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Novel Injectable Calcium Phosphate Bone Cement from Wet Chemical Precipitation Method

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Abstract. Calcium phosphate cement has been prepared via chemical precipitation method for injectable bone filling materials. Calcium hydroxide, $Ca(OH)_2$, and diammonium hydrogen phosphate, $(NH_4)_2HPO_4$, were used as calcium and phosphorus precursors respectively. The synthesized powder was mixed with water at different powder-to-liquid (P/L) ratios, which was adjusted at 0.8, 0.9, 1.0, 1.1 and 1.2. The influence of P/L ratio on the injectability, setting time and mechanical strength of calcium phosphate cement paste has been evaluated. The synthesized powder appeared as purely hydroxyapatite with nanosized and agglomerated spherical particles. All cement pastes show excellent injectability except for the paste with P/L ratio 1.2. Calcium phosphate cement with P/L ratio 1.1 shows the ideal cement for bone filler application with good injectability, the initial and final setting times of 30 min and 160 min, and the compression strength of 2.47 MPa. The result indicated that the newly developed calcium phosphate cement is physically suitable for bone filler application. This paper presents our investigation on the effect of P/L ratio on the handling and mechanical properties of calcium phosphate cement prepared via wet chemical precipitation method.

1. Introduction

Calcium phosphate cement (CPC) is clinically accepted for bone cement application. This is attributed to their excellent biological properties, injectability and ability to harden *in vivo* [1,2]. CPC can be moulded and shaped to fill the defect sites by using injection needle. The commercial CPC is made of tetracalcium phosphate (TTCP) and α–tricalcium phosphate (α-TCP) which will transform to hydroxyapatite (HA) upon contact with water, forming apatite cements [3].

CPC can be synthesized via dry methods (i.e. solid-state and mechanochemical synthesis) and wet methods (i.e. chemical precipitation, hydrolysis, sol-gel, hydrothermal, emulsion and sonochemical methods) [4]. Wet chemical methods is the most common method used in preparation of HA due to their ability to control the morphology and mean size of CPC as well as its pore size by adjusting the reaction parameters compared to dry methods [4,5]. The synthesis of CPC via wet chemical precipitation method is the most favorable route due to the ease in experimental procedure, low synthesis temperature, high homogeneous purity products, low cost as well as high yield [4-10].

In this work, novel calcium phosphate cement has been successfully synthesized through wet chemical precipitation method. The synthesized powder was mixed with water at various powder-to-liquid (P/L) ratios. The present work aims at investigating the effect of P/L ratio on the mechanical and handling (i.e. injectability, setting time) properties of CPC, and an optimized condition was defined at which the obtained cement is physically suitable for bone filling materials.

2. Materials and Methods

2.1. Synthesis of powder

Calcium hydroxide ($Ca(OH)_2$) was supplied by PC Laboratory Reagent and diammonium hydrogen phosphate ($(NH_4)_2HPO_4$) by Friendemann Schmidt Chemical, Germany. CPC was synthesized based on the following reaction:

$$5Ca(OH)_2 + 3(NH_4)_2HPO_4 \rightarrow Ca_5(PO_4)_3OH + 6NH_4OH + 3H_2O \quad (1)$$

The HA powders were prepared via modified wet chemical precipitation method, using calcium hydroxide, $Ca(OH)_2$, and diammonium hydrogen phosphate, $(NH_4)_2HPO_4$, as the calcium and phosphorus precursors respectively, with distilled water as the solvent. Calcium-to-phosphorus (Ca/P) ratio was 1.67. Calcium and phosphorus solution was prepared separately, by dissolving each precursor in distilled water. Then, calcium solution was added drop wise into the phosphorus solution. The pH of the mixture was adjusted at pH 11 by adding 25% ammonia solution. The mixture was then refluxed at 90℃. The precipitate formed was left for overnight (18 hours) aging at room temperature. This was followed by washing with distilled water and filtering. The filtered precipitate was dried overnight (18 hours) in an oven at 85℃ and then crushed. Figure 1 summarizes the wet chemical precipitation method.

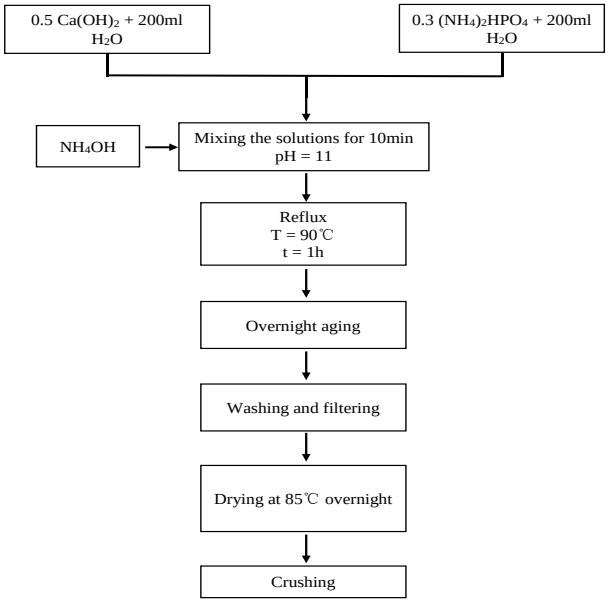

Figure 1. Flowchart of the wet-chemical precipitation synthesis.

