Synthesis And Characterization Of Nanocrystalline Hydroxyapatite Powder; And The Effects Of Oxide-based Sintering Additives On Tricalcium Phosphate

2005

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SYNTHESIS AND CHARACTERIZATION OF NANOCRYSTALLINE HYDROXYAPATITE POWDER; AND THE EFFECTS OF OXIDE-BASED SINTERING ADDITIVES ON TRICALCIUM PHOSPHATE

by

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B.E. University of Bombay, 2002

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in the Department of Mechanical, Materials and Aerospace Engineering in the College of Engineering and Computer Science at the University of Central Florida Orlando, Florida

Summer Term
2005
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ABSTRACT

Calcium phosphate (CP) materials have been used extensively for bone replacement and augmentation due to their similarity to the mineral component of bone. In addition to being non-toxic, they are biocompatible, not recognized as foreign materials in vivo, and most importantly, exhibit osteoconductive behavior, being able to help in bone formation during healing. CPs form an intimate physicochemical bond with the host tissue, termed osseointegration. However the main limitation of calcium phosphates is their inherent brittle nature and poor mechanical performance under complex stress states. As a result, these materials have been used clinically only in non-load-bearing applications, primarily as granules. The primary goal of this research was to enhance mechanical performance of CPs, tricalcium phosphate (TCP) and hydroxyapatite (HAp) to be precise, in an attempt to develop controlled strength-loss resorbable/bioactive ceramic bone-grafts for hard tissue engineering.

In my work on TCP, I selected and introduced small quantities of single and multi-oxide sintering additives in TCP, to study their influence on sintering behavior, densification, mechanical properties and biodegradation/biomechanical properties in vitro. Through this research, I could improve mechanical performance of β-tricalcium phosphate (β-TCP) and controlled its rate of biodegradation by introducing of certain additives.

In my second work, I improved mechanical performance of HAp (Ca_{10}(PO_{4})_{6}(OH)_{2} by reducing particle-size of the powder through the synthesis of stoichiometric, nanocrystalline, single phase HAp powder in the range of 2-20 nm. Synthesis of powder was accomplished via a modified low temperature sol-gel technique using ethanol/water as solvent.
Dedicated
to
My Parents
ACKNOWLEDGMENTS

First and foremost, I would like to express gratitude to my advisor Dr. Samar Kalita for his support throughout my studies at UCF. His talents, dedication, and enthusiasm for research will be a continuing source of inspiration. I would also like to thank Dr. Vimal Desai (Director-AMPAC) for his support throughout the materials program. I appreciate him for involving me in the material science department with funding. I would like to thank Dr. Joe Cho and Dr. C. Suryanarayana for serving on my thesis committee and for their valuable suggestions. Also, I am grateful to Mr. Richard E. Zotti for his apt guidance.

Special thanks to Dr. Helge Heinrich of AMPAC for his help in this research and his helpful tips. Besides, I would like to thank Mr. Abdulbaset A. Benwali of MMAE for his help in getting some laboratory aids.

I would like to express sincere gratitude to Ms. Arlene Ollivierre, Ms. Linette Reyes and Ms. Jeanine Clements of MMAE for their help in timely procuring items and materials vital to this project.

I would like to thank Kirk Scammon from the Materials Characterization Facilities at AMPAC for his experimental support. Moreover I would like to thank all my friends and well-wishers, particularly Jayadeep Kudumula, Pavan Gosai, Vikas Somani, Shipeng Qiu and Kartik Brahmbhatt.

Above all I would also like to thank my parents for their constant support, love, and encouragement.
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<td>Calcium phosphate</td>
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<tr>
<td>TCP</td>
<td>Tricalcium phosphate</td>
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<tr>
<td>DCPD</td>
<td>Dicalcium phosphate dihydrate</td>
</tr>
<tr>
<td>DCPA</td>
<td>Dicalcium phosphate anhydrate</td>
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<tr>
<td>TTCP</td>
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</tr>
<tr>
<td>ACP</td>
<td>Amorphous calcium phosphate</td>
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<td>SBF</td>
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CHAPTER 1: INTRODUCTION

1.1 Motivation

Medical procedures to address bone related injury are prevalent in the United States, with around 900,000 hospitalizations due to fractures and over 800,000 grafting procedures annually. To address the need for intervention in these cases, many materials are currently in use to repair or replace bone that has been damaged due to trauma or diseases. These include natural autografts (tissue grafts within the same individual) and allografts (tissue-grafts between two individuals of the same species), as well as a variety of synthetic biomaterials, which can be metallic, ceramic, polymeric or newly developed composites. The use of allografts is limited by possibility of an immunological response and the risk of disease transmission, whereas autografts are restricted by a limited number of donor sites and are associated with additional trauma resulting from the harvesting of bone tissue. In this light, manmade materials stand out as a potential solution, being easily available, processed and modified to suit the needs of a given application. However, many problems persist resulting from the inability to exactly match natural tissue. Metallic materials used in orthopedic industry suffer from mechanical properties far exceeding those of bone, which results in stress shielding and the subsequent weakening of the host bone tissue, which leads to total failure of the implants. Ceramics are a better choice for bone engineering applications because of their compositional resemblance with the bone mineral.

A variety of ceramic materials have been tested and developed for use in the repair of bone defects in the human body [1]. These novel ceramic materials are called bioceramics. Among them, calcium phosphate-based ceramics (CPCs) have received a great deal of attention as preferred materials for a number of biomedical applications, such as, in orthopedics, dentistry
and the drug delivery industry. CPCs exhibit considerably improved biological affinity and activity compared to existing synthetic materials and are materials of choice for bone graft application. An ideal bone graft material should support the activity of osteoblasts in the development of new bone, while simultaneously being resorbed by osteoclasts as a part of the lifelong process of bone remodelling.

1.2 Bone

Bone is a natural composite material, which by weight contains about 60% mineral, 30% matrix and 10% water. Bone is also a living tissue, with about 15% of its weight being due to the cellular content. The matrix of bone is comprised primarily of Type I collagen that is highly aligned, yielding a very anisotropic structure. This organic component of bone is predominantly responsible for its tensile strength. The mineral component of bone is a form of calcium phosphate known as hydroxyapatite (HAp). Stoichiometric HAp has the formula \( \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 \), and has a hexagonal geometry with the unit cell dimensions being 9.42 Å in the a and b directions, and 6.88 Å along the c-axis [2]. However, bone mineral is rarely stoichiometric, containing many substitutions such as magnesium, sodium, potassium, fluorine, chlorine, and carbonate ions. The apatitic mineral in bone is made up of long, flat, plate-like HAp nanocrystals that are approximately 40 nm long, 10 nm wide and 1-3 nm thick and is closely associated with the collagen fibers [3]. This mineral component is responsible for the compressive strength of bone. Inside human body, bones serve a number of different functions: i) provide protection to the internal organs, ii) act a mineral reservoir and iii) provide a site for the cells found in the marrow to differentiate. Nevertheless, its primary purpose is to provide mechanical support for soft tissues and serve as an anchor for the muscles that generate motion.
There are two types of bone, compact or cortical, and cancellous or trabecular (also known as spongy) bone. Compact bone is very dense, consisting of parallel cylindrical units (osteons), and is found in the shafts of the long bones as well as on the outer surface of the smaller bones in the body. Trabecular bone is less dense and is made up of an array of rods and struts that form open-cell foam, the pores of which are filled in by marrow. This type of bone is found at the ends of the long bones and inside the smaller bones (ribs, spine). The anisotropic structure of bone leads to mechanical properties that exhibit directionality. This directionality results from the fact that bone has evolved to be both tough and stiff, two competing properties which are optimized in bone but with an inherent loss in isotropy. Nevertheless, bone exhibits extraordinary mechanical properties, displaying both viscoelastic and semi-brittle behavior. Compact bone has a compressive strength in the longitudinal direction (parallel to the long axis) ranging from 131-224 MPa, and a Young’s modulus between 17-20 GPa [4]. It also exhibits good fracture toughness, which is much higher in the transverse direction than in the longitudinal one. The mechanical properties of trabecular bone are highly dependent on its density. Compressive strength varies with the second power of density, whereas Young’s modulus scales as the second or third power, with values ranging between 5-10 MPa and 50-100 MPa for strength and modulus, respectively [5]. When damaged, bone demonstrates a remarkable capacity for regeneration. Though the detailed process of fracture healing is complex, it can be simplified into three stages: inflammation, repair, and remodeling. In the first stage, the normal wound healing response occurs, resulting in a fibrin clot, when ruptured blood vessels flood the region with growth factors and signaling molecules, attracting cells such as macrophages to digest the damaged tissue. During the repair stage, a callus is formed by the bone cells recruited to the site, osteoblasts, that produce the cartilage-like bone matrix, which eventually mineralizes through
deposition of a non-stoichiometric (calcium deficient) HAp. In the final and longest stage, the bone remolds through a process of resorption and deposition, which enhances the bone to resist the applied environmental stresses. This remodeling process is ongoing throughout an individual’s lifetime. A tunnel is first created by cells called osteoclasts that digest the old bone by releasing acids and enzymes. This space is then invaded by osteoblasts and a blood vessel to supply nutrients and remove waste. The osteoblasts line the walls with new bone matrix that eventually entraps them. These entrapped cells, called osteocytes, are interconnected by microscopic processes called canaliculi, and are nourished by the blood vessel that exists in a cylindrical space called the Haversian canal. This leads to the osteonal structure of bone made up of concentric cylindrical layers (Figure 1). As a result of this inherent regenerative capability, bone is a prime candidate for tissue engineering and reconstruction strategies in dealing with trauma to bone tissues.

Figure 1: Simplified structure of bone
1.3 **Research Objectives**

The primary goal of this research was to develop new generation non-metallic materials for bone-graft applications. This work developed controlled strength-loss \( \beta \)-tricalcium phosphate ceramics and nanostructured hydroxyapatite with improved properties, for possible bone tissue engineering applications. Specific objectives of this research were:

**Specific Objective #1:** To improve mechanical performance of resorbable \( \beta \)-TCP ceramics and to control its rate of resorption by introducing small quantities of MgO, ZnO, SiO\(_2\) and TiO\(_2\) as sintering additives. These additives have shown to improve properties of other phases of calcium phosphate ceramics. The work investigated the effects of these additives on densification, hardness, compression strength, and *in vitro* degradation behavior of \( \beta \)-TCP.

