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Research paper

Calcium Phosphate Bone Cement Prepared Using Wet Precipitation Method at Powder-to-Liquid Ratios of 1.3 and 1.7

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Abstract

Calcium phosphate/poly(ethylene glycol) composite for bone cement use has been developed by incorporating poly(ethylene glycol) (PEG) into calcium phosphate cement (CPC) prepared using wet chemical precipitation method with the powder-to-liquid (P/L) ratios of 1.3 and 1.7. The precursors used in the synthesis are calcium hydroxide, $Ca(OH)_2$, and diammonium hydrogen phosphate, $(NH_4)_2HPO_4$. The effect of PEG addition on injectability, setting behaviour, mechanical properties and anti-washout performance of CPC was investigated. The results indicated that PEG addition significantly improved setting time, injectability, compressive strength as well as anti-washout performance of CPC. The initial and final setting times of PEG free CPC with the P/L ratio of 1.3 are 88 min and 228 min, respectively. The addition of 4% PEG shortened both the initial and final settimg times to 47 min and 182 min, respectively. Without PEG, CPC with the P/L ratio of 1.7 has the compressive strength of 0.25 MPa. The compressive strength increased to 1.553 MPa when 5% PEG was added. The anti-washout properties of CPC/PEG is excellent with no cement dissolution throughout 28 days soaking period.

Keywords: *Calcium phosphate cement; Hydroxyapatite; Injectable; Poly(ethylene glycol); Wet chemical precipitation method*

1. Introduction

CPC has been recognized in biomedical field as injectable bone filling material. This is due to its great biological response, injectability and setting ability [1-3]. Injectable CPC can be injected to fill and take the shape of defect sites, and aids the regeneration of new bone tissues. Preparation of CPC involves the mixing of calcium phosphate powder with water at certain ratios to sets at body temperature via dissolution-precipitation mechanism [2].
Limitations of CPC are due to the poor injectability and low mechanical strength. Polymeric additives are significant approach to enhance performance and improve properties of CPC such as injectability, setting time, cohesiveness, mechanical strength and biological response [4,5]. Some of the additives have been addressed by previous studies including chitosan, alginate, poly(lactic-co-glycolic acid) (PLGA), poly(ethylene glycol) (PEG) and poly(vinyl alcohol) (PVA) [4].
PEG is a polyether composed of glycerol monomers. PEG shows non-toxicity, good water solubility, flexibility and anti-coagulant activity which have been widely used in biomedical field [6]. PEG has been used in preparing premixed CPC as a thickening agent and keeps the cement paste stable [4,6]. PEG is expected to shorten setting time, lower injectability and improve anti-washout performance of CPC [4].
This present work investigated the injectability, setting behavior, mechanical properties and anti-washout performance of CPC synthesized via wet chemical precipitation method at different powder-to-liquid (P/L) ratios and PEG concentrations.

2. Materials and methods

2.1 Synthesis of powder

CPC was synthesized via wet chemical precipitation method based on the procedure reported in the previous work [7]. This route employed calcium hydroxide, $Ca(OH)_2$ and diammonium hydrogen phosphate, $(NH_4)_2HPO_4$ as the calcium and phosphorus precursors respectively, and the solvent used was distilled water. Calcium-to-phosphate (Ca/P) ratio was fixed at 1.67.

2.2 Cement preparation

Preparation of CPC was done by mixing the synthesized HA powder and distilled water at certain ratios. The P/L ratio was varied at 1.3 and 1.7. PEG (MW300, Sigma) addition into CPC with the P/L ratio of 1.3 was varied at 1, 2, 3, 4 and 5 wt%. PEG was varied at 5, 10, 15 and 20 wt% for CPC with the P/L ratio of 1.7. The difference in the amount of PEG added is based on injectability behaviour which will be revealed in the next section.

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2.3 Injectability test

Extrusion method has been employed for the injectability test of CPC, in which a non-needle 5 ml polyethylene syringe was used. The extrusion of the cement paste has been done under compression mode of Lloyd LR 10 K+ Universal Testing Machine ran at 50 mm/min crosshead speed and 300 N maximum load. The result was plotted in graph form of extrusion force (N) against the extrusion time (s).

2.4 Setting time

The initial and final setting times of CPC was determined using Gillmore needle method. Powder and liquid phases were mixed for 2 min, and then the cement paste was put into a plastic mould prior to testing.

