

**SYNTHESIS OF HYDROXYAPATITE POWDERS VIA
MECHANICAL ACTIVATION TECHNIQUE**

by

ZARINA OMAR

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LIST OF ABBREVIATIONS

$\text{Ca}_2\text{P}_2\text{O}_7$	calcium pyrophosphate (CP)
CaCO_3	calcium carbonate (CC)
$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$	hydroxyapatite (HA)
$\text{Ca}_3(\text{PO}_4)_2$	β -tricalcium phosphate (BTCP)
CaO	calcium oxide (CaO)
XRD	x-ray diffractometer
XRF	x-ray fluorescence
TEM	transmission electron microscopy
FT-IR	fourier transform infra-red
TG	thermogravimetric analysis
DSC	differential scanning calorimetry

SINTESIS SERBUK HIDROKSIAPATIT MELALUI TEKNIK PENGAKTIFAN MEKANIKAL

ABSTRAK

Suatu tinjauan permulaan bagi pengisaran bebola halaju rendah telah dijalankan dengan menggunakan bahan mentah kalsium pirofosfat dan kalsium karbonat ($\text{Ca}_2\text{P}_2\text{O}_7 - \text{CaCO}_3$) dengan pertambahan sejumlah amaun air suling untuk menghasilkan hidroksiapatit (HA), $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$. Campuran ini telah dikisar selama 8 jam dengan menggunakan dua alat, iaitu pengisar-aduk dan pengisar-putar. Hasil kisan seterusnya dikalsin pada $1100\text{ }^\circ\text{C}$ dan didapati kedua-dua kaedah berjaya menghasilkan fasa HA tunggal. Satu kajian yang lebih terperinci dilakukan dengan menggunakan campuran yang sama tetapi pengaktifan mekanikal disempurnakan dengan sebuah pengisar bebola planetari berhalaju tinggi untuk tempoh pengisaran, suhu pengkalsinan dan kitaran pengisaran yang berbeza. Perubahan fasa selepas setiap keadaan pengisaran telah dianalisis dengan menggunakan pembelauan sinar-x (XRD) sebelum dan selepas pengkalsinan. Termogravimetri dan kalorimetri pengimbasan pembeza (TG/DSC) telah dijalankan ke atas sampel yang telah dikisar untuk menentukan sifat terma semasa pemanasan. Analisis lain yang turut dijalankan ialah analisis saiz partikel, pendarfluor sinar-x (XRF) dan spektroskopi jelmaan fourier-infra merah (FT-IR). Perubahan fasa telah berlaku semasa pengisaran dan menghasilkan beberapa fasa pertengahan selain bahan asal yang kemudiannya bertukar ke fasa HA tunggal atau campuran HA selepas pengkalsinan. Keputusan yang telah didapati menunjukkan bahawa suhu pengkalsinan yang optimum dipengaruhi oleh tempoh pengisaran dan juga kitaran pengisaran. Suhu terendah yang didapati dalam kajian ini untuk pembentukan fasa tunggal hidroksiapatit (HA) adalah $900\text{ }^\circ\text{C}$ selepas pengisaran selama 6 jam dan kitaran adalah 30 minit pengisaran dan 2 minit rehat. Ini jelas jauh memperbaiki keadaan sebelum ini iaitu suhu kalsin $1100\text{ }^\circ\text{C}$ selepas pengisaran 8 jam.

SYNTHESIS OF HYDROXYAPATITE POWDERS VIA MECHANICAL ACTIVATION TECHNIQUE

ABSTRACT

A preliminary experiment on low-speed ball-milling was carried out using calcium pyrophosphate and calcium carbonate ($\text{Ca}_2\text{P}_2\text{O}_7 - \text{CaCO}_3$) as starting materials with an addition of some amount of distilled water to produce hydroxyapatite (HA), $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$. The mixtures were milled for 8 hours using two equipment i.e. milling-mixer and roll-mill. The milled mixtures were subsequently calcined at 1100 °C and was found that both methods successfully formed a single-phase HA. A more detailed study of the same mixtures but with mechanical activation being effected using a high-speed planetary ball-mill for different milling durations, calcination temperatures and milling cycles. The phase changes after each milling condition were analysed by x-ray diffraction (XRD) before and after calcination. Thermogravimetry and differential scanning calorimetry (TG/DSC) were conducted on the as-milled samples to determine the thermal behavior upon heating. Other analysis was also carried out such as particle size analysis, x-ray fluorescence (XRF) and fourier transformation - infra red (FT-IR) spectroscopy. Phase transformations were found to take place upon milling to produce a few intermediate phases other than the starting materials, which were finally transformed to a single-phase or mixed HA upon calcination. It was found that the optimum calcination temperature is influenced by the milling duration as well as the milling cycle. The lowest calcination temperature obtained in this work to form a single-phase hydroxyapatite (HA) is 900 °C after 6 hours milling using a cycle of 30 minutes milling and 2 minutes pause. This is obviously a significant improvement to the current status in forming a single-phase HA, which requires a calcination temperature of 1100 °C after 8 hours of milling.

CHAPTER 1

INTRODUCTION

1.1 Introduction

Bone repair or regeneration is a common but complicated clinical problem in orthopedic surgery. Every year, millions of people suffer from bone defects arising from trauma, tumor or bone diseases, and inevitably in extreme cases, resulting in death due to insufficient ideal bone substitute (Murugan & Ramakrishna, 2004). Recent advances in materials technology have created numerous possibilities for extensive use of biomedical devices and implants. Current knowledge in medical science and biomaterials engineering, followed by a continuing development of new surgical techniques and synthetic parts, are providing surgeons with the means to improve, restore and replace defective or diseased parts of the human anatomy (Cheang & Khor, 1995).