**Specific Objective #2:** To develop ternary-oxide sintering additives based on MgO-Na\(_2\)O-P\(_2\)O\(_5\) ceramic system to study their influence on sintering kinetics, densification and biomechanical behavior of \( \beta \)-TCP. MgO-Na\(_2\)O-P\(_2\)O\(_5\) additives have shown to improve mechanical properties of HAp ceramics without altering its biocompatibility. Further, \( \beta \)-TCP allows substitutions to take place, which could be beneficial in tailoring its properties through the introduction of certain metal ions that are present in the bone mineral.

**Specific Objective #3:** To develop stoichiometric; nano crystalline, single-phase HAp powders via Sol-Gel route within a short time frame (sol preparation time of 16 h) at a considerable low temperature, to improve is mechanical performance using the benefits of nanotechnology.
CHAPTER 2: LITERATURE REVIEW

Calcium phosphates (CPs) being light in weight, chemically stable and compositionally similar to the mineral phase of the bone are preferred as bone graft materials in hard tissue engineering. They are composed of ions commonly found in physiological environment, which make them highly biocompatible. In addition, these bioceramics are also resistant to microbial attack, pH changes and solvent conditions [6]. CPs exist in various forms and phases depending on temperature and partial pressure of water [7]. HAp, β-TCP, α-TCP, biphasic calcium phosphate (BCP), monocalcium phosphate monohydrate (MCPM) and unsintered apatite (AP) are different forms of commercially available CPs currently used in the biomedical industry. Table 1 summarizes the physical properties of various phases of calcium phosphates. The contemporary health care industry uses CPCs, depending on whether a resorbable or a bioactive material is desired. HAp is the ideal phase for application inside human body because of its excellent stability above pH 4.3, human blood pH being 7.3. Table 2 presents solubility and pH stability of different forms of calcium phosphates in aqueous solution.

Among these forms, particular attention has been placed on tricalcium phosphate [Ca$_3$(PO$_4$)$_2$, TCP] and hydroxyapatite [Ca$_{10}$(PO$_4$)$_6$(OH)$_2$, HAp] due to their outstanding biological responses to physiological environments [8]. Because of the chemical similarity between HAp and the bone mineral, synthetic HAp exhibits strong affinity to host hard tissues. On the other hand, TCP has been proven to be resorbable in vivo with new bone growth, replacing the implanted TCP [9]. This property imparts significant advantage to TCP compared to other biomedical materials, which are not resorbed and replaced by natural bone [10].
Table 1: Physical properties of various phases of calcium phosphate bioceramics

<table>
<thead>
<tr>
<th>Phases</th>
<th>Chemical Formulae</th>
<th>Ca:P Ratio</th>
<th>Crystal Structure</th>
<th>Density</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyapatite (HAp)</td>
<td>Ca_{10}(PO_4)_6(OH)_2</td>
<td>10/6</td>
<td>Hexagonal, P6₃/m space group, cell dimensions a=9.42Å, and c=6.88Å.</td>
<td>3.16 g/cm³</td>
</tr>
<tr>
<td>α-Tricalcium Phosphate</td>
<td>Ca_3(PO_4)_2</td>
<td>3/2</td>
<td>Monoclinic, P2₁/a space group, lattice constants a=12.887 Å, b=27.280 Å, c=15.219 Å, β=126.20°.</td>
<td>2.86 g/cm³</td>
</tr>
<tr>
<td>β-Tricalcium Phosphate</td>
<td>Ca_3(PO_4)_2</td>
<td>3/2</td>
<td>Hexagonal, rhombohedral space group R3, unit cell dimensions a=10.439 Å, c=37.375 Å.</td>
<td>3.07 g/cm³</td>
</tr>
<tr>
<td>Tetracalcium Phosphate</td>
<td>Ca_4P_2O_9</td>
<td>2/1</td>
<td>Monoclinic, space group P2₁, a=7.023 Å, b=11.986 Å, c=9.473 Å, β=90.90°.</td>
<td>3.05 g/cm³</td>
</tr>
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Sources:
Table 2: Solubility and pH stability of different phases of calcium phosphates

<table>
<thead>
<tr>
<th>Phases</th>
<th>Solubility at 25°C, -log(K_{sp})</th>
<th>pH stability range in aqueous solution at 25°C</th>
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<tbody>
<tr>
<td>Hydroxyapatite (HAp)</td>
<td>116.8</td>
<td>9.5-12</td>
</tr>
<tr>
<td>β-tricalcium phosphate (β-TCP)</td>
<td>28.9</td>
<td>Cannot be precipitated from aqueous solutions</td>
</tr>
<tr>
<td>α-tricalcium phosphate (α-TCP)</td>
<td>25.5</td>
<td>Cannot be precipitated from aqueous solutions</td>
</tr>
<tr>
<td>Tetracalcium phosphate (TTCP)</td>
<td>38-44</td>
<td>Cannot be precipitated from aqueous solutions</td>
</tr>
<tr>
<td>Dicalcium phosphate dihydrate (DCPD)</td>
<td>6.59</td>
<td>2.0-6.0</td>
</tr>
<tr>
<td>Dicalcium phosphate anhydrate (DCPA)</td>
<td>6.90</td>
<td>Stable at temperatures above 100°C</td>
</tr>
<tr>
<td>Amorphous calcium phosphate (ACP)</td>
<td>Cannot be measured precisely. However, the following values were reported: 25.7±0.1 (pH 7.40), 29.9±0.1 (pH 6.00), 32.7±0.1 (pH 5.28).</td>
<td>Always metastable. The composition of a precipitate depends on the solution pH value and composition.</td>
</tr>
<tr>
<td>Calcium-deficient hydroxyapatite (CDHAp)</td>
<td>~ 85.1</td>
<td>6.5-9.5</td>
</tr>
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Sources:
One of the major shortcomings of CPs is their poor mechanical strength under complex stress states. Further, it has been proved that the bioactivity of synthetic CPs (micron size powder) is inferior to natural apatite, the bone mineral. It is believed that inferior bioactivity of synthetic CPs is due to the absence of various essential trace ions like Mg$^{2+}$, Zn$^{2+}$, Na$^+$, K$^+$ and F$^-$ which are present in the bone mineral. Additionally, like other ceramic materials, the tensile and compressive strengths of CPs are governed by the presence of voids, pores or interstices, which results during the process of densification while sintering. However, unlike most advanced ceramics, CPs are difficult to sinter and thus are mechanically weak. The resistance to fatigue is another essential factor for (tensile) load-bearing implants. In terms of Weibull factor, n, values of n=50 to 100 usually signify good resistance but values of n=10 to 20 are insufficient and may fail in several months of usage.

Although synthetic calcium phosphate bioceramics are bioactive, their analogy with the bone mineral is generally very poor due to absence of hydrogenophosphate ions, carbonate ions, magnesium, sodium and numerous elements. These trace elements play an important role in overall performance of human bone. It is important to incorporate these elements into the TCP implants, as their biocompatibility is closely dependent on their composition. Drissens et al. [21] found out that densification of calcium phosphate ceramics can be improved by addition of proportional amount of sintering additives. Although significant research has already been done to improve the mechanical properties of TCP ceramics, the strength of these ceramics is still poor which restricts their use to non-load bearing applications. In this research we have studied and analyzed the effects of various oxide-based sintering additives on hardness, densification and characterization of these bioceramics.
Conventional calcium phosphate based ceramic powders suffer from poor sinterability possibly due to their low surface area (typical 2-5 m²/gm). In addition, it has been also recorded that the resorption process of synthetic CPs (conventional forms) is quite different from that of bone mineral. Bone mineral crystals are in nano-size with a very large surface area. They are grown in an organic matrix and have very loose crystal-to-crystal bonds; therefore the resorption by osteoclasts is quite homogeneous. CPs (micron size), on the contrary, present a low surface area and have strong crystal-to-crystal bond. Resorption takes place in two steps: (i) disintegration of particles and (ii) dissolution of the crystals. Nanoscale bioceramics is one of the emerging approaches that have been extensively studied recently by various researchers to find a solution to these long standing problems associated with calcium phosphates. In a recent publication, Kim et al [5] reported that biomineralization of calcium phosphate nano-crystals on ceramics with specific compositions and structures is a core mechanism of bioactivity. This inspires acellular and protein free biomimetic strategies for bio-active materials with new physical, chemical and biological functions.

Crystallization of various salts of CPs like hydroxyapatite (HAp) and β-tricalcium phosphate (β-TCP) depends on Ca/P ratio, presence of water and impurities, and temperature. For instance, in a wet environment and at a lower temperature (<900°C), the formation of hydroxyapatite is most likely to happen, but in a dry atmosphere and at a higher temperature, β-TCP is more likely to form.
2.1 **Tricalcium phosphate**

Tricalcium phosphate is thermodynamically stable only at elevated temperatures [1000-1500°C]. It has been proved to be resorbable *in vivo* with new bone growth replacing the implanted TCP [11]. β-TCP and α-TCP are the two forms of TCP that are known to exist. β-TCP transforms to α-TCP at around 1200°C. The later phase is stable in the range of 700-1200°C [12]. α-TCP, however, has received very little interest in the biomedical field. The disadvantage for using α-TCP is its quick resorption rate, which limits its usage in this area [13]. On the other hand β-TCP, also known as β-whitlockite, is essentially a slowly degrading bio-resorbable calcium phosphate ceramic (CPC) [14] and is a promising material in the field of biomedical applications such as orthopedics. It has also been observed to have significant biological affinity and activity and responds very well to the physiological environments [15]. Because of its slow degradation characteristic, the porous β-TCP is regarded as an ideal material for bone substitutes that should degrade by advancing bone growth [16]. These factors give β-TCP an edge over other biomedical materials when it comes to resorbability and replacement of the implanted TCP *in vivo* by the new bone tissue. Its excellent biocompatibility makes it a possible material to act as a scaffold allowing bone regeneration and in growth. X-ray patterns reveal that β-TCP has a hexagonal crystal structure. It is reported that the resorbability of β-TCP *in vivo* might be strongly related to the characterization and stability of the β-TCP structure [17]. However, although β-TCP degrades slowly compared to α-TCP form, the rate of degradation is uncontrolled [18-22], which limits its usage in most bone engineering applications.

