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# Effect of mixing ratio and pH on the reaction between $Ca_4(PO_4)_2O$ and $CaHPO_4$

S. MATSUYA
*Department of Dental Materials Engineering, Faculty of Dentistry, Kyushu University, Fukuoka 812-8582, Japan*

S. TAKAGI, L.C. CHOW
*American Dental Association Health Foundation, Paffenbarger Research Center, National Institute of Standards and Technology, Gaithersburg, MD 20899, USA*
*E-mail: smatsuya@dent.kyushu-u.ac.jp*

The reaction of $Ca(PO_4)_2O$ (TTCP) and $CaHPO_4$ (DCPA) in an aqueous solution has been shown to be responsible for the hardening of a calcium phosphate cement. This reaction was investigated by monitoring pH changes and composition of solid phases. In the first set of experiments (no attempt to control pH), 2.5 g each of mixtures of TTCP/DCPA, molar ratio from 0.25 to 2, was placed in 12.5 mL of 0.15 mol/L KCl solution, at initial pH about 7, and the pH was allowed to drift for 24 h. Results show that at any time up to 24 h, the pHs were higher for slurries with higher TTCP/DCPA molar ratios. For the slurries with TTCP/DCPA molar ratio of $\geq$ 0.83, the 24 h pHs of the slurries were 9 to 11, whereas for those with TTCP/DCPA of $\leq$ 0.67, the pHs were between 5.3 and 7. The slurries with TTCP/DCPA molar ratios between 0.5 and 1 (Ca/P molar ratio = 1.5 to 1.67) reacted completely within 24 h to form hydroxyapatite (OHAp), $Ca_5(PO_4)_3OH$. In the second set of experiments, 2 g of an equimolar TTCP and DCPA mixture was placed in 20 mL of 0.15 mol/L KCl solution. The pH values were kept constant (6, 8 or 10) by using $H_3PO_4$ and $Ca(OH)_2$ or HCl and KOH as titrant solutions. At pH 8, DCPA and TTCP dissolved at about the same rate, whereas at pH 10, DCPA was consumed more rapidly than TTCP. At both pHs, OHAp was the only product formed. However, at pH 6, the composition of reaction products depended on the types of the titrants used. Specifically when $H_3PO_4$ and $Ca(OH)_2$ were used, hydrolysis of TTCP was the predominant reaction and both octacalcium phosphate and OHAp were formed. But, when HCl and KOH were used, only OHAp was formed. In this case hydrolysis of TTCP and DCPA appeared to proceed independently with TTCP hydrolysis beginning immediately and progressing slowly through 48 h while the DCPA hydrolysis began several hours after the reaction started but was completed in 24 h.

## 1. Introduction

Calcium phosphate cement (CPC) as reported by Brown and Chow [1] has generated significant interest in biomaterials research. This cement is a mixture of either tetracalcium phosphate (TTCP), $Ca_4(PO_4)_2O$, and dicalcium phosphate anhydrous (DCPA), $CaHPO_4$ or TTCP and dicalcium phosphate dihydrate (DCPD), $CaHPO_4 \cdot 2H_2O$. The hardening mechanism of the cement was the exclusive formation of hydroxyapatite (OHAp), $Ca_5(PO_4)_3OH$, by the reaction between TTCP and DCPA (or DCPD) [2–5]. A series of papers reported the use of isothermal conduction calorimetry to study the kinetics of reactions in the mixture with a TTCP/DCPA molar ratio of 0.5 [6–9]. It was concluded that the reaction proceeded in two steps. Stoichiometric OHAp was formed by the reaction between TTCP and DCPA at a TTCP/DCPA molar ratio of 1 in the first step. Then Ca-deficient OHAp was formed by the reaction between the stoichiometric OHAp and excess DCPA in the second step. In this system OHAp formation was controlled by the dissolution rate of DCPA initially and by diffusion of ionic species through the OHAp layer formed on DCPA subsequently. Similar results were obtained in a recent report on the hardening process of the cement [5]. Studies on the reaction between TTCP and DCPD [10, 11] showed that the reaction kinetics of this mixture depended largely on the rate of hydrolysis of TTCP [12]. Additional studies show that TTCP hydrolyzed to form octacalcium phosphate (OCP), $Ca_8H_2(PO_4)_6 \cdot 5H_2O$, [13] or OHAp [12, 14, 15] depending on the pH and solution composition. It is interesting to investigate the effect of pH on the setting reaction of CPC.

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Because TTCP is a basic compound and DCPA is an acidic compound, the dissolution and hydrolysis of the two compounds can be expected to be affected differently by the solution pH.