2.5 Mechanical strength

Compression strength was measured using Lloyd LR 10 K+ Universal Testing Machine operated at 1 mm/s crosshead rate. The cement pastes were left for 48 hours to set after molded in Teflon mold. The sample dimension was 10 mm diameter x 15 mm length.

2.6 Antiwashout test

The antiwashout behavior of CPC with dimension of 10 mm diameter x 15 mm length was investigated by soaking the cement in a Ringer's solution for up to 28 days. The compressive strength of CPC after the immersion was measured at 3, 7, 14, 21 and 28 days. At each interval, samples were washed with distilled water and dried prior to compression test.

3. Results and discussion

3.1 Setting time

CPC incorporated with PEG were prepared using the P/L ratios of 1.3 and 1.7 with different PEG concentrations. Figures 1 and 2 present the setting times of the fabricated CPC. The initial setting time is between 47 min and 88 min, whereas the final setting time is between 182 min to 228 min for CPC/PEG with the P/L ratio 1.3. Figure 1 shows the incorporation of PEG into CPC has improved setting time of CPC by shortening the hardening time of CPC. The entanglement of three dimensional apatite structure with polymer network structure during the hydration process has led to the acceleration of setting [6,8]. However, this is true only for the CPC with PEG content below 5%. This result indicates that a proper amount of PEG is required to improve setting time of CPC. Setting time of CPC/PEG with the P/L ratio 1.7 shows the increase in setting time with PEG content as shown in Figure 2. This result indicates improvement as the cement paste became more workable, which is attributed to the high PEG content used in preparing CPC.

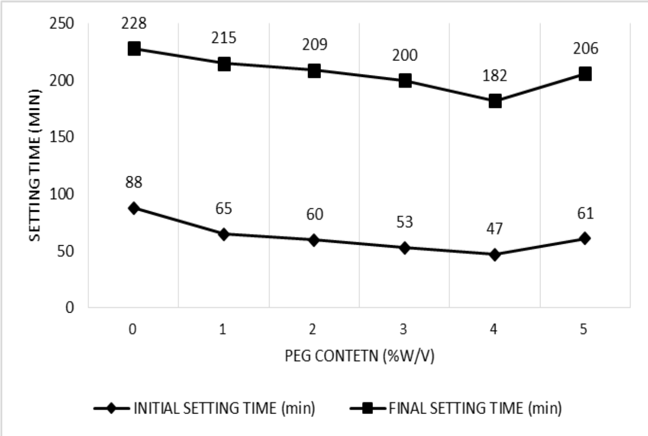

Figure 1: Effect of PEG addition on setting times of CPC prepared with the P/L ratio of 1.3.

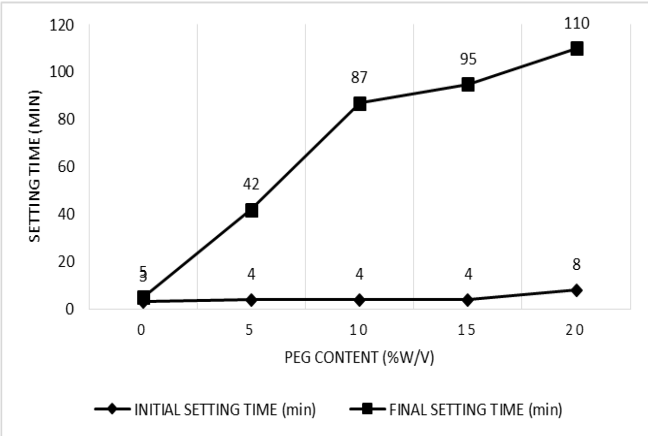

Figure 2: Effect of PEG addition on setting times of CPC prepared with the P/L ratio of 1.7.

3.2 Injectability

The injectability of CPC is illustrated in Figures 3 and 4. In Figure 3, an increase in PEG content improves injectability of CPC as the extrusion load decreased. Figure 4 demonstrates that CPC/PEG with the P/L ratio of 1.7 shows no injectability up to 15% PEG addition and start to become injectable with the addition of 20% PEG. The addition of PEG lowered the friction between CPC particles as compared with paste using water only [9]. On the other hand, the increased in PEG concentration reduced injectability due to the increase in viscosity of cement paste [6].