Biocompatible materials are applied as bone and tissue substitutes for the human body (Cheang & Khor, 1995). Common bone substitution materials are traditional bone substitutes such as autografts, allografts and xenografts. In the next few years, the bone substitutes will bear the risk of infections and immune responses, which may cause other health problems and thus affecting quality of the substitute. As an alternative, there are various synthetic materials, composites and bioceramics. However, none of these materials provides a perfect solution for guided bone healing because there always remain the questions about mechanical stability, long term *in-vivo* biocompatibility and biodegradability (Tadic & Beckmann, 2004).

Artificial implants of all types and designs are increasingly being introduced using a variety of materials ranging from metals and polymers to ceramics (Cheang & Khor, 1995). These ceramics are opted for their excellent biological properties like biocompatibility, good resistance to corrosion and high wear resistance (Balamurugan et al., 2003)

The two calcium phosphate ceramics widely used in clinical applications are β -tricalcium phosphate (β -TCP) and hydroxyapatite (HA) (Cao & Hench, 1996). The use of HA has received particular attention due to its chemical composition which is similar to that of the mineral constituent of bone (Chen et al., 2002). HA which is a highly crystalline and osteoconductive material can be said to be the most stable calcium phosphate at neutral pH and the most prevalent form of calcium phosphate on the market (Mickiewicz, 2001). Thus the preparation of HA is a suitable target in technologies using restorative biomaterials with HA to mimic the chemical composition present in the human body (Rodriguez-Clemente & Lopez-Macipe, 1998). There are many methods to produce HA such as precipitation, solid-state reaction, sol gel, hydrothermal and etc. In the present investigation, a simple process of solid-state reaction to prepare pure hydroxyapatite powder via mechanical activation and subsequently calcined at elevated temperatures.

1.2 Problem statement

Many research works had been carried out to investigate solid-state method of HA synthesis via mechanical milling under various conditions and most of them can be classified into dry and wet processes. The powders prepared by the dry method are usually of irregular forms with large grain size and often exhibit heterogeneity in composition due to inhomogeneous milling (Yoshimura & Suda, 1994). Meanwhile, the wet process can provide finer particles, more homogeneous and more reactive powders.

Another advantage of the wet process is that the by-product is almost water and the probability of contamination during milling is very low.

One of the studies to synthesise HA is by using calcium pyrophosphate and calcium carbonate as starting materials. The chemicals were mixed in water during 8 hours of ball-milling duration with a rotating speed of 170 rpm. The hydroxyl group from the water is needed for the formation of HA during calcination. A single-phase HA was observed after calcination at a temperature of 1100 °C (Rhee, 2002). Another research by Yeong et al. (2001) had attained a single phase HA using a high-energy shaker mill without calcination. The particle size of the HA obtained was ~ 25nm after more than 20 hours of mechanical milling using different starting materials, namely calcium oxide and anhydrous calcium hydrogen phosphate.

High speed planetary ball-milling had also been used in many other studies. Kim et al. (2000), for example, used mixtures of $\text{CaO} - \text{Ca}(\text{OH})_2 - \text{P}_2\text{O}_5$ to synthesize HA via dry intensive milling without calcination. By using a Fritsch planetary ball-mill (790 rpm) with zirconia milling container and balls, the mixture was milled for 5 to 120 min. Every cycle was milled for 10 min and suspended for 10 min (Kim et al., 2000). Silva et al. (2004) used a Fritsch planetary ball mill with stainless steel milling container and balls to mill for 60 hours at 370 rpm. A $\text{CaHPO}_4 - \text{Ca}(\text{OH})_2$ mixture was in pure dry process for 30 min of milling step and 10 min pause to produce nanocrystalline HA powders, also without calcination (Silva et al., 2004). Another example of planetary ball mill investigation is the kinetic study of dry mechanochemistry (without calcination) by two different planetary ball mills (Retsch and Fritsch) using porcelain and agate milling container and balls at 350 rpm (Mochales et al., 2004).

In the present research, a wet method of solid-state reaction was carried out to prepare hydroxyapatite powder using low-speed ball milling and high speed planetary ball-milling with subsequent calcination. The two starting powders, calcium pyrophosphate and calcium carbonate, as used in a previous study (Rhee, 2002) were re-used as starting materials and they were mixed in distilled water. Since there were many researches involving mechanical activation, this research was done to improve the study of Rhee (2002) by using a higher speed planetary ball-milling (400 rpm) with suitable milling duration and different calcination temperatures to produce a single-phase HA.

1.3 Objectives of Research

This study is focused on certain variables such as amount of distilled water used, milling duration and calcination temperature. Therefore, the objectives of the research are:

1. To synthesize single-phase hydroxyapatite by planetary ball-milling from $\text{Ca}_2\text{P}_2\text{O}_7$ and CaCO_3 starting materials with additions of an adequate amount of distilled water.
2. To investigate the optimum milling duration and optimum calcination temperature to form a single-phase hydroxyapatite.
3. To study the effect of using different interval of milling and pause during the milling cycle.
4. To identify the significance of actual milling duration as compared to the milling cycle duration.

