

Head Start:
Graduate Level Resources
in Materials Engineering

Issue 1: Ceramics for Medical Applications

Tanya J. Levingstone

March 2008

Series Editor: Lisa Looney

Publishers:

Dublin City University,
Dublin 9,
Ireland

ISBN 1-87232-752-4

ISSN 1649-8232

Printed in Ireland by Snap Printing

© Dublin City University 2008

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior permission of the publishers.

Head Start: Graduate Level Resources in Materials Engineering

This serial publication includes technology and science topics relevant to research in materials engineering. It is intended to supplement discipline specific undergraduate education and also provide detailed information on specific processing systems.

Forward

Issue 1: Ceramics for Medical Applications, March 2008.

Graduate level research has traditionally involved an initial period of intensive reading. Obvious resources include peer reviewed papers, conference papers and theses. However, for most students considerable time is also spent on technical descriptions of equipment and procedures, and on reading textbooks on relevant topics not covered by their own undergraduate training. The latter can be particularly pertinent to engineers working on a cross discipline project extensively involving materials chemistry or biological systems. While there is no doubt as to the value of a broad understanding of the context of a project, nor the need to understand relevant equipment, chemical processes and biological systems, this information is not generally at research level.

Nonetheless it can be a very time consuming exercise to come 'up to speed'. Add to this the wealth of research being made accessible through electronic databases, and the rapidly growing volume of research being published, and the initial phase of reading oneself into a project can be very daunting.

Having observed many graduate students of the Materials Processing Research Centre at Dublin City University struggle through this process, I noted that we were not building effectively on this type of understanding gained by each student. There has also been confusion as to what is appropriately included in theses, with examiners taking different views on the amount of content to be dedicated to explaining concepts, terminology and systems from the complementary discipline.

From these observations came the idea of a series of publications dedicated to giving graduate students a 'head start'. These are written by graduate students, largely based on their reading of text books in science and engineering disciplines relevant to their project. Where it is appropriate, students have collaborated on a theme. It is intended that the texts consolidate existing MPRC background knowledge on a topic, thus providing a 'fast track' for new researchers to start on their own work on a related project. It is intended they be an open ended serial, with new students and all MPRC members being welcome to submit new titles.

Lisa Looney
Series Editor

Director, Materials Processing Research Centre.
Dublin City University
Ireland

ACKNOWLEDGEMENTS

The author, editor and publisher are grateful to the following for permission to reproduce their copyright material:

Prof. Keith Rogers, Cranfield University (Figure 3.1: hydroxyapatite unit cell)

Elsevier & C.S. Elliot (Figure 3.2: Solubility isotherms of various calcium phosphate phases)

World Scientific Publishing Co, Larry L. Hench, and June Wilson, eds. (Figure 3.3: Phase diagram of the system $\text{CaO-P}_2\text{O}_5$ at high temperature. No water present, Figure 3.4: Phase diagram of the system $\text{CaO-P}_2\text{O}_5$ at high temperature; at a partial water pressure of 500mmHg, and Figure 3.5: Influence of ambient water vapour pressure on phase composition)

The author is grateful for useful discussion with Dr. Tim Prescott during draft stages of this publication. The editorial assistance provided by Dr. Samsun Naher is also acknowledged.

The author would also like to acknowledge the research support provided by the Irish Research Council for Science, Engineering and Technology, funded by the National Development Plan.

CONTENTS

1	BIOMATERIALS.....	1
1.1	INTRODUCTION	1
1.2	PROPERTIES OF BIOMATERIALS	1
1.3	TYPES OF BIOMATERIALS	1
1.3.1	<i>Metals</i>	1
1.3.2	<i>Polymers</i>	3
1.3.3	<i>Ceramics</i>	3
1.3.4	<i>Composites</i>	4
2	BIOCERAMICS	5
2.1	INTRODUCTION	5
2.2	CLASSIFICATION OF BIOCERAMICS	5
2.2.1	<i>Virtually Inert Ceramics</i>	5
2.2.2	<i>Bioactive Ceramics</i>	6
2.2.3	<i>Resorbable Bioceramics</i>	6
2.3	COMPOSITIONAL CLASSIFICATION OF BIOCERAMICS	7
2.3.1	<i>Oxide Ceramics</i>	7
2.3.2	<i>Carbons</i>	8
2.3.3	<i>Glasses</i>	8
2.3.4	<i>Calcium Phosphate Ceramics</i>	9
3	HYDROXYAPATITE.....	11
3.1	INTRODUCTION	11
3.2	CHEMICAL STRUCTURE	11
3.3	SUBSTITUTIONS	12
3.4	BIOLOGICAL CALCIUM PHOSPHATE.....	14
3.5	BIOCOMPATIBILITY	15
3.6	DISSOLUTION PROPERTIES	15
3.7	THERMAL BEHAVIOUR	17
3.7.1	<i>Introduction</i>	17
3.7.2	<i>Processes Involved in the Thermal Decomposition of HA</i>	17
3.7.3	<i>Effect of Crystal Structure and Atmospheric Conditions</i>	20
3.8	MECHANICAL PROPERTIES.....	22
4	PRODUCTION OF HYDROXYAPATITE POWDERS	24
4.1	INTRODUCTION	24
4.2	WET CHEMICAL METHODS	24
4.2.1	<i>Hydrolysis</i>	24

4.2.2	<i>Precipitation</i>	25
4.3	SOLID STATE REACTIONS METHODS	26
4.4	HYDROTHERMAL METHOD	26
4.5	OTHER PROCESSES	27
4.5.1	<i>The Melt Growth Method</i>	27
4.5.2	<i>The Flux Growth Method</i>	27
4.5.3	<i>Sol-Gel Method</i>	27
4.6	POWDER PROCESSING	28
4.6.1	<i>Atomization</i>	29
4.6.2	<i>Agglomeration</i>	29
5	CALCIUM PHOSPHATE COATINGS	31
5.1	INTRODUCTION	31
5.2	COATING APPLICATION METHODS.....	31
5.2.1	<i>Physical Vapour Deposition (PVD)</i>	31
5.2.2	<i>Chemical Vapour Deposition (CVD)</i>	31
5.2.3	<i>Electrophoretic Deposition (EPD)</i>	32
5.2.4	<i>Biomimetic Coatings</i>	32
5.2.5	<i>Sol-gel Coatings</i>	32
5.2.6	<i>Thermal Spraying</i>	32
5.3	PLASMA SPRAYING	33
5.4	COATING PROPERTIES.....	34
5.4.1	<i>Chemical Composition</i>	34
5.4.2	<i>Coating Crystallinity</i>	37
5.4.3	<i>Coating Adhesion</i>	37
5.4.4	<i>Coating Microstructure</i>	38
5.4.5	<i>Residual Stress</i>	40
5.4.6	<i>Coating Thickness</i>	40
5.4.7	<i>Coating Strength</i>	40
6	REFERENCES	42

Figures

FIGURE 3.1: HYDROXYAPATITE UNIT CELL [25]	12
FIGURE 3.2: SOLUBILITY ISOTHERMS OF VARIOUS CALCIUM PHOSPHATE PHASES [39].....	16
FIGURE 3.3: PHASE DIAGRAM OF THE SYSTEM $\text{CaO-P}_2\text{O}_5$ AT HIGH TEMPERATURE. NO WATER PRESENT [32]	21
FIGURE 3.4: PHASE DIAGRAM OF THE SYSTEM $\text{CaO-P}_2\text{O}_5$ AT HIGH TEMPERATURE; AT A PARTIAL WATER PRESSURE OF 500MMHG [32]	21
FIGURE 3.5: INFLUENCE OF AMBIENT WATER VAPOUR PRESSURE ON PHASE COMPOSITION [32].....	22
FIGURE 5.1: ATMOSPHERIC PLASMA SPRAYING.....	34
FIGURE 5.2: XRD PATTERN FOR HA	36
FIGURE 5.3: SEM MICROGRAPH OF THE MICROSTRUCTURE OF A PLASMA SPRAYED HYDROXYAPATITE COATING.....	39

Tables

TABLE 1.1: SOME BIO-METALLIC MATERIALS AND THEIR APPLICATIONS [1, 2]	2
TABLE 1.2: MECHANICAL PROPERTIES OF METALS USED FOR IMPLANTS [2]	2
TABLE 1.3: SOME POLYMERS AND THEIR APPLICATIONS ADAPTED FROM [1]	3
TABLE 1.4: SOME BIOCERAMICS AND THEIR APPLICATIONS ADAPTED FROM [1]	4
TABLE 1.5: SOME BIOCOMPOSITES AND THEIR APPLICATIONS	4
TABLE 2.1: CLASSIFICATION OF BIOCERAMICS [8, 9]	6
TABLE 2.2: SOME CALCIUM PHOSPHATE COMPOUNDS [13, 18]	9
TABLE 3.1: POSSIBLE SUBSTITUTIONS IN THE APATITE STRUCTURE	13
TABLE 3.2: COMPARISON OF BONE AND HYDROXYAPATITE CERAMICS ADAPTED FROM [9]	14
TABLE 3.3: THERMAL EFFECTS ON HYDROXYAPATITE	19
TABLE 3.4: MECHANICAL PROPERTIES OF HA AND BONE ADAPTED FROM [2]	22
TABLE 5.1: ADVANTAGES AND DISADVANTAGES OF SOME COATING TECHNIQUES	33
TABLE 5.2: MAXIMUM ALLOWABLE LIMITS FOR TRACE ELEMENTS [82]	35
TABLE 5.3: J.C.P.D.S. STANDARDS FOR CALCIUM PHOSPHATE MATERIALS	36

1 Biomaterials

1.1 Introduction

There are numerous materials that have been identified as being safe for use within the human body. These materials are termed biomaterials. Biomaterials have been defined as 'any material that is used to replace or restore function to a body tissue and is continuously or intermittently in contact with body fluids' [1]. They include metals, polymers, ceramics and also composite materials.

1.2 Properties of Biomaterials

There are a number of important properties that a material must have in order for it to be suitable for use in the body. It should have a biocompatible chemical composition that does not induce adverse tissue reaction. This means that it should be non-toxic, non-carcinogenic, non-allergic and non-inflammatory. It must also be bio-functional, with sufficient strength and wear resistance to withstand the environment in which it is placed. Depending on the application for which it is used, it may also need to be able to stable over long periods, have specific degradation rates or encourage bone ingrowth.

1.3 Types of Biomaterials

1.3.1 Metals

Metals are used for a wide range of medical applications. These include orthopaedic implants, implants, plates and screws for oral and maxillofacial surgery, components for devices used in cardiovascular surgery, e.g. pacemakers, valve replacements and stents [1]. Surgical and dental instruments are also made from metallic materials. Due to the requirements for biocompatibility, relatively few metals are suitable for medical applications. Those most widely used for structural applications are titanium, titanium alloys, cobalt-base alloys and various grades of stainless steel. Metals used for other applications include commercially pure titanium, shape memory alloys (based on the nickel-titanium binary system), zirconium alloys, tantalum, niobium and precious metals, such as silver. Some examples of the metals used for various applications are given in *table 1.1*. The mechanical properties of various metals used for medical applications are given in *table 1.2*.

Table 1.1: Some bio-metallic materials and their applications [1, 2]

<i>Application</i>	<i>Metal</i>
Joint prostheses	316L stainless steel, cobalt-base alloys, titanium and titanium alloys
Bone screws and pins	Austenitic stainless steel, 316L stainless steel, titanium alloys
Angioplasty	Shape-memory alloys e.g. nickel titanium alloys and copper-base alloys
Pacemaker cases	Commercially pure titanium alloy
Pacemaker electrodes	304, 316 and 316L stainless steel, cobalt alloys, tungsten bronzes, zirconium, tungsten, tantalum and titanium.
Medical staples	304, 316 and 316L stainless steel, nickel titanium alloys
Vascular stents	Nickel titanium alloys
Dental implants	Titanium and titanium alloys
Dental crowns and bridges	Porcelain-fused to metal (PFM) type: gold alloys, palladium alloys, nickel alloys, cobalt-chromium alloys, titanium and titanium alloys

Table 1.2: Mechanical properties of metals used for implants [2]

<i>Material</i>	<i>Young's Modulus (GPa)</i>	<i>Tensile strength (MPa)</i>	<i>Fracture Toughness (MPam^{1/2})</i>
Cobalt-chromium alloys	210	400-1030	120-160
Stainless steel (316L)	193	515-620	20-95
Ti-6Al-4V	114	900-1172	44-66

1.3.2 Polymers

Polymers are long chain molecules derived from many repeating units called monomers [3]. They are typically classified into three groups, thermoplastics, thermosets and elastomers. Although all three groups are used for medical applications, thermoplastics are most widely used [1]. Some of the polymers most commonly used for medical applications include silicone, nylon, ultra high molecular weight polyethylene, PVC and polyurethane. They are used for a wide range of applications for example replacement joint components, implants, such as facial and breast implants, heart valves, lenses, sutures, cements and adhesives. Some of these applications are detailed below in *table 1.3*.

Table 1.3: Some polymers and their applications (Adapted from [1])

<i>Application</i>	<i>Polymer</i>
Knee, hip, shoulder joints	Ultrahigh molecular weight polyethylene
Finger joints	Silicone
Sutures	Polylactic and polyglycolic acid, nylon
Tracheal tubes	Silicone, acrylic, nylon
Heart pacemaker	Acetal, polyethylene, polyurethane
Blood vessels	Polyester, polytetrafluoroethylene, PVC
Gastrointestinal segments	Nylon, PVC, silicones
Facial prosthesis	Polydimethyl siloxane, polyurethane, PVC
Contact lenses	Hydrogels
Bone cement	Polymethyl methacrylate

1.3.3 Ceramics

Ceramics have been used for a long time in the medical industry. They have mainly been used for dental and orthopaedic applications. This is due to the chemical similarity between the composition of certain ceramic materials and that of tissues such as bone and teeth. Examples of the applications of various bioceramics are given in *table 1.4*. The types of bioceramics that are currently used are discussed further in the following chapters.

Table 1.4: Some bioceramics and their applications (Adapted from [1])

<i>Application</i>	<i>Ceramic</i>
Joint replacements	alumina, zirconia
Artificial tendons and ligaments	poly(lactic acid) (PLA)-carbon-fibre composites
Dental Implants	alumina, hydroxyapatite, surface-active glasses
Coatings for chemical bonding	hydroxyapatite, surface-active glasses
Bone filler	alumina

1.3.4 Composites

A composite material is a physical mixture of two or more distinct constituents [4]. There is no chemical bonding or alloying between the constituents. Composite materials have properties very different to the properties of their constituents. By adjusting the proportions of the constituent materials used, the materials properties of the composite can be tailored for the specific application. In general a composite just consist of two constituents, a matrix phase, which forms the bulk of the material, and a reinforcing phase, which generally provides strength. For some applications bioactive particles, which encourage bone growth, are used as the reinforcing phase. Composite materials are widely used in medical applications. Some examples of composite materials used for various applications are given in *table 1.5*.