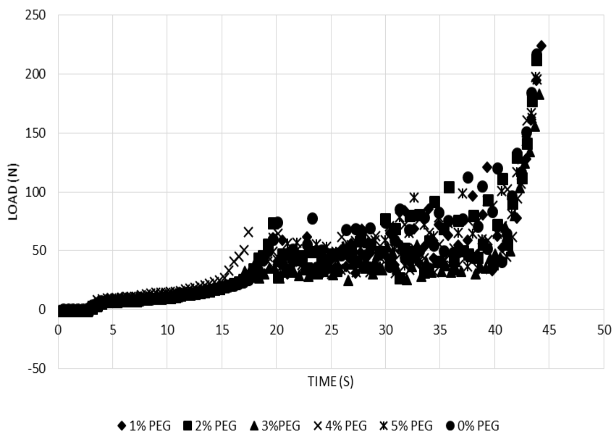

Figure 3: Effect of PEG addition on injectability of CPC prepared with the P/L ratio of 1.3.

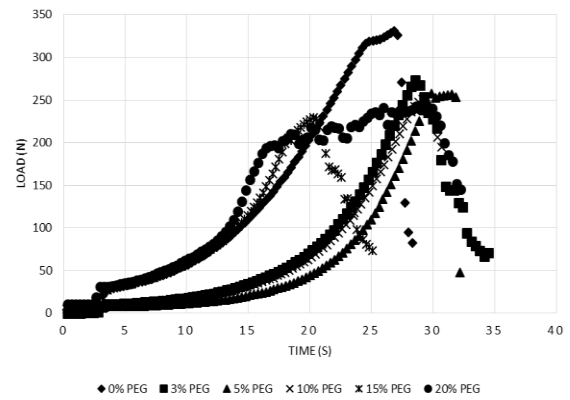

Figure 4: Effect of PEG addition on injectability of CPC prepared with the P/L ratio of 1.7.

3.2 Mechanical strength

The mechanical strength of CPC was determined through compression test. When PEG is added into CPC with the P//L ratio of 1.3, the strength is in the range of 1.167 MPa to 1.786 MPa as presented in Figure 5. CPC with the P/L ratio 1.7 have strength range from 0.25 MPa to 1.553 MPa when PEG is added as revealed in Figure 6. This results indicate that the incorporation of PEG has improved compressive strength of CPC. The formation of a spatial net structure of colloidal particles that join together through Van der Waals force during the hydration reaction between PEG solution and CPC powder strengthened the network of cement paste [6,8]. The dissolution of PEG formed PEG-OH bond and dissolution of HA released Ca^{2+}. PEG-OH can attract Ca^{2+} to form the bond of PEG-O-Ca^{2+}-O-PEG [10].

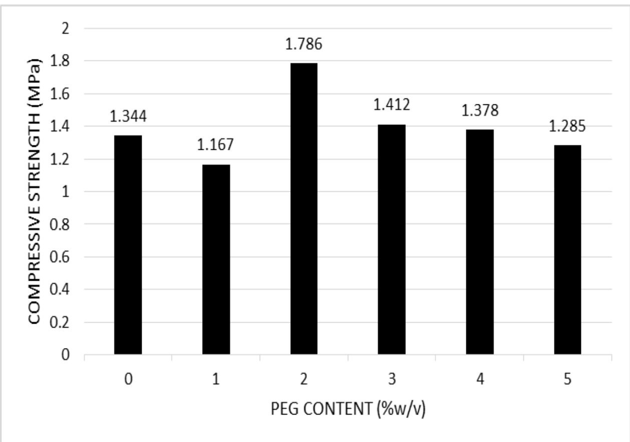

Figure 5: Effect of PEG addition on the compressive strength of CPC prepared with the P/L ratio of 1.3.

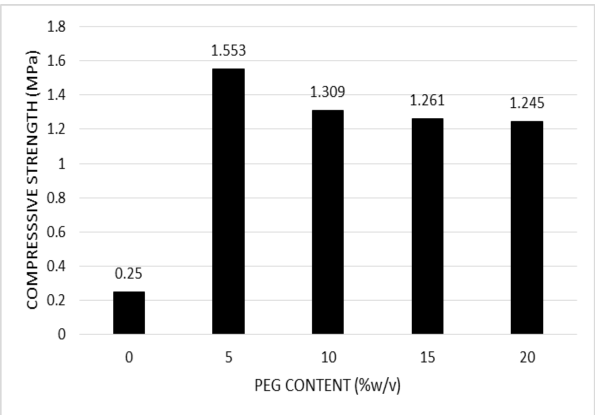

Figure 6: Effect of PEG addition on the compressive strength of CPC prepared with the P/L ratio of 1.7.