1.4 Research Scope

In general, the research is divided into two parts which using a low speed milling (0-100 rpm) and a high speed milling (>100 rpm). The first part is using a low-speed ball-milling method for a preliminary study to determine whether the chosen starting materials ($\text{Ca}_2\text{P}_2\text{O}_7$ and CaCO_3) can be used to synthesis hydroxyapatite according form the study of Rhee (2002). A milling-mixer and a roll mill were used for this study and the results were compared. The investigation involved the characterization of the starting materials and the determination of the phase(s) produced before and after calcination. The characterizations of mixtures were carried out by XRD (x-ray diffraction) analysis and particle size analysis.

The second and major part of the study involves the application of mechanical activation using a high-speed planetary ball milling to produce hydroxyapatite. By using the same starting materials, the mixtures were milled at 8, 16 and 60 hours, and subsequently calcined. TG/DSC was used to study the thermal events and estimate the calcination temperatures required by the mixtures. Particle size analysis was also carried out to determine the changes in particle size after different milling durations.

The study is focused on the effect of milling duration and calcination temperature to determine the optimum conditions for the formation of hydroxyapatite. XRD was used to determine the phases formed. Other analyses used to characterize the samples were XRF (x-ray fluorescence) to determine the chemical elements present and FT-IR (Fourier transform infra-red) spectroscopy to observe the development of functional groups. Subsequently, the effect of using different milling cycles on the temperature of single-phase HA formation was also investigated. Finally, the effect of the actual total milling duration on the changes that take place in the samples was evaluated and placed into perspective in determining the most significant factor during mechanical activation.

CHAPTER TWO

LITERATURE SURVEY

2.1 Introduction

In the early 1970s, biomaterials began to be used in certain implant applications (Cao & Hench, 1996) and since then, the development and applications of biomaterials have been continuously expanded. The most rapidly developing component of the biomaterials field is the use of various types of biomaterial which can substantially expand the surgeon's ability to restore many impaired functions of an organ (Dubok, 2000).

The use of hydroxyapatite (HA) as a biomaterial has received particular attention due to its chemical composition which is similar to that of the mineral constituent of bone. The bioactive properties of HA allow the formation of tissue and bone on and around the material which encourages better fixation of implants (Chen et al., 2002). Therefore, research works are continuously being carried out to understand the HA material and the possibilities of wider usage of HA as an implant in the human body.

This review starts with an overview of the bone structure and the development of bone graft as the main bone substitute material. Then the biomaterial concept will be described in more detail starting with definitions and examples. As HA is the most studied calcium phosphate material, the properties of HA have been presented thoroughly. This is followed by a review into the types of processing methods to produce HA together with their respective advantages and limitations. Some examples from recent literature were also reviewed to amplify the diversity of processing methods beginning from the starting materials up to the final product.

2.2 Bone Structure

Bone is a natural composite material, which by weight contains about 60% mineral, 30% matrix and 10% water. Bone is also a living tissue, with about 15% of its weight being due to a cellular content. The bone mineral has commonly been referred to as a perfectly stoichiometric compound calcium hydroxyapatite $[\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]$. However, the bone mineral is not simply a hydroxyapatite ceramic, and it should be named as a biological calcium–deficient carbonate apatite (Mickiewicz, 2001).

The apatitic mineral in bone is closely associated with the collagen fibers and is made up of long, flat, plate–like nanocrystals that are approximately 40 nm long, 10 nm wide and 1–3 nm thick. This mineral component gives rise to the compressive strength of bone. In the body, bone serves a number of functions:

- a) providing the cells in the marrow that differentiate into blood cells
- b) acting as a calcium reservoir
- c) provide mechanical support for soft tissues
- d) as an anchor for the muscles that generate motion (Mickiewicz, 2001).