In this work, I endeavored to improve sinterability of β-TCP, enhance its mechanical strength, and control its rate of biodegradation by introducing small quantities of various oxide-
based sintering additives. This research developed and investigated the effects of these additives on β-TCP ceramic with regard to its densification, hardness, compression strength, and in vitro degradation behavior.

2.2 **Hydroxyapatite**

Hydroxyapatite (\((\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2)\), HAp) is a bioactive ceramic widely used as powders or in particulate forms in various bone repairs and as coatings for metallic prostheses to improve their biological properties [23]. HAp is thermodynamically the most stable calcium phosphate ceramic compound at the pH, temperature and composition of the physiological fluid [24]. Recently, HAp has been used for a variety of biomedical applications, including matrices for drug release control [25]. Due to the chemical similarity between HAp and mineralized bone of human tissue, synthetic HAp exhibits strong affinity to host hard tissues. Formation of chemical bond with the host tissue offers HAp a greater advantage in clinical applications over most other bone substitutes, such as allografts or metallic implants [26].

HAp possesses a hexagonal structure with a \(P6_3/m\) space group and cell dimensions \(a=b=9.42\text{Å},\) and \(c=6.88\text{Å}\), where \(P6_3/m\) refers to a space group with a six-fold symmetry axis with a threefold helix and a mirror plane [27]. It has an exact stoichiometric Ca/P ratio of 1.67 and is chemically very similar to the mineralized human bone [28]. However, in spite of chemical similarities, mechanical performance of synthetic HAp is very poor compared to bone. In addition, the bone mineral presents a higher bioactivity compared to synthetic HAp.

Many researchers have observed that the mechanical strength and fracture toughness of HAp ceramics can be improved by the use of different sintering techniques which include addition of a low melting secondary phase to achieve liquid phase sintering for better
densification [29-31], incorporation of sintering additives to enhance densification through grain boundary strengthening [32-34], and use of nanoscale ceramic powders for better densification contributed by large surface area to volume ratios of nano size powders. It is believed that nanoscale HAp has the potential to revolutionize the field of biomedical science from bone regeneration to drug delivery. During past ten years, much attention has been given to nanostructured HAp calcium phosphate ceramic, with major research emphases of production of nanoscale powders to improve the mechanical as well as biological properties. Importance and advantages of nano crystalline HAp were highlighted by Sarig and Kahana (2002) [35]. In their work, Sarig et al. [35] could synthesize HAp with 300nm edges, which were loosely aggregated into spherulites of 2–4 mm dimensions. Nanocrystalline HAp powders exhibit improved sinterability and enhanced densification due to greater surface area [36], which could improve the fracture toughness as well as other mechanical properties [37]. Moreover, nano HAp is also expected to have better bioactivity than coarser crystals [38-42].

Nanoscale β-TCP exhibits significant biological affinity and activity and responds very well to the physiological environments. Also owing to its slow degradation characteristic, the porous β-TCP is regarded as an ideal material for bone substitutes that should degrade by advancing bone growth. It also finds applications in drug delivery systems and as bone substitutes.

To augment its usage in this area, Murugan et al. [46] prepared and characterized nano HAp composite bone paste with a natural polysaccharide, chitosan, using wet chemical method at low temperature. Their findings suggest that the HA/chitosan composite paste would be highly beneficial for the particle immobilization upon implantation and may be a candidate bioreabsorbable material as bone substitute.
Chen *et al.* [47] from Xiamen University, China, prepared and characterized nano-sized hydroxyapatite particles and hydroxyapatite/chitosan nano-composite for use in biomedical materials. They were able to produce nano-HAp particles of 20–30 nm width and 50–60 nm length and particles of almost homogeneous microstructure so that they can be useful in producing uniform nano materials. The nano-structured HAp/chitosan composite, promises to have excellent biomedical properties for use in the clinics.

Recently, in 2004, Rauschmann *et al.* [48], assessed the material properties of a calcium sulphate nanoparticulate HAp composite material and analyzed its *in vitro* uptake and release of vancomycin (antibacterial used for treating infections in different parts of the body, usually given in combination with other antibiotics) and gentamicin (antibacterial used for treating infections of the skin) antibiotics. Their results suggest this composite to be a new treatment option in osteomyelitis (acute or chronic bone infection usually caused by bacteria) owing to its good biocompatibility and sufficient antibiotic release.

W. Zhang *et al.* [49], of Tsinghua University (Beijing) described their use of conventional and high-resolution transmission electron spectroscopy (HRTEM) to study nanofibrils of mineralized collagen. They have found a key mechanism behind how these fibrils self-assemble. They have also demonstrated for the first time that HAp crystals associate specifically with the surfaces of collagen fibrils. They observed that the HAp crystals align themselves with the long axis of the collagen fibrils. Previously, other researchers had found that anions on the collagen molecules act as nucleation sites for HAp crystals and that the positions of the hydroxyl groups in HAp crystals lie along the same axis as the carbonyl groups in collagen.
A significant amount of research expected in this area (nano-regime) for much enhanced applications in drug delivery systems and as resorbable scaffolds that can be replaced by the endogenous hard tissues with the passage of time.
CHAPTER 3: EXPERIMENTAL METHODS

3.1 Experimental procedure for single oxide sintering additive system

3.1.1 Materials and methods

β-TCP powders (NC/FCC grade) with the average particle size of 3 µm were acquired from Rhodia chemicals, Chicago, Illinois. The TCP powders, approved by National Formulary (NF), were mixed with various sintering additives at different wt.% ratios. Sintering additives were selected based on earlier research [50-55], and the presence of metal ions in the composition of bone mineral [56]. The selected additives were magnesium oxide (MgO, Alfa Aesar, 96% pure), zinc oxide (ZnO, Alfa Aesar, 99% pure), silicon (IV) oxide (SiO$_2$, Alfa Aesar, 99.5% pure), titanium (IV) oxide, (TiO$_2$ anatase, Alfa Aesar, 99.9% pure). These additives were introduced in the TCP ceramic powder separately at different wt. % (1.0 wt.%, 2.5 wt.% and 4 wt%), followed by homogeneous mixing in a mortar and a pestle for 30 min. Consequent powders of variant compositions were uniaxially compacted in a steel mold, with an internal diameter of 10 mm at a pressure of 37.5 MPa using a 12-ton press from Carver (3851-0 Model C). Compositions of powder mixture of TCP with different sintering additives are presented in Table 3.

Green ceramic structures were measured for their density and then sintered in a muffle furnace, in air, at different sintering temperatures - 1150°C and 1250°C, separately for 6 h. A sintering cycle was developed to achieve better densification and to avoid cracks in the sintered specimens by introducing several soaking temperatures and tailoring the rate of heating and cooling. The consequent cycle had several steps: first, infusion at 150°C to stabilize the furnace; second, infusion at 550°C to remove residual stresses from the green structures; and the final
Table 3: Compositions of calcium phosphate ceramics studied

<table>
<thead>
<tr>
<th>Type</th>
<th>Base Powder: Pure TCP</th>
<th>Additive Composition (wt%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCP</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>A1.0</td>
<td>1.0%</td>
<td>MgO</td>
</tr>
<tr>
<td>A2.5</td>
<td>2.5%</td>
<td>MgO</td>
</tr>
<tr>
<td>A4.0</td>
<td>4.0%</td>
<td>MgO</td>
</tr>
<tr>
<td>B1.0</td>
<td>1.0%</td>
<td>ZnO</td>
</tr>
<tr>
<td>B2.5</td>
<td>2.5%</td>
<td>ZnO</td>
</tr>
<tr>
<td>B4.0</td>
<td>4.0%</td>
<td>ZnO</td>
</tr>
<tr>
<td>C1.0</td>
<td>1.0%</td>
<td>SiO₂</td>
</tr>
<tr>
<td>C2.5</td>
<td>2.5%</td>
<td>SiO₂</td>
</tr>
<tr>
<td>C4.0</td>
<td>4.0%</td>
<td>SiO₂</td>
</tr>
<tr>
<td>D1.0</td>
<td>1.0%</td>
<td>TiO₂</td>
</tr>
<tr>
<td>D2.5</td>
<td>2.5%</td>
<td>TiO₂</td>
</tr>
<tr>
<td>D4.0</td>
<td>4.0%</td>
<td>TiO₂</td>
</tr>
</tbody>
</table>

Infusion at 1150°C or 1250°C for densification. A slow heating rate of 1°C/min was used for better densification. Sintered ceramic structures were measured for their density and then, were subjected to mechanical characterization and bioresorbability analysis. Samples sintered at 1150°C showed poor densification and, therefore, were not characterized for their mechanical and biodegradation behavior.

3.1.2 Phase identification and microstructural analysis

X-ray powder diffraction (XRD) technique was used to study the effect of sintering temperature and additives on phase purity of TCP ceramics. Sintered ceramic structures of variant composition were crushed and ground to fine powder, manually, using a mortar and a
pestle. Powder samples of variant composition (TCP, A1.0, B1.0, C1.0 and D1.0) were placed in the specimen holder of Rigaku diffractometer, separately, and then analyzed, using Ni-filtered CuKα radiation (λ =0.1542 nm) at 40 kV and 40 mA settings. The XRD patterns were recorded in the 2θ range of 15 to 65 degrees, with a step size of 0.02 degrees and step duration of 0.5 s.

Scanning electron microscopy (SEM) was used to observe and analyze the microstructure of sintered ceramic structures to study and understand the influence of sintering aids on grain size and surface porosity after sintering. Specimens of pure TCP and TCP reinforced with 1.0 wt% of additives (A1.0, B1.0, C1.0, and D1.0) sintered at 1250°C for 6 h, were only observed under SEM for microstructural analysis. Specimens used for SEM examination had average dimensions of 8 mm in diameter and 2.3 mm in thickness. These specimens were gold-coated for 1 min using a magnetron sputter coater from Emitech Inc. and placed inside a Jeol SEM, Model 6400F (Tokyo, Japan) for observation.

