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Hydrolysis of dicalcium phosphate dihydrate to hydroxyapatite

M. T. FULMER, P. W. BROWN
Department of Materials Science and Engineering, The Pennsylvania State University, 136 Materials Research Laboratory, University Park, PA 16802, USA

Dicalcium phosphate dihydrate (DCPD) was hydrolysed in water and in 1 M Na_2HPO_4 solution at temperatures from 25–60 °C. Hydrolysis was incomplete in water. At 25 °C, DCPD partially hydrolysed to hydroxyapatite (HAp). Formation of HAp is indicative of incongruent DCPD dissolution. At the higher temperatures, hydrolysis to HAp was more extensive and was accompanied by the formation of anhydrous dicalcium phosphate (DCP). Both of these processes are endothermic. When hydrolysis was carried out in 1 M Na_2HPO_4 solution, heat absorption was greater at any given temperature than for hydrolysis in water. Complete hydrolysis to HAp occurred in this solution. The hydrolysis of DCPD to HAp in sodium phosphate solution was also endothermic. The complete conversion of DCPD to HAp in sodium phosphate solution would not be expected if the only effect of this solution was to cause DCPD dissolution to become congruent. Because of the buffering capacity of a dibasic sodium phosphate solution, DCPD hydrolysed completely to HAp. Complete conversion to HAp was accompanied by the conversion of dibasic sodium phosphate to monobasic sodium phosphate. The formation of DCP was not observed indicating that the sodium phosphate solution precluded the DCPD-to-DCP dehydration reaction. In addition to affecting the extent of hydrolysis, reaction in the sodium phosphate solution also caused a morphological change in the HAp which formed. HAp formed by hydrolysis in water was needle-like to globular while that formed in the sodium phosphate solution exhibited a florette-like morphology. © *1998 Chapman & Hall*

1. Introduction

The mechanisms of $CaHPO_4 \cdot 2H_2O$ (DCPD) growth and dissolution are of interest because of the importance of this calcium phosphate in the development of dental caries and as a constitutent in calcium phosphate cements [1]. One of the factors influencing the conversion of DCPD to HAp is its incongruent dissolution. Incongruent DCPD dissolution results in hydroxyapatite (HAp) formation thereby affecting the morphological relationship between these biologically important calcium phosphates [2]. Although it has been suggested that DCPD dissolution is congruent [3], other observations indicate this is not correct [4]. Significant in that study is the complete hydrolysis of DCPD to HAp in dilute suspension. Complete hydrolysis can occur at high liquid-to-solids ratio, generally 100-to-1. Investigations of the hydrolysis behaviour of DCP have resulted in a similar conclusion [5, 6]. DCP and DCPD exhibit similar hydrolysis behaviour because their solubilities are very similar [7]. Although the absence of epitaxy between DCPD and HAp has been reported [8], HAp formation significantly reduces the rate of DCPD hydrolysis at 25 °C even though the extent of hydrolysis is insufficient to attain the invariant point between them (unpublished observation). These observations illustrate that the extent and rate of DCPD hydrolysis are dependent on the proportions of solution and DCPD present and eventually either the DCPD is entirely consumed or the DCPD-HAp invariant point is reached.