Table 1.5: Some biocomposites and their applications

<i>Application</i>	<i>Composite</i>
Dental restoration	BIS-GMA (a resin monomer) reinforced with quartz, barium glass or colloidal fillers
Bone plates	polymer composites e.g. carbon fibre (CF)/epoxy, glass fibre (GF)/epoxy
Vascular grafts	pellathane-type polyurethane matrix with Lycra-type polyurethane fibres
Total hip replacements	CF/ polystyrene (PS), CF/ carbon (C)
Bone grafts	polymers e.g. PLLA, PEG, gelatine, reinforced with bioactive particles

2 Bioceramics

2.1 Introduction

Ceramics are compounds between metallic and non-metallic elements; most frequently oxides, nitrides and carbides [5]. Ceramics tend to have a low energy state, which means that they tend to be stable and may well be considered the most chemically and biologically inert of all materials. The wide range of materials that falls within this classification includes ceramics that are composed of clay materials, cement and glass [6]. Unlike metals and polymers, ceramics are difficult to shear plastically due to the nature of the ionic and covalent bonding holding them together and also the minimum number of slip systems [7].

Ceramics in the form of pottery have been used by humans for thousands of years. In the past properties such as their inherent brittleness, susceptibility to notches or microcracks, low tensile strength and low impact strength has limited their use. However, within the last 100 years, improvements in the techniques used for the fabrication of ceramics have lead to their use as 'high tech' materials [5].

More recently it has been recognised that the characteristic properties of hardness, durability and chemical resistance displayed by ceramics mean that many can withstand the hostile environment within the body. Over the past forty years ceramics have been specifically designed for the repair and reconstruction of diseased and worn out body parts. These ceramics are termed 'bioceramics' [8]. They are now used for many important applications in the body as outlined in *table 1.4*.

2.2 Classification of Bioceramics

No foreign material that is implanted into living tissue can be completely compatible. Any material that is recognized as foreign elicits some form of response from living tissue. Bioceramics can be classified according to the response that they initiate within the body. There are three main classes; virtually inert, bioactive and resorbable bioceramics. Examples of materials that fall into each of these classifications are given in *table 2.1*.

2.2.1 Virtually Inert Ceramics

Virtually inert ceramics have minimal interaction with their surrounding tissue. They therefore maintain their physical and mechanical properties while in the body and are also resistant to corrosion and wear. Examples include aluminium oxides, zirconia ceramics and single phase calcium aluminates. Virtually inert ceramics may be used for structural support, such as bone plates, bone screws and femoral heads, and also non-structural support, such as drug delivery devices and ventilation tubes.

Table 2.1: Classification of Bioceramics [8, 9]

<i>Type of Bioceramic</i>	<i>Interaction with tissue</i>	<i>Type of Attachment</i>	<i>Example</i>
Virtually Inert	Little or no biological response	Mechanical fixation	alumina (Al_2O_3), zirconia oxide (ZrO_2)
Bioactive	Promote a distinct and positive response from tissue	Chemical bonding	hydroxyapatite (HA), bio-active glasses and glass-ceramics
Resorbable	Gradually dissolve within the body	Replaced by tissue	calcium phosphate cements, bio-active glasses and tricalcium phosphate

2.2.2 Bioactive Ceramics

Bioactive ceramics or surface-reactive ceramics undergo chemical reactions at their surface. They thereby allow the formation of a chemical bond between the implant and the tissue. The type of interface that forms mimics the type of interface that is formed when natural tissues repair themselves [8]. Examples of bioactive ceramics include glasses, such as the commercially available glass Bioglass®, and calcium phosphate ceramics such as hydroxyapatite. Bioactive ceramics have many applications including coatings for metal prosthesis, in reconstruction of dental defects, as replacements for middle ear ossicles, as bone plates and screws and for filling spaces vacated by bone screws, donor bone, excised tumours and diseased bone loss.

2.2.3 Resorbable Bioceramics

Resorbable implants gradually dissolve when placed into the body and are replaced by natural tissues. In order for the implant to be successful the dissolution rate must match the repair rates of the body tissue [10]. Dissolution rate depends on the composition and structure of the material. The concept of using synthetic resorbable ceramics as bone substitutes was introduced by Hentrich in 1971 [11]. Examples of bioresorbable materials include porous calcium phosphates, such as tricalcium phosphate, bioglass, zinc-calcium-phosphorous oxide (ZCAP) ceramics, zinc-sulphate-calcium-phosphate (ZSCAP) ceramics, aluminium-calcium-phosphate (ALCAP) ceramics and ferric-calcium-phosphorous-oxide (FECAP) ceramics.

2.3 Compositional Classification of Bioceramics

Bioceramics can be classified according to their compositions. The major groups are oxide ceramics, glasses and calcium phosphate bioceramics.

2.3.1 Oxide Ceramics

The major types of oxide ceramics are alumina (Al_2O_3)-based ceramics and zirconia (ZrO_2)-based ceramics. Other simple oxides that have been investigated for use in biomedical applications include $\text{CaO}.\text{Al}_2\text{O}_3$, $\text{CaO}.\text{TiO}_2$ and $\text{CaO}.\text{ZrO}_2$.

Alumina (Al_2O_3)-based ceramics

Alumina ceramics are reportedly the first bioceramics to be widely used clinically [12]. They have many favourable characteristics including good strength, high wear resistance, good biocompatibility and excellent corrosion resistance. They have good hardness with values ranging from 20 to 30GPa [7]. Both single and polycrystalline alumina have been used clinically. The most stable phase is $\alpha\text{-Al}_2\text{O}_3$. MgO , CaO and Y_2O_3 have been added to alumina in low percentages to control its granular growth, and consequently the densification [13].

Because of its high wear resistance, alumina is currently used for the bearing surfaces in joint replacements. It is also used for other applications, such as porous coatings for femoral stems, porous bone spacers, middle ear implants and for dental implants.

Zirconia-based ceramics

Zirconia-based ceramics have become a popular alternative to alumina as a structural ceramic because of their substantially higher fracture toughness [12]. They have better reliability, a higher flexural strength and a lower Young's modulus than alumina and can also be polished to a superior surface finish. Zirconia-based ceramics also have excellent biocompatibility and, although they are not quite as hard as alumina, they have excellent wear and friction resistance. One disadvantage of these ceramics is the fact that zirconia undergoes a volume change of about 5% during phase changes at high temperature, which can cause fracture. Zirconia is therefore generally stabilized with a dopant, such as yttria (Y_2O_3) or magnesium oxide (MgO), which promotes the formation of a more stable cubic phase [13, 14]. Zirconia-based ceramics produced with the use of a stabiliser is referred to as partially stabilised zirconia [7]. Partially stabilized zirconia is used for the bearing surfaces in joint replacements. Oxidized zirconia has also recently been introduced for this application. Zirconia dental implants have also been produced although they are not widely used.

2.3.2 Carbons

The biocompatibility of carbon has long been recognized. It is available in numerous different forms. These include pyrolytic carbon, crystalline diamond, graphite, noncrystalline glassy carbon and carbon fibres. Some carbons have been found to have excellent thrombo-resistance properties and are used for applications such as artificial heart valves and pacemaker electrodes. The main types used for this application are low temperature isotropic (LTI) pyrolytic carbon, vitreous (glassy) carbon and ultra-low temperature isotropic (ULTI) carbon [9]. The composition, structure and fabrication of these three carbons are similar to those of graphite and other industrial forms produced from pure elemental carbon [1].

Other carbons that are used in the medical industry include diamond-like carbons and carbon fibres. Diamond-like carbons have high hardness, wear resistance, optical transparency, chemical inertness, low friction and good adhesion properties [15]. They have been found to have excellent biocompatibility. Their use as a protective coating for implants, produced using vapour deposited methods, has been investigated. These coatings have produced good results but they are difficult and costly to manufacture.

High strength carbon fibres were developed in the 1950's for the aerospace industry [16]. They have since found application in numerous other areas including the biomedical industry. They have high strength and a high modulus of above 50 million PSI. These fibres can be incorporated into other materials to form a high stiffness structure. Carbon fibres can be formed in many ways. The final properties depend on the processing technique used. They are used for applications such as bone plates, implants and artificial tendons and ligaments.

2.3.3 Glasses

It was discovered by Hench et al. in 1969 that bone can bond chemically to certain glass compositions [17]. The main glasses used for implantation are $\text{SiO}_2\text{-CaO-Na}_2\text{O-P}_2\text{O}_5$ and $\text{Li}_2\text{O-ZnO-SiO}_2$ systems [7]. Many glasses are based on a formula called 45S5, signifying 45 wt% SiO_2 and 5 to 1 molar ratios of CaO and P_2O_5 [1]. Glasses with lower molar ratios of CaO to P_2O_5 do not bond to bone. The most reactive glass compositions have been shown to develop a stable, bonded interface with soft tissues.

It is possible to design glasses with properties specific to a particular clinical application [17]. The main advantage of bioactive glasses is the rapid tissue bonding they induce. The primary disadvantage is mechanical weakness and low fracture toughness due to their amorphous two-dimensional glass network [17]. Two commercially available bioactive glasses are Cervital® and Bioglass®.

2.3.4 Calcium Phosphate Ceramics

Calcium phosphate can be crystallized into various calcium phosphate ceramics depending on the Ca:P ratio, presence of water, impurities and temperature [7]. Examples of phases formed include tri-calcium phosphate, tetracalcium phosphate and hydroxyapatite. Calcium phosphate ceramics have received a lot of research attention due to their chemical similarity to calcified tissue (bones, teeth). They have been used in dentistry and medicine for about thirty years.

Table 2.2: Some Calcium Phosphate Compounds [13, 18]

<i>Chemical Definition</i>	<i>Symbol</i>	<i>Phase</i>	<i>Chemical Formula</i>	<i>Ca/P Ratio</i>
Monocalcium phosphate hydrate	MCP		$\text{Ca}(\text{H}_2\text{PO}_4)_2$	0.50
Dicalcium phosphate anhydrous	DCPA	Monetite	CaHPO_4	1.00
Dicalcium phosphate dihydrate	DCPD	Brushite	$\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$	1.00
Octocalcium phosphate	OCP		$\text{Ca}_8\text{H}_2(\text{PO}_4)_6 \cdot 5\text{H}_2\text{O}$	1.33
α -Tricalcium phosphate	α -TCP		$\alpha\text{-Ca}_3(\text{PO}_4)_2$	1.50
β -Tricalcium phosphate	β -TCP	Whitlockite	$\beta\text{-Ca}_3(\text{PO}_4)_2$	1.50
Tetracalcium phosphate	TTCP	Hilgenstockite	$\text{Ca}_4(\text{PO}_4)_2\text{O}$	2.00
Oxyhydroxyapatite	OHA		$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_{2-2x}$ $(\text{O}_4)(\overset{\uparrow}{\text{I}})_x$	
Oxyapatite	OXA		$\text{Ca}_{10}(\text{PO}_4)_6\text{O}$	1.67
Hydroxyapatite	HA		$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$	1.67
Amorphous calcium phosphate	ACP		N/A	

Calcium phosphate ceramics can be used in block form for applications such as spinal fusion and bone space filling, for example after the removal of a tumour. They can also be used in granule form to help repair damaged bone in procedures such as alveolar ridge augmentation and maxillofacial surgery. In loading bearing applications their inherent brittleness requires them to be used as a coating material on a tougher substrate. These coatings are used to

encourage the ingrowth of bone material and are used for the fixation of dental implants and joint replacement components. More recently they have shown potential for use as percutaneous implants and as drug release ceramics. Calcium phosphate can also be used for calcium phosphate cements (CPC). There are two types, apatite CPC and brushite CPC. Different calcium phosphate compounds along with their chemical composition and Ca/P ratio are summarised in *table 2.2*.

3 Hydroxyapatite

3.1 Introduction

Hydroxyapatite (HA), as discussed above, is a calcium phosphate bioceramic. The similarity between these calcium phosphate bioceramics and the mineral component of bone is reported to have been first recognised in 1788 by Proust and by Klaprota [19]. This similarity led to the development of many commercial and non-commercial calcium phosphate materials, including ceramic HA, non-ceramic HA, coralline HA, β -TCP, and biphasic calcium phosphates. The first successful repair of a bony defect with a calcium phosphate reagent, described as triple calcium phosphate compound, was reported by Albee in 1920 [20].

In the late sixties and early seventies other researchers, such as Levitt and Monroe, developed methods for the production of ceramic materials for use in dental and medical applications [21]. In the mid-seventies Jarcho et al. in the USA, deGroot et al. and Denissen in Europe, and Aoki et al. in Japan began to work simultaneously but independently towards the development and commercialization of hydroxyapatite [21].

Hydroxyapatite is now used in many orthopaedic applications. It has been used to form spacers in several shapes e.g. as an iliac bone spacer inserted into the defected iliac bone after an iliac bone is removed as an autobone graft [22]. HA can be filled into bone defects resulting from the removal of bone tumours. It can be used on its own or mixed with autograft bone chips. HA coatings and HA composite coatings can be used as coatings on hip and knee replacements. HA is also used in bioactive bone cements.

3.2 Chemical Structure

Hydroxyapatite crystallizes to form a hexagonal structure and because of this structure is recognised as belonging to the 'apatite' family. Compounds in this family all have a similar hexagonal structure but have different compositions. Apatite was first named as a mineral by Werner in 1786 [19]. The name was derived from the Greek word "to deceive", [19], because it had been confused with several other minerals of similar appearance including beryl, amethyst, olivine and fluorite. Calcium apatites have the general chemical formula $\text{Ca}_5(\text{PO}_4)_3\text{X}$, where X is an electronegative element or group such as halogen or an OH group [23]. As shown in *table 2.2* HA has the formula $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ and a Ca/P ratio of 1.67. Other examples of calcium apatites include fluorapatite (FA), $\text{Ca}_5(\text{PO}_4)_3\text{F}$ and chlorapatite (CA), $\text{Ca}_5(\text{PO}_4)_3\text{Cl}$.

