PO_4)_6(OH)_2$	Bioactive
Hydroxyapatite (sintered at low temperature)	$Ca_{10}(PO_4)_6(OH)_2$	Biodegradable
Tricalcium phosphate	$Ca_2(PO_4)_3$	Biodegradable

The major drawbacks to the use of ceramics and glasses as implants are their brittleness and poor tensile properties (see Table 2.4). Although they can have outstanding strength when loaded in compression, ceramics and glass fail at low stress when loaded in tension or bending. Among the biomedical ceramics, alumina has the highest mechanical properties, but its tensile properties are still below those of metallic biomaterials. Additional advantageous properties of alumina are its low coefficient of friction and wear rate. From these properties, alumina has been used as a bearing surface in joint replacements.

Table 2.4: Mechanical properties of ceramic biomaterials (Dee et al., 2002)

Materials	**Young's Modulus, E (GPa)**	**Compressive Strength, (MPa)**	**Tensile Strength, (MPa)**
Alumina	380	4500	350
Bioglass-ceramics	22	500	56-83
Calcium phosphates	40-117	510-896	69-193
Pyrolytic carbon	18-28	517	280-560

The mechanical properties of calcium phosphates and bioactive glasses make them unsuitable as load-bearing implants. Clinically, hydroxyapatite has been used as a filler for bone defect and as an implant in load-free anatomic sites (for example, nasal septal bone and middle ear). In addition, hydroxyapatite has been used as a coating on metallic orthopedic and dental implant to promote their fixation in bone. In these cases, the underlying metal carries the load, whereas the surrounding bone strongly bonds to the hydroxyapatite.

2.2.3 Polymeric biomaterials

Synthetic polymeric materials have been widely used in medical disposable supply, prosthetic materials, dental materials, implants, dressings, extracorporeal devices, encapsulants, polymeric drug delivery systems, tissue engineered products, and orthodoses as that of metal and ceramic substituents. The main advantages of the polymeric biomaterials compared to metal or ceramic materials are ease of manufacturability to produce various shapes (latex, film, sheet, fibers, etc.), ease of secondary processablility, reasonable cost and availability with desired mechanical and physical properties. The required properties of polymeric biomaterials are similar

to other biomaterials, that is, biocompatibility, sterilizability, adequate mechanical and physical properties, and manufacturability as given in Table 2.5 (Wong and Bronzino, 2007).

Table 2.5: Requirement for Biomedical Polymers (Wong and Bronzino, 2007)

Properties	**Description**
Biocompatibility	Noncarcinogenesis, nonpyrogenicity, nontoxicity, and nonallergic response
Sterilizability	Autoclave, dry heating, ethylenoxide gas, and radiation
Physical property	Strength, elasticity, and durability
Manufacturability	Machining, molding, extruding, and fiber forming.

The mechanical properties of polymers depend on several factors, including the composition and structure of the macromolecular chains and their molecular weights. Table 2.6 lists some mechanical properties of selected polymeric biomaterials. Compared with metals and ceramics, polymers have much lower strengths and moduli but they can be deformed to a greater extent before failure. Consequently, polymers are generally not used in biomedical applications that bear loads (such as body weight). Ultra high molecular weight polyethylene (UHMWPE) is an exception, as it is used as a bearing surface in hip and knee replacements. The mechanical properties of polymers, however, are sufficient for numerous biomedical applications (some of which are listed in Table 2.6).

Table 2.6: Mechanical properties of biomedical polymers (Dee et al., 2002)

Polymer	**Tensile Strength, MPa**	**Young's Modulus, E, MPa**	**Elongation, %**
Polymethylmetacrylate (PMMA)	30	2.2	1.4
Nylon 6/6	76	2.8	90
Polyethylene terephthalate	53	2.14	300
Polylactic acid	28-50	1.2-3	2-6
Polypropylene	28-36	1.1-1.55	400-900
Polytetrafluoroethylene	17-28	0.5	120-350
Silicone rubber	2.8	Up to 10	160
Ultra high molecular weight polyethylene (UHMWPE)	≥35	4-12	≥300

2.3 Calcium phosphate ceramics

Calcium phosphate-based bioceramics have been in used in medicine and dentistry for nearly 20 years. Applications include coating of orthopedic and dental implants, alveolar ridge augmentation, maxillofacial surgery, otolaryngology, and scaffolds for bone growth and as powders in total hip and knee surgery (Hench et al., 1998).