The kinetics of DCPD dissolution (e.g. [9, 10]) and the growth of DCPD (e.g. [10]) have been studied. Dissolution has been shown to be diffusionally controlled [9] with rates governed by the Burton, Cabrera, Frank (BCF) mechanism [10]. However, the kinetics of dissolution will be strongly affected in the event of HAp formation because of the effect of incongruency. Once HAp appears, the reaction involves both dissolution and crystallization events. The term hydrolysis will be used in this paper when discussing these processes. The hydrolysis of DCPD should also be expected to depend on the reaction temperature. HAp has been shown to exhibit retrograde solubility [11, 12] while DCPD has been shown to exhibit a maximum in its solubility product at about 25 °C [3]. A decrease in the kinetics of dissolution may be the result of retrograde solubility in two ways. The concentration gradient between the surfaces of the dissolving DCPD crystals and the bulk solution will be reduced and the overgrowth by HAp will occur at a lower extent of dissolution. Therefore, the investigation of the extent of and the rate of the hydrolysis of DCPD under conditions where HAp forms is of interest. A prior study demonstrated that the rate of HAp formation by the reaction between DCPD and tetracalcium phosphate ($Ca_4(PO_4)_2O$) is significantly increased in sodium phosphate solutions [13]. The effect was attributed to the dissolution of DCPD becoming congruent in the sodium phosphate solutions. The present study was undertaken to determine the effects of temperature and solution chemistry on DCPD hydrolysis. This was done by measuring the heat evolution/absorption characteristics of DCPD hydrolysis reactions depending on the temperature and on the presence of sodium phosphate. In an attempt to separate the effects of HAp formation and temperature on the kinetics of DCPD hydrolysis rates of heat evolution were determined under conditions where DCPD dissolution is incongruent (in water) and congruent (in Na_2HPO_4 solution).

2. Materials and methods

2.1. DCPD preparation

DCPD was prepared at 25 °C. Equimolar amounts of monocalcium phosphate monohydrate (MCPM) and $Ca(OH)_2$ were reacted in water as follows

$$Ca(H_2PO_4)_2 \cdot H_2O + Ca(OH)_2 \xrightarrow{H_2O} 2CaHPO_4 \cdot 2H_2O \tag{1}$$

Typically, a batch was prepared by weighing 36.60 g MCPM and 10.76 g calcium hydroxide at a liquid-to-solids ratio of 10, using 500 ml deionized water (resistivity = 16.7 mΩ). The $Ca(OH)_2$ powder was added to solution first due to its lower solubility. It was determined that the simultaneous addition of $Ca(OH)_2$ and MCPM resulted in the formation of large DCPD agglomerates containing residual $Ca(OH)_2$ even after long periods of reaction. This problem was overcome by introducing the $Ca(OH)_2$ to solution first and allowing the suspension to stir for 3 h to achieve a saturated solution of $Ca(OH)_2$. After MCPM was added, the suspension was allowed to stir for 10 min. Following this, the DCPD was filtered using a Büchner funnel with Whatman no. 40 fine crystallite filter paper. This procedure produced DCPD having a plate-like morphology and a crystallite size of a few micrometres [14].

2.2. Kinetics of hydrolysis

Isothermal calorimetry, using an envelope-type calorimeter (Thermonetics Corp., San Diego, CA) [15, 16], was used to determine the heat evolution during the hydrolysis of DCPD at a liquid-to-solids ratio of 5. This ratio was selected to allow incomplete DCPD hydrolysis to HAp in water. Rates of heat evolution were determined at constant temperatures by separately equilibrating the liquid and solid reactants. The liquid was contained in a syringe and the solid reactants in a gold-plated copper calorimeter cup. The cup was sealed with "Parafilm" to minimize endothermic effects of water evaporation. After thermal equilibration had been achieved, the liquid was injected on to the DCPD allowing the reaction to initiate. The calorimeter cup is surrounded by thermopiles in the isothermal calorimetric system used; thus heat evolution or absorption as a result of hydrolysis is converted to a voltage output. In a typical experiment, 0.5 g DCPD and 2.5 ml solution were used. The voltage output was determined at 1 min intervals and collected using a microprocessor. Using the appropriate thermoelectric coefficient, the rate of heat absorption can be determined. Integration of the rate data allows the total heat absorbed to be determined. These data were plotted versus time. The rates of DCPD hydrolysis in water and in 1 M Na_2HPO_4 were determined at 25, 38, 45 and 60 °C. The extent of heat loss from the calorimeters increased with increasing temperature, primarily because of the evaporation of water. To compensate for this, the heat loss at 60 °C was determined by inoculating water on to an inert powder ($Al_2O_3 \cdot 3H_2O$). This determination indicated the heat loss was 1 kJ h^{-1} and this correction factor was used in reporting the heat absorption data obtained at 60 °C.