The structure of calcium HA is reported to have been determined by Beevers and McIntyre and later refined by Kay et al. [21]. The unit cell contains Ca, PO₄ and OH ions closely packed together to represent the apatite structure. Most researchers suggest that hydroxyapatite has a hexagonal crystal structure with a space group, P6₃/m [21, 24]. The unit cell for this structure can be seen in *figure 3.1*. This space group is characterised by a six-fold c-axis perpendicular to three equivalent a-axes (a₁, a₂, a₃) at angles of 120° to each other. The ten calcium atoms belong to either Ca(I) or Ca(II) subsets depending on their environment. Four calcium atoms occupy the Ca(I) positions: two at levels z = 0 and two at z = 0.5. Six calcium atoms occupy the Ca(II) positions: one group of three calcium atoms describing a triangle located at z = 0.25, the other group of three at z = 0.75, respectively. The six phosphate (PO₄) tetrahedral are in a helical arrangement from levels z = 0.25 to z = 0.75. The network of PO₄ groups provides the skeletal framework which gives the apatite structure its stability. The oxygens of the phosphate groups are described as one O_I, one O_{II} and two O_{III} [21]. The dimensions of the unit cell at room temperature are: a₀ = b₀ = 9.11 Å and c₀ = 6.86 Å [23].

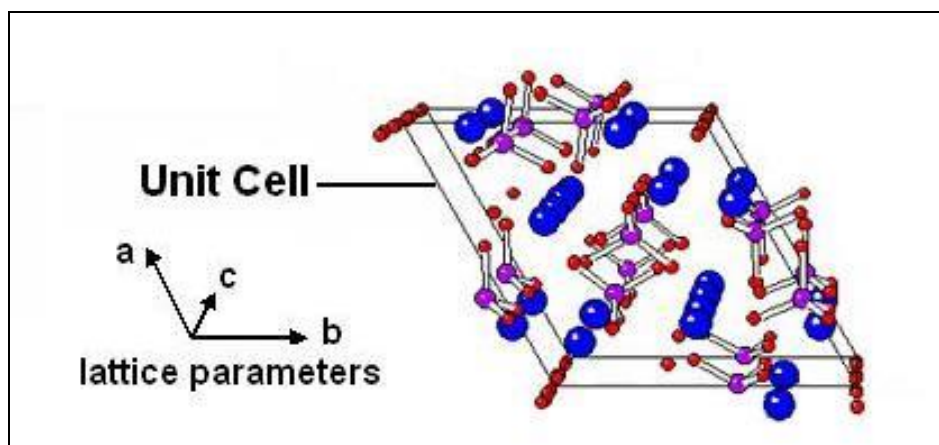


Figure 3.1: Hydroxyapatite Unit Cell [25]

However, this structure is usually associated with non-stoichiometric HA containing impurities. A hexagonal P6₃ structure has been suggested for stoichiometric HA [26]. This structure gives a poor least squares fit to XRD diffraction and thus its acceptance is limited. Two monoclinic models have also been suggested, P2₁/b [27] and P2₁ [28]. These have been found to give a better fit to diffraction patterns and also to be more energetically favourable models of the structure of HA [28]. The calculated density of hydroxyapatite is 3.219 g/cm³ [7].

3.3 Substitutions

The apatite structure is a very hospitable one, allowing the substitutions of many other ions. Substitutions can occur for the (Ca), (PO₄) or (OH) groups. These substitutions result in changes in the properties of the crystal including changes in lattice parameters, morphology

and solubility. Differences in lattice parameters between substituted and unsubstituted HA reflect the size and the amount of the substituting ions. The possible substitutions for each group are shown in *table 3.1*.

Table 3.1: Possible Substitutions in the apatite structure

Ca_{10}		$(PO_4)_6$		$(OH)_2$	
Sr^{2+}	Na^+	AsO_4^{3-}	CO_3^{2-}	F	S^{2-}
Pb^{2+}	Ln^{3+}	VO_4^{3-}	CO_3F^{3-}	Cl	O^{2-}
Cd^{2+}		SiO_4^{4-}		Br	O^2
Mn^{2+}		SO_4^{2-}		I	H_2O
Mg^{2+}		HPO_4^{2-}		CO_3^{2-}	

Cl substitution causes the loss of hexagonal symmetry but exhibits monoclinic symmetry, because of the alternating positions of the Cl atoms, and causes an enlargement of the cell in the b direction. Substitution of F for OH, causes a contraction in the a-axis dimension without changing the c-axis [7]. This is because symmetrically shaped fluoride allows closer coordination with the nearest calcium than asymmetric hydroxyl, with its two atoms, does [7]. This substitution generally causes an increase in the crystallinity leading to greater stability of the structure [21]. This increased stability is reflected in the observation that F-substituted apatites are less soluble than F-free synthetic and biological apatites.

Carbonate, CO_3 , can substitute either for the hydroxyl (OH), Type A substitutions, or the phosphate (PO_4) groups, Type B substitutions [21]. These two types of substitutions have opposite effects on the lattice parameters, a-axis and c-axis dimensions. In the case of Type A, the substitution of larger planar CO_3 group for smaller linear OH group, causes an expansion in the a-axis and contraction in the c-axis dimensions. For the Type B, the substitution of smaller planar CO_3 group for a larger tetrahedral PO_4 group causes a contraction in the a-axis and expansion in the c-axis dimensions. Coupled CO_3 for PO_4 and Na for Ca substitutions cause changes in the size and shape of the apatite crystal: from acicular crystals to rods to equi-axed crystals with increasing carbonate content and dissolution properties: the CO_3 substituted apatite being more soluble than CO_3 -free synthetic apatites [21]. Other ions which may substitute for calcium in the apatite structure include strontium (Sr) and magnesium (Mg). The substitution of Sr for Ca or Mg for Ca causes an increase in the extent of dissolution of the apatite.

3.4 Biological Calcium Phosphate

In biological systems, apatite or apatitic calcium phosphates occur as the principal inorganic constituent of bone and tooth. They comprise approximately 70 wt% of natural bone [29]. They also occur as the major crystalline components in pathological calcification such as dental and urinary calculi and stones [30].

Biological apatites have a similar composition and crystallinity to HA. They contain many impurities and are typically calcium deficient and carbonate substituted. The Ca/P ratio of biological apatite can be as low as 1.50. The stoichiometry of HA varies with its location in the body and also is known to increase with age [30]. It has been proposed that the crystallographically disorder of biological apatites is caused by this carbonate substitution into the apatite lattice [31]. The non-stoichiometry of biological apatites led to speculations that they could form from precursor phases such as amorphous calcium phosphate (ACP) or octocalcium phosphate (OCP), which may initially form and then hydrolyze to apatite. To date the exact structure of biological apatites remains undefined.

The minor elements associated with biological apatites are magnesium, (Mg^{2+}), carbonate, (CO_3^{2-}), sodium, (Na^+), chloride, (Cl^-), potassium (K^+), fluoride (F^-), and acid phosphate, (HPO_4^{2-}). Trace elements include strontium, (Sr^{2+}), barium, (Ba^{2+}), and lead, (Pb^{2+}). Some of these minor and trace elements may be surface rather than lattice-bound. Lattice bound elements will contribute to changes in lattice parameters. Surface elements do not affect lattice parameters, but do contribute to changes in the crystal properties [21]. Minor elements such as magnesium and carbonate have been shown to cause a decrease in crystallinity and an increase in the extent of dissolution of synthetic apatites [21]. The main constituents of bone and HA are compared in *table 3.2*.

Table 3.2: Comparison of bone and hydroxyapatite ceramics (Adapted from [9])

Constituents (wt%)	Bone	HA
Ca	24.5	39.6
P	11.5	18.5
Ca/P ratio	1.65	1.67
Na	0.7	Trace
K	0.03	Trace
Mg	0.55	Trace
CO_3^{2-}	5.8	-

3.5 Biocompatibility

The biocompatibility of synthetic HA is not only suggested by its composition but also by results of in vivo implantation. It has been shown to produce no local or systemic toxicity, no inflammation, and no foreign body response [32]. Examples of such studies are those completed by Ducheyne et al., [33], Ducheyne and Qiu, [34] and Buma et al. [35].

3.6 Dissolution properties

The rate of in vitro dissolution of HA depends on the composition and crystallinity of the HA. Factors such as the Ca/P ratio, impurities like F^- or Mg^{2+} , the degree of micro- and macroporosities, defect structure and the amount and type of other phases all have significant effects on biodegradation. The rate of dissolution is also dependent on the type and concentration of the surrounding solution, the pH of the solution, the degree of saturation of the solution, the solid/solution ratio and the length of time for which it is suspended in the solutions.

Only two calcium phosphate materials are stable at room temperature when in contact with aqueous solutions. The pH of the solution determines which one is stable. At a pH lower than 4.2, dicalcium phosphate (DCP) is the most stable, while at higher pH, greater than 4.2, hydroxyapatite (HA) is the stable phase [32, 36]. The solubility of various calcium phosphates in an aqueous solution is shown in *figure 3.2* below. Solubility is given in terms of the calcium content present in the solution and varies depending on the pH of the solution.

The mechanism of degradation of calcium phosphate in the body is unclear. Some researchers believe that cellular interaction has little effect on the dissolution kinetics. Others believe that the process is a physio-chemical one, in which particles are ingested by osteoclast-like cells attached to the surface and that intracellular dissolution of these particles occurs [37]. The dissolution process is known to be initiated at dislocations and grain boundaries. Incoherent grain boundaries, without lattice continuity, are more sensitive to dissolution than semi-coherent grain boundaries [38].

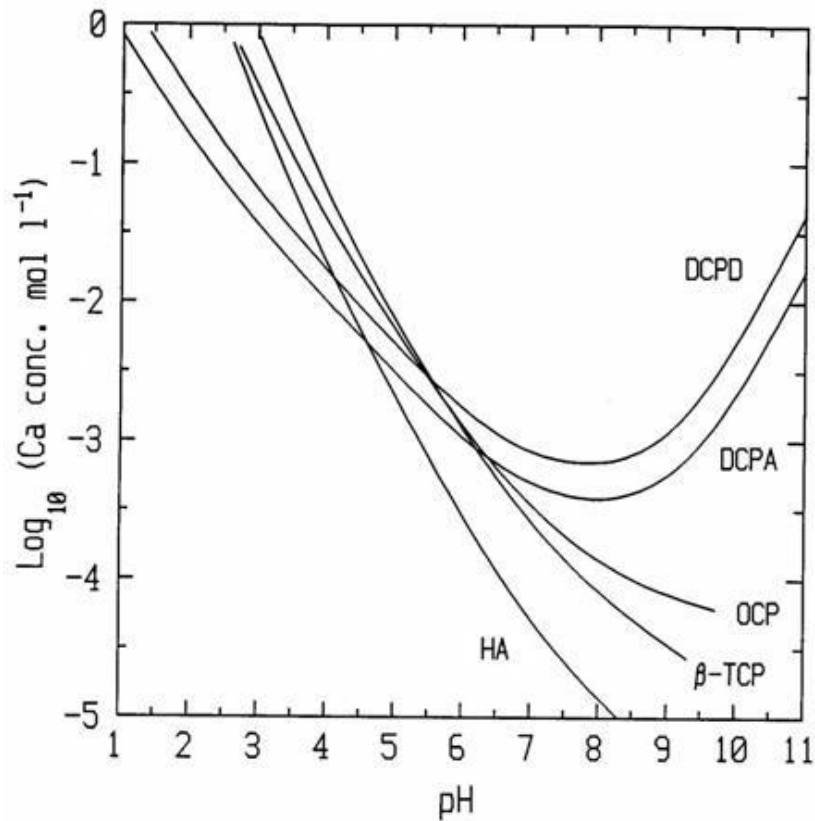
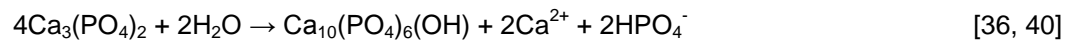
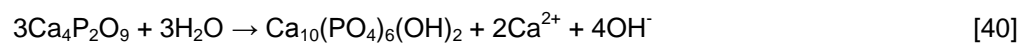


Figure 3.2: Solubility Isotherms of various calcium phosphate phases [39]

Unstable phases may interact with body fluids at 37°C and reprecipitate as hydroxyapatite on the implant surface. In these conditions HA forms by the following reactions:



or



Variations in the material properties of calcium-phosphate coatings affect the bone bonding mechanism and the rate of bone formation. Local supersaturation in the constituent ions of the bone mineral phase, arising from enhanced solid-solution exchange at the coating surface, could be a cause of bone tissue growth enhancement [32].

3.7 Thermal Behaviour

3.7.1 Introduction

The thermal properties of HA powders are important as various high temperature methods are used in the production of HA components and HA coatings, for example, sintering and plasma spraying. During plasma spraying, the temperatures reached within the plasma flame can be as high as 16,600°C [41]. This will depend on the gases used as well as the spraying parameters selected. When the hydroxyapatite powder particles experience these high temperatures thermal decomposition occurs, changing the balance of HA phases. This leads to HA coatings with significantly different crystal structure, phase composition and morphology than the original starting powder. The changes occurring need to be understood so as to ensure that the coating produced has the required composition.

3.7.2 Processes Involved in the Thermal Decomposition of HA

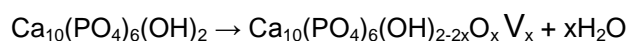
It is widely accepted that the heating of HA leads to three processes, 1) evaporation of water, 2) dehydroxylation, and 3) decomposition.

Evaporation of water

Hydroxyapatite contains two types of water in its structure, absorbed water, both on the surface of the powder, and lattice water which exists within the lattice structure of the powder. When HA is heated at low temperatures the first change to occur is that absorbed water begins to evaporate. As the temperature is increased the lattice water then starts to evaporate. This has been reported by Sridhar et al. [42] to cause a contraction in the a-lattice dimension of the crystal structure.

Dehydroxylation

At higher temperatures, dehydroxylation occurs where hydroxyapatite gradually loses its hydroxyl (OH⁻) group. The dehydroxylation reaction, which has been reported by many authors, [42, 43] is as follows:



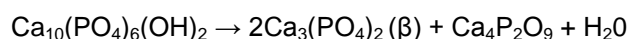
Where V is vacancy and $x < 1$

If heating is carried out in an atmosphere free of water, H₂O is eliminated as it forms. This favours the formation of a hydroxyl ion deficient product, known as oxyhydroxyapatite (OHA).

OHA has a large number of vacancies in its structure, a bivalent oxygen ion and a vacancy substitute for two monovalent OH⁻ ions of HA [42]. The weight loss due to dehydroxylation of HA can be calculated theoretically to be ~1.8% [44]. If heating is carried out in a moist atmosphere stabilised HA results [45].