2.2. Preparation of CPC

CPC was prepared by mixing powder and liquid phase for two minutes. The as-synthesized powder was used as the powder phase, and liquid phase is distilled water. P/L ratios were varied at 0.8, 0.9, 1.0, 1.1 and 1.2. The pastes were the put into a mould for further characterizations and properties evaluation.

2.3. Powder characterization

The as-synthesized powder was characterized for morphology and phase analysis. X-ray Diffraction (XRD) was used for phase analysis using an Empyrean PANalytical XRD system was operated by using CuKα radiation (λ = 1.5406 Å). Scan speed of 2 °per minute and a step size of 0.02 °over the 2θ

range of 20-60 ° were applied. Field Emission Scanning Electron Micsroscopy (FESEM) JEOL JSM 6700F was employed for morphological evaluation.

2.4. Injectability test

The injectability test was done using Lloyd LR 10 K+ Universal Testing Machine under compression mode. This is called extrusion method, in which the cement paste was extruded out of non-needle 5ml polyethylene syringe. The extrusion was done by applying a crosshead speed of 50 mm/min and a maximum load of 300 N.

The result of this extrusion method was recorded as the evolution of extrusion force (N) against the extrusion time (sec) and plotted in y and x axes respectively. The injectability tests were evaluated for CPC with different P/L ratios.

2.5. Setting time

The determination of the setting time of CPC was done using Gillmore needle method. After mixing the powder and liquid phases for two min, the paste was put into a polyethylene mould of 8 mm diameter x 12 mm length dimension. This work determined the setting time for CPC with different P/L ratios.

The initial and final setting times were determined by applying the thick and thin needle respectively in vertical position until no visible indentation was observed. Using Gillmore needle apparatus, initial setting time is the time when CPC able to resist the small fixed pressure applied by a thick Gillmore needle, while final setting time is the time when CPC able to resist the high fixed pressure applied by thin Gillmore needle [1,2].

2.6. Mechanical test

The measurement of compression strength was done using Lloyd LR 10 K+ Universal Testing Machine. The cement pastes were molded in Teflon moulds and left to dry for 48 hours, followed by compression tests on the 10 mm diameter x 15 mm length specimen at 1 mm/s crosshead rate.

3. Results and Discussion

Numerous studies on calcium phosphate cement development have used more complex synthesis routes and the synthesis time is relatively long [6, 10-15]. The modified wet chemical precipitation method in the present work is simpler and shortened the synthesis time.

Figure 2 shows the XRD patterns of the synthesized powder. The peaks present in the figure attributed to the standard data of HA (card no. 024-0033) as the main phase. The sharp and clear peaks confirmed the phase purity and crystallinity degree of the synthesized powder.

The FESEM image of synthesized HA powder is presented in Figure 3. The micrograph shows the agglomeration of spherical HA particles. The picture also is an evidence of the formation of nano size powder. This is in agreements with previous studies done by Yousefi *et al.* [11] and Dhanalakshmi *et al.* [12].

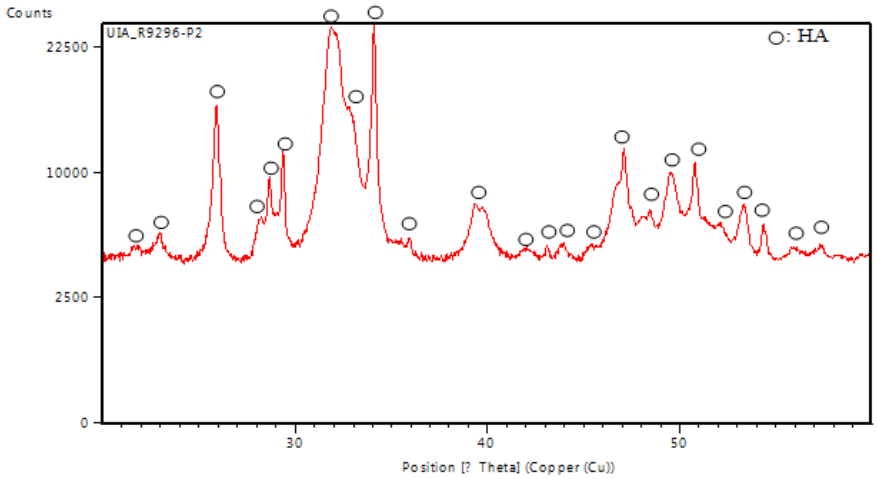

Figure 2. XRD pattern of the synthesized HA powder.