2.3. X-ray diffraction analysis

When further heat absorption was no longer observed, X-ray diffraction analyses were carried out to determine the compositions of the solids present. X-ray diffraction analyses were performed on an automated diffractometer (Scintag, Inc., Sunnyvale, CA) using a step size of 0.02°, scan rate of 2° min^{-1}, and a scan range between 20° and 35° 2θ.

2.4. Scanning electron microscopy

The morphologies of these solids were observed by SEM. The variations in pH during DCPD hydrolysis at 60 °C were also determined. Microstructural development was observed using a conventional dual-stage scanning electron microscope (DS130, Topcon Technologies, Inc., Pleasanton, CA).

3. Results and discussion

3.1. Hydrolysis of DCPD in water

The calorimetric curves for the hydrolysis of DCPD in water at 25, 38, 45, and 60 °C are shown in Fig. 1. The calorimetric curve for DCPD hydrolysis at 25 °C shows that hydrolysis occurred at this temperature but at a very slow rate. Slight heat absorption was observed shortly after the addition of the water. Subsequent to this, the rate of heat absorption was negligible. An X-ray diffraction pattern of the solids present after 20 h reaction indicated a small proportion of HAp, and residual unreacted DCPD. The rate of hydrolysis was greater at 38 °C than at 25 °C and was accompanied by the absorption of heat. At 38 °C, after an exotherm due to the wetting and initial dissolution of DCPD occurred, an endotherm was observed over the remainder of the study. The total heat adsorbed for reaction at 38 °C was 8 kJ mol^{-1}. After 10 and 20 h reaction, the phases identified by X-ray

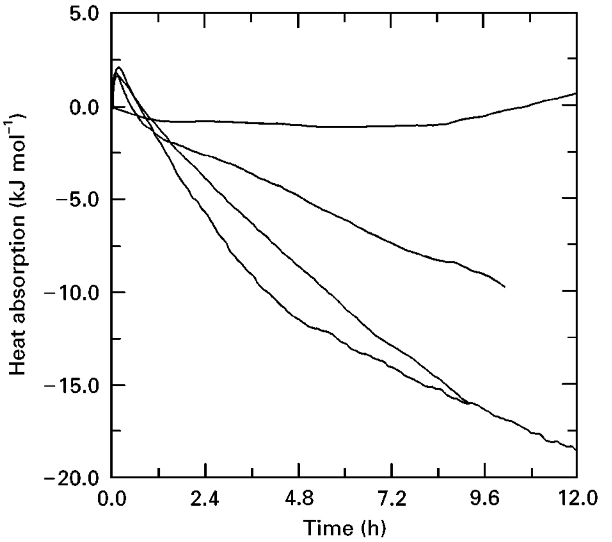

Figure 1 Calorimetric curves showing the extent of heat absorption with time when DCPD is hydrolysed in water at 25, 38, 45 and 60 °C

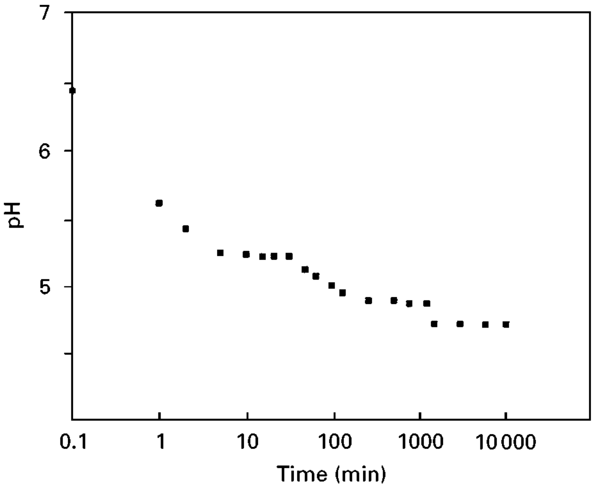

Figure 2 The variation in pH with time when DCPD is hydrolysed in water at 60 °C.

diffraction were unreacted DCPD and small proportions of HAp.