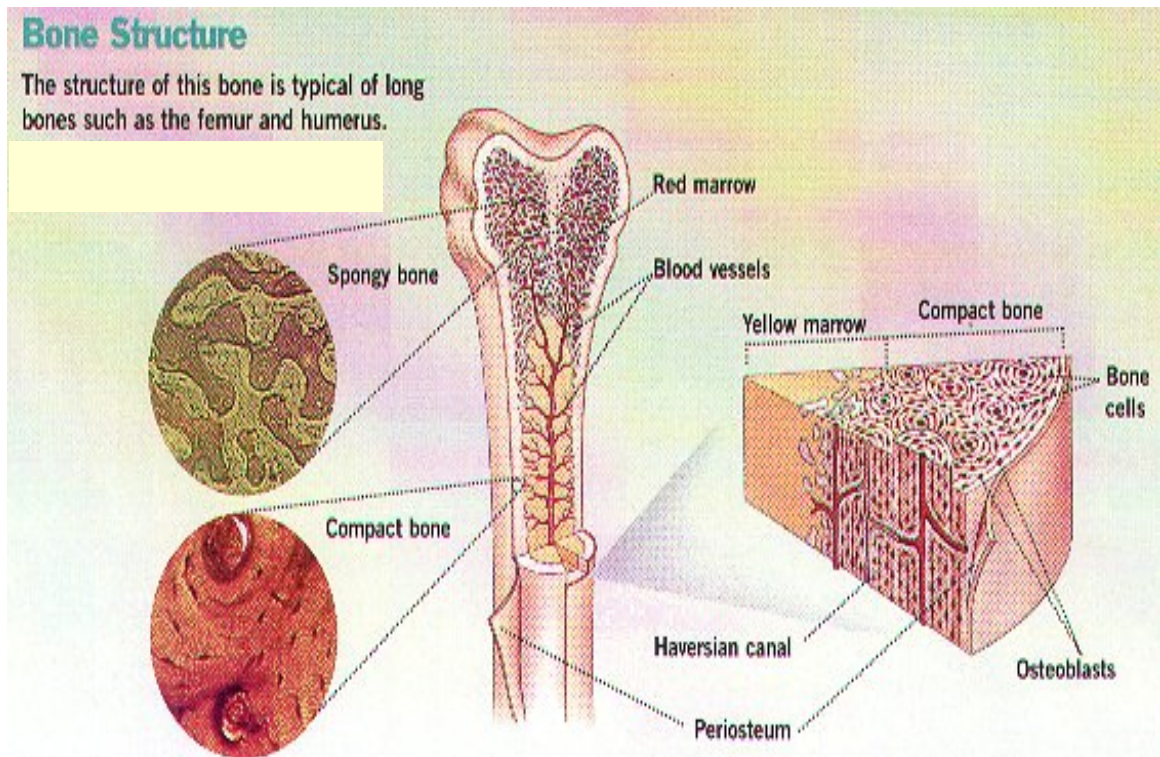


Figure 2.1: Bone structure (Johnson, 2006)

There are two types of bone as shown in Figure 2.1, viz compact or cortical bone and cancellous or trabecular bone (also known as spongy bone). Compact bone is very dense, consisting of parallel cylindrical units and is found in the shafts of long bones. Meanwhile, the trabecular bone is less dense and is made up of an array of rods and struts that form an open cell foam, the pores of which are filled in by marrow. This type of bone is found at the ends of the long bones and inside the smaller bones (Mickiewicz, 2001)

2.3 Bone Graft

Nowadays, bone fracture and damage are serious health problems in clinical cases. Bone repair or regeneration becomes a common and complicated problem in orthopaedic surgery (Murugan & Ramakrishna, 2004).

A bone substitute can be defined as an implanted or transplanted tissue from another part of the body or from another person, to serve as a replacement. The purpose of bone substitutes are:

- a) to provide linkage or splintage as well as to promote osteogenesis (e.g. filling bony cavities or defects and replacing crushed bones)
- b) as scaffolding upon which new bone is laid upon
- c) it can be used on repairing the bone destructive complications (Agale, 1999).

Common traditional bone substitution materials are autografts, allografts and xenografts (Tadic & Beckmann, 2004). Autografts are bone grafts whereby the bone is removed and transplanted within the same individual (from one site to another). The drawback is that the acquisition of these bone transplants are achieved with certain impact to the patient including additional surgical incisions, increased operating time, increased post-operative morbidity, weakened bone donor sites and potential complications such as infection (Agale, 1999).

Bone grafts whereby the bone is transferred from one individual to another of the same species are called allografts. The donor may be alive or deceased but the disadvantage of this grafting technique is that the donor to host transfer is not immunologically acceptable. The possibility of transmitting viruses or bacteria may limit the use of allografts. Xenografts are bone grafts whereby the bone is transferred from other mammalian species. These grafts tend to be less effective than allografts despite antigenicity treatment. Antigenicity means the ability of a substance to trigger an immune response in a particular organism. Generally, the graft must be impregnated with the host marrow. However, it elicits an acute antigenic response with a high failure rate (Agale, 1999).

As an alternative, synthetic biomaterials or called bone graft substitutes have been developed and clinically tested. Bone graft substitutes are commercially produced synthetic products that mimic the human bone. They are safe and proven alternative to autograft (a person's own bone) and allograft (bone from another person). They provide a suitable environment for the body to repair or produce its own bone, either replacing the bone graft substitute over time with original bone, or combining with the bone graft substitute to form a strong repaired bone. Bone graft substitutes can be manufactured to provide distinct advantages over human bone, such as:

- a) 100% free from all risk of possible human infective agents.
- b) Stronger than the human bone, allowing faster mobilisation and shorter hospitalisation following surgery.
- c) Reliable availability, ensuring enough bone is available for any surgical operation.
- d) Reliable quality.
- e) More predictable response in the human body in terms of new bone growth.

Calcium phosphate – based bone substitute material should ideally be implanted with a design in consideration that the osteoclastic resorption will be able to slowly and gradually degrade the implanted material. If a material is not resorbed by the osteoclasts, such as crystalline alumina (mostly used as caps on metallic implants used in hip arthroplasty) or zirconia, then such bioinert materials may not be used as a successful bone substitute bioceramic. Some of these materials implanted into bone defects are often encapsulated by a fibrous tissue and do not adhere to bone due to lack of bioactivity, and thus is isolated from the surrounding bone and remains as a foreign body. To overcome the above intricacy, bioactive materials, e.g. hydroxyapatite has been proposed as a substitute for defective bones or teeth. It is known to be biocompatible and bioactive, i.e.

ability to form a direct chemical bond with the surrounding tissues, osteoconductive, non-toxic, non-inflammatory and non-immunogenic agent (Murugan & Ramakrishna., 2004)

2.4 Biomaterial

A biomaterial can be defined as “a material intended to interface with the biological systems to evaluate, treat, augment or replace any tissue, organ or function of the body” (Williams, 1992). Biomaterials available presently include three basic types: bioactive materials which form direct chemical bonds with the bone or even with the soft tissue of a living organism; various bioresorbable materials which are actively included in the metabolic processes of an organism with predictable results, and bioinert high strength materials (Dubok, 2000).

The concept of bioactivity is defined as: “A bioactive material is one 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” (Cao & Hench, 1996). It is an intermediate between resorbable and bioinert materials. A bioactive material creates an environment compatible with osteogenesis (bone growth), with the mineralizing interface developing as a natural bonding junction between living and non – living materials. This concept has now been expanded to include a large number of bioactive materials with a wide range of rates of bonding and thickness of interfacial bonding layers (Cao & Hench, 1996).

