

**SCHOOL OF MATERIALS AND MINERAL RESOURCES ENGINEERING  
UNIVERSITI SAINS MALAYSIA**

**PRELIMINARY STUDY OF SELF-SETTING 45S5 BIOGLASS  
GRANULAR CEMENT**

**By**

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Dissertation submitted in partial fulfillment  
of the requirements for the degree of Bachelor of Engineering with Honours  
(Materials Engineering)

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## DECLARATION

I hereby declare that I have conducted, completed the research work and written the dissertation entitled “**Preliminary study of Self-Setting 45S5 bioglass granular cement**”. I also declare that it has not been previously submitted for the award of any degree or diploma or other similar title of this for any others examining body or University.

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# **KAJIAN AWAL Pengerasan-DIRI SIMEN BIOKACA**

## **BERBUTIR 45S5**

### **ABSTRAK**

Objektif kajian ini adalah untuk mengkaji kesan kepekatan larutan kalsium fosfat berasid dan masa rendam dalam kalsium fosfat berasid terhadap ciri-ciri simen biokaca berbutir 45S5. Larutan kalsium fosfat berasid yang mengandungi kepekatan fosforik asid sebanyak 25mmol/L dengan kepekatan MCPM yang berbeza (25 mmol/L, 50 mmol/L, 75 mmol/L dan 100 mmol/L) didedahkan kepada 45S5 granul simen biokaca pada suhu 25°C dengan masa rendam yang berbeza (2, 4, 6 dan 8 jam) untuk mengkaji kemampuan pengerasan. Beberapa kaedah pencirian seperti XRD, SEM, FTIR, pengukuran nilai pH dan ujian mampatan telah dijalankan terhadap simen biokaca berbutir 45S5 untuk memahami kebolehan pengerasan-diri spesimen tersebut. Analisa XRD dan SEM menunjukkan bahawa wujudnya hablur DCPD yang terbentuk dan bersambung antara satu sama lain pada permukaan simen biokaca berbutir 45S5. hablur DCPD yang terbentuk semakin banyak apabila kepekatan larutan kalsium fosfat berasid juga ditingkatkan. Selain itu, kajian ini juga menunjukkan bahawa nilai pH simen biokaca berbutir 45S5 yang telah direndam selama 8 jam adalah rendah selepas direndam dalam larutan HBSS hanya selama satu hari. Kajian ini juga menunjukkan kekuatan mampatan bagi spesimen yang telah mengeras iaitu pada 8 jam pendedahan kepada larutan kalsium fosfat berasid dengan kepekatan MCPM sebanyak 100mmol/L adalah 0.116 Mpa. Kajian ini berjaya membuktikan bahawa kesan kepekatan kalsium fosfat berasid dan kesan masa pendedahan larutan asid kalsium fosfat 45S5 granul biokaca pada suhu 25°C telah berjaya.

# **PRELIMINARY STUDY OF SELF-SETTING 45S5 BIOGLASS GRANULAR CEMENT**

## **ABSTRACT**

The objectives of this study is to investigate the effect of different concentration of acidic calcium phosphate solution and soaking time on the 45S5 bioglass granular cement. The acidic calcium phosphate solution contain different concentration of MCPM (25 mmol/L, 50 mmol/L, 75 mmol/L and 100mmol/L) were imposed to 45S5 bioglass granules at temperature of 25°C (for 2, 4, 6 and 8 hours) to see its setting ability. Several characterization methods such as XRD, SEM, FTIR, measurement of pH value and compression test were carried out on 45S5 bioglass granular cement in order to understand its setting properties. XRD and SEM analysis result showed that the DCPD crystal are present and bridging to each other between the surface of 45S5 bioglass granular cement. The DCPD crystal that are form were increased when the concentration of acidic calcium phosphate is increased. Moreover, this study also shows the pH value of 45S5 bioglass granular cement that has been soak for 8 hours with acidic calcium phosphate solution are low after the specimen are immersed into HBSS solution for 1 day. On the other hand, this study also shows the compression strength for the specimen that are fully set at 8 hours of soaking time with acidic calcium phosphate solution with concentration of MCPM 100 mmol/L is 0.116 Mpa. Therefore, this study proved that the effect of concentration acidic calcium phosphate solution and the soaking time able to set the 45S5 bioglass granular at temperature 25°C.

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# CHAPTER 1

## INTRODUCTION

### 1.1 Research background

Many different kinds of biomaterials, including metals, polymers, ceramics, bioactive glasses, calcium carbonates, calcium sulphates, and calcium phosphates, have been developed for the purpose of bone restoration applications. One of the synthetic materials that is frequently employed as biomaterials among all of these biomaterials is 45S5 bioglass. Glasses are amorphous, non-crystalline solids that are usually made of silica-based materials and other minor additives. Bioglass 45S5 contains more calcium and phosphorus and less amount of silica when compared to soda-lime glass. The term 45S5 refers to glass with a  $\text{SiO}_2$  content of 45wt% and a calcium to phosphorus ratio of 5:1. The Apatite crystals is form due to the high calcium to phosphorus ratio; calcium and silica ions can serve as crystallisation nuclei (Chen et al. 2006). Because it has a composition that is very similar to that of hydroxyapatite, which is a component of bone mineral, the specific composition of Bioglass 45S5 is an excellent choice for use in biomedical applications. This commonality enables Bioglass 45S5 to be incorporated with living bone, which is a significant benefit (Cakraborty et al. 2021). Because of its excellent osteoconductivity as well as osteointegration after being implanted in the bone defect area, 45S5 bioglass has seen widespread application in medical practises and hospitals (Hench, L.L. et. al., 1998). For instance, the research conducted by Hench found that 45S5 bioglass exhibits a high level of both bioactivity and biocompatibility after being implanted into a patient's bone associated defect area (Jones, J.R. et. al., 2013). When compared to other

types of glass, the bioactive glass composition has a softer composition. Machining it, particularly with diamond tools, or grinding it into powder are both viable options. Because it rapidly absorbs moisture and reacts with it, Bioglass 45S5 needs to be kept in a dry environment when it is being stored. The discovery that an artificial substance could make a chemical link with bone led to the development of a number of additional bioactive glasses, and the first formulation of such a material was the bioactive glass known as Bioglass 45S5. Its potential to avoid an immune reaction and fibrous encapsulation are two examples of why its biocompatibility is one of the most important medical advantages that offers. The primary use for is in the repair of bone injuries or flaws that are too large to be repaired by the body's normal process of regeneration. As a result, on the basis of the benefits of 45S5 that were reported in the prior study, the purpose of this study is to investigate whether or not it is possible to use 45S5 bioglass granule as the starting material for the fabrication of 45S5 bioglass granular cement. Both the influence of acidic calcium phosphate solution concentration on the self-setting ability of 45S5 bioglass granule and the effect of soaking duration on the characteristics of 45S5 bioglass granule will be examined and investigated in this project. The characteristics of the set specimens were analysed with characterization techniques such as Scanning Electron Microscopy (SEM), X-ray Diffraction (XRD), X-ray Fluorescence (XRF), pH value measurement (pH measurement), Fourier transform infrared (FTIR) analysis, mechanical strength test and Density testing.