3.1.3 Mechanical characterization

Mechanical properties of sintered ceramic structures containing various sintering additives were evaluated in terms of their hardness and compression strength. Sintered ceramics of all composition types (TCP, A1.0, B1.0, C1.0, D 1.0, A2.5, B2.5, C2.5, and D2.5) were indented with a Vickers diamond indenter and the indentation size was measured automatically to find their hardness in a Vickers hardness tester (LECO 700). Specimens used for hardness testing had an average dimension of 8 mm in diameter and 2.3 mm in thickness. The test was carried out with a major load of 1 kg for 5 s loading. Two samples of each of the composition type were tested for their hardness at three different locations. The average of these readings were calculated and compared for analysis.
To determine mechanical strength under uniaxial compressive loading, the sintered ceramic specimens of selected compositions (TCP, A1.0, B1.0, C1.0, and D1.0) were tested in a fully automated tensile tester from Instron (Model 3369) with a constant crosshead speed of 1 mm/min. Six cylindrical samples of each of these compositions with diameter to height ratio of 1:1.5 (approx.) were prepared and then sintered at 1250°C for 6 h. The compression samples had an average diameter of 7.5 mm with an average height of 11.5 mm. Only samples containing 1.0 wt.% of additives were subjected to compression testing.

### 3.1.4 Biodegradation study

The rate of degradation of sintered ceramic structures of different compositions was determined in terms of their weight-loss in a protein free dynamic simulated body fluid (SBF). SBF has been widely used by researchers to test bioactivity of materials by examining the formation of apatite layer on the surface of testing materials. The *in vivo* formation of an apatite layer on the surface of a bone grafting material can be reproduced in a cellular SBF which is prepared to have an ion concentration nearly equal to that of human blood plasma [57-59] (Na\(^+\) 142.0, K\(^+\) 5.0, Ca\(^{2+}\) 2.5, Mg\(^{2+}\) 1.5, Cl\(^-\) 147.8, HCO\(_3\)\(^-\) 4.2, HPO\(_4\)\(^{2-}\) 1.0, and SO\(_4\)\(^{2-}\) 0.5 mM, and a pH of 7.3, as shown in Table 4. In our work, we used SBF to determine effect of selected sintering additives on biodegradation of TCP. Samples containing 1.0 wt% of additives were prepared and immersed in a dynamic SBF solution for weeks. A tank having compartments for placing the samples separately was selected. A set of fifteen samples of composition types TCP, A1.0, B1.0, C1.0 and D1.0 were placed in perforated plastic containers and then these containers were placed inside the tank. The tank was filled with freshly prepared SBF and was observed for 5 weeks, in a state of constant flow. SBF was replaced every week with a freshly prepared one to maintain its
ionic concentration. At the end of each week, three samples of each of these compositions were taken out from the tank, dried at 100°C in a furnace and measured for their weight to calculate weight loss as a result of time. Dried specimens were also tested for their hardness, to understand the effect of biodegradation on their mechanical property.

Table 4: Ion concentrations of human blood plasma and SBF

<table>
<thead>
<tr>
<th>Ionic Concentration (mM)</th>
<th>Na⁺</th>
<th>K⁺</th>
<th>Ca²⁺</th>
<th>Mg²⁺</th>
<th>Cl⁻</th>
<th>HCO₃⁻</th>
<th>HPO₄²⁻</th>
<th>SO₄²⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human blood plasma</td>
<td>142.0</td>
<td>5.0</td>
<td>1.5</td>
<td>2.5</td>
<td>103.0</td>
<td>27.0</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>SBF</td>
<td>142.0</td>
<td>5.0</td>
<td>1.5</td>
<td>2.5</td>
<td>148.8</td>
<td>4.2</td>
<td>1.0</td>
<td>0.5</td>
</tr>
</tbody>
</table>

SBF buffered at pH 7.3 with tris-hydroxymethylaminomethane and 1M HCl.

3.2 Experimental procedure for multi oxide sintering additive system

In this work, I investigated the effects of three different compositions of MgO-Na₂O-P₂O₅-based additives on the phase transition and sintering behavior of β-TCP.

3.2.1 Materials and methods

β-TCP powder (NC/FCC grade) with the average particle size of 3 µm was acquired from Rhodia chemicals, Chicago, IL, for this research. Three different compositions of MgO-Na₂O-P₂O₅-based additives were selected and prepared based on its ternary-oxide phase diagram. Constituent powders were mixed in stoichiometric ratios based on their phase compositions.
Sintering additive mixtures were heat treated at 0.5 $T_m$, where $T_m$ is the melting temperature of corresponding phase mixture. Heat-treated additives were crushed and ground into fine powder using a mortar and pestle. TCP powder, national formulary (NF) approved, was mixed with small quantities of as-prepared MgO-Na$_2$O-P$_2$O$_5$-based additives using ball milling and then pressed into green pallets via uniaxial pressing in a steel mold. Starting powders used in the preparation of sintering additives were magnesium oxide (MgO, Alfa Aesar, 96% pure), phosphorous pentoxide (P$_2$O$_5$, Alfa Aesar, 98.5%, min) and sodium carbonate (Na$_2$CO$_3$, Alfa Aesar, 95% pure). Table 1 presents composition of the additives and abbreviation used in this paper to represent different compositions of TCP integrated with these additives.

As-prepared powder of variant compositions were uniaxially compacted in a press mold made of steel having an internal diameter of 10 mm at a pressure of 37.5 MPa using a 10-ton press from Carver Inc. Green ceramic structures were measured for their density and then sintered in a muffle furnace, in air, at 1250°C for 6 h for densification. A sintering cycle suitable for TCP ceramics was developed to achieve improved densification and to avoid cracks in the sintered specimens by introducing several soaking temperatures and tailoring the rate of heating and cooling. The consequent cycle had several steps: first, infusion at 150°C to stabilize the furnace; second, infusion at 550°C to remove residual stresses from the green structures; and the final infusion at 1250°C for densification. A slow heating rate of 1°C/min was used for better densification. Sintered ceramic structures were measured for their density and then, were subjected to mechanical characterization and bioresorbability analysis.
Table 5: Compositions of tricalcium phosphate (TCP) ceramic doped with MgO-Na₂O-P₂O₅-based sintering additives.

<table>
<thead>
<tr>
<th>Type</th>
<th>Base Powder: Pure TCP Additive Amount (wt%)</th>
<th>Compositions of Additives (wt%)</th>
<th>MgO</th>
<th>Na₂O</th>
<th>P₂O₅</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCP</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>I</td>
<td>1.0%, 2.5%, 4.0%</td>
<td>35 12 53</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>1.0%, 2.5%, 4.0%</td>
<td>60 25 15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>1.0%, 2.5%, 4.0%</td>
<td>50 25 25</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.2.2 **Phase identification and microstructural analysis**

X-ray powder diffraction (XRD) technique was used to study the effect of sintering temperature and additives on phase purity of TCP ceramics. Sintered ceramic structures of variant composition were crushed and ground to fine powder, manually, using a mortar and a pestle. Powder samples of variant composition (TCP, I1.0, II1.0 and III1.0) were placed in the specimen holder of Rigaku diffractometer, separately, and then analyzed, using Ni-filtered CuKα radiation (λ =0.1542 nm) at 40 kV and 40 mA settings. The XRD patterns were recorded in the 2θ range of 15 to 65 degrees, with a step size of 0.02 degrees and step duration of 0.5 s.

Scanning electron microscopy (SEM) was used to observe and analyze the microstructure of sintered ceramic structures to study and understand the influence of sintering aids on grain size and surface porosity after sintering. Specimens of pure TCP and TCP reinforced with 1.0 wt% of additives (II1.0, III1.0 and III1.0) sintered at 1250°C for 6 h, were only observed under SEM for microstructural analysis. Specimens used for SEM examination had average dimensions of 8 mm in diameter and 2.3 mm in thickness. These specimens were gold-coated for 1 min.
using a magnetron sputter coater from Emitech Inc. and placed inside a Jeol SEM, Model 6400F (Tokyo, Japan) for observation.

### 3.2.3 Mechanical characterization

Mechanical properties of sintered ceramic structures containing various sintering additives were evaluated in terms of their hardness and compression strength. Sintered ceramics of all composition types with 1 wt% and 2.5 wt% sintering additives were indented with a Vickers diamond indenter and the indentation size was measured automatically to find their hardness in a Vickers hardness tester (LECO 700). Specimens used for hardness testing had an average dimension of 8 mm in diameter and 2.3 mm in thickness. The test was carried out with a major load of 1 kg for 5 s loading. Two samples of each of the composition type were tested for their hardness at three different locations. The average of these readings were calculated and compared for analysis.

To determine mechanical strength under uniaxial compressive loading, the sintered ceramic specimens of selected compositions (TCP, II1.0, III1.0 and III1.0) were tested in a fully automated tensile tester from Instron (Model 3369) with a constant crosshead speed of 1 mm/min. Six cylindrical samples of each of these compositions with diameter to height ratio of 1:1.5 (approx.) were prepared and then sintered at 1250°C for 6 h. The compression samples had an average diameter of 7.5 mm with an average height of 11.5 mm. Only samples containing 1.0 wt.% of additives were subjected to compression testing.
3.2.4 Biodegradation study

The rate of degradation of sintered ceramic structures of different compositions was determined in terms of their weight-loss and degradation in hardness in a protein free dynamic simulated body fluid (SBF) as discussed in section 3.1.4.

3.3 Experimental procedure for nanocrystalline hydroxyapatite

In this research, we synthesized nanocrystalline, stoichiometric, single-phase HAp powders in the range of 2-10 nm within a short time frame (sol preparation time of 16 hrs) through low temperature Sol-Gel techniques.

3.3.1 Materials and method

A 0.025 mol of triethyl phosphite (Fisher, USA) was first hydrolyzed with a fixed amount of distilled water (the molar ratio of water to phosphite is fixed at 8) in a nalgene bottle under vigorous stirring. A stoichiometric amount, 0.045 mol of calcium nitrate (Fisher, USA) dissolved first in 25 ml of distilled water, was added drop wise into the hydrolyzed phosphite sol. The mixed sol solution was then continuously agitated for additional 4 min and kept static (aging) at 50°C. Measured amount of the mixed sol was sampled after an aging time of 125 min. This aged sol was then subjected to thermal treatment at 85°C for 20hrs until a white, dried gel was obtained. The dried gels were further doped with magnesium and zinc in 1 wt%, 2.5 wt% and 4 wt% addition. The doped gels were further calcined at 250°C, 350°C for 3 h and at 500°C for only 15 min, at a constant heat rate of 15°C/min, followed by furnace cool. Phase composition of the dried gel and HAp powders were determined by X-ray powder diffraction analysis (XRD)
with Ni-filtered CuKα radiation (Rigaku Corp.; 40 kV, 40 mA). The morphology of the powders was analyzed in a transmission electron microscope (HR-TEM; Technai-Phillips). As-synthesized nano-HAp powders were uniaxially compressed using a steel mold having an internal diameter of 10 mm at a pressure of 37.47 MPa. Compositions of powder mixture of TCP with different sintering additives are presented in Table 9.

Table 6: Compositions of calcium phosphate ceramics studied

<table>
<thead>
<tr>
<th>Type</th>
<th>Synthesized base Powder: Pure HAp Additive Composition (wt%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAp</td>
<td>—</td>
</tr>
<tr>
<td>A1.0</td>
<td>1.0% MgO</td>
</tr>
<tr>
<td>A2.5</td>
<td>2.5% MgO</td>
</tr>
<tr>
<td>A4.0</td>
<td>4.0% MgO</td>
</tr>
<tr>
<td>B1.0</td>
<td>1.0% ZnO</td>
</tr>
<tr>
<td>B2.5</td>
<td>2.5% ZnO</td>
</tr>
<tr>
<td>B4.0</td>
<td>4.0% ZnO</td>
</tr>
</tbody>
</table>

3.3.2 Phase identification and powder morphology

X-ray powder diffraction (XRD) technique was used to study the effect of calcining temperature and dopants on phase purity of HAp ceramics. Calcined ceramic powders were ground to fine powder, manually, using a mortar and a pestle. Powder samples of variant composition (Pure nano HAp, A and B) were placed in the specimen holder of Rigaku diffractometer, separately, and then analyzed, using Ni-filtered CuKα radiation (λ =0.1542 nm)
at 40 kV and 40 mA settings. The XRD patterns were recorded in the 2θ range of 15 to 65 degrees, with a step size of 0.02 degrees and step duration of 0.5 s.

Transmission electron microscopy (TEM) was used to observe and analyze the morphology of the as-synthesized powders calcined at 500°C for 15 min. Powders calcined at lower temperatures were not analyzed for their particle size. Powder specimens of pure HAp and HAp doped with 1.0 wt% of additives (A and B) calcined at 500°C for 15 min, were observed under TEM for microstructural analysis.

3.3.3 Densification study

Green ceramic structures were measured for their density and then sintered in a muffle furnace, in air, at 1150°C, 1250°C and 1300°C, separately for 6 h. A sintering cycle was developed to achieve better densification and to avoid cracks in the sintered specimens by introducing several soaking temperatures and tailoring the rate of heating and cooling. The consequent cycle had several steps: first, infusion at 150°C to stabilize the furnace; second, infusion at 550°C to remove residual stresses from the green structures; and the final infusion at 1250°C and 1300°C, respectively for densification. A slow heating rate of 1°C/min was used for better densification. Sintered ceramic structures were measured for their density and then, were subjected to mechanical characterization and bioresorbability analysis.

3.3.4 Mechanical characterization

Mechanical properties of sintered ceramic structures containing various sintering additives were evaluated in terms of their hardness and compression strength. Sintered ceramics
of composition types (Pure HAp, A and B) were indented with a Vickers diamond indenter and the indentation size was measured automatically to find their hardness in a Vickers hardness tester (LECO 700). Specimens used for hardness testing had an average dimension of 8 mm in diameter and 2.3 mm in thickness. The test was carried out with a major load of 1 kg for 5 s loading. Two samples of each of the composition type were tested for their hardness at three different locations. The average of these readings were calculated and compared for analysis.

To determine mechanical strength under uniaxial compressive loading, the sintered ceramic specimens of compositions (Pure HAp, A and B) were tested in a fully automated tensile tester from Instron (Model 3369) with a constant crosshead speed of 1 mm/min. Six cylindrical samples of each of these compositions with diameter to height ratio of 1:1.5 (approx.) were prepared and then sintered at 1300°C for 6 h. The compression samples had an average diameter of 7.5 mm with an average height of 11.5 mm.

3.3.5 Biodegradation study

The rate of degradation of sintered ceramic structures of different compositions was determined in terms of their weight-loss and degradation in hardness in a protein free dynamic simulated body fluid (SBF) as discussed in section 3.1.4.
CHAPTER 4: RESULTS AND DISCUSSION

4.1 Effect of single oxide sintering additives on tricalcium phosphate ceramics

4.1.1 Densification study

Green ceramic structures prepared via uniaxial pressing were measured for their bulk density and were subjected to pressure-less sintering. Two sets of four green specimens of all composition types (TCP, A1.0, B1.0, C1.0, D1.0, A2.5, B2.5, C2.5, D2.5, A4.0, B4.0, C4.0, and D4.0) were sintered at 1150 °C and 1250 °C separately, for 6 h to study the effect of sintering temperature and the amount of sintering additives on densification of TCP. Each sintered specimen was measured for its bulk density and the average of each of the compositions. The average sintered densities for different compositions were plotted as a function of percentage of sintering additives at two different temperatures – 1150 °C and 1250 °C and are presented in figure 2(a) and figure 2(b). It is evident from figure 2(a) that sintering at 1150 °C did not improve densification of TCP. The highest sintered density of 2.77 g/cc was recorded for composition type B1.0 at 1150 °C. Pure TCP showed a maximum density of 2.50 g/cc at this temperature. Sintering at 1250 °C significantly improved the densification of all compositions including pure TCP, in comparison to 1150 °C. A remarkable improvement in sintered density was achieved in composition types A1.0 (3.39 g/cc), which showed the highest sintered density compared to pure TCP (3.04 g/cc). The theoretical density of β-TCP is reported to be 3.12 g/cc [23]. Addition of SiO$_2$ (C1.0, C2.5, C4.0) and TiO$_2$ (D1.0, D2.5, D4.0) showed a negative effect on densification of TCP as shown in figure 2 and figure 3. At 1250 °C, composition types B1.0 and B2.5 showed marginal increase in density, compared to pure TCP.
Figure 2: Influence of oxide-based sintering additives on densification of tricalcium phosphate (TCP) ceramics. Sintering was done at 1150 °C and 1250 °C respectively.

These results can be explained with the help of microstructures of these dense structures having different compositions as shown in figure 6 (SEM micrographs). Figure 6 shows that although we sintered samples of all compositions (A, B, C, D) at the same sintering temperature (1250 °C) for 6 hrs, voids were seen in the sintered compacts of compositions C and D; whereas good crystalline microstructures with no visible pores, were observed in case of compositions A and B. It is known that decrease in porosity increases density in a bulk material. This explains why the compositions A and B showed the higher sintered density at 1250 °C compared to other
compositions. These results can also be explained with the help of XRD patterns (Figure 5) of sintered ceramics of different compositions. As one can see here, the crystallinity of the $\beta$-TCP ceramic increased with the addition of 1.0 wt.% of MgO and ZnO (composition A and B, respectively) compared to $\beta$-TCP pure and compositions C and D. Additionally, it is clear from figure 2a and b that with increasing sintering temperature sintered density improved for $\beta$-TCP ceramics, which is line with what is reported in literature [24].

Figure 3 presents the plot of volume shrinkage as a function of composition for specimens sintered at 1250 °C. A considerable increase in volume shrinkage was observed for the composition A1.0. This can also be co-related with the densification process (figure 2b) and can be explained with the help of figure 6. It is clear from the SEM pictures that the grain distribution in composition A is uniform with distinct grain boundaries and no visible cracks or pores. This resulted in a very dense sintered compact. It is worthwhile to note that the composition type A2.5 and A4.0 showed a marginal increase in volume shrinkage. This can be confirmed from figure 3 as the sintered density of compositions A2.5 and A4.0 is greater than that of pure TCP.

4.1.2 **Phase identification and microstructural analysis**

Results of X-ray powder diffraction revealed that presence of sintering additives and sintering temperature (1250°C) did not alter the phase purity of TCP ceramics. Figure 4 shows X-ray diffraction patterns of sintered compacts for the compositions TCP, A1.0, B1.0, C1.0 and D1.0. Peaks in each X-ray diffraction pattern were recorded and verified using standard JCPDS file, no. 9-169. Compared to XRD pattern of pure TCP, the crystallinity of TCP powders
increased on addition of some of the sintering additives but no obvious phase change was noticed from these XRD patterns. Composition type A1.0, and B1.0 exhibit high crystalline peaks at about 31.5°. Almost identical patterns were recorded for all these compositions, which suggest that the presence of 1.0 wt.% of sintering aids did not alter phase-purity of TCP. Compositions with higher percentage of sintering additives were not analyzed for their phases.

Sintered ceramic structures were observed under an SEM to understand, compare and analyze the effects of sintering additives on microstructure and correlate them with physical and mechanical properties. Results of scanning electron microscopy are shown in figure 6a, b, c, d, and e for structures sintered at 1250 °C of composition type TCP, A1.0, B1.0, C1.0 and D1.0, respectively. Micrographs of all of these compositions showed clear demarcation in the grain...
Figure 4: XRD patterns of sintered TCP ceramics doped with oxide-based sintering additives (1.0 wt.%). Sintering was done at 1250 °C.
Figure 5: SEM micrographs of metal ion-doped sintered tricalcium phosphate. Specimens were sintered at 1250 °C.
boundaries and therefore, their grain diameter could be easily calculated. Linear intercept method was employed to calculate average grain diameter of the sintered structures. The average grain sizes were calculated to be 3.14 µm, 4.19 µm, 3.19 µm, 7.23 µm, and 6.81 µm, respectively, for composition types TCP, A1.0, B1.0, C1.0 and D1.0. SEM results showed that presence of sintering additives increased the grain size of the sintered ceramics compared to pure TCP. The grain growth is significant for composition types C1.0 and D1.0, and therefore, we believe these compositions showed lower sintered density compared to pure TCP. Also from their micrographs, it is clear that these structures had surface porosity, which had contributed to poor densification during sintering. Composition types TCP and B1.0 showed very little difference in their grain sizes as well as their sintered densities at 1250 ºC. In contradiction, composition type A1.0 showed significantly improved sintered density although its grain size was slightly higher than that of pure TCP at 1250 ºC. Our explanation for this behavior is that although these was an increase in grain diameter of the composition type A1.0, the sintering additive present in the structure (1.0 wt.% MgO) had improved the grain boundary properties thereby improving its sintered density at 1250 ºC. SEM micrograph of this composition (A1.0) also showed that the sintered structure was fully dense without any surface porosity, which had contributed to its improved sintered density.

4.1.3 Mechanical property evaluation

4.1.3.1 Vickers hardness testing

Results of Vickers hardness testing revealed that the presence of certain sintering additives could significantly enhance the hardness of TCP ceramics. Hardness testing was performed on specimens sintered at both at 1150 ºC and 1250 ºC for pure TCP and TCP
containing 1.0 wt.% and 2.5 wt.% of additives (TCP, A1.0, B1.0, C1.0, D1.0, A2.5, B2.5, C2.5, and D2.5). The average hardness of each of these composition types were calculated and plotted as a bar chart as shown in figure 7 as a function of composition. It can be observed from figure 7, presence of sintering additives influenced hardness of TCP both positively and negatively. With respect to sintered structure of pure TCP, some composition types showed higher hardness while some other compositions showed relatively lower hardness. In accordance with our densification studies, specimens sintered at 1150 °C showed significantly lower hardness in comparison to the specimens sintered at 1250 °C. The highest hardness value of 302 HV was achieved for the composition type A1.0 sintered at 1250 °C, which had also shown the highest sintered density. At 1250 °C, composition types A1.0, A2.5, B1.0, B2.5, and D1.0 showed enhanced hardness compared to pure TCP although some of these compositions showed nearly equal or lower sintered density than pure TCP. We believe that presence of additives improved grain boundary
properties of TCP thereby improving its mechanical properties. Composition type C1.0 showed a hardness value very close to that of pure TCP in spite of its low sintered density (figure 7) and higher grain size (figure 5c). To bring out the relationship between sintered density and hardness, separate graphs showing variation of hardness as a function of sintered density for structures sintered at 1150 °C and 1250 °C. These graphs are shown in figure 8 and figure 9. It is clear from these figures that with the increase in density of sintered structures their hardness also improved with exception to composition type D1.0 at 1250°C.

![Graph showing hardness vs. density plots for dense TCP structures containing 1.0 wt% of single-oxide sintering additives sintered at 1250°C.](image)

Figure 7: Hardness vs. density plots for dense TCP structures containing 1.0 wt% of single-oxide sintering additives sintered at 1250°C.

### 4.1.3.2 Compression testing

TCP ceramics integrated with 1.0 wt% of different sintering additives were subjected to mechanical testing to determine their failure strength under uniaxial compressive loading. Sintered ceramic structures with average dimensions of 7.5 mm in diameter and 11.5 mm in...
height of composition types TCP, A1.0, B1.0, C1.0, and D1.0 were evaluated for their compression strengths in a fully automated screw driven tensile tester from Instron. Average compression strengths of different compositions were evaluated and were compared with that of pure TCP structures processed under the same conditions. Results from compression test are shown in Table 5.

Table 7: Compressive strengths of Pure TCP and TCP reinforced with 1.0 wt.% of additives

<table>
<thead>
<tr>
<th>Type</th>
<th>Compression Strength (MPa)</th>
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<tbody>
<tr>
<td>TCP</td>
<td>29.7 ± 4.2</td>
</tr>
<tr>
<td>A1.0</td>
<td>90.9 ± 5.1</td>
</tr>
<tr>
<td>B1.0</td>
<td>71.3 ± 3.1</td>
</tr>
<tr>
<td>C1.0</td>
<td>41.5 ± 4.2</td>
</tr>
<tr>
<td>D1.0</td>
<td>29.9 ± 2.2</td>
</tr>
</tbody>
</table>

Composition type A1.0 showed the highest failure strength (91 MPa) under compressive loading, which is a 206% improvement, compared to compression strength of pure TCP structures (30 MPa), processed under the same conditions. SEM micrographs (Figure 6) give the best explanation as to why compositions A, B and C showed significantly higher compression strength compared to pure β-TCP. As seen here, composition A had almost equiaxed grains with no pores, and had the highest compression strength. Although pores were present in compositions C and D (Figure 5c and 5d), the pores were larger in number for D compared to C. This explains why C showed higher compression strength and higher hardness compared to D.
From these results, it can be concluded that some of these sintering additives can be used to improve mechanical performance of resorbable β-TCP ceramics, which has many potential applications in hard tissue engineering. Structures prepared via high pressure pressing routes such as cold isostatic pressing and hot isostatic pressing will possibly possess even higher mechanical properties.

4.1.4 Biodegradation study

Figure 8: Biodegradation of β-TCP reinforced with single-oxide sintering additives in SBF.

Figure 8 represents the biodegradation study for sintered compacts with 1.0 wt.% additives. All the compositions with 1.0 wt% sintering additives were selected due to their excellent densification and hardness values. It is evident from the figure that composition A with 1.0 wt.% addition degrades at a slower rate as compared to the other compositions. In fact there
is no major loss of weight in the samples having composition A, also their hardness values are not affected. Composition B and C degrades at much slower rate as compared to commercial TCP. Composition D was observed to be degrading at a much higher rate as compared to all other single oxide systems.

Figure 9 represents the hardness plot for the samples, which were kept in the SBF (simulated body fluid) for a specific period of time. A batch of 6 samples each were taken out of the fish tank containing the SBF and were subjected to the Vickers hardness. It was observed that composition A with 1.0 wt% of sintering additives showed a considerable increase in hardness value about 20% when compared to the hardness of pure TCP. The hardness of composition A remained constant even after 6 weeks. Composition B showed about 2.0% increase in hardness when compared to pure TCP. Similar trend was observed for the hardness values for composition B after 6 weeks. Composition C and D showed a decrease in hardness about 10%. There was a constant decrease in the hardness values and the hardness trend after each week.
Figure 9: Effect of biodegradation on hardness of TCP ceramics doped with different sintering additives at various time points.

4.1.5 Conclusions

We have done densification, hardness and biodegradation studies on the various oxide based sintering additives. Composition A showed better densification and hardness values as compared to the other compositions. A maximum sintered density of 3.39 g/cc was achieved for the composition A having 1.0 wt.% sintering additives, sintered at 1250°C for 6 hours. Although most of these sintering additives did not increase sintering density appreciably, their presence did significantly improve the hardness of pure TCP. On average, 20-30 % increase in hardness value was recorded for some of the compositions when compared to pure TCP compacts under the same environment. Compression testing results showed that some of these sintering additives
improved failure strength of commercial TCP. On an average, a 30% increase in the failure strength was observed for the samples with composition A (1 wt.% of additives), sintered at 1250 °C for 6 hours. Biodegradation study for composition A revealed no significant change in densification value as well as hardness value.

4.2 Effects of multi-oxide sintering additives on tricalcium phosphate bioceramics

4.2.1 Densification study

Green ceramic structures prepared via uniaxial pressing were measured for their bulk green density and were subjected to pressure-less sintering. Two sets of four green specimens of all composition types (TCP, I1.0, II1.0, III1.0, I2.5, II2.5, III2.5, I4.0, II4.0 and III4.0) were sintered at 1250 °C for 6 h to study the influence of sintering and the amount of sintering additives on densification of TCP. Each sintered specimen was measured for its bulk density and the average for each composition was calculated. The average sintered densities for all compositions were plotted as a function of percentage of sintering additives at 1250 °C as shown in figure 11. Results showed that sintering at 1250 °C improved the densification of all compositions. A remarkable improvement in sintered density was achieved in composition I4.0 (3.33 g/cc) compared to pure TCP (3.04 g/cc).

The results of densification study can be explained in context with the SEM micrographs as shown in figure 13. From the micrographs it is clear that pure TCP and composition I shows a very good crystalline structures with clear grain boundaries which are distinctly visible, whereas we do not see perfectly crystalline structures for composition II and III. Looking at this micrographs it is clear that there is a significant grain growth for compositions II and III leading
to lower densification values, whereas a crystalline grains with uniform grain size are observed in composition I. This explains why the compositions I and pure TCP showed the higher sintered density than other two compositions studied.

![Graph showing the influence of MgO-Na₂O-P₂O₅-based additives on sintered density of tricalcium phosphate bioceramic. Specimens were sintered at 1250 °C.](image)

**Figure 10:** Influence of MgO-Na₂O-P₂O₅-based additives on sintered density of tricalcium phosphate bioceramic. Specimens were sintered at 1250 °C.

4.2.2 **Phase identification and microstructural analysis**

Results of X-ray powder diffraction of the sintered ceramics revealed that presence of MgO-Na₂O-P₂O₅ additives and the sintering temperature of 1250 °C did not significantly alter phase purity of β-TCP. Figure 12 shows X-ray diffraction patterns of sintered ceramics for the composition types TCP, I1.0, II1.0 and III1.0. Peaks in each XRD patterns were recorded and
verified using standard JCPDS file, no. 9-169. Compared to XRD pattern of pure TCP, the crystallinity of TCP powders increased on addition of some of the sintering additives. Some $\beta$-TCP did change into $\alpha$-TCP, which is in line with what is reported in literature. Transformation of $\beta$-TCP to $\alpha$-TCP can start at a temperature as low as 800 $^\circ$C, and it is extremely difficult avoid this phase transformation.