Bioresorbable materials are designed to degrade gradually over a period of time and be replaced by the natural host tissue. This leads to a very thin interfacial thickness. This is the optimal solution to the biomaterials problem if the requirements of strength and short-term performance can be met. Natural tissues can repair themselves and are gradually replaced throughout life. Thus, bioresorbable materials are based on the same

principles of repair which have evolved over millions of years. Porous or particulate calcium phosphate ceramic materials such as tricalcium phosphate (TCP) are successful resorbable material for hard tissue replacements when low loads are applied to the material (Hench, 2001). No material implanted in an organism is absolutely bioinert because each will stimulate a reaction in the living tissue. Maximum bioinertness is commonly found in the most refractory oxide ceramics which have the strongest chemical bonds, and thus, not attacked by even the various fermentation systems of the organism (Dubok, 2000)

Generally, there are three classes of biomaterials: metals, polymers and ceramics. The main metals in clinical use are titanium and stainless steel. All of them are inert and biocompatible. Metal implants are used for load bearing purposes such as joint prostheses, screws and plates. On the other hand, polymers are easy to mould, cheaper and are even stronger than certain bones. The material is not resorbable which will be an advantage for augmentation surgery. Augmentation is referring to the stage of a disease in which the symptoms go on increasing (Dubok, 2000).

The use of HA as a bioceramic has received particular attention due to its chemical composition which is similar to that of the mineral constituent of bone. The bioactive properties of HA allow the formation of tissue and bone on and around the material and thus encouraging better fixation of implants (Liu et al., 2002). Therefore, research is continuously been pursued to understand the behaviour of HA in body environment.

2.5 Hydroxyapatite

Hydroxyapatite (HA) with the chemical formula $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ has been extensively used in medicine for implant purposes owing to its similarity with the mineral constituents found in hard tissue (teeth and bones). Because of its high level of biocompatibility, it is commonly the material of choice for fabrication of dense and porous bioceramics (Riman & Suchanek, 2002).

It is well known that HA crystallites in different parts of a living body have different morphological characteristics, depending on their specific function (Vandiver & Dean, 2005). HA has favourable osteo-conductive and bio-active properties which promote rapid bone formation and strong biological fixation to bony tissue (Zdujic et al., 1999). HA also has the ability to absorb organic chemical. HA is a well-studied system that is normally found to be associated with different phosphates produced during certain synthesis conditions. The grade of the biological and chemical stability of these systems is closely associated with the amount and ratio of these different phases. For example, systems containing large amount of phosphate phase are very bioactive, but can dissolve easily in body fluids (Rodriguez-Clemente & Lopez-Macipe, 1998).

Nowadays, the use of HA as a filler in synthetic composites are meant for bone augmentation and restoration which are almost a standard technology. An increasing number of new HA containing biocompatible systems is reported every year (Liu et al., 1997). Table 2.1 showed the physico-chemical properties of synthetic HA.

Table 2.1: Physico – chemical properties of synthetic hydroxyapatite (Yoshimura & Suda, 1994)

Properties	Values
Theoretical Formula	$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$
Space Group	Hexagonal Monoclinic
Lattice Parameters	$a = 9.41 - 9.44 \text{ \AA}$ $c = 6.84 - 6.94 \text{ \AA}$
Theoretical Density	3.16 g/cm^3
Moh's Hardness	5
Heat Capacity	$184.07 \text{ cal/Kmol at } 298.16\text{K}$
Thermal Expansion Coefficient	$11 - 14 \times 10^{-6} \text{ K}^{-1}$
Melting Point	$1614 \text{ }^\circ\text{C}$
Surface Energy	$S(001) = 95 \pm 25 \text{ MPa}$ $S(100) = 480 \pm 30 \text{ MPa}$
Stiffness Coefficient at R.T. (Mbars)	$C_{11} = 1.434, C_{33} = 1.805$ $C_{44} = 0.415, C_{12} = 0.445$ $C_{13} = 0.575, C_{66} = 0.495$
Dielectric Constant	$7.40 - 10.47$
Optical Frequency	$2.71 (\parallel c)$ $2.69 (\perp c)$

Although pure HA ceramics have excellent biocompatibility, their mechanical strengths are insufficient. One of the most effective methods to improve the mechanical properties of HA is to fabricate them into composites. This fabrication requires the preparation of homogenously dispersed powder mixtures, followed by sintering (Yoshimura & Suda, 1994). In fabrication process, a fine powder phase with a minimized degree of particle agglomeration is needed as the starting material in order to achieve a dense and uniform microstructure (Xue et al., 1999). The fine particles will cause a larger contact area of the particles and stronger bodies can be fabricated (Deng et al., 1994).

Figure 2.2 shows an electron microscopy of fine particles of HA. The production of submicron monolithic HA powders is actively being investigated as they exhibit greater surface area. Indeed, nanometer - sized HA is also expected to have a better bioactivity than coarser crystals. This in turn would provide improved sinterability and enhanced densification (Muralithran & Ramesh, 2002).