## **1.2 Problem statement**

The usage of 45S5 bioglass granular as a replacement material for bone defects illness has seen widespread use in clinical and hospital settings. However, a few studies have



shown that 45S5 bioglass granular has a "flush out" feature after being implanted in a big bone defect area. The term "flush out" refers to the process in which liquid flows through out of the body while the bone is being repaired. As a result of this problem, there have been a few studies that suggest the "flush out" phenomenon could be able to be remedied by enabling the granule to set all by itself. An earlier study found that exposing atricalcium phosphate granular to an acidic calcium phosphate solution made it possible for the granular to harden into the desired shape. (Khairul et al., 2015). In the meantime, a number of studies have reported that the calcium carbonate granules hardened after being exposed to an acidic calcium phosphate solution in a manner analogous to that used in the previous example. (Eddy et al. 2018). Because it enables the 45S5 bioglass to set by itself, the acidic calcium phosphate solution contributes to the resolution of the "flush out" problem, which had been a source of contention. As a consequence of this finding, an acidic calcium phosphate solution is going to be utilised in an effort to establish the capability of setting 45S5 bioglass granular. The effect of the amount of time spent soaking also has an effect on the characteristics of the specimen. The 45S5 bioglass granular cement is given more time to set by itself when the soaking period is increased along with the concentration of the acidic calcium phosphate solution. When compared to some other calcium phosphate that has been widely used in making a granular cement that has a short time for it to set by itself, which makes it difficult to be done in medical bone repairing, 45S5 bioglass may have a longer time to set by itself than the other calcium phosphate. This is because 45S5 bioglass is made from a different type of calcium phosphate. It was anticipated that the findings of this study will establish a measurement on how 45S5 bioglass granular could be set by a dissolution-precipitation reaction.

### **1.3 Objectives**

There are two research objectives set in this project:

1. To study the effect of acidic calcium phosphate solution concentration on the self-setting ability of 45S5 bioglass granular cement.
2. To evaluate the effect of soaking time on the preparation of the 45S5 bioglass granular cement investigate.

### **1.4 Research approach**

For the purpose of this study, 45S5 bioglass granules were produced by the melt-quench approach. For setting reaction, various concentrations of an acidic calcium phosphate solution were utilised at a temperature of 25°C. For the purpose of determining the characteristics of self-setting 45S5 bioglass granular cement, a number of characterization procedures including X-Ray Diffraction (XRD), X-Ray Fluorescence (XRF), Scanning Electron Microscope (SEM), pH measurement and compression testing were carried out.

The main material used in this project is 45S5 bioglass granular. 45S5 bioglass granular was prepared by mixing  $\text{SiO}_2$ ,  $\text{Na}_2\text{CO}_3$ ,  $\text{CaCO}_3$  and  $\text{P}_2\text{O}_5$ . using milling machine for 6 hours. After milling process, the mixture was then melted into the furnace with temperature of 1400°C. The melted mixture was then quenched into the distilled water and the glass frits inserted into the oven with temperature of 80°C overnight for drying. The glass frits then put into the milling jar to achieve 45S5 bioglass into powder form using planetary milling. The powder was then compressed into pellet shape using hand press machine. The

compacted body was then crushed using agate mortar and sieve to get 45S5 bioglass granules with 300-600  $\mu\text{m}$  size range. Different concentration acidic calcium phosphate solution was prepared by dissolving the Monocalcium Phosphate Monohydrate (MCPM) into the diluted 0.025mmol/L of phosphoric acid solution.

The 45S5 bioglass granules and acidic calcium phosphate solution with varying concentrations of MCPM were put into a Perspex mould with dimensions of 6 mm in diameter and 3 mm in thickness using a ratio of 0.12ml of liquid to 0.2g of granules. In order to stop the setting reaction, the specimen was given an acetone wash after it had been left to set for the allotted amount of time. The raw materials were analysed with X-Ray Diffraction (XRD), Scanning Electron Microscope (SEM), and X-Ray Fluorescence (XRF), while the set of specimens were analysed with Scanning Electron Microscope (SEM), X-Ray Diffraction (XRD), pH analysis, and Fourier-Transform Infrared Spectroscopy (FTIR) test to investigate the surface morphology, microstructure, functional groups, and phase presence. In addition, the compressive strength of the 45S5 bioglass granular cement was evaluated by means of a measurement in order to ascertain its mechanical qualities. An investigation into the pH of the HBSS solution that the 45S5 bioglass granular cement was subjected to was one of the tasks that were carried out as part of this study.

The value of pH was determined by immersing 45S5 bioglass granular cements formed from a mixture of 45S5 bioglass granules and varied amounts of acidic calcium phosphate solution in Hanks' Balanced Salt Solution (HBSS) for 1, 3, and 7 days at a temperature of 37°C. Figure 1.1 illustrates the processes involved in the production of 45S5 bioglass granular cements as well as

the characterisation of specimens.

