Effect of Poly(Vinyl Alcohol) Addition on the Properties of Hydrothermal Derived Calcium Phosphate Cement for Bone Filling Materials

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Abstract. The effect of addition of poly(vinyl alcohol) on hydrothermal derived calcium phosphate cement has been studied. The precursors used to prepare the cement were calcium oxide (CaO) and ammonium dihydrogen phosphate (NH4H2PO4); the reaction was conducted in water at 80-100°C. To improve properties of CPC, poly(vinyl alcohol) (PVA) of 1wt% and 2wt% was added to the liquid phase of CPC and the results were compared to CPC without PVA addition. The addition of PVA was proved to bring remarkable effects on cohesion, setting time and mechanical strength of CPC which make it suitable physically for injectable bone filler applications.

1. Introduction

Calcium phosphate cements (CPC) has shown great interest as one of the materials for bone graft applications because of excellent biological behavior, non-toxicity, biocompatibility, and osteoconductivity[1]. CPC is generally produced by chemical reaction between two phases which are powder phase and liquid phase[2,3]. The preparation of cement using hydrothermal method is most favorable because its ability to produce highly crystalline cement with high yield, controlled morphology and stoichiometric Ca/P ratio[5]. Nevertheless, there are certain drawbacks that need to be considered which gives limitation to its clinical applications[2,6]. CPC has shown poor injectability and in certain cases, the phase separation between powder and liquid might occur[7]. The cements also have tendency to disintegrate after injected and contact with blood or other physiological solutions in body because of weak cohesion[7]. Numerous works have been reported to increase integrity of CPC by adding polymeric binder such as poly(vinyl alcohol) (PVA), poly(lactic-co-glycolic acid) (PLGA), chitosan fibers, polyamides and others to either powder or liquid phase of CPC paste with the aim to improve their handling and mechanical properties[6]. Among these polymers, PVA is of great interest from the viewpoint of improving cohesion and setting time of CPC. PVA is one of the hydrophilic biocompatible polymer that was widely used in biomedical applications. The high hydrophilicity and easy swelling when...
absorbing water have made PVA as one of the materials suitable to maintain stability of the CPC during storage[8]. In this report, the effect of PVA addition on the handling and mechanical properties of hydrothermal derived CPC will be presented.

2. Materials and Methods

2.1 Synthesis of powder.
The calcium phosphate cement (CPC) was prepared using a hydrothermal method as we reported elsewhere[9]. The chemical reaction to synthesize CPC powder is as follows:

\[5\text{Ca(OH)}_2 + 3(\text{NH}_4)\text{HPO}_4 \rightarrow \text{Ca}_5(\text{PO}_4)_3\text{OH} + 3\text{NH}_4\text{OH} + \text{H}_2\text{O}\]

(1)

The composition of CPC consists of calcium oxide (CaO) and ammonium dihydrogen phosphate (ADP), \(\text{NH}_4\text{H}_2\text{PO}_4\). The stoichiometric composition of hydroxyapatite (HA) produced is referred to 0mol% excess of CaO. The synthesized HA was then dried overnight at 80°C until the dry powder was produced. To make CPC paste, the dried powder (p) and distilled water (w) were mixed homogenously for 3min at the ratio of (3:2) p/w mass-ratio for preparation of filler materials. The evaluation of the effect of PVA addition on the CPC paste was done by addition of 1 and 2wt% of PVA to the filler materials. The paste was then filled into the 10mm diameter and 15mm height PTFE (Teflon) mold by hand-spatulation. Figure 1 shows the flowchart of the method to produce CPC.

2.2 Physical and Mechanical characterization
The dried powder obtained was subjected to physical and mechanical characterization. XRD was used for crystal structure and phase analysis using Empyrean, PANalytical XRD system. The scanning done at scan speed of 2° per minute and a step size of 0.02° over the 2θ range of 20-60°. The diffraction patterns obtained from the XRD analysis was compared to powder diffraction files from JCPDS database to determine the phase of HA. Morphological analysis on the powder was done using JEOL, JSM 6700F.

2.3 Injectability test
The injectability test was done by extrusion of 5 ml non-needle syringe with 2.68mm inner diameter of canula filled with paste as the working sample. The force applied on the syringe ejector spindle was determined by recording the evolution of the extrusion force (N) against the extrusion time (sec) using of a Lloyd universal testing machine, LR 10 K+ model, at a crosshead speed of 50mm/min and a maximum load of 300N. The injectability results for CPC samples with addition of 1 and 2wt% of PVA were evaluated.

2.4 Setting time test
To identify the setting time, Gillmore method was used to measure (3:2) p/w ratio of CPC with the addition of PVA. After homogenously mixed, the CPC paste was moulded into PTFE (Teflon) mold. The initial and final setting times were determined by holding the light and heavy needles in vertical position and applied to the cement surface until no visible indentation formed.

2.5 Mechanical test
The compression test was done using the Lloyd LR 10 K+ Universal Testing Machine on 10mm diameter x 15mm length specimens at 1mm/min crosshead rate for all samples of CPC.