In this study, pH changes in mixtures with TTCP/DCPA ratios of 0.25 to 2 in a 0.15 mol/L KCl solution were measured to understand how the TTCP/DCPA ratio affects the reaction process. The reaction in an equimolar mixture of TTCP and DCPA, which reflects the TTCP/DCPA ratio in the CPC, was additionally investigated at constant pH levels of 6, 8 or 10 by titration of acids and/or bases.

## 2. Materials and methods

TTCP was synthesized by heating a mixture of $CaHPO_4$ and $CaCO_3$ (Baker Analytical Reagents, J. T. Baker Chemical Co., NJ, USA) at 1500 °C for 6 h. The Ca/P molar ratio in the mixture was 1.9, which was lower than the Ca/P ratio of stoichiometric TTCP ($Ca/P = 2$), to avoid the possibility of formation of CaO. Our preliminary study showed that a small amount of CaO in the TTCP caused an increase in pH in the cement slurry and retarded the setting of the cement. The TTCP was ground by hand to yield a median particle size of 12.4 μm. DCPA was a commercial reagent grade chemical and was ground in a volume fraction of 95% ethanol in a centrifugal agate ball mill for 3 d; the median particle size was 0.6 μm. Particle sizes were determined by a sedimentation method based on Stoke's law with the use of a particle size analyzer (SA-CP3, Shimadzu, Columbia, MD, USA). Mixtures with the following TTCP/DCPA molar ratios were prepared: (A) 2, (B) 1, (C) 0.83, (D) 0.67, (E) 0.5, and (F) 0.25.

In the first series of experiments, 2.5 g of each of the mixtures (A) through (F) was placed in 12.5 mL of 0.15 mol/L KCl solution under constant stirring with a magnetic stirrer, and the pH was followed for 24 h with the use of a combination pH electrode (Orion Research, Cambridge, MA, USA). Results from a previous study [16] showed that the standard uncertainty in similar slurry pH measurements was about 0.15 pH unit ($n = 3$). At selected time intervals, a predetermined amount of the slurry was withdrawn and filtered. The composition of the solid phase was determined by X-ray diffraction (XRD) analysis. The XRD patterns of the specimens were recorded with the use of a powder diffractometer system (Rigaku Denki Co. Ltd, Tokyo, Japan) that utilized graphite-monochromatized $CuK_\alpha$ radiation ($\lambda = 0.154$ nm) generated at 40 kV and 25 mA. The estimated standard uncertainty of $2\theta$ measurement is 0.01° and the minimum amount of a phase to be detected by XRD in the present system is about 0.03 mass fraction.

In the second series of experiments, the reaction of the equimolar mixture (B) was studied under a constant pH of 6, 8, or 10. In this experiment, 2 g of the mixture was placed in 20 mL of 0.15 mol/L KCl solution under constant stirring. The pH was kept constant by titration of an acid or base. Two combinations of acid and base were used because as the reaction proceeded, the solubilities of TTCP and DCPA, and thus the reaction rate would vary depending on whether the acid titrant was $H_3PO_4$ or HCl and whether the base titrant was $Ca(OH)_2$ or KOH. This is because the nature and amounts of the acid and/or base added for pH control affects the solubilities by changing the Ca/P ratio in the solution [17]. In system I, titration was performed with the use of 0.3 mol/L $H_3PO_4$ in 0.15 mol/L KCl as the acid and 0.15 mol/L $Ca(OH)_2$ in 0.15 mol/L KCl as the base. Because the solubility of $Ca(OH)_2$ is very low, titration of the $Ca(OH)_2$ was in practice accomplished by simultaneous addition of 0.15 mol/L $CaCl_2$ and 0.3 mol/L KOH (both solutions having a 0.15 mol/L KCl background to maintain constant ionic strength throughout the reaction). In system II, titration was conducted with the use of 0.3 mol/L HCl and 0.3 mol/L KOH in 0.15 mol/L KCl. The volumes of the titrants were recorded with time. Based on the precision of the pH electrode, the volume and the buffer capacity of the reaction solution, and the acid (or base) concentration of the titrant solutions, the standard uncertainty of the titrant volume measurement is estimated to be 0.01 mL. As before, at selected time intervals, a predetermined amount of the slurry was withdrawn and filtered. The composition of solid phase was determined by XRD.