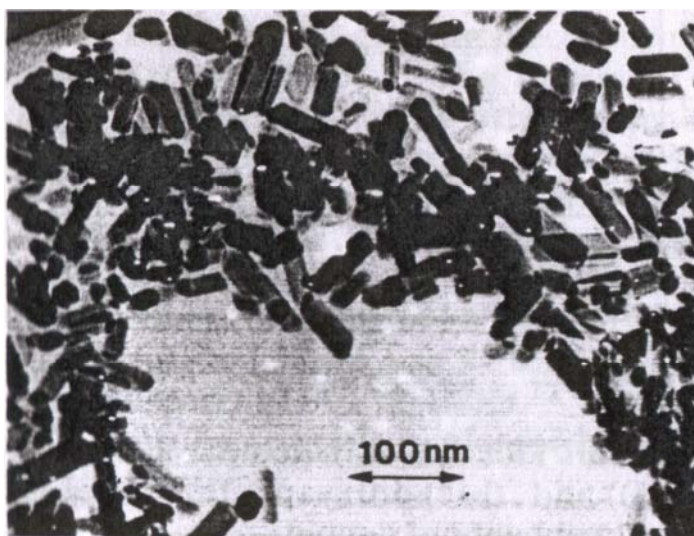


Figure 2.2: Fine crystals of HA (Yoshimura & Suda, 1994)

2.6 Synthesis of Hydroxyapatite Powders

Most of the ceramic processing methods need precise controls for the preparation of HA. Thus, the compositions and properties of the final products are strongly influenced by the various parameters such as nature of the starting materials used, pH of the solutions, reaction times and temperatures (Kim et al., 2000). Preparative methods for HA are largely divided into three classes. First is the wet chemical method (precipitation and hydrolysis) at relatively low temperatures, second is the hydrothermal method using high temperature-high pressure aqueous solutions and the third is the conventional solid-state reaction methods (wet and dry process) (Yoshimura & Suda, 1994).

2.6.1 Wet Chemical Method

The wet method utilizes either precipitation from mixed aqueous solutions or the hydrolysis of calcium phosphates. Many experiments on the preparation of HA by this method have been reported in order to investigate the formation mechanism of calcium phosphates in vitro and in vivo (Yoshimura & Suda, 1994). HA is usually prepared by precipitation under the very basic conditions and sintering the precipitate at 950° to 1100° C (LeGeros, 1994). However, the powders prepared by this method usually are poorly crystallized, inhomogeneous in composition and irregularly formed. HA powders produced by the wet process also possess a high surface area and fine particle size. However they are non-stoichiometric (Ca-deficient) and are of low crystallinity (Yoshimura & Suda, 1994).

2.6.2 Hydrothermal Method

Another method to produce hydroxyapatite is by a hydrothermal. The hydrothermal method involves reactions in an aqueous environment, conducted at relatively high temperatures and pressures with respect to the ambient conditions. The hydrothermal fluid environment is thus created in a pressurized and heated sealed system where the reactants are housed. The temperature and pressure can vary in the range of 80° to 400°C (in some cases even higher) and small autogeneous pressures of up to 100 MPa or more, respectively (Ganguli & Chatterjee, 1997).

Liu et al. (1997) had produced a well-crystallized HA powder by using hydrothermal treatment at 109 °C in a pressurized pot for 3 hours. However, all samples had a Ca/P molar ratio of 1.64-1.643 which were slightly calcium – deficient than the stoichiometric HA. This calcium – deficient HA could transform into other phases such as TCP which later could weaken the strength of dense specimens.

2.6.3 Solid-State Reaction

Mechanical alloying and mechanical milling have been the most popular methods for producing powders in the solid state (Suryanarayana, 2004). A characteristic feature of all solid-state reactions is that they involve the formation of product phases at the interfaces of the reactants. The solid-state reactions initiated by intensive milling in high-energy ball mills could be a good choice for ceramic powder preparation. An important criterion for intensive milling is the mechanical activation of highly dispersed materials or the formation of new product because of a solid-state reaction (mechanochemical reaction) (Stojanovic, 2003).

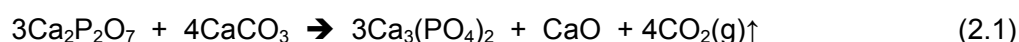
A solid-state reaction which is usually a dry process has generally been used for the processing of ceramic powders and for studying phase stabilities. The powders prepared by this method however, usually have irregular forms with a large grain size and often exhibit heterogeneity in composition due to incomplete reaction resulting from small diffusion coefficients of ions within solids (Yoshimura & Suda, 1994).

Meanwhile, a wet process which had been widely adopted provide finer, more homogeneous and more reactive powders. The advantages of the wet processes are that the by-product is almost water and the probability of contamination during processing is very low. Wet milling has the advantage of producing finer particles than dry milling and is also known for greater utilization of the energy which is linked with the economics of the operation (Ganguli & Chatterjee, 1997).

Intensive milling increases the area of contact between the reactant powder particles due to reduction in particle size and allows fresh surfaces to come into contact. This allows the reduction to proceed without the necessity for diffusion through the product

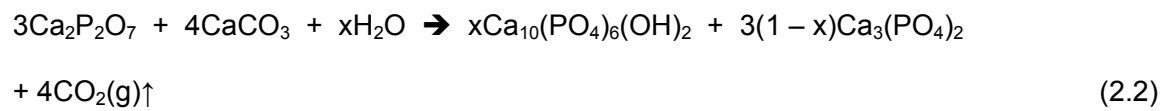
layer. As a consequence, the solid-state reactions that normally require high temperatures will occur at a lower temperature during calcination. Alternatively, the particle refinement and consequent reduction in diffusion distances (due to microstructural refinement) can at least reduce the reaction temperatures significantly, even if they do not occur at room temperature. Further, mechanical treatment of ceramic powders can reduce particle size and enable obtainment of nanostructured powders (Suryanarayana, 2004).