Calcium phosphate has been synthesized and used for manufacturing various forms of implants, as well as for solid or porous coatings on other implants. There are mono-, di-, tri-, and tetra-calcium phosphates, in addition to the hydroxyapatite and β-whitlockite, which have ratios of 5/3 and 3/2 for calcium and phosphorus (Ca/P), respectively. The stability in solution generally increases with increasing

Ca/P ratios (Park and Lakes, 2007). Different phases are used in different applications depending upon whether a degradable or a bioactive material is desired (Billotte, 2000). Table 2.7 summarized various phases of calcium phosphate currently used in the biomedical industry.

Table 2.7: Various phases of calcium phosphate ceramics (Guelcher and Hooinger, 2006)

Phases	**Chemical formulae**	**Mineral name**	**Ca/P ratio**
Hydroxyapatite (HA)	$Ca_{10}(PO_4)_6(OH)_2$	Apatite	1.67
α-Tricalcium phosphate (α-TCP)	$Ca_3(PO_4)_2$	Whitlockite	1.5
β-Tricalcium phosphate (β-TCP)	$Ca_3(PO_4)_2$	Whitlockite	1.5
Dicalcium phosphate dihydrate (DCPD)	$CaHPO_4.2H_2O$	Brushite	1.0
Dicalcium phosphate anhydrous (DCPA)	$CaHPO_4$	Monetite	1.0

The stable phases of calcium phosphate ceramics depend considerably upon temperature and the presence of water, either during processing or in the use environment. At body temperature, only two calcium phosphates are stable in contact with aqueous media, such as body fluids; at pH < 4.2, the stable phase is $CaHPO_4.2H_2O$ (DCPD or brushite, C_2P), whereas at pH ≥ 4.2, the stable phase is $Ca_{10}(PO_4)_6(OH)_2$ (HA) [Hench, 1991]. At higher temperatures, other phases, such as $Ca_3(PO_4)_2$ (β-tricalcium phosphate, C_3P, or TCP) and $Ca_4P_2O_9$ (tetracalcium phosphate) are present. The unhydrated, high-temperature calcium phosphate phases interact with water, or body fluids at 37^{o}C to form HA. Thus, the solubility of a TCP surface approaches the solubility of HA and decrease the pH of the solution which

further increases the solubility of TCP and enhances resorption (Hench, 1991). The presence of micropores in the sintered material can increase the solubility of these phases (Jarcho, 1981).

There is a wide variation in the mechanical properties of synthetic calcium phosphates, as given in Table 2.8. The mechanical behavior of calcium phosphate ceramics strongly influences their application as implants. Tensile and compressive strength and fatigue resistance depend on the total volume of porosity. The wide variations of properties are due to the variations in the structure of polycrystalline calcium phosphates due to variations in the manufacturing processes. Depending on the final firing conditions, the calcium phosphate can be calcium hydroxyapatite or β-TCP. In many instances, however, both type of structure exist in the same final product.

Table 2.8: Physical properties of synthetic calcium phosphates (Park and Lakes, 2007)

Properties	**Values**
Elastic modulus (GPa)	40-117
Compressive strength (MPa)	294
Bending strength (MPa)	147
Hardness (Vickers, GPa)	3.43
Poisson's ratio	0.27
Density (Theoretical, g/cm^3)	3.16

Sintering of calcium phosphate ceramics usually occurs at 1000-1500^{o}C, following compaction of the powder into a desired shape. The phase formed at high temperature depends not only on temperature but also on the partial pressure of water (ρ_{H2O}) in the sintering atmosphere. When water is present, HA can be formed and is a

stable phase up to 1360°C. Without water, C_4P and C_3P are stable phases (Hench, 1991).

The temperature range of HA stability increases with ρ_{H2O}, as does the rate of phase transitions of C_3P or C_4P to HA. Because of kinetics barriers that affect the rates of formation of the stable calcium phosphate phases, it is often difficult to predict the volume fraction of high-temperature phases that are formed during sintering and their relative stability when cooled to room temperature.