## 3. Results

Fig. 1 shows the pH of the various slurries as a function of time. The pHs were higher for slurries with higher TTCP/DCPA ratios throughout the 24 h reaction. The pH for slurries B to F showed a steep increase within the first ten min whereas the pH for slurry A showed a larger and broad peak during a 3 h time span. In more acidic slurries (E and F), the pH fell steadily from about 8 to 6 and then slowly to about 5.5. The rest of the slurries exhibited a minimum in pH followed by an increase in pH to a plateau. The minimum pH increased from 6.4 to 8.2 for slurries E to A with increasing TTCP/DCPA molar ratio from 0.5 to 2. With slurry A, the pH curve showed two peaks around 40 min and 5 h after the start of mixing; and then the pH increased up to 11. XRD analysis showed that OHAp was the only reaction product of TTCP and DCPA in all cases. Both reactants, TTCP and DCPA, were completely consumed after 24 h except in slurries A and F; unreacted TTCP was present in slurry A and

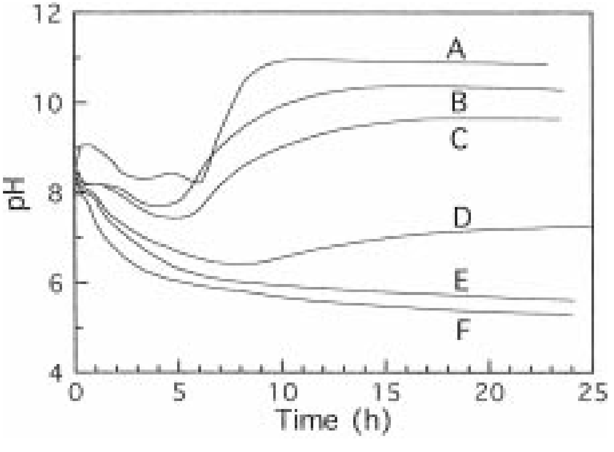

*Figure 1* pH changes with time for the TTCP/DCPA slurries A–F with various mixing ratios: (A) TTCP/DCPA = 2, (B) 1, (C) 0.83, (D) 0.67, (E) 0.5, (F) 0.25.

DCPA in slurry F. XRD patterns of samples taken at various times during the reaction from slurry B (TTCP/DCPA = 1) showed that DCPA was consumed more rapidly than TTCP, and at 4 h, only OHAp and TTCP were present, although OHAp was the only phase present at 24 h. In slurry E (TTCP/DCPA = 0.5), TTCP and DCPA were consumed at approximately the same rate throughout the reaction and only OHAp was present at 24 h despite the fact that the Ca/P ratio of the product is 1.5, a value significantly lower than the Ca/P ratio of stoichiometric OHAp.

Fig. 2 shows the titration curves of the acid and base to maintain constant pH levels of 6, 8, or 10 in system I, i.e. $H_3PO_4$ and $Ca(OH)_2$ were used as the acid and base titrants, respectively and the slurry B was used. At each pH, both the acid and base were titrated at different times during the course of the reaction. This indicates that when the pH is kept at a constant level, the net reaction released base at certain times yet it also released acid at different times. At pH 6, acid was titrated initially to counteract the increase in pH observed in non-pH-stated experiments (Fig. 1). After the initial rapid titration of acid, the titration rate gradually decreased and ceased at about 20 h. A very small amount of base titration occurred at about 45 h after the start of titration. At pH 8, each of the acid and the base were titrated at two time intervals during the experimental period. The acid was first titrated up to 1.5 mL within 1 h. A small amount of base titration occurred at 3 h and this was followed by a second acid titration at 5 h. The base titration occurred again at 20 h and the titration rate slowly decreased with time. At pH 10, the base was titrated at the start of the reaction at a relatively constant rate until it ceased at about 7 h. This was followed by titration of the acid which continued until about 25 h. The base titration occurred again at around 36 h at a steady rate through the remaining experimental period in a way similar to the base titration curve at pH 8 (Fig. 2).

Titration curves in system II (Fig. 3) were similar to those in system I at pH levels of 8 and 10 even though the amounts of titration were considerably smaller. At pH 6, the initial acid titration occurred more rapidly and ended earlier in system II than in system I; the base titration occurred sooner (9 h as compared with 45 h in system I) as well and titration volume was higher.

Figs 4 and 5 show X-ray diffraction patterns of solid phases during the reaction at pH 8 and 10, respectively, in system I. The DCPA was totally consumed after 4 h at pH 8 and after 6 h at pH 10, whereas TTCP still remained after 16 h at pH 8 and after 24 h at pH 10. At 45 h OHAp was the only phase present at both pHs. The rate of OHAp formation was greater at pH 8 than at pH 10.