A larger endotherm was observed when the reaction was carried out at 45 °C. In this case heat absorption was 12 kJ mol^{-1}. Unreacted DCPD, and a larger proportion of HAp were observed by X-ray diffraction after 10 and 20 h reaction at this temperature. X-ray diffraction analysis was also carried out on the solids present in a sample which had been held for 10 wk at 45 °C. In addition to DCPD and HAp, DCP was also observed. This indicates that two reactions were occurring. One was the hydrolysis of DCPD to HAp, and the second was the conversion of DCPD to DCP. The conversion of DCPD to DCP at 45 °C was not expected based on a literature citation [17] which indicated dehydration occurred at a minimum temperature of about 60 °C. The pH of the solution after 2 wk reaction was 5.24. This pH value is generally consistent with previously reported values of 5.13–5.28 at 37.5 °C for the DCPD-HAp invariant point [18].

When hydrolysis occurred at 60 °C an initial exotherm was still observed. This was followed by an endotherm comparable to that observed at 45 °C. Heat was still being adsorbed after 12 h indicating that reaction had not yet reached completion. X-ray diffraction of the solids present after 12 h reaction showed DCP and a relatively low proportion of DCPD. The only phase identified by X-ray diffraction after 20 h reaction was DCP.

A slight amorphous hump was also observed in the X-ray diffraction patterns obtained after 12 and 20 h. After maintaining these samples at 60 °C for 10 wk, weak HAp peaks could be observed in the pattern indicating the presence of a small proportion of this solid. The amorphous hump was no longer observed. These findings indicate that heat absorption is associated with the conversion of DCPD to HAp at 25 and 38 °C and to DCP at 45 and 60 °C. Comparing the rates of heat absorption at 45 and 60 °C suggests the rate of DCPD conversion to DCP does not exhibit a strong temperature dependence, at least over this range. When DCPD was hydrolysed at 60 °C for 10 wk, HAp diffraction peaks were observed indicating the slow hydrolysis of DCP to HAp.

The pH of solution held at 60 °C was monitored over time to determine the variation in pH associated with DCPD hydrolysis at a liquid-to-solids ratio of 5. As shown in Fig. 2 the pH decreased during the first day before reaching a constant value. The initial pH of the deionized water was 6.45. Within the first 5 min hydrolysis the pH reached a value of 5.22, where it remained for the next 25 min. After this time, the pH began to drop again to a steady state pH value of approximately 4.88. The pH remained at this value for about a day. Finally, the pH decreased to a value of 4.7 where it remained until the termination of the study. The variations in the pH did not occur monotonically but occurred in steps. Hydrolysis at 60 °C resulted in the complete conversion to DCP. These variations in pH with time are in accord with the formation of HAp, which results in the acidification of the solution. While the mechanistic path taken is indeterminant, the final pH is that of the invariant point between DCP and HAp (~4.7). This value is substantially below the value of 5.24 observed when DCPD was still present.

The morphologies of the products obtained after the hydrolysis of DCPD in water at 25 and 38 °C were very similar. The micrograph shown in Fig. 3 illustrates the microstructure observed after 2 wk of reaction at 25 °C. The morphology of the unreacted DCPD can be seen along with that of a minor amount of a solid which exhibits the needle-like morphology typical of HAp. The solids present after hydrolysis at 45 °C showed a morphology different from that observed at the lower temperatures. Fig. 4 shows the presence of polygonal crystallites typical of those which have been observed previously for DCP [14]. Unreacted DCPD, which was identified by X-ray diffraction, was intermixed among the DCP crystallites. The products formed at 60 °C are shown in Fig. 5. Compared to 45 °C, relatively more polygonal DCP crystallites can be discerned at this temperature.

A second solid having a globular morphology can also be observed in the micrograph. Based on the identification of HAp by X-ray diffraction analysis, it would appear that globular material is HAp.