Starting powders can be made by mixing into an aqueous solution the appropriate molar ratios of calcium nitrate and ammonium phosphate which yield a precipitate of stoichiometric HA. The Ca^{2+}, PO_4^{3-} and OH^- ions can be replaced by other ions during processing or in physiological surroundings; e.g., fluorapatite and carbonated apatite. Flourapatite is found in dental enamel and carbornated apatite is present in bone (Hench, 1998).

2.3.1 Biological apatite

Biological apatites constitute the mineral phase of calcified tissue such as bone, dentine and enamel in the body and also some pathological calcifications. They are similar to synthetic HA but they differ from HA in composition, stoichiometry and physical and mechanical properties. Biological apatites are usually calcium-deficient as a result of various substitution at regular HA lattice points. It is therefore not appropriate to simply refer to biological apatite as hydroxyapatite. Table 2.9 presents the composition of biological apatite and hydroxyapatite. Table 2.10 shows the properties of biological apatite and hydroxapatite.

Table 2.9: Composition of biological apatite and hydroxyapatite (Donglu Shi, 2004)

Major constituent	Biological apatite		Hydroxyapatite
	In enamel (wt%)	In bone (wt%)	
Ca	36.00	24.50	39.60
P	17.70	11.50	18.50
Na	0.50	0.70	
K	0.08	0.03	
Mg	0.44	0.55	
F	0.01	0.02	
Cl	0.30	0.10	
CO_3^{2-}	3.20	0.58	
Silicon	0.003	0.04	
Ca:P (molar ratio)	1.62	1.65	1.67

Table 2.10: Properties of biological apatite and hydroxyapatite (Donglu Shi, 2004)

Property	Biological apatite		Hydroxyapatite
	In enamel	In bone	
Lattice parameter / nm			
a	0.9441	0.9419	0.9423
c	0.6882	0.6880	0.6875
Crystal size/ nm	130x30	25x(2.5-5.0)	in micrometers
Elastic modulus/ GPa	14	7-30	10
Tensile strength/ MPa	70	50-150	~100

2.3.2 Hydroxyapatite

Hydroxyapatite (HA) is the most important among the calcium compounds since it is found in natural hard tissues as mineral phase. Among the most interesting properties of hydroxyapatite as a biomaterial is its excellent biocompatibility. It appears to form a direct chemical bond with hard tissue. In addition, hydroxyapatite acts as reinforcement in hard tissues and is responsible for the stiffness of bone, dentine, and enamel (Wong and Bronzino, 2007).

According to Park and Lake, (1992), the mineral part of bone and teeth is made of a crystalline form of calcium phosphate similar to hydroxyapatite. The apatite family of mineral crystallizes into hexagonal rhombic prisms, with the space group being $P6_3/m$ and has unit cell dimensions a = 9.432 and c = 6.875 . The unit cell contains a complete representation of the apatite crystal, consisting of Ca^{2+}, PO_4^{3-}, and OH^- groups closely packed together in arrangement shown in Figure 2.1. The atomic structure of hydroxyaptite projected down the c-axis onto the basal plane. The hydroxyl ions lie on the corners of the projected basal plane and they occur at equidistant interval (3.44) along the columns perpendicular to the basal plane and parallel to the c-axis. Six of the ten calcium ions in the unit cell are associated with the hydroxyls in these columns, resulting in strong interactions among them.