Figs 6 and 7 show X-ray diffraction patterns of the solid phases during the reaction at pH 6 in systems I and

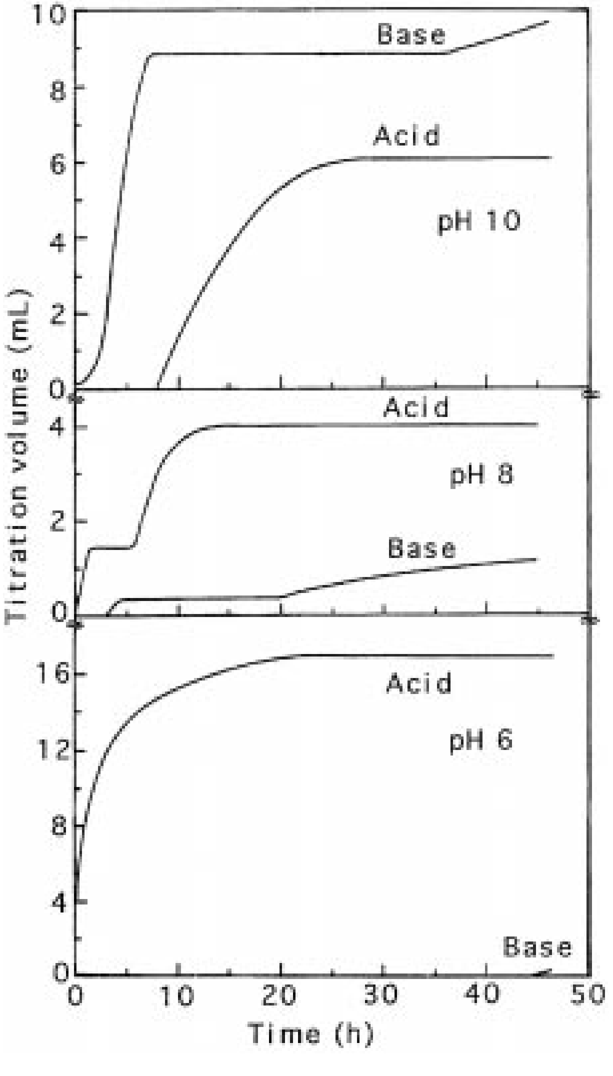

*Figure 2* Titration volume of acid (0.15 mol/L $H_3PO_4$) and base (0.3 mol/L KOH and 0.15 mol/L $Ca(OH)_2$) with time at pH 6, 8, and 10 in system I.

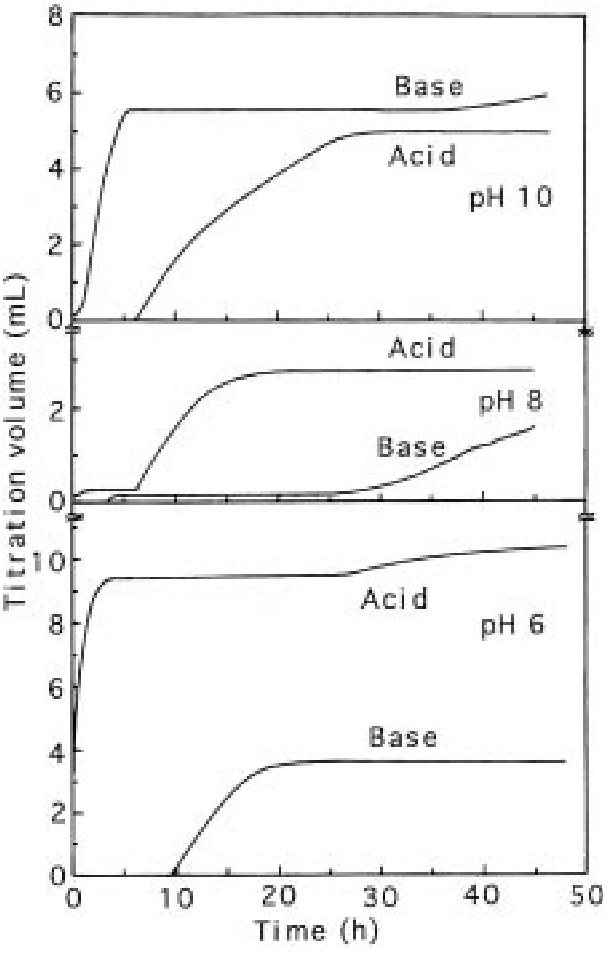

*Figure 3* Titration volume of acid (0.3 mol/L HCl) and base (0.3 mol/L KOH) with time at pH 6, 8, and 10 in system II.