3. Results and Discussion
The addition of 1 and 2wt% of PVA has shown remarkable effects on injectability, setting time, morphology, cohesiveness, density and mechanical strength of calcium phosphate cement. The addition of 1 and 2wt% of PVA to CPC was able to extrude all paste from the syringe as shown in Figure 2. CPC without PVA shows good injectability and started to increase load for paste extrusion at 40s. However, the paste has shortened the extrusion time to 37s and 33s for 1 and 2wt% PVA added to CPC, respectively, due to absorption of water molecules by PVA which leads to more viscous and poor injectability of CPC paste. Additionally, Figure 3(a) and (b) represents both CPC without PVA and CPC with 1wt% PVA, able to extrude all the paste from the syringe. Meanwhile, there are little paste still remained in the syringe as shown in Figure 3(c) for CPC with 2wt% PVA. Overall, the increase in the concentration of PVA decreases the injectability.

![Figure 2](image1.png)  
**Figure 2.** Injectability of (3:2) p/w ratio CPC at different wt% of PVA:  
(a) 0%, (b) 1% and (c) 2%.

![Figure 3](image2.png)  
**Figure 3.** Moldable forms of calcium phosphate cement for different wt% of PVA:  
(a) 0%, (b) 1% and (c) 2%.

Figure 4 shows the initial and final setting time of CPC as the function of PVA concentration. The initial setting time of CPC without PVA is 11min, and decreased to 6 and 3min respectively, when PVA concentration of 1 and 2wt% was added. While, the final setting time of non-PVA CPC paste was 87min, and it decreased to 56 and 38min when PVA was added to the concentration of 1 and 2wt%, respectively. Rajzer et al reported that addition of PVA with the presence of glycerol to CPC increases the setting time, might be caused the high viscosity of glycerol [8].

The presence of hydroxyapatite was marked by a strong x-ray peak at (31.733; 2θ). The clear and sharp peak shown in Figure 5 proves that the phase purity and crystallinity of the hydroxyapatite powder. The crystallinity of CPC was also mentioned previously in the study done by Wang et al [10] and Yousefi et al [11]. CPC without PVA shows slightly higher peak of HA compared to CPC with PVA addition.

Figure 6 presents FESEM for fine powder of HA where nanosize particles of 100nm long are clearly shown in CPC without PVA. The powder also formed agglomerated particles of a needle like.
morphology. After addition of 1 wt% PVA, fine powder of HA with nanosize particles of 100nm long still visible but there is more agglomeration of spherical size particles compared to CPC without PVA. The addition of 2 wt% PVA to CPC gave different looks to microstructure of CPC where the powder particles have been covered by PVA particles, making the CPC particles invisible.

**Figure 4.** Influence of the concentration of PVA on the setting time of CPC.

![Graph showing initial and final setting time of CPC with different PVA concentrations](image)

**Figure 5.** XRD peak of CPC without PVA (above) and CPC with the addition of 2 wt% PVA (below).

![XRD peaks of CPC](image)

**Figure 6.** Morphology of the nanosized particles of CPC without PVA (a), CPC with 1 wt% PVA (b) and CPC with 2 wt% PVA (c) tested using FESEM.

![Morphology images](image)

In general, the addition of PVA was very effective in improving the compression strength of the CPC. This test is beneficial to determine the strength of the materials and make sure it is able to withstand the load depends on the applications. Results from the compression strength test as shown in Figure 7, proves that the addition of 1 wt% PVA increases the compression strength of CPC from 1.01 to 2.03Mpa and increases up to 2.24MPa after addition of 2 wt% PVA. This shows that PVA addition has improved the mechanical strength of CPC.

Figure 8 shows the relative density of CPC with different wt% PVA added to CPC. After addition of 1 and 2 wt% of PVA to CPC, the density of cement decreased from 1.769 to 1.721 g/cm³. Meanwhile, the relative density of CPC can be calculated as compared to density of hydroxyapatite that is 3.14 g/cm³. From the calculations, the relative density of CPC without PVA, CPC with 1 wt% PVA and CPC with 2 wt% PVA are 43.66%, 44.42% and 45.19%, respectively.
The effect of PVA addition on the physical properties of hydrothermal derived CPC has been investigated. The as-synthesized powder was purely hydroxyapatite (HA) and no tangible change observed in its crystallinity after PVA addition. The microstructure size increased with PVA concentration but still maintain their spherical shape and agglomerate. The results also showed that, the initial and the final setting times of CPC have been faster with 2wt% PVA addition from 8 to 3 min and 87 to 38 min, respectively. However, CPC with 2wt% PVA did not show injectability as excellent as pure CPC showed where some portion of the paste remained in syringe after extrusion. The extrusion time also decreased from 40s to 33s after the PVA addition proving a poorer injectability. CPC’s compression strength increased from 1.01 to 2.24 MPa after addition of 2wt% PVA revealing much better ductility. In this study, PVA has acted as a suitable setting agent for the hydrothermal derived CPC, that helps to reduce setting time and improved compressive strength of the CPC cement. Therefore, the injectable CPC-PVA developed can be a promising material used in hard tissue filling applications.

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