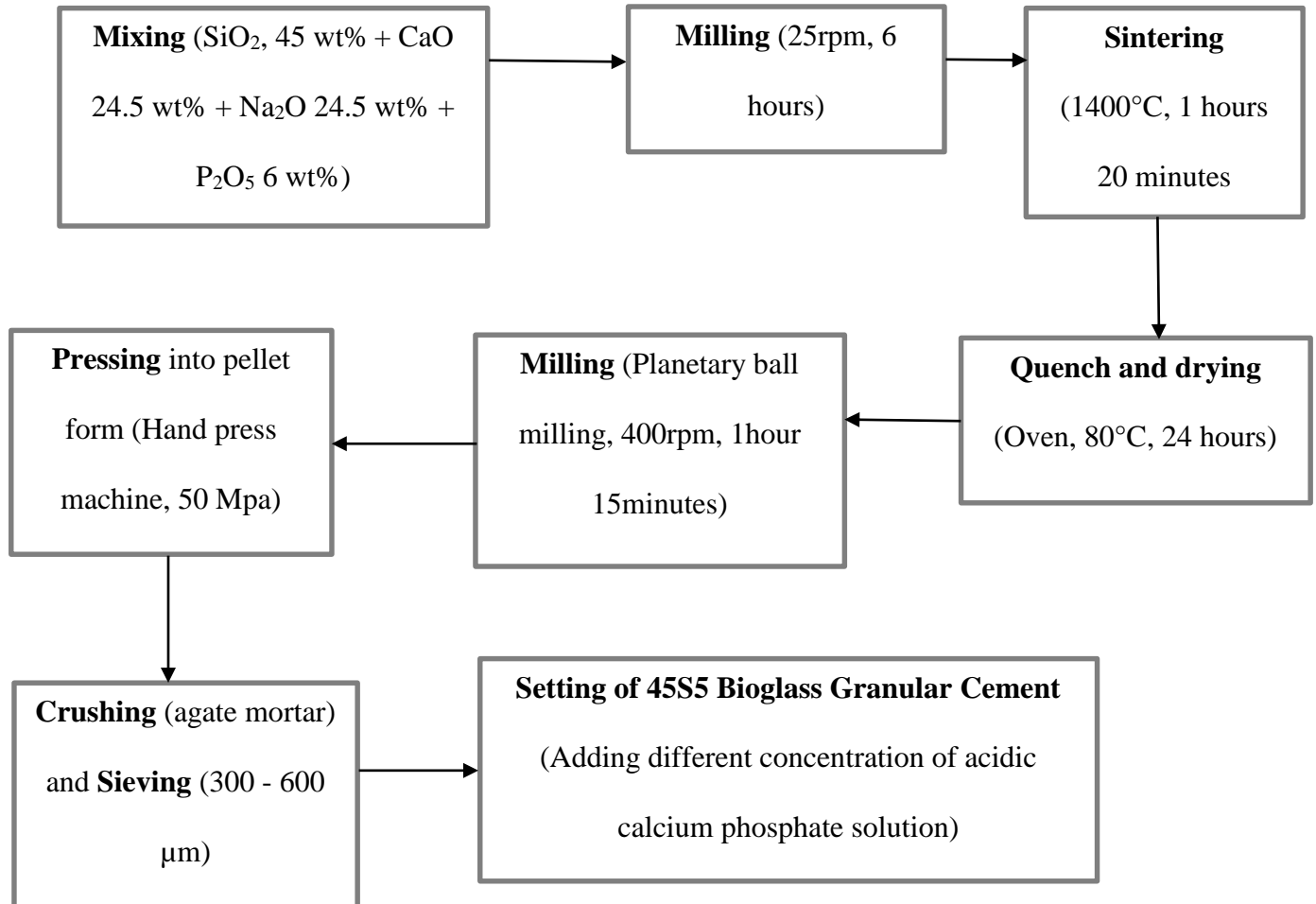


Figure 1.1: Steps of producing 45S5 bioglass granular cement

## **CHAPTER 2**

### **LITERATURE REVIEW**

#### **2.1 Introduction on ceramic as biomaterials**

Ceramic is a type of non-metallic, inorganic substance that is formed by the heating and moulding of non-metallic compounds into desired shapes before being cooled and hardened. Even though they are fragile, ceramics are generally sturdy and resistant to corrosion and chemical attack. Ceramics also have a long lifespan. Ceramics find use in a diverse set of industries, such as mining, aerospace, medicine, food and chemical processing, electronics, industrial, and electrical transmission. Ceramics are also used in the transmission of electricity. The two most important sub-types of ceramics are known as "traditional" and "advanced" ceramics, respectively. Clay or other materials derived from the earth are typically used in the production of traditional ceramics. After being moulded and fired, these materials are subsequently hardened. Enhanced ceramics are made from chemical powders of a high purity that have been manufactured in order to endow them with a variety of improved features. Some of these properties include biocompatibility and osteoconductive capabilities. Biomaterials are materials that can be found in nature or that can be synthesised. These materials are utilised in therapeutic settings to support or repair injured tissue or to manufacture new bone. Biomaterials can be found in nature or can be synthesised. Ceramics containing biological features such as antibacterial and antifungal activity, as well as better sealing qualities, are what make up bioceramic materials. These materials are used in medicinal applications. They have the

potential to break down old tissue while also promoting the creation of new bone or tissue (Raghavendra et al., 2017). There are three distinct types of bioceramic materials: those that are bioinert, those that are bioconductive, and those that are biocompatible. Materials such as alumina, zirconia, and titania are examples of bioinert materials since they do not interact with living tissue and are unaffected by the physiological circumstances of the body (Heimann, 2010). On the other hand, the responses of the organism to these components led to the development of connective tissue. Cements made of calcium carbonate and hydroxyapatite are examples of bioconductive materials that are able to interact with living tissue. Other examples include tricalcium phosphate and hydroxyapatite (Heimann, 2010). Ceramics that are bioconductive form a chemical bond with bone and serve as a medium for greater osteogenesis bonding through this process. Ceramics that are good examples of bioconductivity are calcium phosphate and bioglasses (Heimann, 2010). Materials that are biocompatible, such as bone cement, release chemicals that support the formation of bone and connective tissue. In a clinical environment, any one of these bioceramic materials could be put to use.

The terms osteoconduction and osteoinduction are used to describe the processes that occur when bioceramic materials interact with living tissue. Osteoconduction is the process by which bone cells, blood vessels, and other forms of living tissue form in the space between an implant and the bone that is already there (Albrektsson and Johansson, 2001).. The osteoconduction behaviour of materials with high biocompatibility and bioceramic content is shown to be satisfactory. Osteoinduction refers to the process of stimulating the process of osteogenesis, which ultimately results in the production of bone. Osteoinduction qualities play a significant part in the process of bone healing because of

their ability to stimulate the formation of new bone and bone repair in the area where the defect was (Albrektsson and Johansson, 2001).

## **2.2 Calcium phosphate ceramic as bone substitute materials**

Calcium phosphate ceramic is a type of bioceramic material that is frequently used in orthopaedics and dentistry for bone regeneration and as a bone substitute. These applications include bone replacement and bone regeneration. This is due to the fact that calcium phosphate ceramic possesses excellent osteoconductivity in addition to a chemical composition that is analogous to that of actual bone. It demonstrated an advantageous association with living tissue in addition to an osteoconductive behaviour in immature cells directed toward bone cells. A chemical connection is formed between the calcium phosphate ceramic and the bone along the interface.