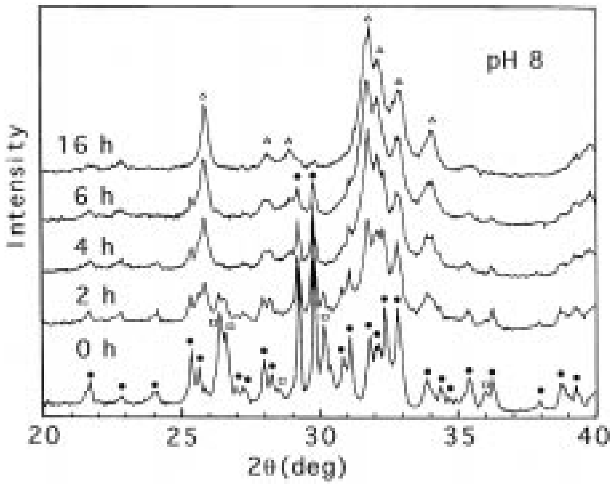

*Figure 4* X-ray diffraction patterns during the reaction at pH 8 in system I; ● TTCP, □ DCPA, △ OHAp.

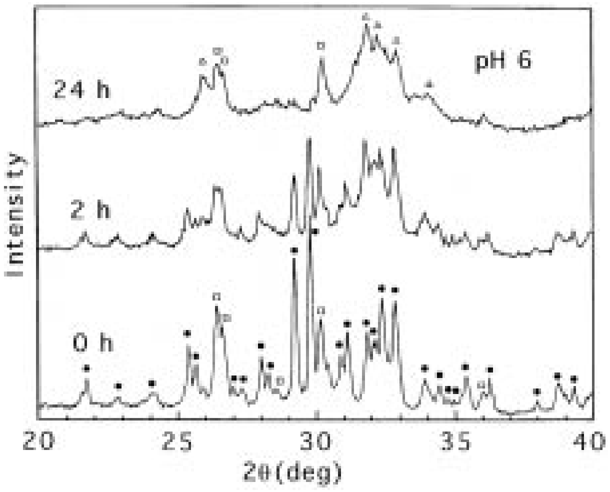

*Figure 6* X-ray diffraction patterns during the reaction at pH 6 in system I; ● TTCP, □ DCPA, △ OHAp.

II. In system I, the reaction at pH 6 was quite different from that at pH 8 and 10 described above. Only a portion of DCPA had reacted and a significant amount of DCPA was present at 24 h while most of the TTCP had been consumed. A small amount of OCP was found in the samples taken after 1 h and the end of the experimental period as evidenced by the presence of a peak at 2θ of 4.8° in XRD patterns. OHAp is by far the major product of the reaction. In system II, DCPA was present at 8 h, but was completely consumed at 24 h. In contrast, significant amounts of TTCP were still present at 24 h. The reaction product was only OHAp and OCP formation was not observed.

## 4. Discussion

### 4.1. Reaction processes in TTCP-DCPA slurries under floating pH conditions

The change in pH with time during the slurry reaction between TTCP and DCPA varied with the TTCP/DCPA ratio of the initial powdered mixture (Fig. 1). The initial pH of the slurry was between 6 and 7, and in all cases a rapid increase in pH was observed immediately after the addition of the powdered mixture. It was suggested that this is due to the rapid dissolution of TTCP which has a higher solubility than DCPA at the initial pH 6 to 7 [1]. The pH reached a maximum of 8 to 8.5 within 10 min except in slurry A which showed a maximum of 9.1 after 0.5 h. The time required for the pH to reach the maximum was longer for slurries with higher TTCP/DCPA ratios. Following the maximum, the pH decreased, probably as a result of the precipitation of OHAp and dissolution of both TTCP and DCPA, with the DCPA dissolving more rapidly because it is more soluble than TTCP above pH 8 at 25 °C, the singular point of TTCP and DCPA [1]. In slurries A, B and C, pHs were approximately constant for a short time period (3 to 6 h) at a level of 8 to 8.5. Similar behavior in pH was reported in an equimolar mixture of TTCP and DCPA [5] and in a cement that contains an equimolar mixture of TTCP and DCPD [11]. The constant pH suggests that during this period, TTCP and DCPA dissolved at approximately the same rate as OHAp precipitated (Equation 1) [18].

$$\mathrm{Ca_4(PO_4)_2O + CaHPO_4 \rightarrow 0.5Ca_{10}(PO_4)_6(OH)_2} \qquad (1)$$

XRD patterns showed that for slurry B (TTCP/

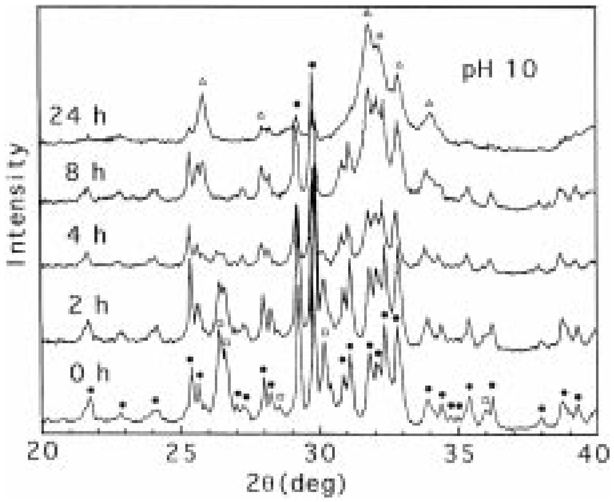

*Figure 5* X-ray diffraction patterns during the reaction at pH 10 in system I; ● TTCP, □ DCPA, △ OHAp.