Decomposition

For temperatures below a certain critical point, HA retains its crystal structure during dehydroxylation and rehydrates on cooling. However, once the critical point is exceeded, complete and irreversible dehydroxylation results. This process is called decomposition. Decomposition of HA leads to the formation of other calcium phosphate phases, such as β -tri-calcium phosphate (β -TCP) and tetra-calcium phosphate (TTCP). The reaction involved in decomposition has been reported by Lazic et al. [46] and Sridhar et al. [42] to be as follows:



At higher temperatures β -tri-calcium phosphate is transformed to α -tri-calcium phosphate.

Temperature Effects on HA

Although there is agreement between researchers about the processes which occur during the thermal decomposition of HA, it is difficult to predict the exact temperatures at which these reactions occur. This is because the reactions do not occur instantly but over a wide temperature range, which depends on a number of factors relating to both the environment and the composition of the HA in question. Researchers have used several techniques, such as thermogravimetric analysis (TGA) [44, 46], Differential Thermal Analysis (DTA) [47, 48], X-ray Diffraction (XRD) [49], and Fourier Transform Infrared Spectroscopy (FTIR) [49], in order to determine the effects of temperature on HA.

The evaporation of water from hydroxyapatite has been reported to occur within a wide temperature range, between about 25°C and 600°C [42, 44, 46, 47]. The total weight loss of absorbed water is reported to be as high as 6.5wt % [46]. A process called decarbonation has been observed by some researchers [44, 47]. The process involves the decomposition of carbon. Carbon may not necessarily present in the crystals originally but may be introduced due to handling or storage. Park et al. [47] reported that decarbonation occurs between 600°C and 700°C and Tampieri et al. [44] noted this decarbonation process at 800°C. Dehydroxylation has been reported by Sridhar et al. [42] to occur between about 850°C and 900°C.

The decomposition of HA has been reported by Sridhar et al. [42] to occur from 1050°C onwards. Tampieri et al. [44] found that decomposition began to occur from 1200°C. Liao et

al. [49] found that HA was stable from 1000°C -1350°C. The highest thermal stability which has been found in the literature is that reported by Deram et al. [48]. The HA powder samples in this study were found not to show any phase transformation up to a temperature of 1450°C.

The decomposition of HA into β -TCP, TTCP and α -TCP has been reported to begin at 1050°C by Sridhar et al. [42], 1200°C by Tampieri et al. [44] and 1400°C by Liao et al. [49]. Tampieri et al. [44] reported the partial melting of HA at 1550°C. Melting temperatures were reported by Fazan [50] to be 1550°C for HA, 1630°C for TeCP and 1730°C for TCP.

Liao et al. [49] investigated the reformation of HA during cooling. It was found that when cooling from 1500°C at 10°C/min there was no phase transformation until a temperature of 1350°C. Characteristic peaks of the reconstruction of HA appeared in the XRD pattern at 1300°C, the intensity gradually increasing with the temperature decrease. The temperature ranges in which reactions occur as HA is heated from room temperature to 1730°C are summarised in *table 3.3*.

Table 3.3: Thermal effects on Hydroxyapatite

Temperature	Reactions
25-600°C	Evaporation of water
600-800°C	Decarbonation
800-900°C	Dehydroxylation of HA forming partially or completely dehydroxylated oxyhydroxyapatite (OHA)
1050-1400°C	HA decomposes to form β -TCP and TTCP
< 1120°C	β -TCP is stable
1120-1470°C	β -TCP is converted to α -TCP
1550°C	Melting temperature of HA
1630°C	Melting temperature of TTCP, leaving behind CaO
1730°C	Melting of TCP

3.7.3 Effect of Crystal Structure and Atmospheric Conditions

The stoichiometry of the HA powder and the partial pressure of water in the surrounding atmosphere have been found to have the greatest effect on the phases formed when HA powder is heated. The consequences of changing these factors have been investigated by numerous researchers.

The effect of stoichiometry on the thermal stability of HA was shown by Fang et al. [51] from experiments in which HA powder samples with Ca/P ratios being 1.52 to 1.67 or 1.68 were heated to 1100°C. The results show that powder with a Ca/P ratio of 1.52 decomposed to TCP, powder with a Ca/P ratio of 1.67 decomposed to TCP and HA, and no decomposition for powder with a Ca/P ratio of 1.68. This clearly illustrates that the stoichiometry is one of the key factors that controls the thermal stability of HA. Tampieri et al. [44] also showed that stoichiometric HA seems to endure thermal treatments at significantly higher temperatures in respect to non-stoichiometric one.

The decomposition of HA also depends on the partial pressure of water (P_{H_2O}) in the surrounding atmosphere. Park et al. [47] report that HA is stable up 1400°C in air or decomposes at 1550°C at $P_{H_2O} = 50\text{mmHg}$. Sridhar et al. [42] found that if performed in a vacuum, HA loses its OH^- at a lower temperature, about 850°C, whereas if HA is heated in a H_2O stream, its structure is then preserved up to 1100°C.

The phase diagrams shown in *figure 3.3* and *figure 3.4* describe the thermal behaviour of $\text{CaO-P}_2\text{O}_5$ system at high temperatures in environments both with and without the presence of water vapour. *Figure 3.3* shows the system when no water vapour is present. It can be seen from the diagram that hydroxyapatite is not stable under these conditions but various other calcium phosphates are, including tetracalcium phosphate (C_4P), α -tricalcium phosphate ($\alpha\text{-C}_3\text{P}$) and mixtures of calcium oxide (CaO) and C_4P .

Figure 3.4 shows the system at a partial water pressure of 500mmHg. Under these conditions HA is found to be stable up to a maximum temperature of 1550°C. If the Ca/P ratio is not exactly equal to 10/6, other calcium phosphates are stable at this temperature, such as CaO or C_4P . *Figures 3.3* and *3.4* illustrate the importance of both partial water pressure and Ca/P ratio in the determination of the stable phases.

Figure 3.5 shows more clearly the effect of partial water pressure on the $\text{CaO} - \text{P}_2\text{O}_5$ system. For a Ca/P ratio higher than 10/6, at temperature of 1300°C, the stable phase is $\alpha\text{C}_3\text{P} + \text{C}_4\text{P}$ if the partial water pressure is 1mmHg. At 10mmHg the stable phases are $\text{HA} + \text{C}_4\text{P}$ and at 100mmHg mixtures of $\text{HA} + \text{CaO}$ are stable.

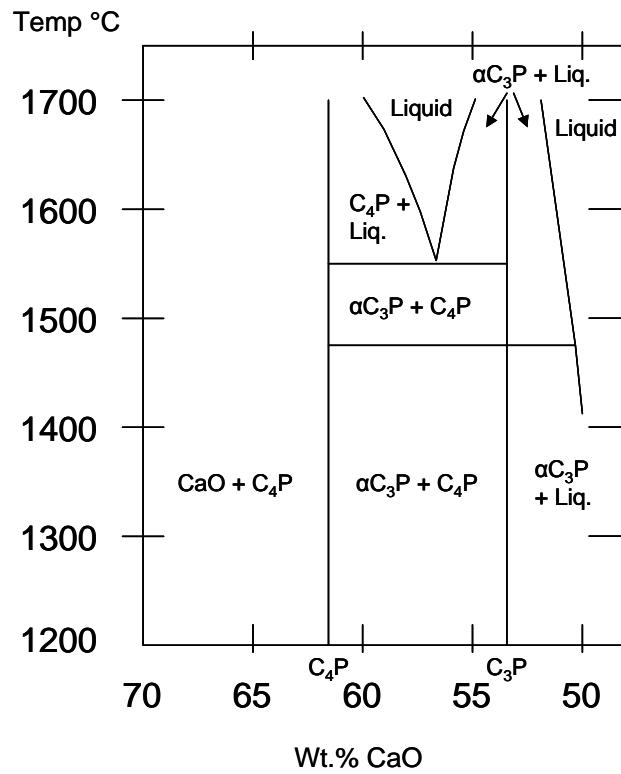


Figure 3.3: Phase diagram of the system CaO-P₂O₅ at high temperature. No water present [32]

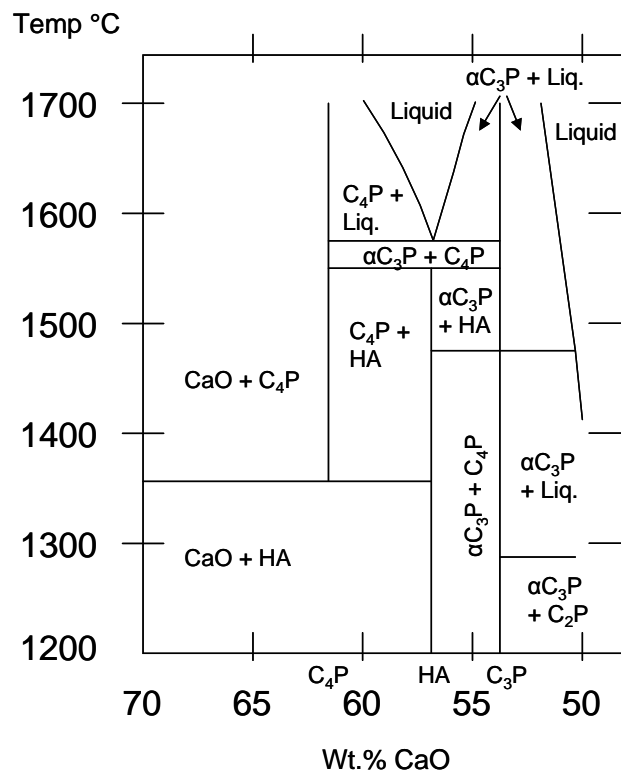


Figure 3.4: Phase diagram of the system CaO-P₂O₅ at high temperature; at a partial water pressure of 500mmHg [32]

It can be concluded that in order to avoid the dehydroxylation and decomposition of HA during plasma spraying a highly stable, crystalline, stoichiometric HA powder should be used. The environmental conditions need to be carefully controlled. Ideally, processing should be carried out in a moist atmosphere. This could involve a moist atmosphere during the actual spraying process or a moist sintering technique after spraying.

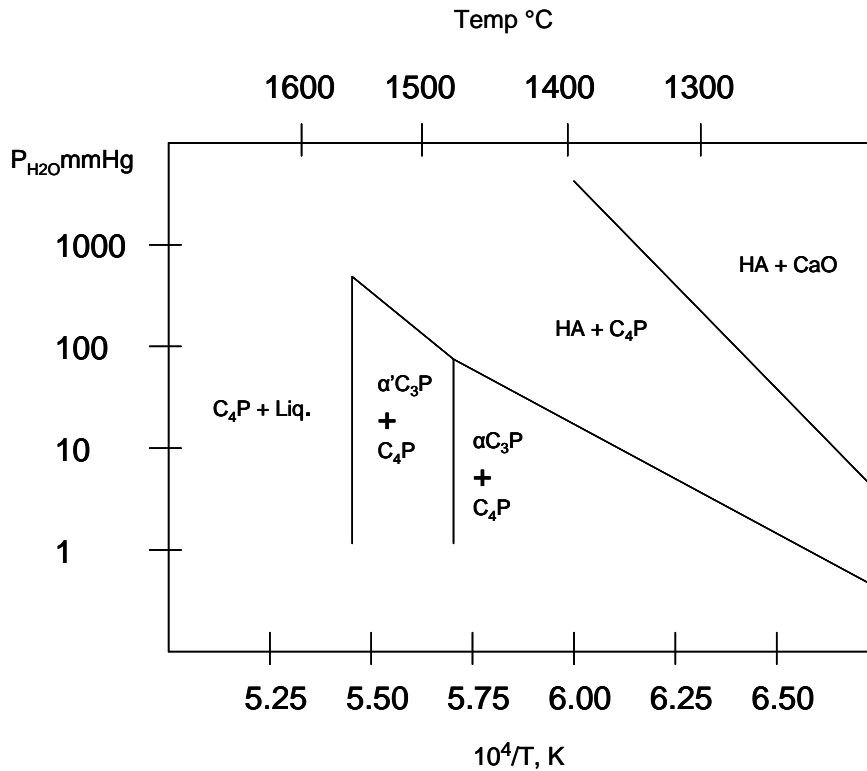


Figure 3.5: Influence of ambient water vapour pressure on phase composition [32]

3.8 Mechanical Properties

The mechanical properties of calcium phosphates vary considerably depending on the methods used in their manufacture [7]. A comparison of the mechanical properties of HA and bone is shown in *table 3.4*.

Table 3.4: Mechanical Properties of HA and Bone (Adapted from [2])

<i>Properties</i>	<i>Cortical Bone</i>	<i>Cancellous Bone</i>	<i>HA Scaffolds</i>
Compressive Strength (MPa)	8-164	23	350-450
Tensile Strength (MPa)	82-114	10-20	38-48
Young's Modulus (GPa)	3.8-11.7	0.2-0.5	7-13

The difference in preparation methods of the HA scaffold materials causes difference in grain size and in composition. Small grain size tends to give greater fracture toughness. Both the tensile and compressive strength of hydroxyapatite depend on the total volume of pores present. These pores can be calcified as either micropores, with diameters of about 1 μ m, or macropores, having diameters of several hundred microns [40]. HA can withstand high compressive force, but is weak in tension, and thus fatigue failure may occur when subjected to tensile or torsional forces.

The resistance of a material to fatigue failure can be described in terms of the Weibull factor, n . Values of 50 to 100 are usually associated with good resistance [40]. The Weibull factor for pure HA was found to be 50 in a dry environment and 12 in a wet physiological environment [50]. Materials that have values between 10 and 20, are susceptible to slow crack growth which produces degradation in properties.

Thus, despite its excellent biocompatibility and osteoconductivity, HA is unsuitable for use in load bearing applications such as the complex physiological loading conditions which occur at the hip joint. It is for this reason that HA is applied as a coating to a substrate, such as a metal alloy, which can provide higher strength and fatigue resistance.

4 Production of Hydroxyapatite Powders

4.1 Introduction

The first synthesis of apatite was that of Daubrée in 1851 who obtained HA by passing phosphorus trichloride vapour over red hot lime [52]. Since then, a number of methods of HA preparation have been reported. They can be divided into three main classes:

- 1) Wet chemical methods
- 2) Solid state reaction methods
- 3) Hydrothermal methods

4.2 Wet chemical methods

The wet chemical method is commonly used for the production of HA as it is relatively easy to conduct. There are two wet chemical routes, hydrolysis and precipitation. These are explained below.

4.2.1 Hydrolysis

In the hydrolysis method, HA is obtained by the hydrolysis reaction of acid calcium-phosphates in an aqueous system. The method may be used to purify powder, and produce small particle sizes [53]. Preparation of calcium-deficient or substituted apatites can also be accomplished by the hydrolysis of ACP, DCPD or DCPA, OCP, α - or β -TCP or tetracalcium phosphate, $\text{Ca}_4(\text{PO}_4)_2\text{O}$, TTCP, in a solution containing OH^- .