Clinical applications of calcium phosphate ceramic include the repair of massive bone defects brought on by tumours, periodontal defects, scaffolding for bone tissue regeneration, and cements for bone healing and regeneration. Some of these clinical applications are listed below (Saikia et al., 2008). Ceramics made of calcium phosphate are used extensively, and two of the most common types are hydroxyapatite and tricalcium phosphate. In order to cure severe defects brought on by tumours, bone graft substitute materials such as hydroxyapatite (HAp) and  $\beta$ -tricalcium phosphate ( $\beta$ -TCP) are often utilised in the treatment process (Saikia et al., 2008). Figure 2.1 illustrates the use of HAp granules and HAp granules as a substitute for bone transplant in the process of filling bone deficiency.

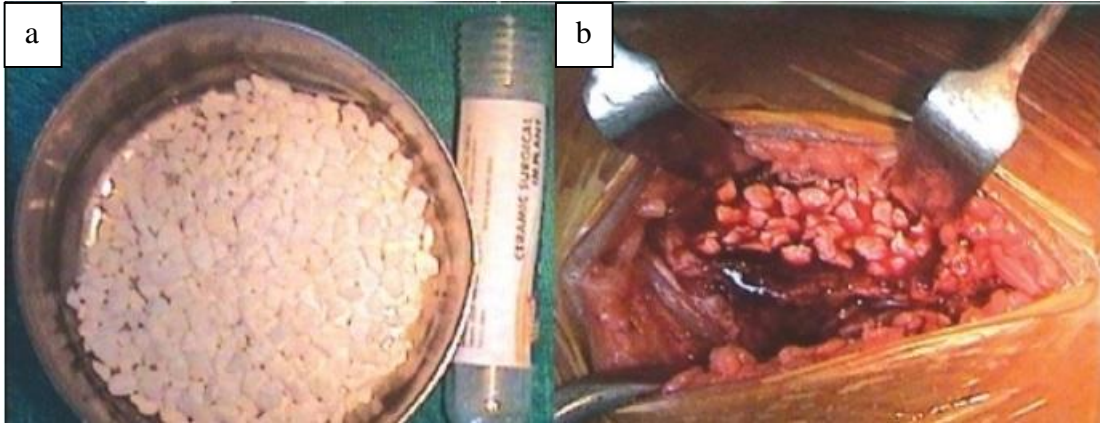


Figure 2.1: (a) HAp granules (b) HAp granules used as bone substituent materials (Saikia et al., 2008).

### 2.3 Type of calcium phosphate groups

The inorganic molecule known as calcium phosphate is made up of calcium cations ( $\text{Ca}^{2+}$ ), orthophosphate ( $\text{PO}_4^{3-}$ ), metaphosphate ( $\text{PO}_3^-$ ), and pyrophosphate ( $\text{P}_2\text{O}_7^{4-}$ ) anions. On rare cases, the presence of hydrogen  $\text{H}^+$  and hydroxide  $\text{OH}^-$  ions is observed (Eliaz and Metoki, 2017). Calcium phosphates are categorised as either acidic or basic according to the Ca/P ratio of the compound. Calcium phosphate that is basic has a Ca/P ratio that is larger than 1.67, in contrast to the Ca/P ratio of acidic calcium phosphate, which is less than 1.67. (Chen et al., 2013). Calcium phosphates are a type of substance that are known as important inorganic minerals in roughly sixty percent of all native human bones. This is because calcium phosphates are composed of a calcium cation and a phosphate anion. Calcium phosphate compound has seen extensive use in the field of bone regeneration applications because to the osteoconductive and, in some instances, osteoinductive qualities that it possesses. The ability to osteoinduce progenitor cells to develop into osteoblastic lineages is referred to as osteoinductive, whereas the ability to osteoconduct



bone formation on the surface of materials is referred to as osteoconduction (Albrektsson & Johansson, 2001). Both osteoinductive and osteoconductive processes promote the adhesion and proliferation of cells. The capacity of a cell to adsorb proteins from the extracellular matrix has a significant impact on the cell's ability to adhere to a surface. It is affected by the surface properties of calcium phosphates, such as their surface roughness, crystallinity, solubility, phase content, porosity, and surface energy. Additionally, it is controlled by the phase content of the calcium phosphates. (Jeong et al., 2019).  $\alpha$ -tricalcium phosphate ( $\alpha$ -TCP), hydroxyapatite (HAp), monocalcium phosphate monohydrate (MCPM), dicalcium phosphate dihydrate (DCPD), tetracalcium phosphate (TTCP), and  $\beta$ -tricalcium phosphate ( $\beta$ -TCP) are some of the different types of calcium phosphate compounds. Other types include dicalcium phosphate dihydrate (DCPD), tetracalcium (MCPM). Each of these compounds will have a unique Ca/P ratio as well as a unique solubility, with greater Ca/P ratio compounds having a lower solubility than the other compounds. Monocalcium phosphate monohydrates (MCPM), dicalcium phosphate dihydrates (DCPD), anhydrous calcium phosphate (DCPA), octacalcium phosphate (OCP), and tricalcium phosphate are a few examples of acidic calcium phosphate (TCP). Hydroxyapatite (HAp) and tetracalcium phosphate (TTCP) are two examples of calcium phosphates that have a basic structure (Chen et al., 2013).

### **2.3.1 Monocalcium phosphate monohydrate (MPCM)**

The molecular formula for the inorganic compound monocalcium phosphate monohydrate (MCPM), often known as calcium dihydrogen phosphate, is written as  $\text{Ca}(\text{H}_2\text{PO}_4)\text{H}_2\text{O}$ . Another frequent name for this substance is calcium dihydrogen

phosphate. It has a Ca/P ratio of 0.5, making it the phase of calcium phosphate that is the most acidic. MCPM is a chemical that is water-soluble and is used in dentistry as a component of self-setting calcium phosphate cements and as a sealant. In addition, MCPM is utilised in other applications. The extreme acidity of pure MCPM, on the other hand, renders it incompatible with biological systems (Eliaz and Metoki, 2017). The graphical representation of MCPM, which is utilised as a component in self-setting calcium phosphate cement, can be seen in Figure 2.2 below..

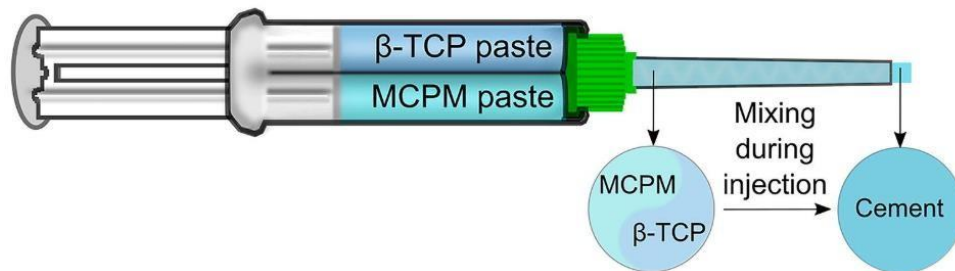


Figure 2.2: Graphical diagram of MCPM used as component of self-setting calcium phosphate cement (Luo et al., 2018).

### 2.3.2 Dicalcium Phosphate Dihydrate (DCPD)

Brushite, commonly known as dicalcium phosphate dihydrate (DCPD), is an acidic calcium phosphate that has the chemical formula  $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$  with a Ca/P ratio of 1.0. Brushite can also be found under the name brushstone. An acidic calcium phosphate solution with a pH between 4 and 5 was all that was needed to quickly produce DCPD at room temperature. (Rey, 1998). The substance known as DCPD is osteoconductive, as well as biocompatible and biodegradable. In the field of medicine, DCPD is utilised both as a calcium phosphate cement and as an intermediate component for the remineralization of teeth.

### 2.3.3 Tricalcium Phosphate

$\text{Ca}_3(\text{PO}_4)_2$  is the chemical formula for TCP, which is more commonly known as tricalcium phosphate. It has a Ca/P ratio of 1.5 in its make-up. TCP is a material that is biocompatible and makes a contribution to the growth of tough tissues. It is possible to use it for tooth and bone mending due to the fact that it has a high solubility and the ability to mediate cell processes in vivo (He et al., 2017). The look of TCP is identical to that of biological apatite, which is found in the bone tissue of humans. TCP can be found in four different polymorphic forms, including  $\beta$ -TCP for use at low temperatures,  $\alpha$ -,  $\alpha'$ -, and  $\gamma$ -TCP for use at high temperatures. Even though  $\alpha$ - and  $\beta$ -TCP have the identical chemical composition, the degree to which they are soluble is affected by changes in their crystallographic structures. According to Rey et al. (1998),  $\alpha$ -TCP is more stable at temperatures that are higher than 1125 °C, whereas  $\beta$ -TCP more stable at temperatures that are lower than 1125°C. Because it can only exist at very high temperatures and pressures,  $\alpha'$ - and  $\gamma$ '-TCP are not attractive to study because of this property. They are difficult to produce in a single phase and immediately revert back into  $\alpha$ -TCP as soon as the temperature drops below their critical temperature of 1430°C. The temperature resistance of TCP is depicted in figure 2.3. TCP is an osteoconductive substance, meaning that it encourages the growth of bone either within its pores or on its surface (Al-Sanabani et al., 2013).

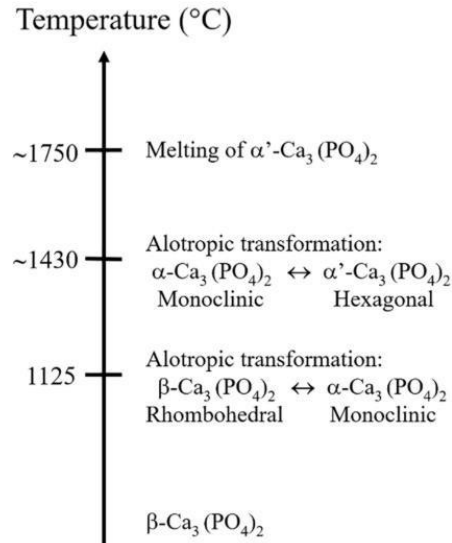


Figure 2.3: Thermal stability of TCP (Casas-Luna et al., 2018).

### 2.3.3.1 $\alpha$ -Tricalcium Phosphate

$\alpha$ -tricalcium phosphate, also known as  $\alpha$ - $\text{Ca}_3(\text{PO}_4)_2$ , is yet another form of calcium phosphate that has been shown to have a number of applications to its advantage. As a result of the material's high level of solubility,  $\alpha$ -TCP has been used into bone cements and several other bone substitutes (Carrodegua and De Aza, 2011). The material is nonetheless biocompatible despite the fact that  $\alpha$ -TCP is more soluble than  $\beta$ -TCP and that it hydrolyzes into hydroxyapatite (HAp) more quickly. This demonstrates that the incorporation of  $\alpha$ -TCP material into both self-setting bone cements and biodegradable ceramics for the purpose of bone healing is beneficial (Carrodegua and De Aza, 2011). Additionally, when  $\alpha$ -TCP is exposed to the liquid phase, it will harden and create a very rigid substance that can be utilised to fill in bone flaws. This material can be used to fill in bone deformities.

It should be noted that the temperature range of 1150 to 1500°C is where  $\alpha$ -TCP is thermodynamically stable (Kolmas et al., 2015). Therefore, as it requires quick cooling after the sintering process, the manufacturing of  $\alpha$ -TCP is particularly challenging to manage. According to a study by Karashima et al. (2009), polyurethane foam burning can be used to create porous  $\alpha$ -TCP foam scaffolds. These porous  $\alpha$ -TCP foam scaffolds are easily converted to HAp by a hydrothermal process at temperatures between 100 and 200°C (Karashima et al., 2009). Figure 2.4 displays SEM images of  $\alpha$ -TCP foam granules that were treated hydrothermally with distilled water at 100°C and 200°C for 24 hours after being immersed in distilled water at 37°C.

According to the findings of another piece of research, crystals of dicalcium phosphate dihydrate (DCPD) were produced on the surface of the  $\alpha$ -TCP foam granules after they were subjected to an acidic calcium phosphate solution composed of monocalcium phosphate monohydrate (MCPM:  $\text{Ca}(\text{HPO}_4) \cdot 2\text{H}_2\text{O}$ ) and phosphoric acid solution. This solution was used to treat the foam granules ( $\text{H}_3\text{PO}_4$ ). These precipitated DCPD crystals instantly bridged the  $\alpha$ -TCP foam granules after they had formed (Shariff et al., 2016). Figure 2.5 shows SEM images of  $\alpha$ -TCP foam granules before and after exposure to 0.3 mol/L MCPM–0.1 mol/L  $\text{H}_3\text{PO}_4$  and 1.0 mol/L MCPM–1.0 mol/L  $\text{H}_3\text{PO}_4$  solutions for 60 min at 25°C.