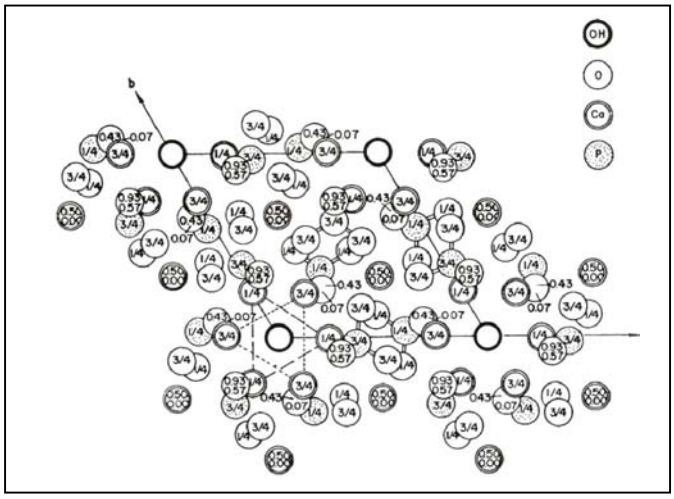

Figure 2.1 The atomic arrangement of calcium hydroxyapatite
(Hench and Wilson, 1993)

The theoretical composition of pure HA is 39.68 wt% Ca and 18.45 wt% P with Ca/P molar ratio of 1.667. In dense HA material, variations in Ca/P ratios after sintering are reflected by the β-TCP/HA ratios which in turn reflect the purity. If the

Ca/P ratio is 1.67, only HA will be observed in the x-ray diffraction. If the Ca/P ratio is lower than 1.67, β-TCP and other phases such as tetracalcium phosphate (TTCP) will be presented with the HA phase, depending on the temperature and condition of sintering. If Ca/P ratio is higher than 1.67, CaO will be present with the HAp phase (Hench and Wilson, 1993).

The synthetic HA is used in hard tissue replacement applications since it is capable of undergoing bonding osteogenesis and is chemically stable for long periods of time *in vivo* (Kobayashi et al., 2006). However, despite its chemical similarity to bone mineral, synthetic HA differs significantly in terms of its microstructure and macrostructure to its nearest biological equivalentcortical bone. Cortical bone is a composite material with an advanced structure consisting of collagen fibre-HA crystallite networks at the molecular level, a lamellar structure at the microstructural level and aligned cylindrical units at the macrostructural level (Ruys et al., 1995). At present, applications for synthetic HA are restricted to areas free of dynamic load bearing because synthetic HA is known for its weakness and brittleness (Zhang et al., 2003).

Synthetic HA is simply a fine-grained polycrystalline ceramic. This large difference in structure accounts for the low fracture toughness of synthetic HA in relation to bone: HA ≈ 0.6-1.5 MPa $m^{1/2}$; bone ≈ 2-12 MPa $m^{1/2}$ (Ruys et al., 1995).

To produce synthetic HA powders with the desired properties, wet-chemical methods (precipitation, hydrothermal technique and hydrolysis of other calcium phosphates) and dry processes (solid-state reaction) can be used. In general, the wet-

chemical methods allow the production of materials with good crystallinity, physiological stability, and with the morphological characteristics of the hard tissue, but some of the physical, chemical, and mechanical properties of the final product usually depend on the specific method used in the synthesis (Donadel et al., 2005).

2.3.3 Tricalcium phosphate

The chemical formula of tricalcium phosphate (TCP) is $Ca_3(PO_4)_2$. TCP has four polymorphs: α, β, γ and super-α. The γ-polymorph phase is a high-pressure phase, and the super-α polymorph phase is observed at temperature above approximate 1500^{o}C. Therefore the most frequently observed TCP polymorphs in the field of bioceramics are: α and β-TCP. β-TCP is table up to 1125^{o}C. But above this temperature and up to 1430^{o}C, α-TCP becomes the stable phase. Supper α-TCP forms between 1430^{o}C and the melting point 1756^{o}C (Guelcher and Hollinger, 2006).

TCP is a resorbable temporary bone space filler material. When implanted, TCP will interact with body fluids to form HA as follows (Grook, 1984):

$$4Ca_3(PO_4)_2 + 2H_2O \rightarrow Ca_{10}(PO_4)_6(OH)_2 \text{ (surface)} + 2Ca^{2+} + 2HPO_4^{2-} \qquad (2.1)$$

This reaction will decrease with the pH of the local solution and further increases the solubility of TCP. Theoretically, resorbable TCP is an ideal implant material. After implantation, TCP will degrade with time and be replaced with natural tissues. It leads to the regeneration of tissues instead of their replacement and so solves the problem of interfacial stability. However, in clinical applications, some limitations restrict the use of resorbable TCP: