



UNIVERSITI TEKNIKAL MALAYSIA MELAKA

**CHARACTERIZATION OF CALCIUM PHOSPHATE FOR
BONE FILLER**

This report submitted in accordance with requirement of the Universiti Teknikal Malaysia Melaka (UTeM) for the Bachelor Degree of Manufacturing Engineering (Engineering Materials) (Hons.)

by

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ABSTRACT

Calcium phosphate (CaP) is one of the widely used materials to support bone ingrowth and to promote bone integration. Among CaP materials, synthetic hydroxyapatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) and β -tricalcium phosphate (β -TCP, $\text{Ca}_3(\text{PO}_4)_2$) are well-known for their potential in biomedical applications. In this study, HA powder has been synthesized via a chemical precipitation technique. The uncalcined HA produced by this method underwent a calcination treatment to produce a much more crystalline powder at different temperatures of 800 °C, 900 °C and 1000 °C. The samples were heated then at three different of sintering temperatures of 1100 °C, 1200 °C and 1300 °C to determine the optimised temperature for maximum phase transformation of HA to TCP. The powder sample was analysed by characterization techniques such as Thermogravimetric Analysis (TGA), X-ray Diffraction (XRD), and Raman Spectroscopy. Next, fabrication of hydroxyapatite pellet by uniaxial pressing was also included in this study. This study also investigated the effect of double heat treatment on porosity and hardness of the pellet. On the other hand, the porous HA scaffold was first produced by dipping a polyurethane (PU) foam with slurry. The HA scaffold was obtained from sintering at 1000 °C was then coated with PLA and its three dimensional fully-interconnected porous structure was found to be maintained. The structure and interconnectivity of both the single HA scaffold and the composite HA/PLA scaffold were determined by Scanning Electron Microscopy (SEM).

ABSTRAK

Kalsium fosfat (CaP) adalah satu daripada bahan yang digunakan secara meluas untuk menyokong pertumbuhan tulang dan membantu integrasi tulang. Antara jenis-jenis CaP, sintetik hydroxyapatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) dan trikalsium fosfat (β -TCP, $\text{Ca}_3(\text{PO}_4)_2$) adalah bahan yang sangat dikenali kerana penggunaannya di dalam bidang bioperubatan. Dalam kajian ini, serbuk HA telah dihasilkan melalui proses pemendakan kimia. Serbuk HA yang tidak dikalsin mengalami rawatan kalsinasi untuk mendapatkan serbuk yang mempunyai habluk yang lebih baik dengan suhu yang berbeza iaitu 800 °C, 900 °C and 1000 °C. Kemudian, sampel telah dipanaskan dengan mengguna suhu sinter yang berbeza seperti 1100 °C, 1200 °C and 1300 °C untuk mengenalpasti suhu yang tepat untuk menghasilkan transformasi maksimum fasa HA kepada fasa TCP. Sampel serbuk itu dianalisis oleh teknik pencirian seperti TGA, XRD dan Raman spektroskopi. Seterusnya, penghasilan HA pellet dengan menggunakan tekanan sehalu termasuk dalam kajian ini. Kajian ini menyiasat kesan rawatan haba berganda kepada keliangan dan kekerasan pellet itu. Selain itu, perancah HA yang berliang di hasilkan bermula dengan merendam span ke dalam sluri. Perancah HA yang di sinter di suhu 1000 °C kemudiannya di saluti dengan PLA dan struktur berliang 3D yang bersambung sepenuhnya dapat dikekalkan. Struktur dan antara sambungan perancah bagi kedua-dua perancah HA dan perancah komposit HA/PLA dicirikan dengan SEM.

DEDICATION

To my beloved family members especially my mother, Hamidah bt Drani who always stand behind me. Thank you for all you did. This work is dedicated to them.

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LIST OF ABBREVIATION

ASTM	American Society for Testing and Materials
ACP	Amorphous Calcium Phosphate
CaP	Calcium Phosphate
DCPD	Dicalcium Phosphate Dehydrate
HA	Hydroxyapatite
OCP	Octacalcium Phosphate
PLA	Poly (lactic acid)
PU	Polyurethane
PVA	Polyvinyl Alcohol
SEM	Scanning Electron Microscopy
TCP	Tricalcium Phosphate
TGA	Thermogravimetric Analysis
wt%	by weight percent
X	Magnification power
XRD	X-ray Diffraction
β -TCP	Beta- Tricalcium Phosphate

CHAPTER 1

INTRODUCTION

1.0 Background

Bone damage can occur due to several factors such as disease, injury, and trauma and others. Thus in the presence of damage, treatment is sought to repair, replace or regenerate the bone to gain their normal function (O'Brien, 2011). Conventional methods (autograft and allograft) may possess high risks cause such as infection or inflammation and often pose discomfort among patients. Thus, a new material such as synthetic bone filler is required in order to overcome this problem. Figure 1 shows the typical fracture and structure of the bones.



Figure 1.0: The humeral head and vertebra fracture and the structure of the normal bone and osteoporotic spongy bone (Daniela *et al.*, 2011).

The bone filler in the form of scaffold can be inserted or implanted to the part of the injured bone to stimulate the new tissue regeneration and also act as bridge to connect to the remaining bone. Highly porous scaffold will act as a template to guide the growth of new tissue. Figure 2 shows the example of a ceramic scaffold.



Figure 1.0: The ceramic scaffold used in biomedical field (Tian et al., 2011).

The most common ceramic biomaterials used for scaffold is calcium phosphate. Calcium phosphate (CaP) materials like synthetic hydroxyapatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) and β -tricalcium phosphate (β -TCP, $\text{Ca}_3(\text{PO}_4)_2$) are famous for their potency in bone tissue engineering and drug delivery applications. Calcium phosphate materials have attracted a lot of research attention in current years because of being chemically identical to bones and teeth. They are excellent biomedical materials due to their outstanding biocompatibility and are nontoxic. Calcium phosphates are a group of bioactive synthetic materials (Al- Sanabani et al., 2013).

HA is an inorganic phase of bones denoted by $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$. HA is crystallographic owing to the hexagonal system and have the space group $\text{P6}_3/\text{m}$ and identified by a six fold a - axis perpendicular to three equivalent a -axes (a_1 , a_2 , a_3) at angles 120° to each other (Dorozhkin, 2012). The calcium to phosphate (Ca/P) ratio for HA is 1.67. This material can be classed based on its porosity, phase and processing method. It has very good biocompatibility and bioactive, which is can induce osteoconduction and osseointegration activities.

Tricalcium phosphate (TCP) exists in many polymorphs but only two phases (α and β) that are commonly used as biomaterials. The Ca/P ratio for TCP is 1.5. It

is tertiary phase of calcium phosphate and acts as rich origins for calcium and phosphorus which can be easily assimilated and absorbed (Shamsul, 2013). β -TCP is greatly biocompatible and able to sets up a resorbable interlocking network within the injury site to encourage healing. Hence, HA is determined as nonresorbable whilst TCP is determined as a restorable material in bone tissue engineering.

The HA powder can be synthesized by many methods such as precipitation, sol- gel, hydrothermal route and mechanochemical methods. The most widely used is aqueous chemical precipitation. The uncalcined HA produced by the wet chemical precipitation method cannot be used directly in the body. They need to undergo calcination treatment to produce more crystalline HA powder. Next, TCP is the phase of secondary HA after being sintered at certain temperature.

Almost all ceramic body must be sintered to produce a microstructure or phase with the required properties. Sintering of pure HA particles is typically reported to take place above 1000 °C. The option of right sintering temperature is vital as it has an effect on the properties of the final sample. Most researchers compromise that pure HA (ratio Ca/P=1.67) is stable in air and argon atmospheres at temperatures up to 1200 °C (Mouthuy, Crossley & Ye, 2013).

Recently, polymer/ceramics scaffolds were used as alternatives strategies in tissue engineering. Composites systems, based on polymer and ceramics materials, offer the possibility to produce constructs with increased mechanical properties and biocompatibility. As human bones are very complex composite structures, composites are a clear choice of replacement materials that are potentially able to mimic the structure and properties for use in bone repair. Tanner (2010) summarized that the few main reasons for using composites are because the mechanical properties of the prosthesis can be tailored to be comparable with bone tissue. The stiffness of the implant needs be similar to that of natural bone, however only few materials have been published to have stiffness close to those of cortical bones. Secondly, the initial strength of the prosthesis needs to be higher than the bone. Thirdly, by using composite, the biological properties can be tailored according to the applications.

Rich et al. (2002) reported that degradation appeared to be increased in filled composite compared to an unfilled polymer when adding 40, 60 and 70 wt.% of bioactive glass (S53P4) filler particles in poly (ϵ -caprolactone-co-DL-lactide) matrix. Polylactic (PLA) is among the most commonly used synthetic bioabsorbable polymer. The stereochemistry of PLA is complex as it consist of chiral carbon that enable it to exist in three stereoisomeric forms, L and D and racemic mixture of L/D. Poly-L-lactides are more commonly used compared to poly-D-lactide for implants because the L-monomer is naturally present in the isomer (Nair and Laurencin, 2007)

1.1 Problem Statement

Phases and crystallinity of HA powders can be influenced by thermal treatment. The uncalcined HA powders produced by wet chemical precipitation method are normally amorphous and may contain unreacted chemical groups that are not suitable for use directly in the human body. Thus, the HA powders produced by this method need to undergo calcination process to produce more crystalline HA powder as well as to remove unreacted chemical group. Further process at higher temperature is needed to encourage phase transform into tricalcium phosphate (TCP).

The uncalcined HA also can be directly transformed into TCPs without prior calcination treatment but this route will required higher temperature compared to calcined HA. Thus, the temperature value will influence the amount of crystallinity and types of phases that occur in the calcium phosphate powder. Therefore, it is important to identify and optimise the calcination temperature and heat treatment process in order to produce a desired crystalline calcium phosphate. Fabrication of biodegradable composite scaffold that guide and stimulate tissue generation is still a major issue. The effect of PLA coating in fabricating uniform porous HA scaffold still needs to be studied to produce adequate pore sizes, interconnectivity and mechanical properties in accordance with the injured tissue.

1.2 Objectives

1. To relate the effect of calcination temperature towards the crystallinity of HA powder.
2. To identify the most suitable sintering temperatures for maximum TCP phase transformation from HA phase.
3. To investigate the effect of PLA coating in fabricating uniform porous 3-D HA scaffolds.

1.3 Scope of study

In this study, the calcium phosphate (HA) was treated to a calcination process at a range of temperatures of 800 °C, 900 °C and 1000 °C (Cimdina, 2012), and a sintering process at 1100 °C, 1200 °C and 1300 °C (Aminzare et al., 2013) in order to optimise their crystallinity transformation as well as the formation of TCP phases. Thermogravimetric Analysis (TGA) was used to characterize the uncalcined powder to identify the thermal properties of the HA powder. All samples were characterized prior to and after the treatment using characterization techniques such as X-ray Diffraction (XRD). From XRD results, the most suitable temperature for calcination and sintering process were identified. The uncalcined HA and the powder calcined using the most suitable calcination temperature were characterized by Raman spectroscopy. Next, the pellets were produced based on characterization using XRD. Then, the sintered pellets will be characterized by Vickers microhardness, porosity test and Scanning Electron Microscopy (SEM). The last stage of this study was the fabrication of porous HA scaffold and HA/PLA scaffold to relate the time of squeezing the foam in slurry with interconnectivity of scaffold. The polyurethane foams used to fabricate scaffold were characterized by SEM.

CHAPTER 2

LITERATURE REVIEW

2.0 Introduction

Bone is a dynamic and highly vascularised tissue that continues to reforming in a whole lifetime of an individual. It plays an important role in locomotion and also makes sure the skeleton has enough load-bearing capacity. Instead of these structural roles, bone is usually involved in homeostasis through its storage of Ca and P ions (M. Stevens, 2008). Bone can be damaged by disease, injury and trauma and thus, bone require treatments to facilitate their repair, replacement or regeneration. Bone filler in the form of scaffold will act as a template for tissue formation during the bone healing.

Ceramic biomaterials especially calcium phosphate is one of the best option for bone scaffold. Calcium phosphate such as hydroxyapatite (HA) which is the crystalline type of calcium phosphate is important in development of 60-70 percent of bone tissue. Both synthetic and naturally occurring HA and tricalcium phosphate (TCP) have been used for biomedical especially in orthopaedic applications (Shamsul *et al.*, 2013).

2.1 Bone Structure

Bone is an enormous and dynamic configuration of extracellular proteins and minerals that held an important role in calcium and phosphate homeostasis, blood

circular component formation, organ protection and structural support against gravity (Kobayashi *et al.*, 2014). Bone is a type of connective tissue contains a collagen framework combined with mainly calcium and phosphate salts. Appropriate precipitation and crystallization of these salts produce the formation of hydroxyapatite, a mineral compound in charge for providing bone its rigidity.

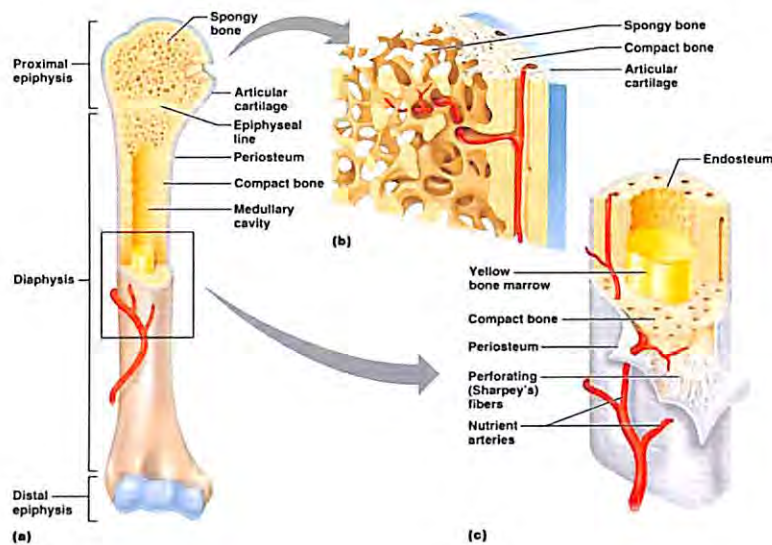


Figure 2.0: The overall bone structure (a) which consist two parts as spongy bone or cancellous bone (b) and compact bone or cortical bone (c) (Steele & Bramblett, 1988).

The upper layer of a bone consist a thin layer of dense connective tissue named as periosteum. This can be segmented into two layers, an outer fibrous layer containing majority fibroblasts and an inner cambium layer, including progenitor cells which grow into osteoblasts which are the cells responsible for bone formation. The periosteum's function to give a good blood supply to the bone and a place for muscular attachment. Below the periosteum is a thin layer of compact bone or called cortical bone, which gives the bones strength. In cortical bone, there are osteon that contain bone cell and Extracellular Matrix (ECM) while Harvesian canal in the cortical bone acts as pathway for blood vessel. A bony matrix has a dense composition of organic and inorganic salts that have gaps between them called lacunae contain bone cell known as osteocytes. These cells deal with each other by projecting cytoplasmic processes through tube-like structures called as canaliculi.

These canal comprise fluid consisting of calcium and phosphate ions that also contribute to the composition of the bone matrix.

There is another structure known as spongy or cancellous bone. This is a more porous, lightweight type of bone with an irregular arrangement of tissue which permits highest strength. In a long bone, this structure location normally found at either end of the bone whereas in flat or irregular bones it is a thin layer found just inside the compact bone. Interestingly, compact bone makes up to 80% of the bones weight, with spongy bone contribute the additional 20%, although it is much larger surface area. For biomedical applications, when cancellous bone is used for the treatment of the bone defect, it is known as a bone graft (Way, 2003).

2.2 Biomaterial

Biomaterials is defined as a substance or a mixture of a substances, other than drugs produced either from natural or synthetic origin which can be utilized for any periods of time as whole or as part of the system that heals, regenerates, or replaces any tissue, organ or function of the body (Newman, 2007) . Later, de Leeuw (2010) claimed the term biomaterial as a material of natural or manmade origin that is utilized to replaces the functions of living tissues of the human body. Typically, there are three groups of biomaterial which are metals, polymers (synthetic and natural) and ceramics are used in the fabrication of scaffold for tissue engineering.

Among the biomaterials that can be acquired, bioceramics display some of the most attractive properties. Biomaterials when implanted into the body cause some reaction with the host tissues and bioceramics show all the possible tissue or implant reactions. Due to the tissues response, bioceramics can be divided into :

- I. **Bioinert:** Bioinert materials are biocompatibility materials but cannot provide any interfacial biological bond between implants and bone.