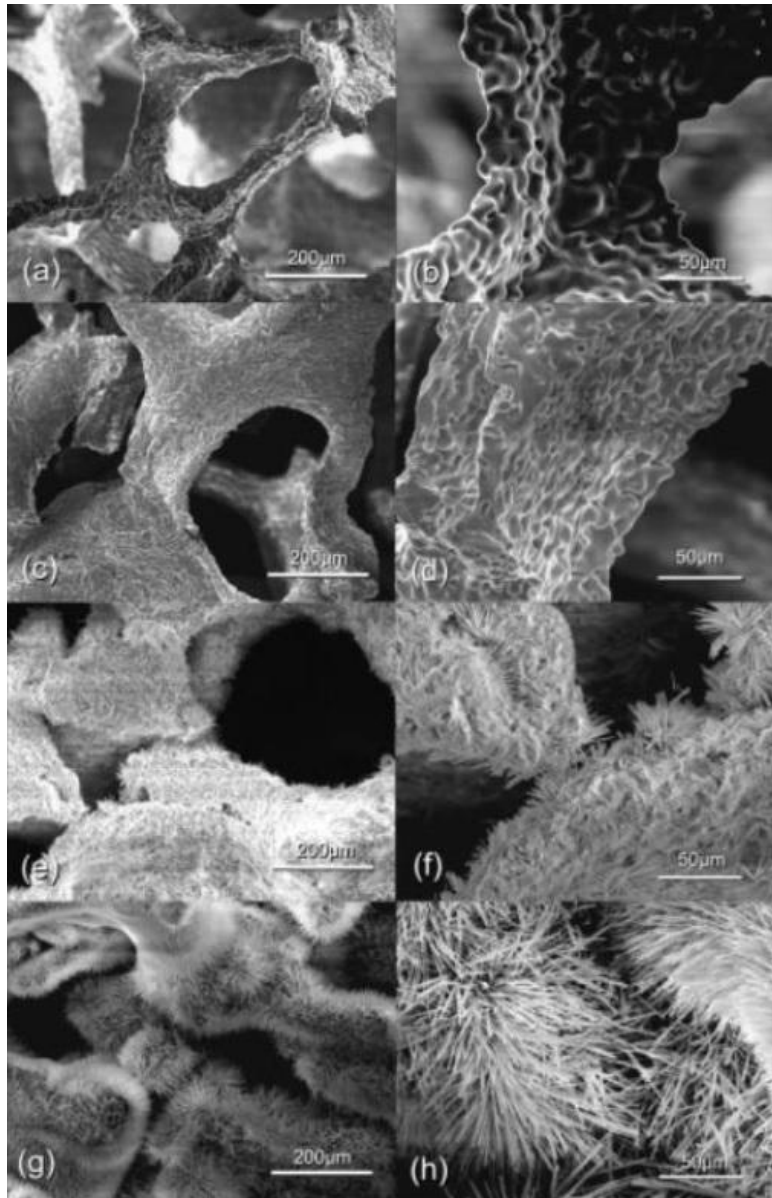


Figure 2.4: SEM images of  $\alpha$ -TCP foam granules (a and b) and specimens after immersion in the distilled water at 37°C (c and d) and after hydrothermal treatment with distilled water at 100°C (e and f) and 200°C (g and h) for 24 hours (Karashima et al., 2009).

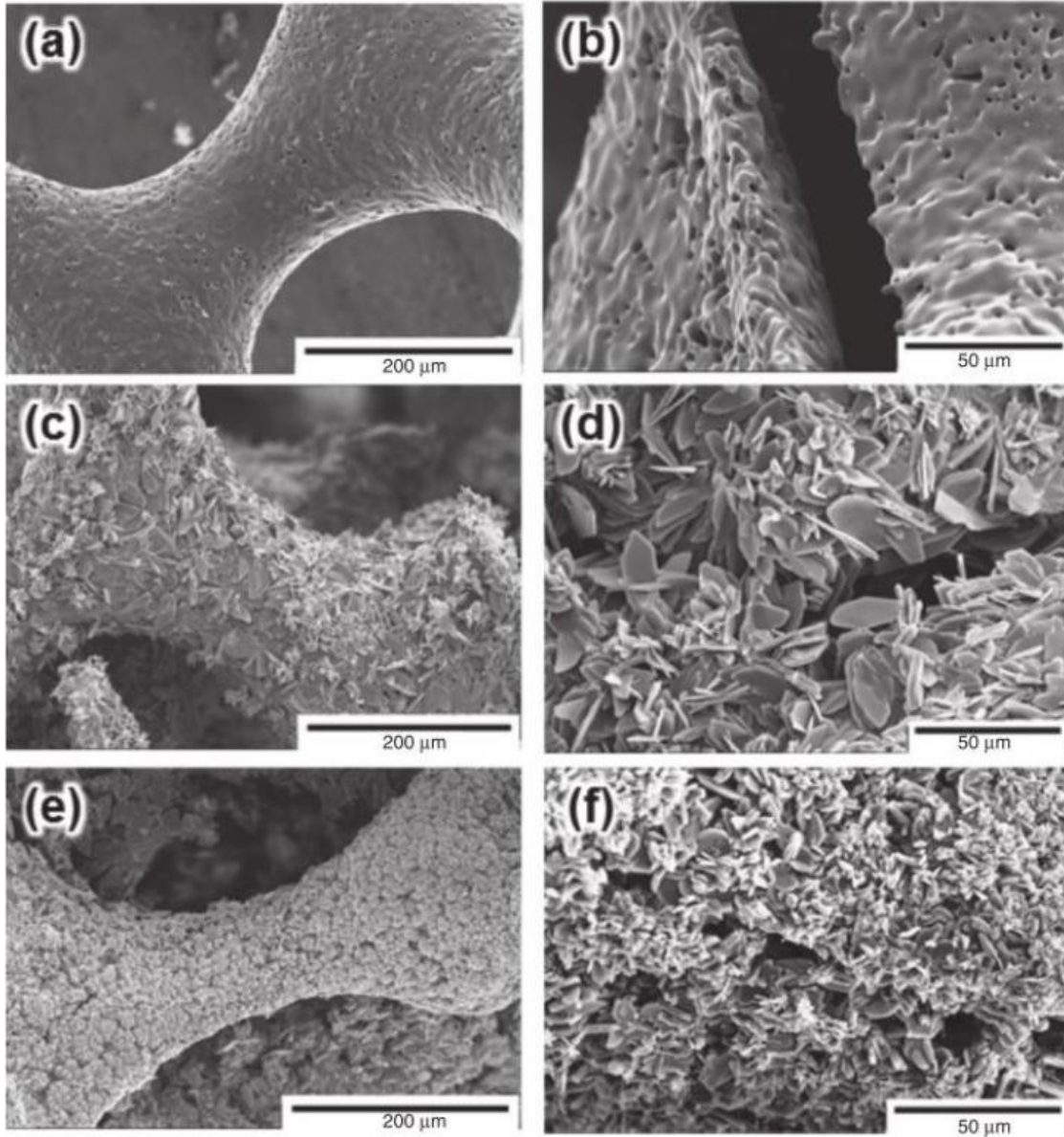


Figure 2.5: SEM images of  $\alpha$ -TCP foam granules (a, b) before and after exposure to (c, d) 0.3 mol/L MCPM–0.1mol/L H<sub>3</sub>PO<sub>4</sub> and (e, f) 1.0 mol/L MCPM–1.0 mol/L H<sub>3</sub>PO<sub>4</sub> solutions for 60 min at 25°C (Shariff et al., 2016).