![XRD patterns of sintered TCP doped with different compositions of MgO-Na$_2$O-P$_2$O$_5$-based additives.](image)

Figure 11: XRD patterns of sintered TCP doped with different compositions of MgO-Na$_2$O-P$_2$O$_5$-based additives.
Sintered ceramic structures were also observed under an SEM to understand, compare and analyze the effects of additives on their microstructure and correlate them with physical and mechanical properties. Results of SEM examination are shown in figure 13a, b, c, d, and e for composition types TCP, II1.0, II1.0 and III1.0, respectively. Linear intercept method was employed to calculate average grain diameter of the sintered structures of different compositions.
The average grain sizes were calculated to be 3.14 µm, 4.13 µm, 6.53 µm and 7.12 µm, respectively, for composition types TCP, I1.0, II1.0 and III1.0. From these calculations it is clear that the presence of sintering additives increased grain diameter of the sintered ceramics compared to pure TCP. The grain growth is significant for composition types II1.0 and III1.0, and therefore, we believe these compositions showed lower sintered density compared to pure TCP. Also from these micrographs, it is visible that these structures had surface porosity, as explained earlier, which had contributed to poor densification during sintering. In contradiction, composition type I1.0 showed significantly improved sintered density although its grain size was slightly higher than that of pure TCP at 1250 ºC. Our explanation for this behavior is that although there was an increase in grain diameter of the composition type I1.0, the sintering additive present in the structure (1 wt% MgO) had improved the grain boundary properties thereby improving its sintered density at 1250 ºC.

4.2.3 Mechanical property evaluation

4.2.3.1 Vickers hardness testing

Results of Vickers hardness test revealed that the presence of certain sintering additives could significantly enhance the hardness of TCP ceramics. Hardness testing was performed on sintered specimens containing 1.0 and 2.5 wt.% of additives (TCP, I1.0, III1.0, I2.5, II2.5 and III2.5). The average hardness of each of these composition types were calculated and plotted as a function of composition as shown in figure 15. It can be observed from figure 14 that the presence of sintering additives influenced hardness of TCP both positively and negatively. A maximum hardness value of 241 HV was achieved for the composition type I1.0 whereas the hardness of pure TCP, processed under the same condition, was measured to be (172.10 HV). In
relative term, this improvement corresponds to 40% increase in hardness. Overall, composition types I1.0, I2.5 and III1.0 showed improved hardness compared to pure TCP. In general, structures with greater sintered density showed higher hardness. However, it is interesting to note that some of these compositions (I.25 and III1.0) showed improved hardness values although they exhibited nearly equal or lower sintered density than pure TCP. We believe that this exception is possibly due to the improvement in grain boundary properties of TCP by the introduction of these sintering additives. To bring out the relationship between sintered density and hardness, separate graphs showing variation of hardness as a function of sintered density for structures sintered 1250 °C. These graphs are shown in Figure 15. It is clear from these figures that with the increase in density of sintered structures their hardness also improved with exception to composition type III1.0.

Figure 13: Vickers hardness of pure TCP and TCP doped with different compositions of MgO-Na₂O-P₂O₅ additives, expressed in % with respect to hardness of pure TCP.
Figure 14: Variation of hardness as a function of sintered density of TCP and TCP integrated with MgO-Na$_2$O-P$_2$O$_5$-based sintering additives.

### 4.2.3.2 Compression testing

TCP ceramics integrated with 1.0 wt% of different sintering additives were subjected to mechanical testing to determine their failure strength under uniaxial compressive loading. Sintered ceramic structures with average dimensions of 7.5 mm in diameter and 11.5 mm in height of composition types TCP, II1.0, III1.0 and III1.0 were evaluated for their compression strengths in a fully automatic screw driven tensile tester from Instron. Average compression strengths of different compositions were evaluated and were compared with that of pure TCP structures processed under the same conditions. Results from compression test are presented in table 8.
Table 8: Influence of MgO-Na$_2$O-P$_2$O$_5$ additives on failure strength of tricalcium phosphate (TCP) under uniaxial compressive loading.

<table>
<thead>
<tr>
<th>Type</th>
<th>Compression Strength (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCP</td>
<td>29.7 ± 4.2</td>
</tr>
<tr>
<td>I 1.0</td>
<td>72.3 ± 2.9</td>
</tr>
<tr>
<td>II 1.0</td>
<td>26.1 ± 1.7</td>
</tr>
<tr>
<td>III 1.0</td>
<td>12.7 ± 3.4</td>
</tr>
</tbody>
</table>

Composition type I 1.0 showed the highest failure strength (72.3 MPa) under compressive loading, which is a 143 % improvement, compared to compression strength of pure TCP structures (30 MPa). Structures of composition type III 1.0 showed poor densification and relatively lower hardness, also their compressive strengths (26 MPa and 12 MPa) were slightly lower than that of pure TCP. SEM micrographs (figure 14) give the best explanation as to why these compositions showed ultimate compression strength. As seen here, composition I had almost equiaxed grains with no pores, and had the highest compression strength. Although pores were present in compositions II and III (Figure 14c and 14d), the pores were larger in number for III compared to II. This explains why II showed higher compression strength and higher hardness compared to III.

From these results, it can be concluded that some of these sintering additives can be used to improve mechanical performance of resorbable β-TCP ceramics, which has many potential applications in hard tissue engineering. Structures prepared via high pressure pressing routes such as cold isostatic pressing and hot isostatic pressing will possibly possess even higher mechanical properties.
4.2.4 **Biodegradation study**

Biodegradation studies conducted in a dynamic SBF showed that these sintering additives could tailor the rate of resorption of TCP ceramics. Figure 16 shows the rate of resorption of sintered ceramics structures of variant composition measured in terms of their weight loss at different time points.

It is clear from figure 16 that composition type I1.0 showed weight loss after the 2 week of degradation study where as for all other compositions (TCP, II1.0 and III1.0), there was an increase in weight loss with time.

![Figure 15: Degradation behavior of pure TCP and TCP doped with MgO-Na$_2$O-P$_2$O$_5$-based sintering additives in a dynamic simulated body fluid (SBF).](image-url)
Presence of MgO, Na₂O and P₂O₅ as sintering aids proved to decrease the rate of resorption of TCP. Influence of sintering additives on the degradation of mechanical behavior of TCP ceramics was studied by evaluating the hardness of sintered specimens of variant compositions, as they dissolved in SBF, with time. A set of two specimens of each composition type was removed from the SBF solution at set time points (day 7, 14, 21, 28 and 35) and tested in a Vickers hardness tester in three different locations. The average hardness was calculated for each composition at separate time points.

![Graph showing the effect of biodegradation on mechanical property of pure TCP and TCP doped with MgO-Na₂O-P₂O₅-based sintering additives as a result of immersion in a dynamic simulated body fluid (SBF).](image-url)

Figure 16: Effect of biodegradation on mechanical property of pure TCP and TCP doped with MgO-Na₂O-P₂O₅-based sintering additives as a result of immersion in a dynamic simulated body fluid (SBF).
The results were plotted as a function of time, as shown in Figure 17; where hardness is expressed in percentage with respect to the hardness of pure TCP structure prior to immersion in SBF. It is apparent from figure 18 that for composition type I1.0, no decrease in hardness was observed for the five-week dissolution study. However, for all other composition types (TCP, II1.0, C1.0 and D1.0), hardness decreased with time, in different rates. Composition types C1.0 and D1.0 showed a continuous decline in hardness, whereas; for B1.0 the rate of decrease in hardness was marginal. Structures of A1.0 and B1.0 maintained much higher hardness compared to pure TCP structure, throughout the experiment. Although our biodegradation study using SBF showed promising results with regard to the development of controlled resorbable ceramic bone implants, further in vitro and in vivo experimentation of these ceramics is critically essential and a must for their successful application as bone grafts.

4.2.5 Conclusions

Influence of MgO-Na$_2$O-P$_2$O$_5$ sintering additives on the densification, microstructure, hardness, mechanical strength and biodegradability of tricalcium phosphate ceramics was studied. Uniaxially compacted ceramic structures were sintered at 1250°C in a muffle furnace, and were characterized for different properties. Phase analysis using X-ray powder diffraction technique revealed that the presence of these additives did not alter the phase purity of TCP ceramics. Densification results proved that sintered density of TCP ceramics could be significantly improved by incorporating MgO-Na$_2$O-P$_2$O$_5$ sintering additives in small quantities. A maximum sintered density of 3.33 g/cc was achieved for the composition type I having 4.0 wt.% sintering additives, sintered at 1250°C for 6 h. Although some of the composition types did not show improved densification, they showed improvement in hardness, in comparison to
TCP ceramics. On average, 20-30 % increase in hardness value was recorded for some of the compositions when tallied to pure TCP structures processed under the same conditions. Results of mechanical testing under uniaxial compressive loading showed a three-fold increase in compression strength for composition type II.0 compared to pure TCP. Maximum compression strength of 72.3 (± 2.9) MPa was achieved in this composition. Biodegradation studies conducted in dynamic SBF brought out the fact that these additives could tailor the rate of degradation of TCP, as per requirements.

4.3 Synthesis and characterization of nanocrystalline hydroxyapatite

4.3.1 Phase identification and powdery morphology

In our research, we have synthesized nanocrystalline HAp powder using water-based sol-gel technique and studied the influence of Mg and Zn doping (1.0 wt%) on morphology of the powder and mechanical properties. Phase evaluation at different calcination temperatures was recorded using XRD. Diffraction patterns of the amorphous dried gel and calcined powder at different temperatures (250°C for 2 h, 350°C for 2 h and 500°C for 15 min) are shown in figure 19. The figure also includes XRD patterns of powder doped with 1.0 wt % of MgO and ZnO, separately (calcined at 500°C). The peaks in these diffraction patterns were verified using standard JCPDS file # 9-432 for HAp (Ca₁₀(PO₄)₆(OH)₂), which confirmed phase purity of the synthesized powders.
Figure 17: XRD patterns of synthesized nano HAp powders.

XRD traces of the powders calcined at 500°C showed that the apatite phase first appeared at 500°C and the HAp content increased with increase in calcination temperatures. Results presented in figure 19 show that the dried gel exhibits highly amorphous characteristics. No clear peaks of any phase are visible. The powders calcined at 250°C and 350°C exhibits two broad peaks at about 31° with a considerable amount of amorphous phase.
The patterns due to the as-prepared material bears with it the characteristic amorphous phase but not with much resolution and intensity. While the powders calcined at 250°C, 350°C and 500°C showed gradual increase in intensities. The powders contained no other crystalline phase other than HAp. According to explanation presented by van der Houwen et al. [18], the broad patterns around at (002) and (211) indicate that the crystallites are very tiny in nature with much atomic oscillations [18]. They observed similar peaks during the organic ligands-assisted growth of calcium phosphate. The XRD patterns of the calcined powder at 500°C showed increase in intensity of the peaks as shown in figure 19. XRD analysis using JCPDS showed that these peaks corresponds to (002), (210), (211), (202), (220), (310), (222), and (213) planes. Further no crystalline impurity phase was observed, which indicated that the produced powder is single phase crystalline HAp. Our results are in line with what is reported in the literature [17, 45]

Morphology of synthesized powders was analyzed using transmission electron microscopy. The TEM micrographs of pure HAp (calcined at 500 °C), and HAp powder doped with 1.0 wt% MgO (A1.0) and 1.0 wt% ZnO (B1.0) are shown in Figure 20a, b and c. It is evident from figure 20 that pure phase HAp powder produced after calcination at 500°C is in nano range (<100 nm). Average particle size of this powder was found to be 40-90 nm in diameter. Powder particle size was refined when we doped the amorphous powder with the selected dopants. TEM analysis revealed that the average particle size of composition A (nano HAp doped with Mg) powder, calcined at 500°C, were in the range of 2-10 nm and for composition B (nano HAp doped with Zn), were in the range of 20-50 nm. (Figure 20b and c)
Figure 18: TEM micrographs of metal ion-doped HAp.

4.3.2 Densification Study

The green ceramic compacts prepared via uniaxial pressing were subjected to pressure less sintering in a muffle furnace at 1250 °C and 1300 °C, separately for 6 h. These sintering
temperatures were selected from available literature where it is reported that HAp shows best densification around 1300 °C [37] and the densification process continues with the increasing sintering temperature in the temperature range of (1000-1300 °C) [60]. Above 1300 °C, density decreases as a result of phase transformations [60]. Four green specimens were sintered at each of these sintering temperatures to study the effect of particle size and sintering temperature on densification of HAp ceramics. Green and sintered densities, measured for these nanostructured ceramics, are presented in Figure 20. A comparative analyses with synthetic commercial HAp powder of micron-size range [38] showed that nano-Hap exhibit improved densification compared to micron size powder, sintered at same the temperature. Sintering of nano HAp at 1250 °C and 1300 °C showed significantly higher densification than micron-size powder. The highest density of HAp (micron) ceramics, processed under similar conditions, was reported to be 2.93 g/cc[38]. Whereas in our work, an average sintered density of 3.07 g/cc was recorded for the specimens sintered at 1250 °C that is equivalent to 95% of theoretical density of HAp. Theoretical density of HAp is 3.16 g/cc [13].

A marginal increase in densification was recorded for the specimens sintered at 1300 °C for 6 hrs compared to the specimens sintered at 1250°C. The highest sintered density was recorded at 1300°C, which was calculated to be 3.12 g/cc, equivalent to 97% of the theoretical density. We did not conduct the densification studies above 1300 °C as it is already established by other workers that sintering of HAp ceramics above this temperature lead to phase change and significantly deteriorate its mechanical properties.
Figure 19: Influence of oxide-based sintering additives on densification of HAp ceramics. Sintering was done at 1250°C and 1300°C for 6 hours, respectively.

Figure 19 shows the densification plots for pure HAp and HAp doped with different amount of MgO and ZnO. It is evident from this figure that the HAp doped with magnesium 1.0 wt% showed the densification of 3.12 g/cc at 1250°C and a maximum densification of 3.29 g/cc at 1300°C. Doping of zinc with the pure HAp did not improve its densification.
4.3.3 **Mechanical property evaluation**

4.3.3.1 **Vickers hardness testing**

![Graph showing Vickers hardness testing results](image)

Figure 20: Effect of additives on hardness of nano-HAp ceramics.

Results of Vickers hardness testing revealed that the presence of dopants could significantly enhance the hardness of HAp ceramics. Hardness testing was performed on specimens sintered at 1300°C for pure HAp, MgO1.0 and ZnO1.0. These results are presented in Figure 22 as a function of sintered density. It is clear from these figures that with the increase in density of sintered structures their hardness also improved.
4.3.3.2  Compression testing

Dense sintered structures (8mm in diameter and 15 mm in height) of pure nano-Hap and nano-Hap doped with MgO and ZnO, separately, were subjected to mechanical testing under compressive loading in a fully automated screw driven tensile tester from Instron Inc. Five samples of each composition were tested and average compression strength of each of these composition were calculated. These results are presented in table 9, which clearly shows that presence of small amount of Zn and Mg enhanced mechanical performance under compressive loading.

Table 9: Compressive strengths of Pure HAp and HAp doped with 1.0 wt.% of additives

<table>
<thead>
<tr>
<th>Type</th>
<th>Compression Strength (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAp</td>
<td>210.8± 17.8</td>
</tr>
<tr>
<td>A1.0</td>
<td>281.3± 15.6</td>
</tr>
<tr>
<td>B1.0</td>
<td>223.3± 12.4</td>
</tr>
</tbody>
</table>

Composition A1.0 showed the highest compressive strength of 281 MPa, which is a 33% improvement, compared to compression strength of pure HAp structures (210 MPa). Zn doping (composition B1.0) improved compressive strength of nano –HAp by 6%. Our research showed that mechanical properties for HAp ceramics could be significantly improved by reducing particle size (nano-synthesis), which could be further enhanced by doping with small amounts of certain additives. No results on mechanical properties of nanostructured HAp ceramics are currently available in the literature. It is expected that structures prepared via high pressure pressing routes will further improve mechanical properties nanostructured HAp. Our results have
significance with respect to the development of non-metallic bone grafts for load-bearing orthopedic applications. As of now, only metallic materials such as stainless steel, titanium alloys and cobalt chrome steels are used in making load-bearing prostheses, which have many shortcomings, particularly due their high strength and stiffness. Compressive strength of cortical bone is reported to be in the range of 100-230 MPa. Our research showed compressive strength of nano HAp in the range of 210-280 MPa, which is relatively higher than that of cortical bone. In porous form, strength of our newly developed materials will definitely be lowered and fall within the range of strength mentioned for cortical bone. These new materials will possibly be great significance in developing cortical bone substitutes.

### 4.3.4 Biodegradation Study

![Biodegradation study graph](image)

Figure 21: Biodegradation of metal ion-doped sintered HAp ceramics in a dynamic simulated body fluid (SBF).
Figure 21 represents the biodegradation study for sintered compacts with 1.0 wt.% additives. Compositions with 1 wt% sintering additives were selected due to their excellent densification and hardness values. It is evident from the figure that composition A with 1.0 wt.% addition degrades at a slower rate as compared to the other compositions. In fact there is no major loss of weight in the samples having composition A, also their hardness values are not affected. Composition B degrades at much slower rate as compared to HAp.

![Graph showing biodegradation study](image)

Figure 22: Effect of biodegradation on hardness of HAp ceramics doped with different sintering additives at various time points.
Figure 22 represents the hardness plot for the samples, which were kept in the SBF (simulated body fluid) for a specific period of time. A batch of 6 samples each were taken out of the fish tank containing the SBF and were subjected to the Vickers hardness. It was observed that composition A with 1.0 wt% of sintering additives showed a considerable increase in hardness value about 20% when compared to the hardness of pure HAp. The hardness of composition A remained constant even after 6 weeks. Composition B showed about 2% increase in hardness when compared to pure HAp. Similar trend was observed for the hardness values for composition B after 6 weeks.

4.3.5 Conclusions

The phenomenon of sol to gel and gel to ceramic during the synthesis of nano hydroxyapatite powders via water-based sol-gel techniques was investigated using high resolution TEM and X ray diffractometry. TEM revealed that the particle-size of the powders synthesized were 2-90 nm. XRD results showed the occurrence of nano HAp phase shortly after 250°C for water based sol-gel method and after 350°C for ethanol based method. A maximum sintered density of 3.12 g/cc was achieved for nano HAp sintered at 1300°C. These sintering additives increased the sintering density of pure nano HAp appreciably. On average, 20-30 % increase in hardness value was recorded for some of the compositions when compared to pure nano HAp compacts under the same environment. 33% increase in the failure strength was observed for the samples with composition A (1 wt.% of additives), sintered at 1300 for 6 hours. This study concludes that nanostructured HAp ceramics produced via water based route has the potential to overcome some of the limitations related to mechanical performance of synthetic
hydroxyapatite. However, detailed *in vitro* and *in vivo* studies are necessary to make these ceramics useful as bone grafts in hard tissue engineering applications.
CHAPTER 4: FUTURE DIRECTIONS AND SUGGESTIONS

Future directions are aimed at creating a therapeutic bio-ceramics that has a dual beneficial effect: osteoconductive properties combined with the ability to deliver therapeutic agents, proteins, and growth factors directly into the ceramics. These new bio-ceramics may offer the ability to stimulate bone growth, combat infection, and, ultimately, increase implant lifetime. Detailed in vitro and in vivo studies are necessary to make these bio-ceramics useful as bone grafts in clinics.

In this research, I used the uniaxial press for compaction of the powders; this technique is not accurate because we do not know the actual pressure applied to the punch. I recommend automation in the compaction process, which will automatically press the samples with uniform pressure resulting into denser compacts with better mechanical properties.
REFERENCES