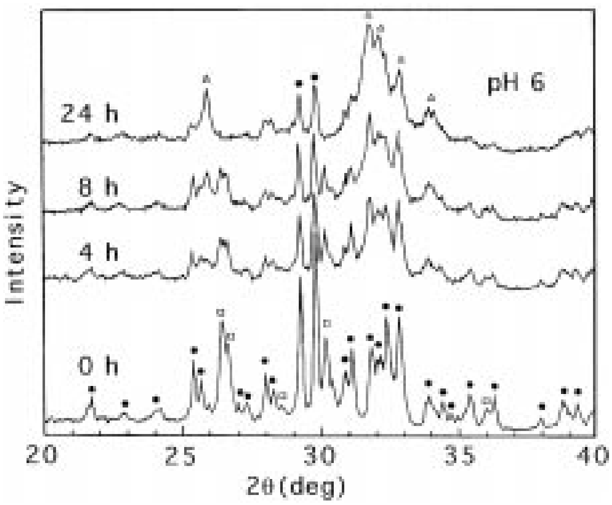

*Figure 7* X-ray diffraction patterns during the reaction at pH 6 in system II; ● TTCP, □ DCPA, △ OHAp.

DCPA = 1) the DCPA was fully consumed by 4 h whereas unreacted TTCP and OHAp product were present. This finding is in contrast to an earlier observation that TTCP was exhausted before DCPA [6, 7], and the discrepancy might be caused by the difference in average particle size of the DCPA used in the studies (> 10 μm in the previous study and 0.6 μm in the present study). The more rapid consumption of DCPA observed in the present study would suggest that despite the fact that the TTCP/DCPA ratio in mixture B reflects the stoichiometry of Equation 1, more than 1 mol of DCPA reacted with each mole of TTCP. Thus, some of the DCPA may react with TTCP following Equation 2 to form a non-stoichiometric or Ca-deficient OHAp [19]. A previous study showed that reaction in a slurry with a TTCP/DCPA ratio of 0.5 follows Equation 2 [6], suggesting the possibility that the reactions occurring in slurries C, D, and E, having TTCP/DCPA ratios of 0.83, 0.67, and 0.5, respectively, may also follow Equation 2.

$$\mathrm{Ca_4(PO_4)_2O} + 2\mathrm{CaHPO_4} \rightarrow 0.667\ \mathrm{Ca_9(HPO_4)(PO_4)_5(OH)} + 0.333\ \mathrm{H_2O} \quad (2)$$

After the period of relatively constant pH, the pH began to increase again in slurries A, B, C and D (Fig. 1). XRD analyzes showed that TTCP was not present in the final product in mixtures B, C, and D, thus after the DCPA was exhausted, TTCP must be consumed by hydrolyzing to form OHAp (Equation 3) or possibly reacting with the non-stoichiometric OHAp formed earlier to form an OHAp with a lower degree of Ca-deficiency, as described by Equation 4.

$$\mathrm{Ca_4(PO_4)_2O} + \mathrm{H_2O} \rightarrow 0.333\ \mathrm{Ca_{10}(PO_4)_6(OH)_2} + 0.667\ \mathrm{Ca(OH)_2} \quad (3)$$

$$\mathrm{Ca_4(PO_4)_2O} + 0.667\ \mathrm{Ca_9(HPO_4)(PO_4)_5OH)} + 0.833\ \mathrm{H_2O} \rightarrow \mathrm{Ca_{9.5}(HPO_4)_{0.5}(PO_4)_{5.5}(OH)_{1.5}} + 0.5\ \mathrm{Ca(OH)_2} \quad (4)$$