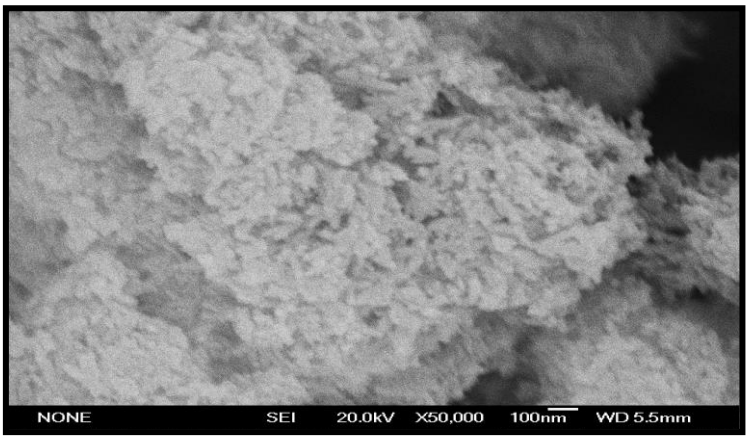

Figure 3. FESEM image of as-synthesized HA powder.

CPC was prepared by mixing the powder and distilled water for two min at different P/L ratios, which are varied from 0.8, 0.9, 1.0, 1.1 and 1.2. Injectability test of CPC as shown in Figure 4 indicated that the increase in powder content increase the extrusion load and injectability become poorer. This happen due to the increase in powder content which increase viscosity of the paste and become hard to be injected. CPC with P/L ratio 1.2 has become unworkable and the paste cannot be extruded out of the syringe.

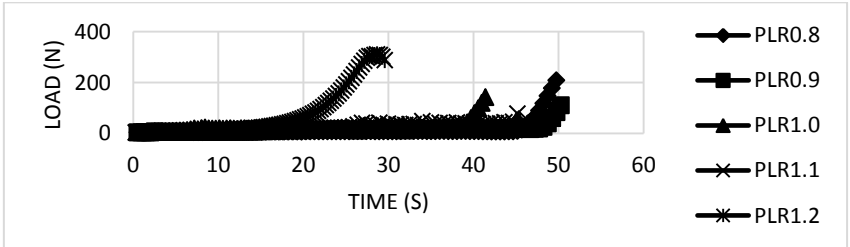

Figure 4. Injectability of CPC at different P/L ratios.

From Figure 5, the increase in P/L ratio shorten the setting time of CPC. This is due to the increase in powder content in the cement paste. P/L ratio 1.1 shows the optimum workable setting times of CPC, with initial setting time of 30 min and final setting time of 160 min. When CPC was prepared using P/L ratio 1.2, the paste was not workable with both initial and final setting times are 3 minutes. This is in a good agreements with the injectability result as the paste with P/L ratio 1.2 also shows no injectability.

The strength of CPC was determined for different P/L ratios. The result for compression test shown in Figure 6. The average strength of CPC ranged from 1.23 MPa to 2.47 MPa. CPC with P/L ratio 1.1 shows the highest strength with 2.47 MPa. It seems the entangled networks of apatite crystals become denser with the increase in powder content [1]. But, P/L ratio 1.2 CPC is an exception because it only forms a wet powder and hence dissolution and reprecipitation might not induced.

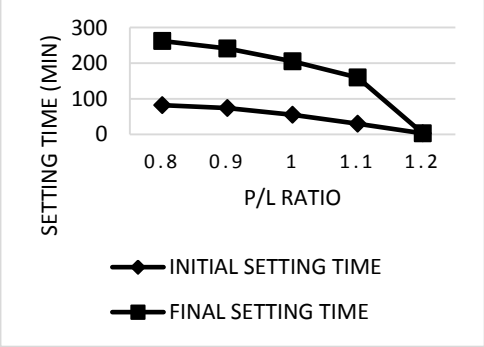

Figure 5. Setting time of CPC with different P/L ratios.

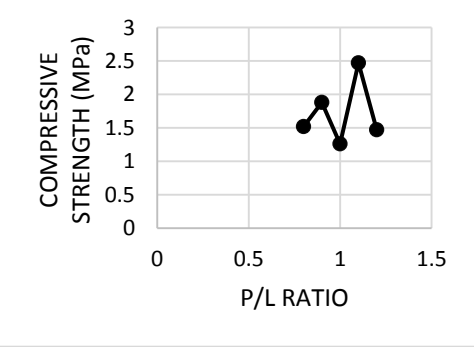

Figure 6. Compressive strength of CPC with different P/L ratios.

4. Conclusion

A novel wet chemical precipitation method has successfully produced a pure nano scale HA by using calcium hydroxide and diammonium hydrogen phosphate. The determination of injectability, setting time and compressive strength have been successfully done to elucidate the effect of P/L ratio on CPC. The results show that the increase in P/L ratio shortened the setting time and improved compressive strength, but reduced injectability. The synthesized CPC has proven its ability as injectable bone filling materials with optimized condition at P/L ratio 1.1.

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