The use of hydrolysis for the production of hydroxyapatite was first reported by Schleede et al. in 1932 [54]. They obtained a precipitate using either tetracalcium phosphate ($\text{Ca}_4(\text{PO}_4)_2\text{O}$) or calcium deficient apatite ($\text{Ca}_9(\text{PO}_4)_9(\text{HPO}_4)\text{OH}$) at a temperature of 90°C. Young and Holcomb synthesised hydroxyapatite by refluxing dehydrated calcium hydrogen phosphate in distilled water for 1 month [53]. The reaction occurring was:



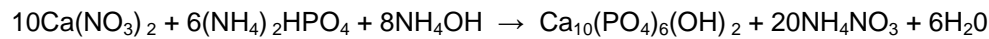
4.2.2 Precipitation

Precipitation occurs by nucleation and growth and is widely used to produce ceramic powders on both the laboratory and industrial scale [53].

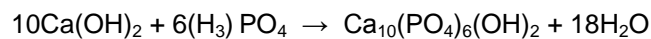
Among the range of precipitation routes, the two most popular are the reaction of:

- 1) Diammonium hydrogen phosphate with calcium nitrate
- 2) Orthophosphoric acid with calcium hydroxide

The reaction when using diammonium hydrogen phosphate with calcium nitrate is as follows [55]:



The major disadvantage of this method is that the purity of the precipitated HA powders is affected by the purity of the calcium nitrate. Aqueous ammonia must also be used to keep the pH of the reaction at around nine. The excess ammonia and ammonium by-products must be removed by extensive washing. The orthophosphoric acid with calcium hydroxide precipitation route is a more convenient process and suitable for the industrial production of HA since the only by-product is water. However, some researchers have found it difficult to obtain HA of stoichiometric composition using this method [56]. The reaction is as follows [55]:



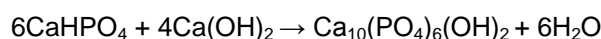
Studies have noted that a number of factors can affect the overall characteristics of the HA produced. These include the reaction temperature, the reactants concentration and the rate of mixing reactants [55]. Because precipitated anions (PO_4^{3-}) are generated slowly in solutions containing the metal ions (Ca^{2+}) it is necessary to add the phosphate solution in drops to the calcium ions-containing solution [56].

Secondary phases may be produced with different reaction pH values, for example in a study by Kweh et al. [55], traces of TCP were detected at a pH of 5 or 7 and at a pH of 11 traces of CaO were identified. A pH of 9 has been found to provide an appropriate environment for the formation of stoichiometric pure HA powders [55]. The correct temperature for the reaction has been found by some authors to be 40°C [56]. LeGeros [30] has reported that the crystallinity of precipitated apatites increases with increasing temperature of preparation. When precipitated at temperatures of 80 to 100°C, apatite is obtained from solution with an initial pH of 4 to 11; the calcium deficiency of the apatite or apatitic precipitation decreasing with increasing pH.

When prepared at temperatures, below 80°C, the pH/temperature dependence of the formation of different calcium phosphate phases (e.g. DCPD, DCPA, OCP) becomes evident unless F is present which promotes the formation of (F,OH) apatite. The reaction conditions and speed of drying the final precipitate can affect the size and shape of the particles. Large particles have been found to result when the addition rate of acid is lowered [56]. One disadvantage relating to the use of wet chemical methods for HA production is that the powder prepared by this method is usually poorly crystallized, inhomogeneous in composition and irregularly formed [52].

4.3 Solid State Reactions Methods

The solid state reaction method is a dry processing method [52]. HA can be produced by mixing calcium compounds and firing them at temperatures above 900°C. An example of a possible reaction is [21]:

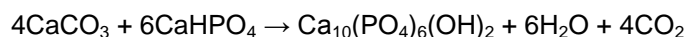


The solid state reaction method can provide high purity products, but the process is chemically restricted to certain compositions, and it is difficult to obtain a precise composition. The resulting powders often exhibit heterogeneity in composition due to incomplete reaction resulting from small diffusion coefficients of ions within solids [52]. The powder particles also tend to have irregular forms with a large grain size.

4.4 Hydrothermal Method

Hydrothermal reactions take place in aqueous solutions under the conditions of high temperature and high pressure. β -TCP, $\text{Ca}_3(\text{PO}_4)_2$ and tetracalcium phosphate (TTCP), $\text{Ca}_4\text{P}_2\text{O}_9$ or $\text{Ca}_4(\text{PO}_4)_2\text{O}$ can easily be converted to HA hydrothermally at these conditions [21]. Pure HA can be obtained by carrying out a hydrothermal reaction of calcium carbonate CaCO_3 and CaHPO_4 or $(\text{NH}_4)_2\text{HPO}_4$ at 275°C under steam pressure of 12,000 psi [50].

The reactions following reactions can be used [21]:



HA powder prepared using the hydrothermal method is well crystallized, compositionally homogeneous, uniform and easily sinterable due to the effects of the high temperature - high

pressure aqueous solutions [52]. Because of this the hydrothermal method has been recognised as an excellent method for the preparation of HA.

4.5 Other Processes

Researchers have also looked at other methods for producing synthetic hydroxyapatite. These methods include the melt growth method, the flux growth method and the sol-gel method.

4.5.1 The Melt Growth Method

The melt growth method has been used for the preparation of single crystals of apatite from a stoichiometric melt. However, the high temperatures conditions required usually result in crystals that are severely strained due to the large temperature gradients present during growth.

4.5.2 The Flux Growth Method

The flux growth method is similar to the melt growth method, except it involves the addition of materials, called fluxes. The fluxes, for example CaF_2 , CaCl_2 and $\text{Ca}(\text{OH})_2$, are mixed with the starting apatite powders and reduce the liquidus temperature far below that needed for the melt growth method, resulting in the production of less strained apatite crystals.

4.5.3 Sol-Gel Method

Sol-gel processing is a chemically based method for producing ceramics, glass, glass ceramics and composites at much lower temperatures than the traditional processing methods [8]. The method involves creating a three-dimensional interconnecting network, termed a gel from a suspension of very small colloidal particles. Colloidal particles are solid particles with very small diameters, (<100nm). A liquid containing a dispersion of these particles is termed a sol. Once a gel is formed it is then dried to a powder. There are three general methods used to form sol-gel materials. These are: [8]

1. Gelation of colloidal powders
2. Supercritical drying
3. Controlled hydrolysis and condensation of metal alkoxide precursors followed by drying at ambient pressure.

The sol-gel process has been successfully applied in the fabrication of both irregularly shaped and spherical powders of calcium phosphates with various Ca/P ratios. The process has a number of advantages for the production of HA powders. It is a low temperature process with the ability to generate nanosized particles. It also has tremendous flexibility to generate nanocrystalline powders, bulk amorphous monolithic solids and thin films [57]. The process also offers a molecular-level mixing of the calcium and phosphorus precursors, which is capable of improving the chemical homogeneity of the resulting HA [58]. The shortcomings of the process are the requirement for expensive alkoxide-based precursors or the need for several complicated steps to ensure complete dissolution of precursors to generate phase pure HA after post-heat treatment [57].

Researchers have used a number of combinations of calcium and phosphorus precursors for sol-gel HA synthesis. Phosphorus alkoxides, mainly triethyl phosphate and triethyl phosphite, seem to be the most frequently used as the phosphorus precursors. The process is affected by differences in chemical activity of the precursors, such as hydrolysis, polycondensation [58]. The temperature that is required to form the apatitic structure depends largely on the chemical nature of the precursors.

Liu et al. [58] reported on some of the synthesis methods used by other researchers. They found that Takahashi et al. [59] used calcium nitrate and phosphonoacetic acid ($\text{HOOCCH}_2\text{PO}(\text{OH})_2$) in an aqueous solution and obtained a pure HA powder at 700°C and Brendel et al. [60] obtained HA at temperatures of 900°C using calcium nitrate ($\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$) and phenyldichlorophosphite ($\text{C}_6\text{H}_5\text{PCl}_2$) as precursors. In their own experiments, Liu et al. [58] produced HA at temperatures of 250°C using triethyl phosphate and calcium nitrate. Kim and Kumta [57] synthesized HA using $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ and P_2O_5 . Deptula et al. [61] carried out a study to produce spherical and irregularly shaped powders. They produced spherical powders using calcium acetate and dehydrated 2-ethyl-1-hexanol and irregular shaped powders were obtained when using calcium nitrate and dehydrated 2-ethyl-1-hexanol.

4.6 Powder Processing

After production of HA, processing may be necessary in order to give a powder with the properties required to produce the HA coating. Important morphological parameters include the particle size, particles shape, porosity, surface parameters, particle flowability, phase composition and homogeneity. Depending on the processing technique used, the powder may require drying after production. Methods used include atomizing, agglomeration and spray drying. This drying process may then be followed by other techniques, such as calcination, crushing, and spheroidizing, which will give the crystallinity and particle size required.

4.6.1 Atomization

The atomization process involves introducing the material into a nozzle at high pressures. The material is atomized as it passes through the nozzle, resulting in a fine spray of powder particles that fall into the powder collector below. Either gas atomization or water atomization can be used. The shape of the resultant particles is dependent on the type used and is also influenced by the method of quenching. Gas-atomized particles are highly spherical whereas water-atomized particles have a more angular shape [62]. The purity of the powder is affected by the atmosphere inside the atomization chamber, the atomization medium and the cooling medium [63].

4.6.2 Agglomeration

The agglomeration process agglomerates very fine powder particles to give an appropriate particle size. Powders manufactured by agglomeration of finer particles must be thoroughly sintered to guarantee mechanical stability. The process is carried out through a sequence of different steps including pelletizing, pressing or spray drying [62]. Variation of the processing parameters leads to large differences in powder densities and surface areas.

Spray drying

Spray drying is a commonly used method in the powder production process. The process combines the atomization and agglomeration methods discussed above. The first step in the spray drying process involves heating a gas source and introducing it into the funnel shaped drying chamber of the spray dryer. The liquid feed material, called a slurry, is then introduced into this drying chamber through separate air jets, causing it to be atomised into a fine spray or mist. The mist particles are then dispersed in the air within the chamber. The extent of atomisation and the length of the time that the particles are in contact with the hot air gas source influence the drying of the particles.

Once mixed with air, the particles are dried and then collected. The coarse, dry particles are collected from the chamber collection point at the base of the drying chamber in buckets. Air borne particles are separated from exhaust air by cyclones. The powder collected from the cyclone is smaller in size than that from the chamber collection point. Powder can be removed from the walls of the spray dryer into the collection points by air brooms, sweepers, pneumatic hammers or vibrators.

There are three main types of spray dryers. They can be distinguished from one another by their flow patterns, which can be co-current, counter current and mixed. The powder produced in the process is relatively porous and so densification may be required. The particle size of

the powder produced can range from about ten microns to a few hundred microns in size. Most HA powders are of the agglomerated spray dried genre.

Calcination/ Sintering

Calcination, or sintering, is a heat treatment that is used to increase both the crystallinity and the density of powder. The process also removes any binders used during spray drying. The increase in crystallinity is due to the growth of the fine crystallites in the agglomerated particles and the transformation of some amorphous phases to crystalline phases. Kweh et al. [55] showed that during the calcinations of HA, α -TCP begins to surface once calcination temperatures reach 1000°C. Therefore, it is necessary to keep the calcination temperature below 1000°C. Cheang and Khor [64] obtained good results from HA feedstock calcined at a temperature of 800°C for 4 hours. Kweh et al. [55] calcined HA at a temperature of 900°C for 2 hours.

Crushing

Particles may need to be crushed in order to give the correct particle size. Ball milling and attrition milling, also called high energy bead milling, are the most commonly used methods. Ball milling uses milling pots and milling balls usually made of porcelain. The attrition mill consists of a chamber containing very small beads, <1mm, generally made of toughened zirconia. The powder is suspended in a slurry within the chamber. It is circulated by a paddle in order to agitate the media. Attrition milling is more effective than ball milling, resulting in finer particle sizes. The particles obtained from milling processes are irregularly shaped and subsequently have poorer flowability than spherical particles. They also have a rather broad particle size distribution.

Spheroidization

The spheroidization process is used to produce spherical particles. Spheroidized HA has been produced by Cheang and Khor [64] using the flame spraying processing, spraying the powder into distilled water using a combustion gun. The resulting HA powder particles are highly dense spherical particles with a glassy smooth texture [64]. They have also been shown to have better flow properties than spray dried, calcined HA [55]. They have shown good results when used for the production of plasma sprayed coatings, resulting in an increase in deposition efficiency and decrease in coating porosity [65].

5 Calcium Phosphate Coatings

5.1 Introduction

As discussed in Chapter 3, the brittleness of calcium phosphate ceramics, such as hydroxyapatite, means that they are unsuitable for use in load bearing applications. For this reason they are used as a coating to a tougher substrate, such as a metal alloy, e.g. steel or titanium. These coatings are used to encourage the ingrowth of bone material and are used for the fixation of dental implants and joint replacement components.

5.2 Coating Application Methods

Numerous coating techniques can be used for the application of bioceramic coatings. These include physical vapour deposition (PVD) techniques, chemical vapour deposition (CVD), electrophoretic deposition (EPD), biomimetic processes, sol-gel methods, and thermal spraying techniques.

5.2.1 Physical Vapour Deposition (PVD)

The physical vapour deposition technique involves bombarding a target material with a high energy ion beam within a vacuum. This results in atom sized particles of the material being sputtered onto a metallic substrate, to form a coating. Many physical vapour deposition techniques have been developed in recent years. These include radio frequency magnetron sputtering, ion beam assisted deposition (IBAD), ion beam deposition (IBD), ion beam mixing (IBM) and techniques that are based on plasma-assisted ion implantation, such as plasma source ion implantation (PSII) and plasma immersion ion implantation (PIII).

5.2.2 Chemical Vapour Deposition (CVD)

The chemical vapour deposition process involves the nucleation and growth of a coating through chemical reactions involved in the gases immediately above the substrate. The process is carried out in a vacuum, at high temperatures, usually about 1000°C. The rate of coating deposition can be controlled by controlling the chemical potential (concentration) of reaction gases.