In mixture A (TTCP/DCPA = 2), the excessive amount of TTCP caused the pH to reach the highest level among all cases and a significant amount of unreacted TTCP was present at the end of the experiment. In either case, the pH increased due to the release of $\mathrm{Ca(OH)_2}$ as a by-product. This analysis is in contrast to the reaction path presented in a previous study [10] that in a TTCP-DCPD cement, the reaction proceeded in two stages: the first stage was formation of a stoichiometric but noncrystalline calcium phosphate and nanocrystalline OHAp by the complete consumption of DCPD and the partial consumption of TTCP; the second stage was stoichiometric or Ca-deficient OHAp formation by the reaction between the intermediate products and the remaining TTCP. In slurry E (TTCP/DCPA = 0.5), which did not show the later increase in pH, both TTCP and DCPA were present at 8 h and neither was present at 24 h. This observation supports the hypothesis that the increase in pH in the later part of the experiment is a result of the presence of TTCP when all of the DCPA has been consumed. In fact, the gradual decrease in pH seen in slurries E and F, which contained excess DCPA, suggests that after TTCP has been fully consumed the excess DCPA may hydrolyze to OHAp (Equation 5) leaving $\mathrm{H_3PO_4}$ in the solution as a by-product.

$$10\mathrm{CaHPO_4} + 2\mathrm{H_2O} \rightarrow \mathrm{Ca_{10}(PO_4)_6(OH)_2} + 4\mathrm{H_3PO_4} \quad (5)$$

## 4.2. Reaction process in TTCP-DCPA slurries under constant pH conditions

In the constant pH experiments, the reaction depended on the pH (6, 8 or 10) and on the composition of titrants used. Of the three pH conditions, the amount of titration volume was the smallest and the reaction proceeded most rapidly at pH 8. Under the pH 8, the pattern of acid and base titration reflected the pH versus. time curve of slurry B in the floating pH experiment (Fig. 1). First the acid was titrated to counteract the increase in pH due to dissolution of the basic TTCP. In both systems I and II, a small amount of base was then titrated at 3 h, the time when a slight decrease in pH occurred in the floating pH experiment. Subsequently, the acid titration was reinitiated after 6 h, again corresponding to the gradual increase in pH that occurred at 6 h in the floating pH experiment. Thus, the reaction under constant pH condition at pH 8 appears to proceed in a similar way as that in the floating pH condition. X-ray diffraction patterns of the solid phase during the reaction showed that DCPA rapidly disappeared within 4 h, while TTCP was still present at 6 h when the acid titration began.

Acid was titrated even at pH 10. The reaction process at pH 10 was similar to that at pH 8 although the reaction rate was much slower. DCPA, which is more soluble than TTCP above pH 8 [17], would dissolve and react faster than TTCP. XRD analyzes indicated that DCPA was consumed more rapidly than TTCP in both the pH 8 and 10 experiments, with the ratio of TTCP/DCPA being higher at pH 10 than at pH 8 during any reaction period. This observation suggests that at pH 10 the DCPA was consumed by reacting with TTCP (Equation 1) as well as with $\mathrm{OH^-}$ derived from titrants at pH 10 (Equations 6 and 7).

$$6\mathrm{CaHPO_4} + 4\mathrm{Ca(OH)_2} \rightarrow \mathrm{Ca_{10}(PO_4)_6(OH)_2} + 6\mathrm{H_2O} \quad (6)$$

$$10\mathrm{CaHPO_4} + 8\mathrm{KOH} \rightarrow \mathrm{Ca_{10}(PO_4)_6(OH)_2} + 4\mathrm{K_2HPO_4} + 6\mathrm{H_2O} \quad (7)$$

A small titration volume of the base at pH 8 also supports the hypotheses. The solubility of DCPA and TTCP was almost the same at pH 8. Acidic DCPA and basic TTCP simultaneously dissolved to form OHAp according to Equation 1. However, at pH 10, DCPA was much more soluble than TTCP, and DCPA itself would be hydrolyzed to OHAp following Equation 6 in system I ($\mathrm{H_3PO_4}$ and $\mathrm{Ca(OH)_2}$ as titrants) and Equation 7 in system II (HCl and KOH as titrants). At pH 6, the reaction process seemed to be much different from that at pH 8 and 10. Titration behavior also depended on the composition of titrants. In system I, only the acid, $\mathrm{H_3PO_4}$, was titrated nearly throughout the reaction, and only a very small amount of base titration occurred at 45 h (Fig. 3). Because formation of OHAp from DCPA would cause base titration and OHAp formation from

TTCP would cause acid titration, the exclusive acid titration observed here suggests that in this system the main reaction was between TTCP and $H_3PO_4$ (Equation 8). This analysis is supported by the observation that most of the DCPA remained unreacted at 24 h when the acid titration ceased.

$$5Ca_4(PO_4)_2O + 2H_3PO_4 \rightarrow 2Ca_{10}(PO_4)_6(OH)_2 + H_2O \tag{8}$$

In this system, a small amount of OCP was formed in addition to OHAp. The OCP formation from TTCP can be expressed by Equation 9,

$$2Ca_4(PO_4)_2O + 2H_3PO_4 + 3H_2O \rightarrow Ca_8H_2(PO_4)_6 \cdot 5H_2O \tag{9}$$