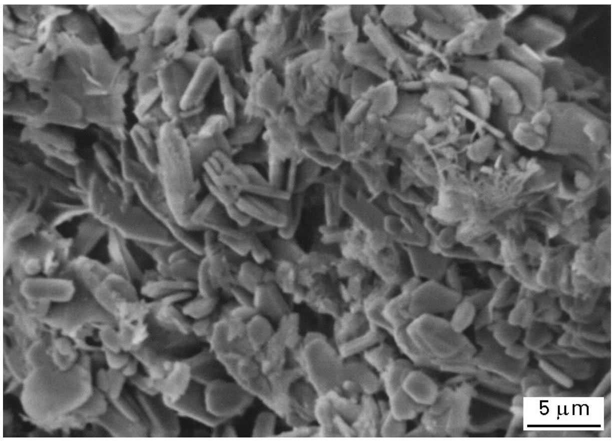

Figure 3 Microstructures of the phases present after the hydrolysis of DCPD in water for 2 wk at 25 °C. Companion X-ray diffraction analysis indicated the presence of DCPD and needle-like HAp.

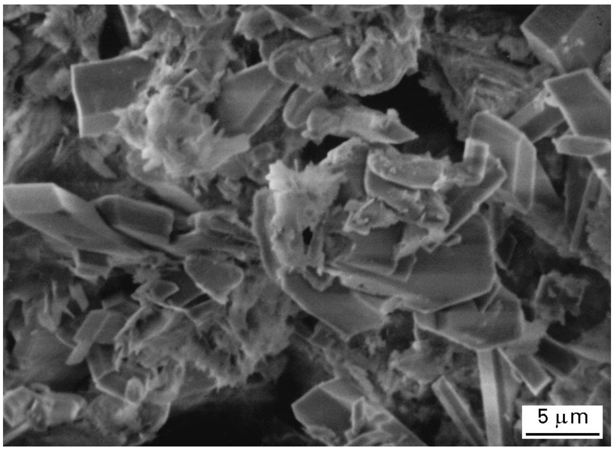

Figure 4 Microstructures of the phases present after the hydrolysis of DCPD in water for 2 wk at 45 °C. Companion X-ray diffraction analysis indicated the presence of DCP (polygonal morphology) and unreacted DCPD.

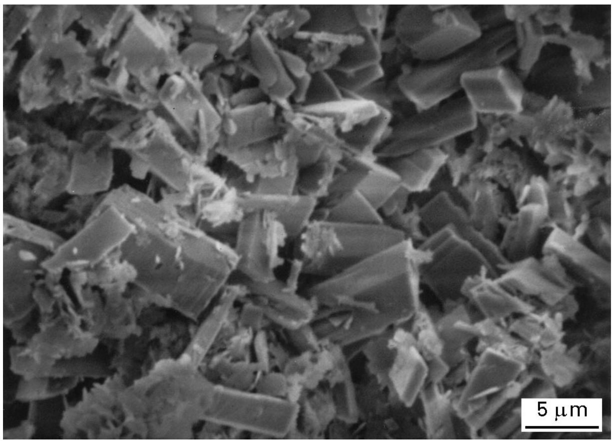

Figure 5 Microstructures of the phases present after the hydrolysis of DCPD in water for 2 wk at 60 °C. Companion X-ray diffraction analysis indicated the presence of DCP (polygonal morphology), HAp (globular) and unreacted DCPD.

3.2. Hydrolysis of DCPD in 1 M Na_2HPO_4 solution

Hydrolysis of DCPD in the basic, phosphate-containing Na_2HPO_4 solution was also investigated by isothermal calorimetry at 25, 38, 45, and 60 °C. Reaction in Na_2HPO_4 solution was chosen because hydrolysis under basic conditions should increase the solubility of DCPD, and should increase the rate of DCPD dissolution. Fig. 6 shows the calorimetric curves as a result of the hydrolysis of DCPD in 1 M Na_2HPO_4 solution at the various temperatures. Comparison of the heat absorption curves shown in Figs 1 and 6 indicate a larger endotherm for hydrolysis at 25 °C in Na_2HPO_4 solution than in water. This is indicative of more extensive DCPD hydrolysis. The X-ray diffraction pattern of the solids present after 20 h hydrolysis at 25 °C indicated HAp and DCPD, but not DCP. Although its relative proportion was lower than that of DCPD, a substantial amount of HAp was present. Thus, the hydrolysis of DCPD to HAp is endothermic, regardless of whether the reaction occurred in water or in sodium phosphate solution. Heat absorption was more rapid when the hydrolysis reaction was carried out at 38 °C. After 10 h reaction, a significant endotherm was observed. After 16 h reaction, X-ray diffraction analysis identified a relatively large proportion of HAp and a lower relative proportion of DCPD. To ensure reproducibility, the hydrolysis experiments at 38 °C were repeated in triplicate and the calorimetric curves were found to be reproducible. Increasing the hydrolysis temperature to 45 °C resulted in more rapid heat absorption. After 3 h, approximately 12 kJ mol^{-1} of heat was absorbed and further reaction could not be detected. Less heat was adsorbed in the reaction at 45 °C than at 38 °C; however, phase analysis by X-ray diffraction at coincident times indicated relatively more HAp, and less DCPD at this temperature. Thus, compared to the other temperatures, heat absorption at 38 °C appeared anomalous in that it was much greater than at 25 or at 45 °C. In

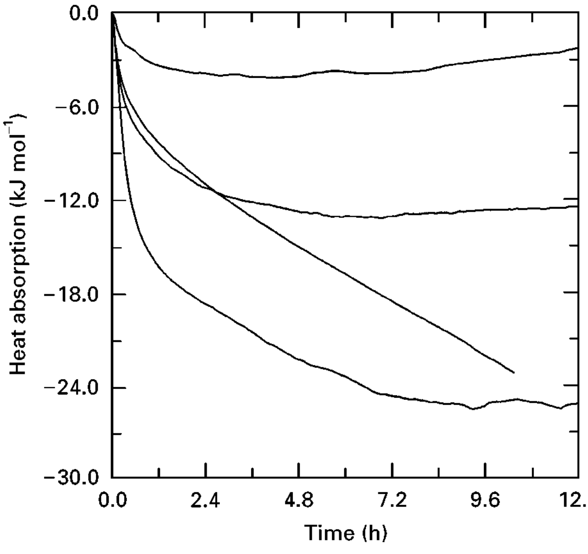

Figure 6 Calorimetric curves showing the extent of heat absorption with time when DCPD is hydrolysed in 1 M Na_2HPO_4 solution at 25, 38, 45 and 60 °C.

spite of this, the proportion of HAp formed increased with increasing temperature. Reaction at 60 °C showed even more rapid early heat uptake. The total heat absorption was the greatest at this temperature. After approximately 16 h reaction only HAp was observed. Compared to hydrolysis in water, both the basic pH conditions, and the presence of phosphates in solution are likely to be important factors increasing the rate of DCPD dissolution; however, the relative importance of these factors remains undetermined.

Microstructurally, the products formed by DCPD hydrolysis in Na_2HPO_4 between 25 and 60 °C are generally similar. Fig. 7 shows the morphology of the products at 25 °C and large florettes can be observed. X-ray analysis identified HAp, along with a relatively low proportion of DCPD. It is apparent that the HAp which formed exhibited a morphology similar to that of the reactant DCPD. X-ray diffraction analysis indicated HAp, and residual sodium phosphate that had precipitated upon drying the products of hydrolysis formed at 60 °C. HAp is minimally soluble in ethanol while the sodium phosphate is quite soluble, thus allowing the latter to be removed. Therefore, the solids were washed in anhydrous ethanol prior to microstructural observation. The morphology observed in this specimen was similar to that observed at 25 °C; however, the florettes do not appear as well ordered, Fig. 8. In addition, smaller plates are observed than when the products formed at 25 °C.

Hydrolysis of DCPD in 1 M sodium phosphate solution precluded the formation of DCP regardless of the temperature; however, heat was absorbed even though DCP did not form. This indicates the hydrolysis of DCPD to HAp to be endothermic. Our prior work indicated that the dissolution of acidic calcium phosphates becomes more congruent in sodium phosphate solutions [13]. Alternatively, the conversion of DCPD to HAp in 1 M sodium phosphate solution would not be expected if its only effect were to make dissolution congruent. However, because the buffering capacity of dibasic sodium phosphate, DCPD can hydrolyse to HAp as follows

$$10CaHPO_4 \cdot 2H_2O + (4Na_2HPO_4)_{aq} \rightarrow Ca_{10}(PO_4)_6(OH)_2 + (8NaH_2PO_4)_{aq} \quad (2)$$

The molar ratios of DCPD and Na_2HPO_4 initially present were about 1.2 : 1, whereas the ratio of DCPD consumed in the formation of HAp to that of Na_2HPO_4 consumed was 2.5 : 1 indicating that sufficient Na_2HPO_4 was present to allow the complete conversion to occur. This mechanism treats the HAp which forms as stoichiometric because of the buffering reaction. However, sodium substitutes for calcium in HAp [19]. In this event the molar ratios will vary. If the limiting composition is assumed to be $Ca_8Na_2(PO_4)_6$ [20], the reaction would be

$$8CaHPO_4 \cdot 2H_2O + (4Na_2HPO_4)_{aq} \rightarrow Ca_8Na_2(PO_4)_6 + (6NaH_2PO_4)_{aq} \quad (3)$$

In this instance the molar ratio of DCPD consumed to Na_2HPO_4 consumed is 2.0. Thus, an adequate amount of dibasic sodium phosphate is still available to allow complete DCPD hydrolysis to occur even if substantial sodium substituted into the HAp which formed.

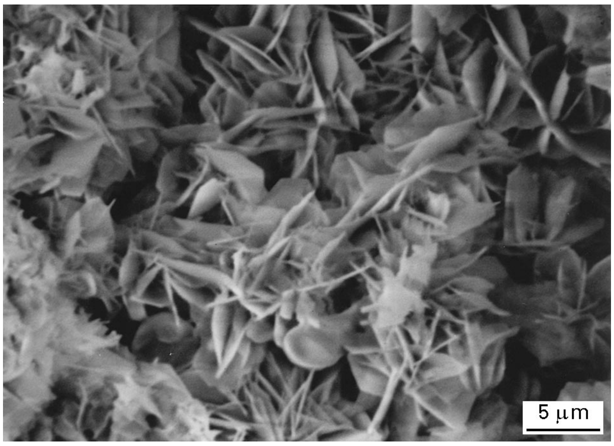

Figure 7 Morphologies of the phases present after DCPD hydrolysis in 1 M Na_2HPO_4 solution at 25 °C. Based on companion X-ray diffraction analysis, the material exhibiting the florette-like morphology is HAp.

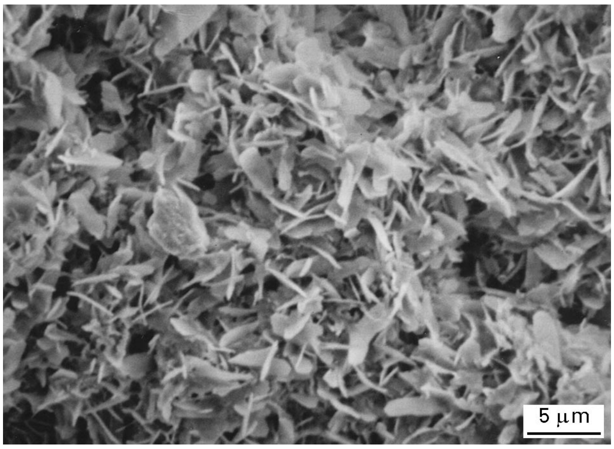

Figure 8 Morphologies of the phases present after DCPD hydrolysis in 1 M Na_2HPO_4 solution at 60 °C. Based on companion X-ray diffraction analysis, only HAp was present.

Comparison of the product morphologies in Figs 3–5, 7, and 8 shows that the temperature affects the HAp morphology when hydrolysis occurs in water, but not when it occurs in sodium phosphate solution. In addition, the morphologies of the HAp formed by the hydrolysis of DCPD in water differ significantly from that formed in sodium phosphate solution. A florette-like HAp morphology was observed in sodium phosphate solution regardless of the hydrolysis temperature, whereas the morphology of HAp formed by DCPD hydrolysis in water varied from needle-like at 25 °C to globular at 60 °C.

Acknowledgement

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