5.2.3 Electrophoretic Deposition (EPD)

The electrophoretic deposition technique involves the suspension of HA particles in isopropanol or other suitable organic liquid. An electric current is then passed through the suspension causing the migration of charged particles towards the counter charged electrode, resulting in deposition. The particles are deposited with minimal change to their original phase. The size of the particles to be deposited by the electrophoresis is particularly important, since the particles must be fine enough to remain in suspension during the coating process [66]. The rate of particle deposition and the thickness of the coating depend on the electric field strength [9]. The pH, ionic strength and viscosity of the solution also affect the properties of coating formed [67].

5.2.4 Biomimetic Coatings

Biomimetic processing is a name given to fabrication strategies that imitate natural processes, such as bone and dental enamel formation [12]. The process is based on the fact that when a scrupulously clean titanium substrate is immersed in either Hank's balanced salt solution or simulated body fluid at 37°C for several days, a bone-like layer is deposited [9]. The resulting coatings are relatively thin, 1-5µm, and are amorphous or amorphous-crystalline structures. They have been shown to be biologically active, but despite this have not yet been used in clinical application [9].

5.2.5 Sol-gel Coatings

The sol-gel process is based on the hydrolysis and condensation of reagents that are mixed in solution, either as a colloidal suspension of inorganic particles, or a metal alkoxides or other organic precursors. The substrate is usually dipped coated by dipping it into the sol. An inorganic network like sponge, called a gel, then forms on the substrate, which after heating densifies to a solid material. The coatings are prepared at room temperature, and then fired at elevated temperatures in the region 400-1000°C [9].

5.2.6 Thermal Spraying

The thermal spraying process involves passing the deposition material through a heating zone where it is melted. The molten particles are then propelled towards the substrate where they are deposited to form a coating. The history of thermal spraying dates back to the late 1800's. There are many different thermal spraying techniques including flame spraying, the spray and fuse process, high velocity oxy-fuel (HVOF) spraying, the electric arc process, the detonation-gun process and plasma arc spraying. Some of the advantages and disadvantages of the various coating techniques are discussed in *table 5.1*.

Table 5.1: Advantages and disadvantages of some coating techniques

Method	Characteristics	References
Electrophoretic Deposition	Leads to impurities Difficult to achieve uniform thickness Low bond strength	[66-69]
Physical Vapour Deposition	Inadequate deposition rate Resultant Ca/P ratio may be too high	[70-74]
Chemical Vapour Deposition	Pure, highly crystalline coating can be produced High bond strength The maximum thickness that can be achieved is only 20µm	[75]
Thermal Spray	High deposition rate Good chemical and microstructural control Coating thickness can easily be controlled Complex shapes can easily to coated	[76-80]

5.3 Plasma Spraying

In this technique, a direct current arc is established between two electrodes. A stream of mixed gases, such as argon and nitrogen, is feed into the arc. The electrical energy causes atoms of the gas to be excited to high energy levels. The atoms then loose some of their electrons and become ionised producing a plasma. This is called a plasma arc or plasma flame. The plasma flame has a very high velocity and can reach temperatures of up to 16,600°C [41]. Powder is fed into the plasma flame by a carrier gas, where it melts and is then accelerated towards the substrate. The molten particles hit the substrate and form the coating. The spraying process is shown in *figure 5.1*.

There are many different plasma arc, or plasma spraying, processes. The different techniques can be distinguished according to the surrounding atmosphere during spraying. Processes

that use air as the spraying atmosphere include, atmospheric plasma spraying (APS), high power plasma spraying (HPPS) and shrouded plasma spraying (SPS). Processes which require special spraying atmospheres include vacuum plasma spraying (VPS), underwater plasma spraying (UPS) and controlled atmosphere plasma spraying (CAPS). Atmospheric plasma spraying and vacuum plasma spraying are the two most commonly used for the production of HA coatings.

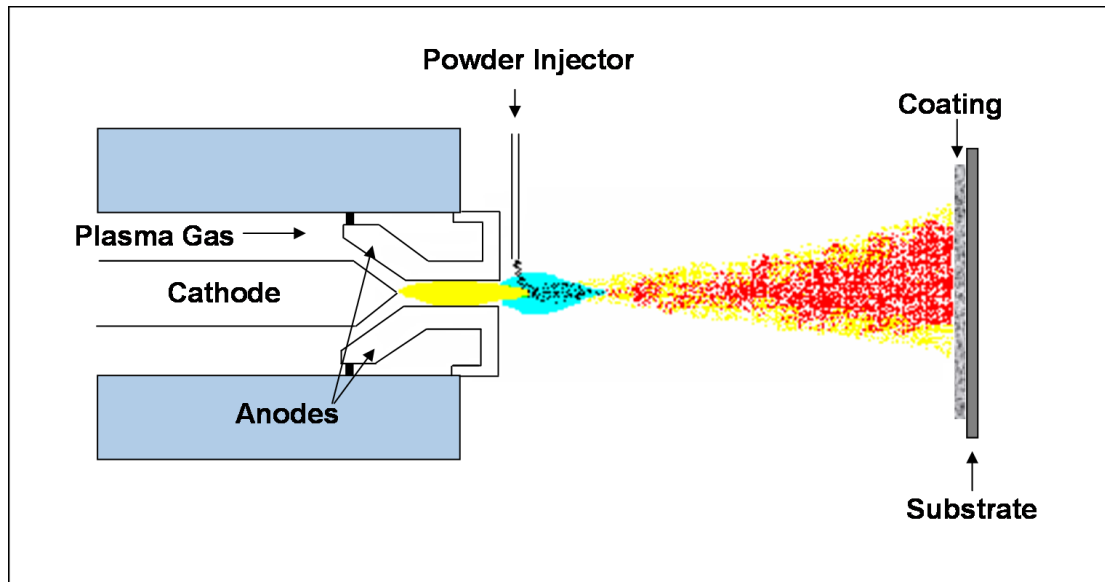


Figure 5.1: Atmospheric Plasma Spraying

5.4 Coating Properties

5.4.1 Chemical Composition

The chemical properties of both HA powder and HA coatings are regulated by standards. According to the ISO standard (ISO 13779-1: 2000) [81] the atomic Ca/P ratio for HA powder has to be between 1.65 and 1.82. The concentration of trace elements present in the coating is given in the *table 5.2*. The maximum allowable total limit of all heavy metals that can be present in the coating is 50 ppm.

The chemical composition of the final coating is dependent on the thermal decomposition occurring during spraying. The ISO standard specification (ISO 13779-2:2000) [82] states that coatings of HA should have a Ca/P ratio in the range of 1.67 to 1.76. The maximum allowable limits for trace elements are the same as that for HA powder (see *table 5.2*).

Table 5.2: Maximum allowable limits for trace elements [82]

<i>Elements</i>	<i>Symbol</i>	<i>ppm., max</i>
Arsenic	As	3
Cadmium	Cd	5
Mercury	Hg	5
Lead	Pb	30

X-ray Diffraction is one of the most important tools for determining the atomic arrangements in matter. It can be used to identify the phases present in samples from raw starting materials to finished product and to provide information on the physical state of the sample, such as grain size, texture and crystal perfection [83]. The technique allows rapid data acquisition, it is a non-destructive technique and samples are acceptable in many forms such as powder, single crystal, or flat polished crystalline materials. The overall size of the sample examined in a given experiment can be as small as $10\mu\text{m}^2$.

In general the use of X-ray Diffraction is restricted to crystalline materials, although some information may be obtained on amorphous solids and liquids. It is recommended as a technique for the verification of the phase composition of plasma-sprayed HA coatings by the Food and Drug Administration (FDA) and required by ASTM F1185-88, "Standard Specification for Composition of Ceramic Hydroxyapatite for Surgical Implants" [84]. A sample XRD pattern for hydroxyapatite is shown in *figure 5.2*.

Phase identification using XRD is based on the unique pattern produced by every crystalline phase. The composition of a sample can therefore be determined by comparing the diffraction pattern with the compilation of standard patterns that have been developed for most known compounds by the Joint Committee of Powder Diffraction Society, (J.C.P.D.S.). The relevant J.C.P.D.S. standards for Calcium Phosphate materials are listed in *table 5.3* below.

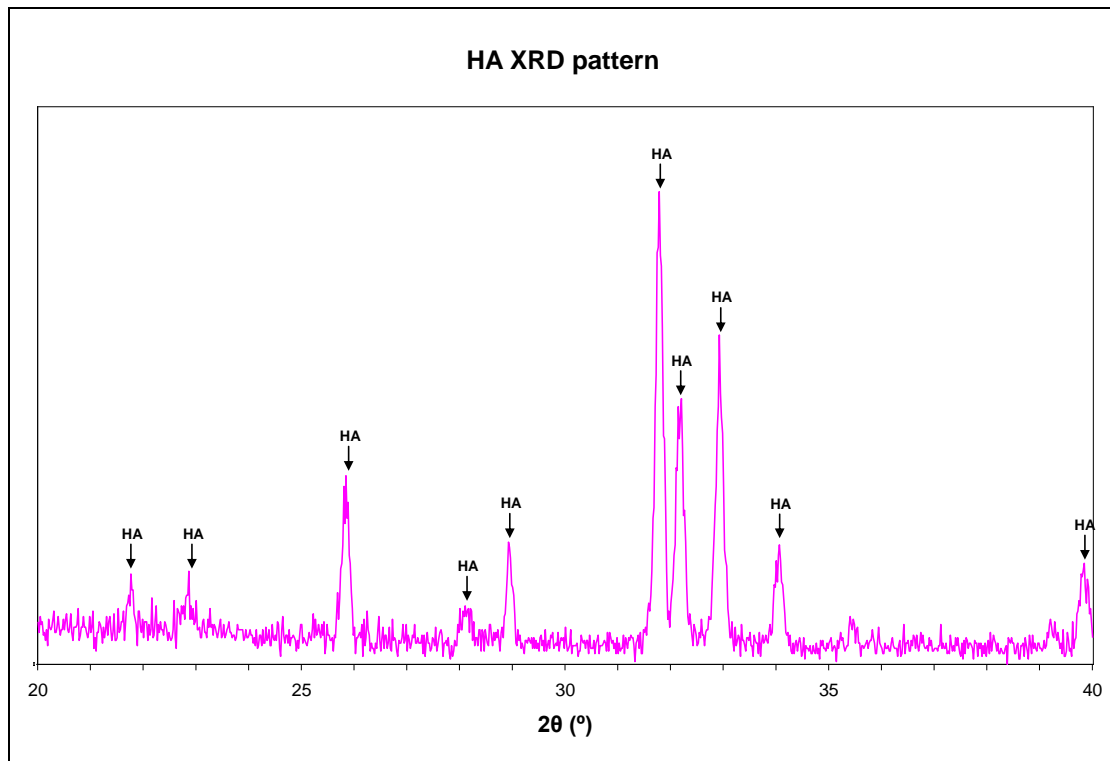


Figure 5.2: XRD pattern for HA

Table 5.3: J.C.P.D.S. standards for calcium phosphate materials

<i>Material</i>	<i>Symbol</i>	<i>Formulae</i>	<i>J.C.P.D.S. reference</i>
Hydroxyapatite	HA	$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})$	9-432
α -Tricalcium Phosphate	α -TCP	$\alpha\text{-Ca}_3(\text{PO}_4)_2$	9-348
β -Tricalcium Phosphate	β -TCP	$\beta\text{-Ca}_3(\text{PO}_4)_2$	9-169
Tetracalcium phosphate	TTCP	$\text{Ca}_4(\text{PO}_4)_2\text{O}$	25-1137
Calcium Oxide	CaO	CaO	4-777
Octacalcium Phosphate	OCP	$\text{Ca}_8\text{H}_2(\text{PO}_4)_6 \cdot 5\text{H}_2\text{O}$	26-1056
Dicalcium phosphate anhydrous	DCPA	CaHPO_4	9-80
Dicalcium phosphate dihydrate	DCPD	$\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$	9-77

5.4.2 Coating Crystallinity

The coating crystallinity is determined by the degree of particle melting and the solidification time of the lamella. As discussed in Chapter 3, coatings that contain a high degree of crystallinity have lower dissolution rates and are thus more stable in vivo. Highly amorphous coatings dissolve quickly leading to the rapid weakening and disintegration of the coating. However, it has been recognised that the amorphous HA content promotes beneficial physiological activity. It is thus desirable for a HA coating to contain both crystalline and amorphous phases.

The ISO standard specification (ISO 13779-1:2000) [81] states that hydroxyapatite powder should have a crystallinity of not less than 95%. The allowable level of other crystalline phases is 5% with the balance being amorphous.

The ISO standard relating to HA coatings, ISO 13779-2:2000 [81], states that in order for a HA coating to have sufficient mechanical properties in vivo the crystalline content should be greater than 45%. The maximum allowable level of other phases is 5%, with the balance being amorphous. In general, the crystallinity of HA coatings is about 65-70% [85].

5.4.3 Coating Adhesion

Although it is well recognised that the coating adhesion is one of the most important parameters affecting the performance of an implant in vivo, the actual mechanisms involved are still not fully understood. Generally, the bottom surfaces of the lamellae are not in full contact with the substrate. The areas that are in contact are called the 'welding points' or 'active zones' [63]. Clearly, the greater the contact area the better the adhesion of the coating will be. In the past researchers, such as Lacefield [10] believed that substrate to coating bonding was entirely mechanical. It is now recognised that a large number of factors are involved in the adhesion mechanism. The main mechanisms are mechanical anchorage, physical interaction and chemical interaction.

Mechanical Anchorage

Mechanical anchorage is the main mechanism involved in coating adhesion. The levels achieved depend on the substrate surface roughness, R_a . The adhesion strength of a ceramic coating is in many cases a linear function of the average surface roughness [62]. Substrate preparation techniques, such as grit blasting, are used to increase roughness prior to spraying. The amount of mechanical anchorage achieved is reduced if a large amount of shrinkage occurs during solidification of the particles.

Physical Interaction

If there is close contact between the atoms of the lamella and the substrate, forces, known as Van der Waals forces, may occur between the atoms. The surfaces must be very close to each other to reach the field of attraction of the atoms, i.e. 0.5nm [63]. These forces contribute to the coating to substrate bonding. In order for them to be present, the surface must be clean and both materials should be in a higher energy state.

Metallurgical Interaction

There are two possible mechanisms of metallurgical interaction: diffusion and chemical reaction between the lamella and substrate. The diffusion occurs mainly by vacancies being present in high concentration in rapidly solidified lamella [63]. According to Fick's law, diffusivity increases with increasing contact temperature [62]. Diffusive adhesion generally plays only a minor role in the overall coating adhesion as rapid cooling and solidification of the particles means that the diffusion depth is very small. The amount achieved can be increased by preheating the substrate. Chemical adhesion results when a chemical compound forms between the coating and substrate.