Based on theoretical thermodynamic calculations in the $CaO\text{-}P_2O_5\text{-}H_2O$ system reported by Duff [20], OCP was stable with respect to TTCP below pH 6.47 at $[Ca^{2+}] = 0.1$ mol/L and below pH 7.97 at $[Ca^{2+}] = 10^{-4}$ mol/L. It was reported that OHAp precipitated from a solution through OCP formation [21]. However, in the present study, it is not certain if the OHAp was formed via OCP because the detected amount of OCP formed was very small and almost constant during the reaction.

In system II with HCl and KOH as titrants, the titration behavior was quite different from that in system I. First, titration of the acid occurred quite rapidly, then ceased at about 3 h. The base titration started at about 8 h and continued for several hours. The acid titration was again initiated at 25 h at a relatively slow rate. XRD analyzes did not show that OCP formation occurred during the reaction. Solubility phase diagrams have been reported in the quaternary system $Ca(OH)_2\text{-}H_3PO_4\text{-}HCl\text{-}H_2O$ at 37 °C at 0.1 mol/L HCl [22]. The difference in solubility at pH 6 between OCP and OHAp was larger than that in the ternary system $Ca(OH)_2\text{-}H_3PO_4\text{-}H_2O$, suggesting that OCP was significantly less stable than OHAp at pH 6 in the quaternary system. This might explain why no OCP was formed in the titration system II. DCPA remained unreacted even after 8 h but disappeared after 24 h. Initiation of the base titration after 8 h was caused by the reaction of DCPA to form OHAp. As described above, at pH 6 little or no reaction of DCPA occurred when $H_3PO_4$ was titrated in system I, and the reaction of TTCP with the titrated $H_3PO_4$ (Equation 8) accounts for the formation of OHAp. However, in system II, the initial reaction of TTCP with the titrated HCl (Equation 10) generates $CaCl_2$ as a by-product thus raising concentration of free $Ca^{2+}$ ions in the solution. It appears that after the $Ca^{2+}$ ion concentration reached a certain level, DCPA would react with the $Ca^{2+}$ ions, liberating $H^+$ ions (Equation 11), causing titration with KOH (Equation 12).

$$3Ca_4(PO_4)_2O + 4HCl \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 2CaCl_2 + H_2O \tag{10}$$

$$6CaHPO_4 + 4Ca^{2+} + 2H_2O \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 8H^+ \tag{11}$$

$$6CaHPO_4 + 4CaCl_2 + 8KOH \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 8KCl + 6H_2O \tag{12}$$

DCPA itself did not hydrolyze into OHAp in 0.15 mol/L KCl solution at pH 6. This fact coincided with the limiting pH for transformation of DCPA to OHAp reported to be 6.02 at 25 °C [23]. However, DCPA was readily hydrolyzed in a 0.15 mol/L KCl solution containing 0.15 mol/L $CaCl_2$; to form well crystallized OHAp within 24 h [24].

It was observed that the base titration was initiated again 20-30 h after both the acid and the base titration ceased at pH levels of 8 and 10. It was reported that OHAp formed by precipitation from solution had Ca deficient nonstoichiometry and poor crystallinity [25]. The Ca-deficient OHAp was expressed by the following general formula, $Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x}$ where $x$ is a number of acid phosphate group. When aging of the OHAp formed at each pH proceeded to form OHAp with a stoichiometric composition ($x = 0$), the acid phosphate should be neutralized and the base would be consumed.

## 5. Conclusion

The reaction of TTCP and DCPA in an aqueous solution depended on their mixing molar ratio. The solution pHs during the reaction up to 24 h were higher for slurries with higher TTCP/DCPA molar ratios. The slurries with TTCP/DCPA molar ratios between 0.5 and 1 (Ca/P molar ratio = 1.5 to 1.67) reacted completely within 24 h to form hydroxyapatite, OHAp. It was also found from the experiment at constant pHs that the reaction process depended on pH. At pH 8, DCPA and TTCP dissolved at about the same rate, whereas at pH 10, DCPA was consumed more rapidly than TTCP. At both pHs, OHAp was the only product formed. However, at pH 6, the composition of reaction products depended on the types of the titrants used. Specifically when $H_3PO_4$ and $Ca(OH)_2$ were used as the titrants, hydrolysis of TTCP was the predominant reaction and both octacalcium phosphate and OHAp were formed. But, when HCl and KOH were used, hydrolysis of TTCP and DCPA appeared to proceed independently and only OHAp was formed.

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