### 2.3.3.2 $\beta$ -Tricalcium Phosphate

$\beta$ -tricalcium phosphate, also known as  $\beta$ - $\text{Ca}_3(\text{PO}_4)_2$ , is utilised rather commonly in medical settings including clinics and hospitals due to the fact that it is both bioactive and biocompatible. It is currently well accepted practise to employ  $\beta$ -TCP in surgical implant applications, cements, and grafting materials for synthetic bone. The most important characteristic of these materials is their capability of forming a direct chemical interaction with bone tissue (Nahar U et al., 2017). Despite the fact that both of these compounds are more soluble than HAp,  $\beta$ -TCP has a lower solubility than  $\alpha$ -TCP does. Because of its high solubility,  $\alpha$ -TCP is more easily dissolved than  $\beta$ -TCP when it is subjected to physiological circumstances (Gallinetti, Canal and Ginebra, 2014). On the other hand, due to the fact that HAp is thermodynamically stable under physiological conditions, it is extremely challenging to dissolve (Durucan and Brown, 2002). Even though  $\alpha$ -TCP has a higher solubility than  $\beta$ -TCP, the bonding of the bone surface will still be negatively impacted as a result of this property. If the dissolution of TCP happens too quickly, the capacity of the bone substitute to develop excellent osteointegration between the surface of the bone substitute and the original will not be successful.

### 2.3.4 Hydroxyapatite (HAp)

Hydroxyapatite, which has the chemical formula  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$  with a Ca/P ratio of 1.67, is considered to be the "golden standard" of ceramics made from calcium phosphate. HAp is far less soluble than  $\beta$ -TCP, and it seems to be the phase that is the most inert in a physiological body environment (Al- Sanabani et al., 2013, Rattanachan et al., 2018).



In addition to this, HAp has a history of being utilised in a variety of clinical applications, such as animal research and orthopaedics. Because of its superior osteoconduction and biocompatibility qualities, HAp is advantageous in this regard (Al-Sanabani et al., 2013, Nyan, 2016, Eliaz and Metoki, 2017). The chemical make-up of human bone and teeth is comparable to that of synthetic HAp. HAp is a filler that can be used to coat and reinforce dental resins for orthopaedic and dental implants. It can also be utilised for other applications. Controlled drug distribution is possible with the help of HAp scaffolds (Eliaz and Metoki, 2017). Table 2.1 presents the results of a comparison between artificial HAp and natural bone and teeth. HAp, on the other hand, has a weak mechanical strength and a poor fracture toughness. Because of this, its application was restricted to load-bearing regions only. The HAp composite that is created when it is mixed with a polymer result in an improvement in the material's mechanical properties.

Table 2.1: Comparison of synthetic HAp with bone and teeth (Al-Sanabani et al., 2013)

Composition, wt %	Enamel	Dentine	Bone	HAp
Calcium	36.5	35.1	34.8	39.6
Phosphorous	17.1	16.9	15.2	18.5
Ca/P ratio	1.63	1.61	1.71	1.67
Total inorganic (%)	97	70	65	100
Total organic (%)	1.5	20	25	-
Water (%)	1.5	10	10	-

## 2.4 Solubility of calcium phosphate groups

The solubility phase diagram of calcium phosphate ceramic is what determines the relative stability of various types of calcium phosphate ceramic at a variety of pH values and temperatures. The relative strength of a calcium phosphate ceramic is directly proportional to its bioresorbability (Chow, 2000, Dorozhkin, 2013). For the purpose of expressing solubility, the  $\log_{10}$  concentration of ions is utilised. At a particular pH value, the fact that there is a larger concentration of ions in the aqueous solution indicates that the calcium phosphate compound has a high propensity to dissolve in the aqueous solution. This demonstrates that the calcium phosphate compound has a high solubility and thermodynamically unstable (Ozdemir et al., 2017). It is said that the calcium phosphate ceramic with the most stable when it has the least amount of solubility compared all between the calcium phosphate ceramics. After the reaction of a self-setting calcium phosphate ceramic had completely set, two significant end products were generated, which are DCPD and HAp. These are the abbreviations for dichlorodiphenylphosphate and hydroxyapatite, respectively (Dorozhkin, 2013). When the pH is higher than 4.2, the DCPD crystal begins to precipitate, and once it does, it is unstable and easily dissolved in aqueous solution, resulting in the release of  $\text{Ca}^{2+}$  and  $\text{PO}_4^{3-}$  ions. When the pH is lower than 4.2, DCPD is the calcium phosphate ceramic that exhibits the greatest degree of thermodynamic stability. When the pH of an aqueous solution is higher than 4.2, HAp is the calcium phosphate ceramic that is the most stable and has the lowest solubility. This demonstrates that HAp rapidly precipitates in aqueous solutions with a pH that is higher than 4.2. The pH threshold of 4.2 may, in practise, correspond to a pH value that is greater (Dorozhkin, 2013). In comparison to other calcium phosphate

ceramics, the HAp phase exhibits the highest level of thermodynamic stability at healthy body conditions with a pH level of 7.4. This suggests that HAp is easily precipitated in conditions that are physiologically relevant to the organism (Ozdemir et al., 2013). Table 2.2 shows the types of calcium phosphate groups with different solubility.