3.2 Antiwashout

Figures 7 and 8 present the effect of PEG addition on the evolution of compressive strength of CPC after soaking in Ringer's solution. Figure 7 shows that after 7 days immersion, the compressive strength of CPC increases with the immersion time for CPC with 0, 1, 2, and 3% PEG contents. The strength increased by 3.0%, 57.7%, 17.0% and 20.0% for the CPC with 0, 1, 2 and 3% PEG contents respectively after 7 days soaking period. Further soaking up to 28 days resulted in a decrease in strength by 53.5%, 543%, 46.1% and 43.8% respectively. However, CPC with 4 and 5% PEG contents show an increase in compressive strength up to 3 days soaking only with 7.2% and 3.9% increase respectively, and then the compressive strength decreased by 25.5% and 40% respectively up to 28 days soaking period. The results presented in Figure 8 revealed that the strength of CPC with 5% PEG increase up to 7 days soaking period, whereas other concentrations up to 3 days soaking only. The increase in strength of the CPC after soaking in Ringer's solution might be attributed to the formation of apatite via biomineralization mechanism. Mohammadi et al. [11] reported that the compressive strength of CPC and apatite formation enhanced with soaking time by soaking CPC in human blood plasma and Ringer's solution. However, hydrophilicity properties of PEG might have causes strength reduction by leaving pores as PEG particles dissolve in the liquid medium, which causes the increase in porosity.

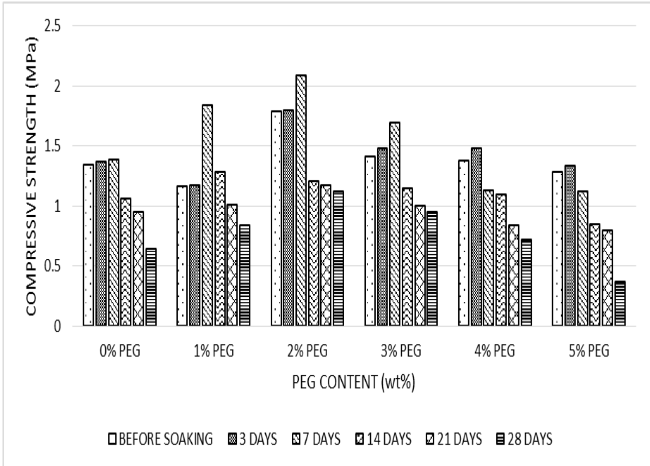

Figure 7: Compressive strength of CPC/PEG with the P/L ratio of 1.3 after soaking in Ringer's solution for 28 days.

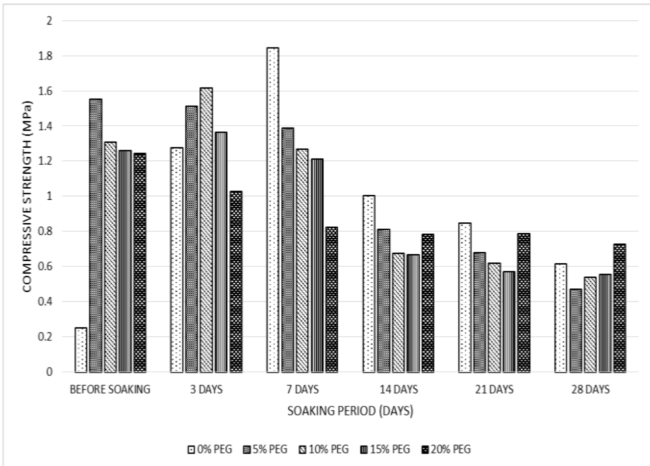

Figure 8: Compressive strength of CPC/PEG with the P/L ratio of 1.7 after soaking in Ringer's solution for 28 days.

4. Conclusion

The wet chemical precipitation derived HA powder has been successfully synthesized by using calcium hydroxide and diammonium hydrogen phosphate. The HA powder was then mixed with distilled water to make CPC at the P/L ratios of 1.3 and 1.7 and PEG concentrations. The present study demonstrated that PEG addition was able to shorten setting time, as well as enhance injectability and mechanical strength. The incorporation of 2% PEG into CPC with the P/L ratio 1.3 showed an optimum condition with 60 min initial setting time, 209 min final setting time and 1.781 MPa compressive strength. The observation of anti-washout performance of CPC/PEG revealed that no dissolution of cement was observed throughout the 28 days soaking period in Ringer's solution which indicated that CPC/PEG has excellent anti washout properties. Hence, CPC/PEG we developed in this study could be a promising candidate for superior injectable bone filling material.

Acknowledgement

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