According to ISO requirements (ISO 13779-2:2000) [82] the adhesion strength should be not less than 15MPa. Ideally, the coating adhesion strength would be as high as possible. The adhesion strength of a plasma sprayed HA coating on a titanium substrate is generally about 28MPa [86]. During adhesive testing of HA coatings, failure is generally a mixture of both adhesive (i.e. at the implant coating-interface) and cohesive failure (i.e. occurring within the coating) [86-88].

5.4.4 Coating Microstructure

The microstructure of a coating greatly affects its performance in vivo. Porosity is an inherent characteristic of all sprayed coating. The degree of porosity depends on the properties of the powder particles when they impinge on the substrate surface. If the particles are highly molten, they can flow over the surface and fill gaps and pores. This results in a denser coating. Semi-molten particles give a more porous coating structure. Porosity can be controlled by varying the particle solidification time. This is achieved by altering spraying parameters, such as the temperature of the plasma flame and the level of substrate heating.

Pores can also be formed due to the liberation of oxygen, nitrogen and hydrogen as the temperature of the material decreases and the solubility of these materials reduces accordingly [89]. In some cases these gases can escape to the atmosphere. Otherwise they remain trapped within the coating.

The optimal microstructure for coatings is under debate. On the one hand a dense coating is necessary in order to prevent coating dissolution. On the other hand porosity allows bone growth into the coating and results in a better bone to coating bond. A large pore size is necessary to allow the ingrowth of bone into HA coatings. Vascular tissue does not appear in pores that are less than 100 μm [8]. The optimal porosity for bone ingrowth has been reported to be 200-400 μm [90]. Pore interconnectivity is also required. The porosity of commercially available HA coatings may vary from 1% to 10% and sometimes may be as great as 50% [91].

The surface roughness of the HA coating influences the ability of bone to bond to it and also affects its dissolution properties. A rough coating surface enhances cell adhesion and proliferation [92]. However, a rough coating will also have a greater surface area exposed to the body fluids. It will therefore dissolve more quickly. An example a typical microstructure of a plasma sprayed HA coating is shown in the SEM micrograph in *figure 5.3*. This coating was produced using the Sulzer Metco 9MB Plasma Spray gun in the National Centre for Plasma Science and Technology (NCPST) in Dublin City University.

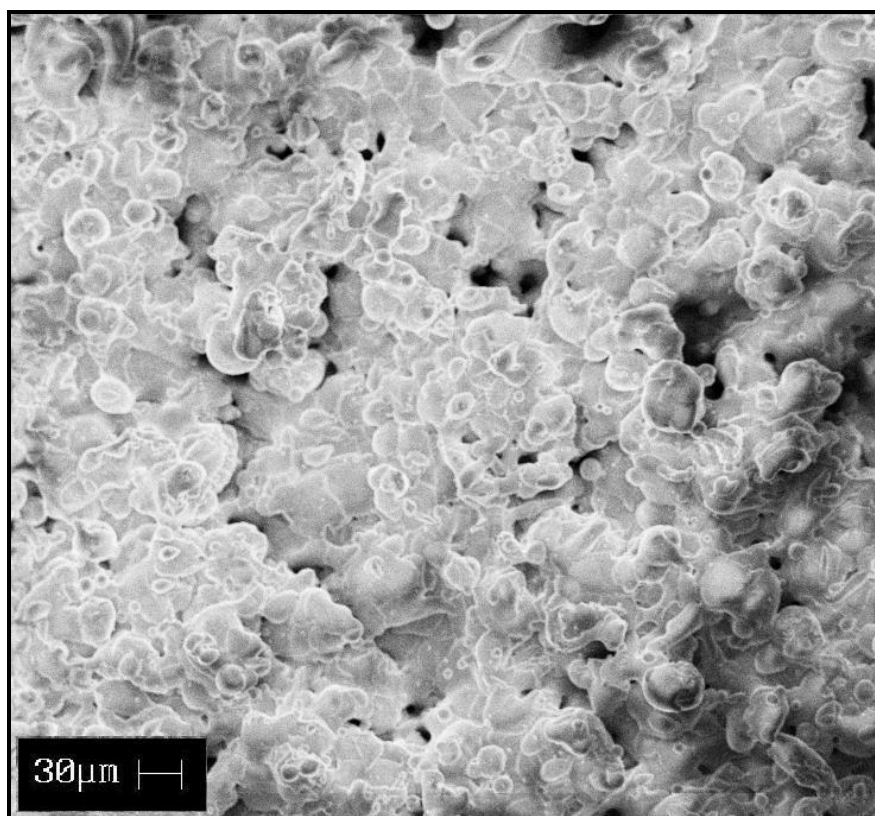


Figure 5.3: SEM micrograph of the microstructure of a plasma sprayed hydroxyapatite coating

5.4.5 Residual Stress

Residual stresses are the internal stresses existing in a body that is under no external load condition [93]. They are generated from inhomogeneously distributed non-elastic changes in dimensions. Residual stresses are inherently induced in any coated deposited by thermal spray methods because of the differences in the thermal properties between the coating and the substrate material. The process is also complicated by the differences between the thermal expansion coefficients of the various phases within the material of the coating and the different temperature ranges experienced by different regions of the component at different times during the process.

The presence of residual stresses leads to crack generation and flaking or peeling of the coating. If spraying parameters are carefully controlled, compressive residual stresses can be generated which can improve the coating characteristics. This is difficult to achieve due to the complexity of the process.

The parameters that affect residual stress generation include the plasma flame temperature, the sprayed particle properties, the substrate temperature and the cooling effects. The coating thickness also affects the residual stresses present. Adding a greater number of layers results in higher residual stresses. Residual stress generation can be reduced by preheating the substrate. The pre-heat temperature selected must be low enough so as not to adversely affect the substrate. Residual stress levels of 44.2MPa were reported by Yang et al. [86] and between about 18 and 41MPa by Tsui et al. [94].

5.4.6 Coating Thickness

The thickness of the final coating is dependent on the number of passes of the plasma gun, the powder feed rate and the deposition efficiency. Thick coatings have better resorption properties and thus provide better protection for the bone from metal-ion released from the substrate; however, they tend to be brittle. The presence of residual stresses in these thicker coatings leads to cracking. Thin coatings perform better mechanically; however, they provide less protection from metal-ion release and also dissolve quickly in vivo. Generally, HA coatings are between 50 μ m and 100 μ m in thickness [95]. The optimal coating thickness has been reported to be 50 μ m [91].

5.4.7 Coating Strength

The mechanical properties of HA coatings depend on a number of important coating characteristics, such as porosity, the number of defects present and the coating thickness. As discussed above, the strength of a coating is inversely proportional to its thickness. The

strength of plasma sprayed HA coatings also depends on the cohesion between the individual particles of the coating.

The requirements for the mechanical properties of HA coatings are outlined in various standards. According to ISO 13779-1:2000 (Implants for Surgery – Hydroxyapatite. Part 1: Ceramic Hydroxyapatite) [81], the compressive strength of sintered hydroxyapatite powder should be not less than 1.5 MPa and the shear strength of HA coatings should be 22-29MPa. No criterion has been suggested for the Young's modulus [91].

6 References

- [1] J. R. Davis, Ed., *Handbook of Materials for Medical Devices*, ASM International, Ohio, 2003
- [2] B. Ben-Nissan and G. Pezzotti, "Bioceramics: An Introduction", in *Engineering Materials for Biomedical Applications*, T. S. Hin, Ed., World Scientific Publishing Co., London, 2004
- [3] A. U. J. Yap, "Biorestorative materials in Dentistry", in *Engineering Materials for Biomedical Applications*, T. S. Hin, Ed., World Scientific Publishing Co., London, 2004
- [4] Z. M. Huang and S. Ramakrishna, "Composites in biomedical applications", in *Engineering Materials for Biomedical Applications*, T. S. Hin, Ed. World Scientific Publishing Co., London, 2004
- [5] William D. Jr., Callister, *Materials Science and Engineering: An Introduction*, 4th ed., New York: John Wiley & Sons, 1997
- [6] A. Toni, A. Sudanese, L. Busanelli, F. A. Zappoli, L. Brizio and A. Giunti, "Cementless arthroplasty using alumina ceramics as a coating and bearing material", in *Hip Surgery: Materials and Developments*, L. Sedel and M. E. Cabanela, Eds., Martin Dunitz Ltd., London, 1998, pp. 267-276
- [7] W. G. Billotte, "Ceramic biomaterials", in *The Biomedical Engineering Handbook*, 2nd ed., Vol. 1, J. D. Bronzino, Ed., CRC Press, Heidelberg; Boca Raton, FL: Springer, 2000, pp. 1-33
- [8] L. L. Hench and J. Wilson, "Introduction", in *An Introduction to Bioceramics*, L. L. Hench and J. Wilson, Eds. World Scientific, Singapore, 1993, pp. 1-24.
- [9] J. W. Nicholson, *The Chemistry of Medical and Dental Materials*, Cambridge, Royal Society of Chemistry, UK, 2002
- [10] W. R. Lacefield, "Hydroxylapatite coatings," in *An Introduction to Bioceramics*, L. L. Hench and J. Wilson, Eds., World Scientific, Singapore, River Edge, N.J, 1993, pp. 223-238.
- [11] R. L. Hentrich, Jr., G. A. Graves, Jr., H. G. Stein and P. K. Bajpai, "An evaluation of inert and resorbable ceramics for future clinical applications", *J. Biomed. Mater. Res.*, vol. 5, pp. 25-51, 1971

- [12] J. F. Shackelford, *Bioceramics*, New Jersey, Gordon and Breach Science Publishers, USA, 1999
- [13] A. Ravaglioli and A. Krajewik, *Bioceramics- Materials, Properties, Applications*, Chapman and Hall, London, 1992
- [14] S. F. Hulbert, "The use of alumina and zirconia in surgical implants", in *An Introduction to Bioceramics*, L. L. Hench and J. Wilson, Eds., World Scientific Publishing Co., Singapore, 1993, pp. 25-40
- [15] M. M. Morshed, B. P. McNamara, D. C. Cameron and M. S. J. Hashmi, "Effect of surface treatment on the adhesion of DLC film on 316L stainless steel", *Surface and Coatings Technology*, vol. 163-164, pp. 541-545, 2003
- [16] A. D. Haubold, R. B. More and J. C. Bokros, "Carbons", in *Handbook of Biomaterial Properties*, J. Black and G. Hastings, Eds., Chapman and Hall, London, 1998, pp. 464-477
- [17] L. L. Hench and O. Andersson, "Bioactive glasses", in *An Introduction to Bioceramics*, L. L. Hench and J. Wilson, Eds., World Scientific Publishing Co., Singapore, 1993, pp. 41-62
- [18] J. L. Lacout, "Calcium phosphates as bioceramics", in *Biomaterials- Hard Tissue Repair and Replacement*, D. Muster, Ed., Elsevier Science Publishers, North- Holland, 1992, pp. 81-95
- [19] A. Myoui, N. Tamai, M. Nishikawa, H. Yoshikawa, N. Araki, T. Nakase and A. Akita, "Three-dimensionally engineered hydroxyapatite ceramics with interconnected pores as a bone substitute and tissue engineering scaffold", in *Biomaterials in Orthopedics*, M. J. Yaszemski, D. J. Trantolo, K. Lewandowski, V. Hasirci, D. E. Altobelli and D. L. Wise, Eds. Marcel Dekker, New York, 2004, pp. 287-300
- [20] F. H. Albee, "Studies in Bone Growth. Triple Calcium Phosphate as a Stimulus to Osteogenesis", *Ann. Surg.*, vol. 71, pp. 32-36, 1920
- [21] Le Geros, Racquel Z. and Le Geros, John P., "Dense hydroxyapatite", in *An Introduction to Bioceramics*, L. L. Hench and J. Wilson, Eds., 1993, pp. 139-180
- [22] H. Oonishi, "Orthopaedic applications of hydroxyapatite", *Biomaterials*, Vol. 12, pp. 171-178, 1991
- [23] L. Calderín, M. J. Stott and A. Rubio, "Electronic and crystallographic structure of apatites", *Phys. Rev. B*, vol. 67, pp. 134106-134113, 2003

- [24] K. Sudarsanan and R. A. Young, "Significant precision in crystal structural details: Holly Springs hydroxyapatite", *Acta Crystallographica, Section B (Structural Crystallography and Crystal Chemistry)*, vol. b25, pp. 1534-43, 1969
- [25] K. Rogers, "The use of diffraction for the analysis of biomaterials", 2nd Annual Biomaterials Workshop, Cranfield University, UK, 2004
- [26] A. T. Sanger and W. F. Khus, "Structural Disorder in Hydroxyapatite", *Zeitschrift Fur Kristallographie*, vol. 199, pp. 123-148, 1992
- [27] J. C. Elliot, P. E. Mackie and R. A. Young, "Monoclinic Hydroxyapatite", *Science*, vol. 180, pp. 1055-1057, 1973
- [28] D. Haverty, S. A. M. Tofail, K. T. Stanton and J. B. McMonagle, "Structure and stability of hydroxyapatite: Density functional calculation and Rietveld analysis", *Phys. Rev. B*, vol. 71, pp. 094103-094112, 2005
- [29] E. C. Shors and R. E. Holmes, "Porous hydroxyapatite", in *An Introduction to Bioceramics*, L. L. Hench and J. Wilson, Eds. London: World Scientific, 1993, pp. 181-198
- [30] R. Z. LeGeros, "Biological and synthetic apatites", in *Hydroxyapatite and Related Materials*, P. W. Brown and B. Constantz, Eds. London: CRC Press, 1994, pp. 3-28
- [31] D. G. A. Nelson, J. D. McLean and J. V. Sanders, "A high-resolution electron microscope study of synthetic and biological carbonated apatites", *J. Ultrastruct. Res.*, vol. 84, pp. 1-15, 1983
- [32] C. P. A. T. Klein, J. G. C. Wolke and K. de Groot, "Stability of calcium phosphate ceramics and plasma sprayed coating", in *An Introduction to Bioceramics*, L. L. Hench and J. Wilson, Eds. London: World Scientific, 1993, pp. 199-221
- [33] P. Ducheyne, J. Beight, J. Cuckler, B. Evans and S. Radin, "Effect of calcium phosphate coating characteristics on early post-operative bone tissue ingrowth", *Biomaterials*, vol. 11, pp. 531-540, 10. 1990
- [34] P. Ducheyne and Q. Qiu, "Bioactive ceramics: the effect of surface reactivity on bone formation and bone cell function", *Biomaterials*, vol. 20, pp. 2287-2303, 12. 1999
- [35] P. Buma, P. J. M. Van Loon, H. Versleyen, H. Weinans, T. J. J. H. Slooff, K. de Groot and R. Huiskes, "Histological and biomechanical analysis of bone and interface reactions around hydroxyapatite-coated intramedullary implants of different stiffness: a pilot study on the goat", *Biomaterials*, vol. 18, pp. 1251-1260, 9. 1997