The calcium and phosphorus normally used as the starting materials in the solid state process are dicalcium phosphate anhydrous, dicalcium phosphate dihydrate, monocalcium phosphate monohydrate, calcium pyrophosphate, calcium carbonate, calcium oxide and calcium hydroxide. Rhee (2002) did a simple process to prepare pure hydroxyapatite powders from calcium pyrophosphate ($\text{Ca}_2\text{P}_2\text{O}_7$) and calcium carbonate (CaCO_3) starting materials via a mechanical activation process and subsequent heat treatment. The experiment was carried out using a conventional ball-milling method and then heat-treated at 1100 °C to form a single-phase of HA. If there is no water during heat-treatment, the HA would transform to tricalcium phosphate and calcium oxide, in accordance to equation (2.1) (Rhee, 2002).

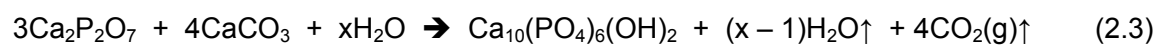


However, if there is x mole of water during heat-treatment, the products of the reaction will be as in equations (2.2) and (2.3) depending on the amount of water.

(a) when $x < 1$ mole



(b) when $x \geq 1$ mole



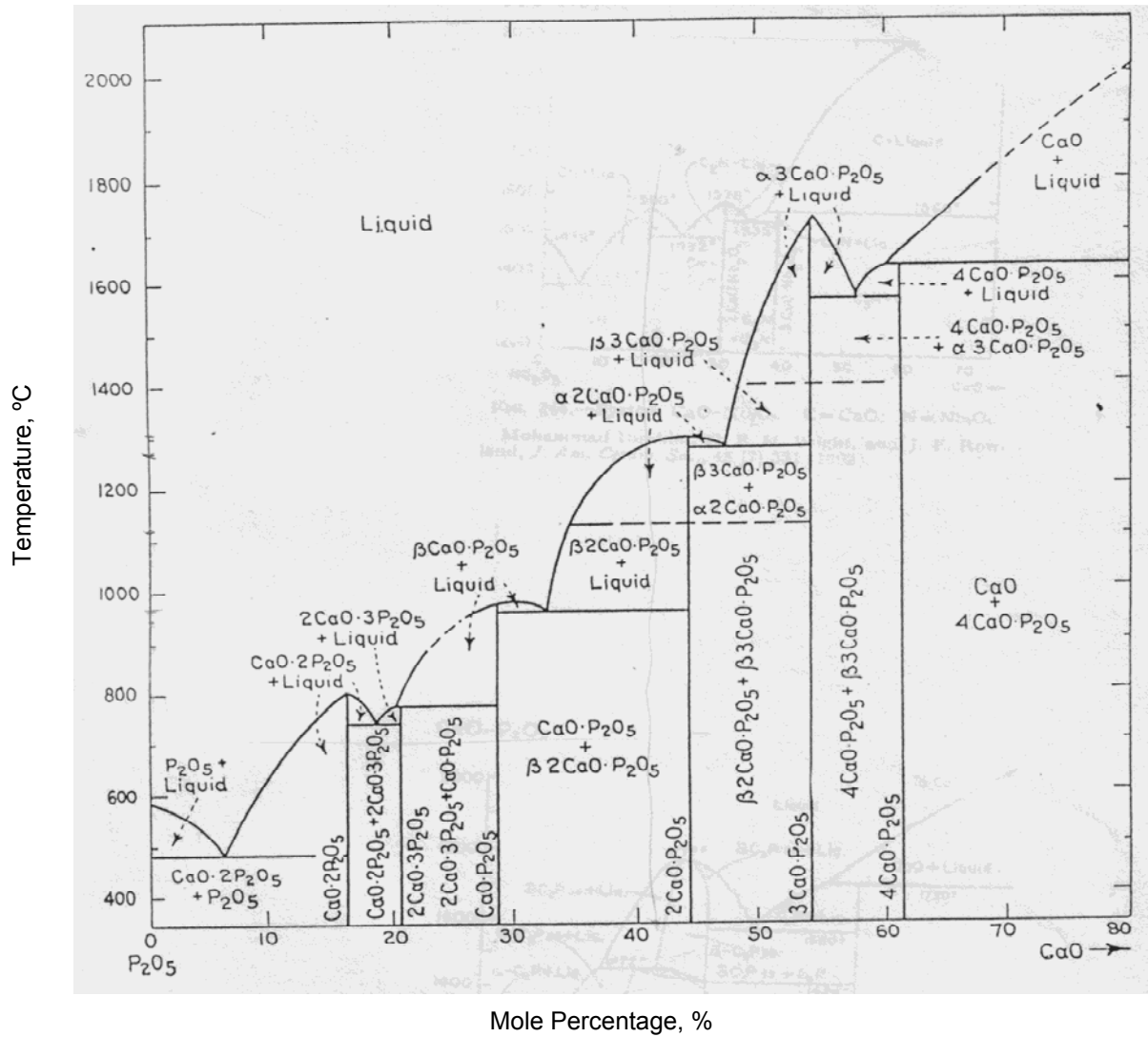
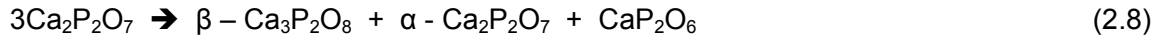
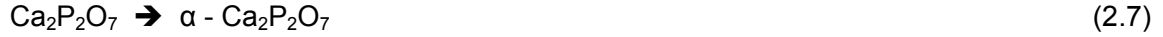