Table 2.2: Solubility of calcium phosphate groups (Kucko et al., 2019)

Calcium Phosphate Compound	Solubility at 25°C (mg/L)
Monocalcium phosphate monohydrate	18,000
Dicalcium phosphate dihydrate	88
$\beta$ -Tricalcium phosphate	0.5
$\alpha$ -Tricalcium phosphate	2.5
Hydroxyapatite	0.3

## 2.5 Bioinert ceramic

After implantation, bioinert ceramics do not display any sort of biological response to the tissues in their immediate environment. This bioinert ceramic is capable of withstanding corrosion when placed in a physiological setting. Oxide bioinert ceramics include alumina and partially stabilised zirconia, while non-oxide bioinert ceramics include carbon and nitride-based ceramics. Alumina and partially stabilised zirconia are examples of oxide bioinert ceramics (Punj et al., 2021). Alumina is frequently utilised in dental repair as well as hip replacement, whereas zirconia is utilised in the production of

ball heads for total hip replacement (THR). Alumina and zirconia are both excellent candidates for hip replacement because of their precise geometries, high levels of stiffness, low levels of porosity, high densities, and superb surface qualities.

## **2.6 Bioactive ceramic**

Bioactive ceramics are ceramics that have been developed to stimulate specific biological activity in order to aid in the regeneration of injured organs. This type of ceramic can be used to help repair damaged organs. When it comes to the process of repairing bone tissues, bioactivity is described as the ability to make direct touch with living bone after implantation in a bone defect location. This is necessary for the healing process. The circumstance in which new bone formation occurs on the surfaces of bioactive ceramics is referred to as osteoconductivity. There are many types of bioactive ceramics, some examples of which are bioglass, sintered hydroxyapatite, and glass ceramic (Ohtsuki et al., 2009).

In addition, bioglass is constructed using the elements silicon oxide, sodium oxide, calcium oxide, and phosphorus pentoxide as its primary constituents. 2017 research by Konofaos and associates Hench's demonstration of the potential of bioglass to connect with bone and soft tissue was presented in the form of a ternary phase diagram (Hench, 2006). As can be seen in Figure 2.6, the composition of bioglass is often made up of 30–60 mol% silica, 10–50 mol% calcium oxide, 5–40 mol% sodium oxide, and 6 mol% phosphorus pentoxides. This composition is also represented by region “I” in the ternary phase diagram (Khalid et al., 2017).

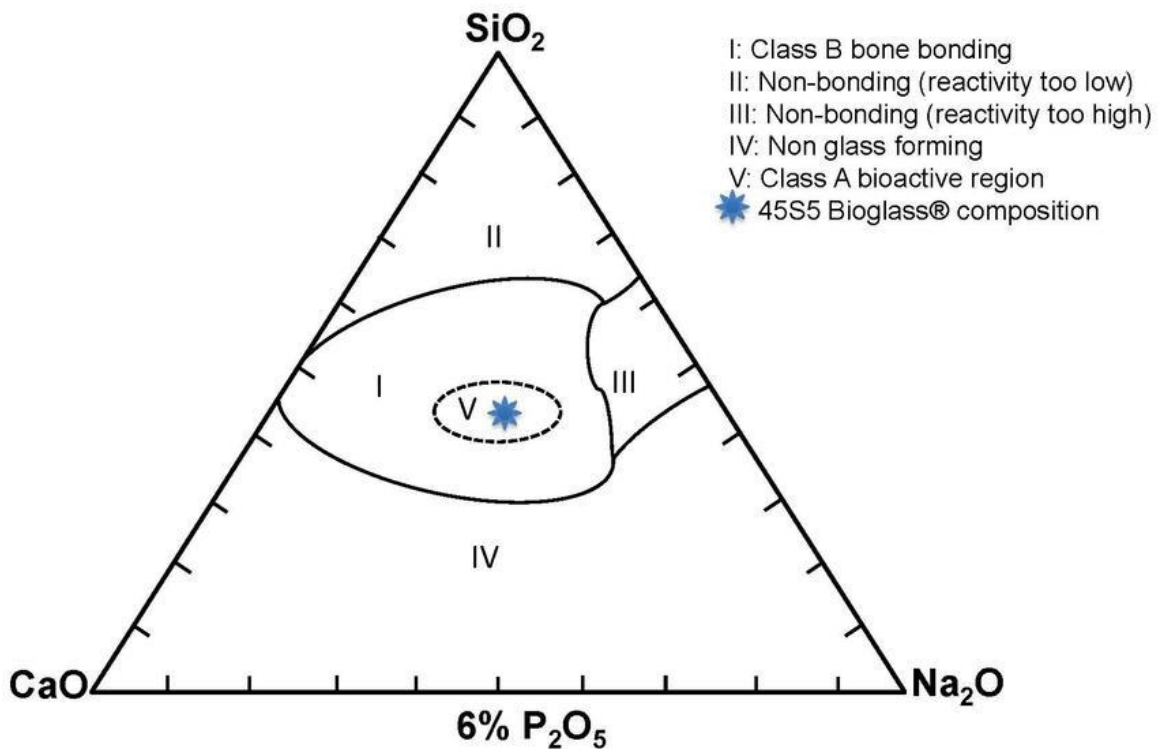


Figure 2.6: Ternary Phase Diagram of Bioglass (Hench, 2015)

As a result, there are two distinct categories of bioglass, designated Class A and Class B, respectively. The formation of new bone as well as osteoconduction and osteostimulation are the outcomes of Class A bioactivity. These materials exhibit osteo-

conductive features because of the quick reaction mechanism that takes place on the surface of the material and causes a critical concentration of soluble silica and Ca ions to dissolve. As a result, these materials also have osteo-productive characteristics. Within the bone defect that has been created surgically, Class A BGs have the potential to encourage the colonisation of their surface by osteogenic stem cells. This, in turn, causes the rapid construction of osteoid bridges between the particles, the mineralization of the matrix, and the development of mature bone structures. This mechanism specifies both an extracellular and an intracellular reaction at the contact because it interacts with the ions that are created from the surface. Class B bioactivity takes place whenever osteoconduction is the only form of conduction. The bioactive chemicals that belong to this category have the ability to form bonds with bone but not with soft tissues. This classification is determined by the amount of silica dioxide present in the ternary system because silica dioxide can form a network and has a major impact on the solubility rate of the other ions (Hench, 2015). These implants solely exhibit osteoconductive qualities, which are exclusively altered by extracellular stimuli, and the most typical example of this is hydroxyapatite. In comparison, the A class implants exhibit both osteoconductive and electrical features.

## **2.7 Bioactive glass**

Bioactive glass, also known as BG, was found to be one of the bioactive materials that belong to Class A and possesses both osteoconductive and osteoinductive capabilities. The literature offered a selection of different BG compositions to choose from. In 1969, Professor Hench was the first person to successfully fabricate bioactive glass, which was