- [36] Schneider, Samuel J. Jr., *Ceramics and Glasses*, vol. 4, ASM International, Ohio, 1991
- [37] K. de Groot, "Calcium phosphate ceramics: Their current status", in *Contemporary Biomaterials- Material and Host Response, Clinical Applications, New Technology and Legal Aspects*, J. W. Boretos and M. Eden, Eds. New Jersey: Noyes Publications, 1984, pp. 477-492
- [38] A. E. Porter, N. Patel, J. N. Skepper, S. M. Best and W. Bonfield, "Comparison of in vivo dissolution processes in hydroxyapatite and silicon-substituted hydroxyapatite bioceramics," *Biomaterials*, vol. 24, pp. 4609-4620, 11. 2003
- [39] C. Ray, "Dissolution properties of calcium phosphates", *2nd Annual Biomaterials Workshop*, Cranfield University, UK, 2004
- [40] K. deGroot, C. P. A. T. Klein, J. G. C. Wolke and J. M. A. de Blicck-Hogervorst, "Chemistry of calcium phosphate bioceramics," in *Calcium Phosphate and Hydroxyapatite Ceramics*, vol. 2, T. Yamamuro, L. L. Hench and J. Wilson, Eds. Florida: CRC Press, 1990, pp. 3-16
- [41] Sulzer Metco [online], www.sulzermetco.com, (Accessed 24th May 2006)
- [42] T. M. Sridhar, U. Kamachi Mudali and M. Subbaiyan, "Sintering atmosphere and temperature effects on hydroxyapatite coated type 316L stainless steel", *Corros. Sci.*, vol. 45, issue 10, pp. 2337-2359, 2003
- [43] Y. Yang, K. Kim, C. M. Agrawal and J. L. Ong, "Interaction of hydroxyapatite-titanium at elevated temperature in vacuum environment", *Biomaterials*, vol. 25, issue 7, pp. 2927-2932, 2004
- [44] A. Tampieri, G. Celotti, S. Sprio and C. Mingazzini, "Characteristics of synthetic hydroxyapatites and attempts to improve their thermal stability", *Mater. Chem. Phys.*, vol. 64, pp. 54-61, 2000
- [45] J. Rodriguez, A. Martin, R. Fernandez and J. E. Fernandez, "An experimental study of the wear performance of NiCrBSi thermal spray coatings", *Wear*, vol. 255, pp. 950-955, 2003
- [46] S. Lazic, S. Zec, N. Miljevic and S. Milonjic, "The effect of temperature on the properties of hydroxyapatite precipitated from calcium hydroxide and phosphoric acid", *Thermochimica Acta*, vol. 374, pp. 13-22, 2001
- [47] E. Park, R. A. Condrate Sr., D. Lee, K. Kociba and P. K. Gallagher, "Characterization of hydroxyapatite: Before and after plasma spraying", *J. Mater. Sci. Mater. Med.*, vol. 13, pp. 211-218, 2002

- [48] V. Deram, C. Minichiello, R. - Vannier, A. Le Maguer, L. Pawlowski and D. Murano, "Microstructural characterizations of plasma sprayed hydroxyapatite coatings", *Surface and Coatings Technology*, vol. 166, pp. 153-159, 2003
- [49] C. Liao, F. Lin, K. Chen and J. Sun, "Thermal decomposition and reconstitution of hydroxyapatite in air atmosphere", *Biomaterials*, vol. 20, pp. 1807-1813, 1999
- [50] F. Fazan, "In vitro behaviour of plasma sprayed hydroxyapatite coatings", Ph.D., University of Birmingham, Birmingham, 2000
- [51] Y. Fang, D. K. Agrawal and D. M. Roy, "Thermal stability of synthetic hydroxyapatite", in *Hydroxyapatite and Related Materials*, P. W. Brown and B. Constantz, Eds. CRC Press, London, 1994
- [52] M. Yoshimura and H. Suda, "Hydrothermal processing of hydroxyapatite: Past, present and future", in *Hydroxyapatite and Related Materials*, P. W. Brown and B. Constantz, Eds. London: CRC Press, 1994, pp. 45-72
- [53] R. A. Young and D. W. Holcomb, Variability of hydroxyapatite preparations, *Calcified Tissue Int*, 34 Supplement 2, pp. 517-532, 1982
- [54] A. Schleede, W. Schmidt and H. Kindt, "Calcium phosphates and apatites", *Elektrochem.*, vol. 38, pp. 633, 1932
- [55] S. W. K. Kweh, K. A. Khor and P. Cheang, "The production and characterization of hydroxyapatite (HA) powders", *J. Mater. Process. Technol.*, vol. 89-90, pp. 373-377, 1999
- [56] A. Afshar, M. Ghorbani, N. Ehsani, M. R. Saeri and C. C. Sorrell, "Some important factors in the wet precipitation process of hydroxyapatite", *Mater Des*, vol. 24, issue 5, pp. 197-202, 2003
- [57] I. Kim and P. N. Kumta, "Sol-gel synthesis and characterization of nanostructured hydroxyapatite powder", *Materials Science and Engineering B*, vol. 111, pp. 232-236, 2004
- [58] D. Liu, T. Troczynski and W. J. Tseng, "Water-based sol-gel synthesis of hydroxyapatite: process development", *Biomaterials*, vol. 22, pp. 1721-1730, 2001
- [59] H. Takahashi, M. Yashima, M. Kakihana and M. Yoshimura, "Synthesis of Stoichiometric Hydroxyapatite by a Gel Route from the Aqueous-Solution of Citric and Phosphonoacetic Acids", *European Journal of Solid State and Inorganic Chemistry*, vol. 32, pp. 829-835, 1995

- [60] T. Brendel, A. Engel and C. Russel, "Hydroxyapatite Coatings by a Polymeric Route", *Journal of Materials Science-Materials in Medicine*, vol. 3, pp. 175-179, May 1992
- [61] A. Deptula, T. Olczak, W. Lada, A. Borello, C. Alvani, L. Lorenzini and A. DiBartolomeo, "Preparation of calcium phosphate powders by water extraction variant of sol-gel process", in *Hydroxyapatite and Related Materials*, P. W. Brown and B. Constantz, Eds. London: CRC Press, 1994, pp. 263-268.
- [62] R. B. Heimann, *Plasma-Spray Coating: Principles and Applications*, VCH Publishers, Cambridge, 1996
- [63] L. Pawlowski, *The Science and Engineering of Thermal Spray Coatings*, Wiley, New York, 1995
- [64] P. Cheang and K. A. Khor, "Addressing processing problems associated with plasma spraying of hydroxyapatite coatings", *Biomaterials*, vol. 17, pp. 537-544, 1996
- [65] S. W. K. Kweh, K. A. Khor and P. Cheang, "An in vitro investigation of plasma sprayed hydroxyapatite (HA) coatings produced with flame-spheroidized feedstock", *Biomaterials*, vol. 23, pp. 775-785, 2002
- [66] A. Stoch, A. Brozek, G. Kmita, J. Stoch, W. Jastrzebski and A. Rakowska, "Electrophoretic coating of hydroxyapatite on titanium implants", *J. Mol. Struct.*, vol. 596, pp. 191-200, 2001
- [67] C. Wang, J. Ma, W. Cheng and R. Zhang, "Thick hydroxyapatite coatings by electrophoretic deposition", *Mater Lett*, vol. 57, pp. 99-105, 2002
- [68] P. Mondragon-Cortez and G. Vargas-Gutierrez, "Electrophoretic deposition of hydroxyapatite submicron particles at high voltages", *Mater Lett*, vol. 58, pp. 1336-1339, 2004
- [69] J. Ma, C. Wang and K. W. Peng, "Electrophoretic deposition of porous hydroxyapatite scaffold", *Biomaterials*, vol. 24, pp. 3505-3510, 2003
- [70] V. Nelea, C. Morosanu, M. Iliescu and I. N. Mihailescu, "Microstructure and mechanical properties of hydroxyapatite thin films grown by RF magnetron sputtering", *Surface and Coatings Technology*, vol. 173, pp. 315-322, 2003
- [71] V. Nelea, C. Morosanu, M. Iliescu and I. N. Mihailescu, "Hydroxyapatite thin films grown by pulsed laser deposition and radio-frequency magnetron sputtering: comparative study", *Appl. Surf. Sci.*, vol. 228, pp. 346-356, 2004

- [72] K. van Dijk, H. G. Schaeken, J. G. C. Wolke and J. A. Jansen, "Influence of annealing temperature on RF magnetron sputtered calcium phosphate coatings", *Biomaterials*, vol. 17, pp. 405-410, 1996
- [73] M. Hamdi and A. Ide-Ektessabi, "Preparation of hydroxyapatite layer by ion beam assisted simultaneous vapor deposition", *Surface and Coatings Technology*, vol. 163-164, pp. 362-367, 2003
- [74] T. N. Kim, Q. L. Feng, Z. S. Luo, F. Z. Cui and J. O. Kim, "Highly adhesive hydroxyapatite coatings on alumina substrates prepared by ion-beam assisted deposition", *Surface and Coatings Technology*, vol. 99, pp. 20-23, 1998
- [75] J. A. Darr, Z. X. Guo, V. Raman, M. Bououdina and I. U. Rehman, "Metal organic chemical vapour deposition (MOCVD) of bone mineral like carbonated hydroxyapatite coatings", *Chemical Communications*, pp. 696-697, 2004
- [76] K. A. Khor, H. Li, P. Cheang and S. Y. Boey, "In vitro behavior of HVOF sprayed calcium phosphate splats and coatings", *Biomaterials*, vol. 24, pp. 723-735, 2003
- [77] A. H. Dent, A. Patel, J. Gutleber, E. Tormey, S. Sampath and H. Herman, "High velocity oxy-fuel and plasma deposition of BaTiO₃ and (Ba,Sr)TiO₃", *Materials Science and Engineering B*, vol. 87, pp. 23-30, 2001
- [78] H. C. Gledhill, I. G. Turner and C. Doyle, "In vitro fatigue behaviour of vacuum plasma and detonation gun sprayed hydroxyapatite coatings", *Biomaterials*, vol. 22, pp. 1233-1240, 2001
- [79] H. C. Gledhill, I. G. Turner and C. Doyle, "Direct morphological comparison of vacuum plasma sprayed and detonation gun sprayed hydroxyapatite coatings for orthopaedic applications", *Biomaterials*, vol. 20, pp. 315-322, 1999
- [80] S. Beauvais, V. Guipont, F. Borit, M. Jeandin, M. Espanol, K. A. Khor, A. Robisson and R. Saenger, "Process-microstructure-property relationships in controlled atmosphere plasma spraying of ceramics", *Surface and Coatings Technology*, vol. 183, pp. 204-211, 2004
- [81] "Implants for surgery- hydroxyapatite. Part 1: Ceramic hydroxyapatite", BS ISO 13779-1:2000, International Organisation for Standards, 2000
- [82] "Implants for Surgery- Hydroxyapatite. Part 2: Coatings of Hydroxyapatite", BS ISO 13779-2:2000, International Organisation for Standards, 2000

- [83] Raymond P. Goehner and Monte C. Nichlos, "X-Ray Powder Diffraction", in *ASM Handbook. - Vol.10 : Materials Characterization*, prepared under the direction of the ASM Handbook Committee, American Society for Metals, Ohio, 1986
- [84] "Standard Specification for Composition of Ceramic Hydroxyapatite for Surgical Implants," ASTM F1185-03, ASTM International, 2003
- [85] Y. C. Tsui, C. Doyle and T. W. Clyne, "Plasma sprayed hydroxyapatite coatings on titanium substrates Part 2: optimisation of coating properties", *Biomaterials*, vol. 19, pp. 2031-2043, 1998
- [86] Y. C. Yang, E. Chang and S. Y. Lee, "Mechanical properties and Young's modulus of plasma-sprayed hydroxyapatite coating on Ti substrate in simulated body fluid", *Journal of Biomedical Materials Research - Part A*, vol. 67, pp. 886-899, 2003
- [87] Y. C. Yang and E. Chang, "Influence of residual stress on bonding strength and fracture of plasma-sprayed hydroxyapatite coatings on Ti-6Al-4V substrate", *Biomaterials*, vol. 22, pp. 1827-1836, 2001
- [88] P. L. Silva, J. D. Santos, F. J. Monteiro and J. C. Knowles, "Adhesion and microstructural characterization of plasma-sprayed hydroxyapatite/glass ceramic coatings onto Ti-6Al-4V substrates", *Surface and Coatings Technology*, vol. 102, pp. 191-196, 1998
- [89] M. P. Taylor, "Assessment of plasma-sprayed hydroxyapatite coatings", Ph.D., University of Birmingham, Birmingham, 1995
- [90] B. D. Boyan, T. W. Hummert, D. D. Dean and Z. Schwartz, "Role of material surfaces in regulating bone and cartilage cell response", *Biomaterials*, vol. 17, pp. 137-146, 1996
- [91] L. Sun, C. C. Berndt, K. A. Gross and A. Kucuk, "Material fundamentals and clinical performance of plasma-sprayed hydroxyapatite coatings: A review", *J. Biomed. Mater. Res.*, vol. 58, pp. 570-592, 2001
- [92] D. D. Deligianni, N. D. Katsala, P. G. Koutsoukos and Y. F. Missirlis, "Effect of surface roughness of hydroxyapatite on human bone marrow cell adhesion, proliferation, differentiation and detachment strength", *Biomaterials*, vol. 22, pp. 87-96, 2001
- [93] Y. Yang and E. Chang, "Measurements of residual stresses in plasma-sprayed hydroxyapatite coatings on titanium alloy", *Surface and Coatings Technology*, vol. 190, pp. 122-131, 2005

- [94] Y. C. Tsui, C. Doyle and T. W. Clyne, "Plasma sprayed hydroxyapatite coatings on titanium substrates Part 1: Mechanical properties and residual stress levels", *Biomaterials*, vol. 19, pp. 2015-2029, 1998
- [95] Y. Yang, J. L. Ong and K. Bessho, "Plasma-sprayed hydroxyapatite-coated and plasma-sprayed titanium-coated implants", in *Biomaterials in Orthopedics* M. J. Yaszemski, D. J. Trantolo, K. Lewandowski, V. Hasirci, D. E. Altobelli and D. L. Wise, Eds. New York: Marcel Dekker, 2004, pp. 401-423