Figure 2.3: Portion of the binary system CaO-P₂O₅ (Knepper et al., 1997)

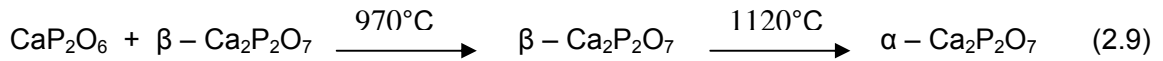
According to Figure 2.5, the possible transformations of a 100 % pure Ca₂P₂O₇ at a temperature of 970 °C can be postulated as below:



Meanwhile at a temperature of 1120 °C, pure $\text{Ca}_2\text{P}_2\text{O}_7$ tends to change into other phases such as:



The stoichiometric ratio for the mixture of $\text{CaO-P}_2\text{O}_5$ to produce hydroxyapatite is in the portion of 42.9 % for P_2O_5 . From Figure 2.5, the changes of the phases can be summarized as below:



Another mechanical activation method was reported by Yeong et al. (2001) which was carried out in a high-energy shaker mill for various time periods which led to the formation and growth of HA nanocrystallites as a result of mechanochemical reaction. Meanwhile, Silva et al. (2004) also used a mechanical activation method in the preparation of HA using a high-speed planetary ball-mill for 60 hours milling (stainless steel as the milling medium) to produce single phase HA. However, the purity of HA was not determined from this lengthy milling period because one of the starting material CaHPO_4 was still present in the XRD results.

On the other hand, calcination processes at high temperatures which are necessary to improve the crystallinity may lower the mechanical properties of the powders (Yoshimura & Suda, 1994). improved sinterability to reduce sintering temperature, could improve the fracture toughness of the HA ceramic (Silva et al., 2004)

2.7 Milling

Comminution is frequently described in the technical literature as milling, grinding and size reduction. All these terms are used interchangeably for a process in which small particles are produced by reducing the size of large ones. In this study, the term milling is commonly used. A wet milling technique produces particles that are finer than a few micrometers. Meanwhile, final powders of dry milling still have agglomerated size distributions of the order of a few microns (Malghan, 1991).

Actual differences between wet and dry comminution are often very large. For example, the power to drive a wet ball mill is as much as 30% less than that required by a dry mill. This difference in energy requirements can be substantially decreased by an appropriate choice of equipment and operating conditions. Another important difference is that wet milling allows the introduction of surfactants, sintering aids, binders and other additives, and results in a better mixing than in dry milling. In dry milling, air or an inert gas is used to keep the particles in suspension. The tendency of fine particles to agglomerate in response to van der Waals attractive forces limits the capabilities of the dry process. As a consequence of being able to control the reagglomeration tendency of fine particles in wet milling, it is used for milling to submicrometer-sized particles (Malghan, 1991).

Milling is an essential step in almost all conventional powder preparation processes because it achieves these important objectives: (Malghan, 1991)

- Deagglomerates by separating particles from clusters
- Decreases the size of powder to eliminate unwanted coarse particles above a certain size

- Increases specific surface area by producing a large quantity of very fine size particles
- Provides surface activation without causing large-scale size reduction
- Homogenizes powder-solvent mixtures
- Facilitate surface chemical and bulk chemical reactions

There are instances in which the goal of milling is just to thoroughly mix the constituents. In many structural ceramic applications for instance, size reduction of raw material powders may not be required. Milling process sometimes cannot be utilized for a single purpose. This is because mixing, surface area, particle size distribution and chemistry are generally interrelated (Malghan, 1991).

2.7.1 Milling Process

Milling is a complex process in which several simultaneous and interrelated physical and chemical processes can occur. No single mechanism can explain the influence of all types of starting materials. The energy provided to the milling process is distributed among different subprocesses within a mill which involve:

- Increased surface energy of powder
- Plastic deformation of the particles
- Elastic deformation of the particles
- Lattice rearrangements (gliding, slipping, twinning) within a particle

The size reduction that occurs in a mill is based on a combination of the following mechanisms: impact with media, abrasion with media and attrition with particles and media. An understanding of the subprocesses, mechanisms and their impact on particle breakage is important to the development of a size reduction knowledge base. These sub-processes are affected by the fluid medium in the mill. Water is the most commonly used liquid, although alcohols or other organics are also sometimes used (Malghan, 1991).

Particle breakage is considered to be the elementary process of milling. Particles are stressed by contact forces that deform and cause stress fields that produce cracks when the stress is large enough. The number of cracks and their directions determine the size and shape of fragments. Crystalline materials tend to exhibit mechanical properties that arise in part, from their crystal structure and associated parameters such as crystallite size and the arrangement of the crystallites within the macro crystal or powder particle (Malghan, 1991). Theoretically, in the size reduction of homogeneous material, the applied stress will be uniform throughout the particle if the crystal lattice were to be perfect (Tkacova, 1989). Therefore, when the stress reaches a level equal to that required for failure, the crystal structure breaks down to produce particles of the same order of size as the primary crystallites. The fracture of a particle involves the propagation of cracks that are either already present or initiated in the particle (Malghan, 1991).

In an ideal size reduction process, the particles from a homogeneous material would be of the same strength, regardless of size. Since no crystal is perfect in a real material because of defects, its behaviour is expected to be nonideal. In practice, two phenomena are observed: