

Solubility of $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ and Formation of Ion Pairs in the System $\text{Ca}(\text{OH})_2 - \text{H}_3\text{PO}_4 - \text{H}_2\text{O}$ at 37.5°C

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The solubility isotherm for $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ (DCPD) in the three-component system $\text{Ca}(\text{OH})_2 - \text{H}_3\text{PO}_4 - \text{H}_2\text{O}$ was determined in the pH range 3.5 to 6.8 by leaching a thermostated column of DCPD with dilute phosphoric acid solutions. In confirmatory experiments, equilibrium was approached both from super- and under-saturation by shaking DCPD with appropriate solutions. The calculated ionic activity product $(\text{Ca}^{++}) \times (\text{HPO}_4^-)$, appeared to be a parabolic function of pH with a minimum near pH 5.0. The pH dependence of the ionic product could be accounted for by considering the ion pairs $[\text{CaHPO}_4]^+$ and $[\text{CaH}_2\text{PO}_4]^+$ as semi-empirical parameters. Under the condition of saturation with respect to DCPD, the activity of the pair $[\text{CaHPO}_4]^+$ must be a constant. The activity of the species $[\text{CaH}_2\text{PO}_4]^+$ was shown to vary directly with hydrogen ion activity. The activities of the two ion pairs were adjusted to give a set of pH-independent ionic activity products with a mean of $2.19 \pm 0.011 \times 10^{-7}$. The stability constants for $[\text{CaHPO}_4]^+$ and $[\text{CaH}_2\text{PO}_4]^+$ are $5.88 \pm 0.031 \times 10^2$ and 7.49 ± 0.039 , respectively. Experiments were conducted to study the hydrolysis of DCPD to more basic calcium phosphates and the kinetics of these transformations is discussed. The significance of the ion pairs in human serum is considered.

Key Words: Solubility of calcium monohydrogen phosphate dihydrate at 37.5°C , calcium-phosphate ion-pairs, solubility of dicalcium phosphate dihydrate, solubility of dibasic calcium phosphate dihydrate.

1. Introduction

Dicalcium phosphate dihydrate (DCPD), $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$, has been found as a component of dental calculi [1]¹ and other biological deposits [2]. A role for DCPD as a nucleating agent [3] in calcification of tissues and its presence at the dental caries site [4] have also been suggested. Also, DCPD has chemical properties which are very helpful for the study of chemical interrelations among the various phosphates of biological significance; its high rate of solution for example, makes it possible to prepare reproducible calcium phosphate solutions within a wide range of concentrations and pH values which can be used in connection with crystal growth studies, calcification,

etc. It has commercial importance as a constituent of fertilizers, feed-grade dicalcium phosphate, and dentifrices.

For these reasons, its solubility is of importance; there is disagreement, however, in reported values of its solubility product constant [5, 6, 7, 8, 9]. Perhaps the most important cause for inconsistent reports is its metastability with respect to the anhydrous salt, CaHPO_4 , and the more basic calcium phosphates, hydroxyapatite (HA), $\text{Ca}_{10}(\text{OH})_2(\text{PO}_4)_6$, and octacalcium phosphate (OCP), $\text{Ca}_8\text{H}_2(\text{PO}_4)_6 \cdot 5\text{H}_2\text{O}$, [10]. Formation of complexes or ion pairs between the calcium and orthophosphate ions, as reported here, also contributes to uncertainty in solubility product constants calculated from solubility data. Its solubility isotherm in the three-component system, $\text{Ca}(\text{OH})_2 - \text{H}_3\text{PO}_4 - \text{H}_2\text{O}$, at 25°C is known [9]. The solubility isotherm and solubility product at physiological temperature, 37.5°C , are reported here. Equilibrations of DCPD with dilute phosphoric acids, using the leaching technique previously described [9], proved successful in minimizing formation of secondary phases. Batchwise equilibrations were used to verify the results obtained with the leaching technique.

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¹ Figures in brackets indicate the literature references at the end of this paper.

2. Methods and Experimental Materials

2.1. Preparation of Materials

Dicalcium phosphate dihydrate was prepared by ammoniating in an ice bath an aqueous solution initially saturated with $\text{Ca}(\text{H}_2\text{PO}_4)_2 \cdot \text{H}_2\text{O}$ and $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$; details are described elsewhere [9]. Chemical analysis of this salt yielded Ca, 23.20 percent and P, 17.93 percent (theoretical: Ca, 23.20 percent and P, 18.02 percent). Petrographically, the preparation appeared as pure, homogeneous DCPD.

Phosphoric acid solutions were prepared from doubly crystallized hemihydrate, $2\text{H}_3\text{PO}_4 \cdot \text{H}_2\text{O}$, and freshly boiled conductance water. The molarities of the final solutions were checked by chemical analysis.

2.2. Leaching Experiments

The leaching apparatus is shown in figure 1. An 8-cm layer of DCPD crystals was poured on top of the fritted glass (medium porosity), F; phosphoric acid solution was poured into the column; the solid was stirred to remove air bubbles; finally about 300 ml of phosphoric acid solution was poured into the reservoir, S, continuously flushing the apparatus with nitrogen. Water, from a constant temperature bath, was pumped through the jackets, W, maintaining the temperature at $37.5 \pm 0.1^\circ\text{C}$ as measured by thermometer T. The effluent from the column was collected in the thermostated cup D in which were mounted glass and calomel electrodes of a commercially available pH meter (claimed relative accuracy ± 0.0037 pH units) and through which flowed a slow current of CO_2 -free and water-saturated nitrogen. When the pH of the solution

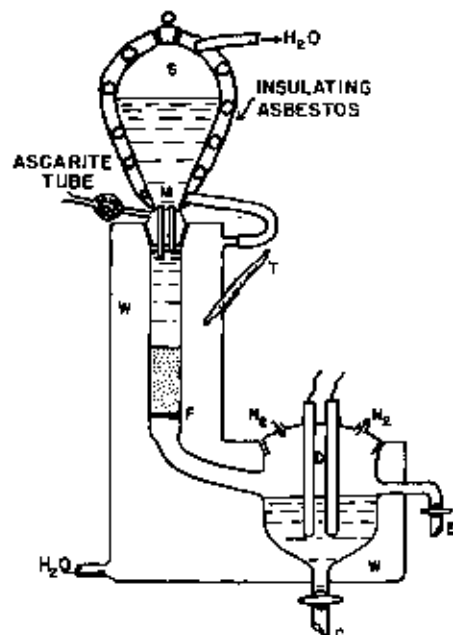


FIGURE 1. Leaching apparatus.

entering the cup D became constant, several samples for analysis were collected through stopcocks C or E. The pH was rechecked several times during sampling and at various flow rates to be sure that the effluent was saturated. Standardization of the pH meter was made with certified NBS buffer standards [11]. The uncertainty in pH measurements was estimated to be about ± 0.008 pH units. The hydraulic head was kept constant by means of the Mariotte valve M. The rate of flow at which the samples were collected was about 25 ml per hour. When faster rates were needed, nitrogen pressures of up to 3 psi were used to supplement the hydraulic head.

2.3. End-Over-End Equilibrations

A series of equilibrations was made in glass-stoppered bottles, each of which contained 5 g of DCPD and 120 ml of phosphoric acid (1.00×10^{-4} , 1.00×10^{-3} , 5.00×10^{-3} , or $5.00 \times 10^{-2}M$) by slowly rotating end-over-end in a water bath at $37.5 \pm 0.1^\circ\text{C}$. In addition to the DCPD, 0.1 g of octacalcium phosphate, $\text{Ca}_8\text{H}_2(\text{PO}_4)_6 \cdot 5\text{H}_2\text{O}$, (OCP), was added to replicates of the two most dilute systems. At selected time intervals the contents of the bottles were filtered through the sintered glass in the thermostated apparatus shown in figure 1; pH values were determined and samples were collected for calcium and phosphorus analyses in the manner described above.

Equilibrium was also approached from supersaturation, taking advantage of the negative thermal coefficient of solubility of DCPD: a column of DCPD in the apparatus shown in figure 1 was leached with $5.00 \times 10^{-3}M$ phosphoric acid at $25 \pm 0.1^\circ\text{C}$; the pH of the effluent was determined and a sample was taken for calcium and phosphorus analyses. The effluent was collected under a CO_2 -free atmosphere in a glass bottle containing about 2 g of DCPD; when the volume was about 120 ml, the bottle was stoppered and equilibrated in a water bath at $37.5 \pm 0.1^\circ\text{C}$ as described above. The pH and the calcium and phosphorus concentrations of the liquid phase were determined after 16 days of equilibration.

2.4. Calcium and Phosphorus Determinations

Calcium was determined colorimetrically by the indirect technique described by Banerjee et al. [12]. Phosphorus was determined using the vanadomolybdate reagent of Brabson et al. [13]. In both analyses, samples were compared directly with blanks and standards in a double beam spectrophotometer. Uncertainties in phosphorus and calcium determinations were estimated as 1.0 and 2.5 percent of the amounts present, respectively.

3. Calculations

3.1. Apparent Solubility Product Constants, K'_{sp}

The ionic strength, μ , is defined in these calculations

by

$$\mu = P[\nu + H^+ / 2P + \Phi / \lambda] \quad (1)$$

in which P and H^+ represent molar concentrations of phosphorus and hydrogen ion and the other symbols are defined as:

$$\nu = 2M/P \quad (2)$$

$$\Phi = \frac{(H^+)}{2K_2 f'} + \frac{2}{f''} \quad (3)$$

$$\lambda = \frac{(H^+)^2}{K_1 K_2} + \frac{(H^+)}{K_2 f'} + \frac{1}{f''} \quad (4)$$

In eqs (2), (3), and (4), (H^+) and M represent the hydrogen ion activity and the molar concentration of calcium, respectively, K_1 and K_2 are the first and second dissociation constants for phosphoric acid, and f' and f'' are the molar activity coefficients for the species $H_2PO_4^-$ and HPO_4^{2-} , respectively. The numerical values for K_1 and K_2 used here were 6.53×10^{-3} [14] and 6.57×10^{-8} , respectively. The value of K_2 at 37.5 °C was interpolated by means of the equation

$$pK_2 = 7.1994 - 1.135 \times 10^{-2} X + 1.998 \times 10^{-5} X^2$$

$$- 6.64 \times 10^{-5} X^3 \text{ with } X = (T \text{ °K} - 298.15)/5$$

derived from a portion (0–45 °C) of the experimental data of Bates and Acree [15].

Equations (1), (2), (3), and (4) are consistent with the assumptions that the only ionic phosphate species present in significant concentrations are $H_2PO_4^-$ and HPO_4^{2-} and that the contribution of hydroxyl ion to the ionic strength is negligible in comparison with that of the other ionic species present. These assumptions are justifiable in the pH range of the present investigation.

An approximate ionic strength was obtained by the use of eqs (1) to (4) assuming unitary values for f' and f'' , improved ionic activity coefficients, f_i , were then calculated from the extension of the Debye-Hückel limiting law,

$$-\log f_i = \frac{AZ_i^2 \sqrt{\mu}}{1 + B a_i \sqrt{\mu}} \quad (5)$$

in which Z_i represents the valence of the i th ion, a_i its distance of closest approach, and A and B are temperature-dependent constants; the numerical values chosen [16] for B and A were 0.331×10^8 and 0.522 , respectively; the numerical values for a_i were Ca^{++} , 6×10^{-8} cm; HPO_4^{2-} and $H_2PO_4^-$, 4×10^{-8} cm [17]. With activity coefficients obtained by the use of eq (5), a new value for μ was calculated from eqs (1) to (4) and iteration was continued until convergence was attained, which usually occurred after three cycles.

The activity of HPO_4^{2-} , (HPO_4^{2-}) , was calculated from

$$(HPO_4^{2-}) = P/\lambda \quad (6)$$

and a solubility product for dicalcium phosphate dihydrate, K'_{sp} , was calculated according to eq (7), assuming a value of unity for the activity of water,

$$K'_{sp} = M f_{Ca} (HPO_4^{2-}) = MP \frac{f_{Ca}}{\lambda} \quad (7)$$

The solubility product calculated in this way was found to be dependent on concentration and is referred to here as the "apparent" solubility product. A more nearly constant value, K_{sp} , was obtained by allowing for the presence of the ion pairs, $[CaHPO_4]^0$ and $[CaH_2PO_4]^+$ as described below.

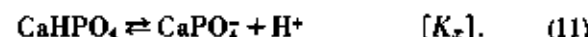
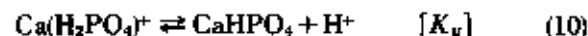
3.2. Stability Constants

The several stability and ionization constants considered in this paper are defined as the equilibrium constants of the following reactions in solution:

(a) Associative reactions (stability constants)



(b) Dissociative reactions (ionization constants)



For systems saturated with respect to DCPD, the concentration of the uncharged species $[CaHPO_4]^0$, X^0 , is given by

$$X^0 = K_x^* (Ca^{++})(HPO_4^{2-})/f_x = K_x^* K_{sp}/f_x \quad (12)$$

in which (Ca^{++}) is the activity of ionic calcium and K_{sp} is the activity product $(Ca^{++})(HPO_4^{2-})$. Therefore, X^0 is constant, assuming, as customary, that the activity coefficient, f_x , of an uncharged species in a dilute electrolyte solution is unity. The activity, (Y^+) , of the charged species $[CaH_2PO_4]^+$ is given by

$$(Y^+) = Y^+ f_{Y^+} = X^0 (H^+)/K_v \quad (13)$$

in which Y^+ represents the concentration of the species $[CaH_2PO_4]^+$; accordingly, the activity of the charged species is proportional to the activity of hydrogen ion. In the calculations reported here, it was assumed that $f_{Y^+} = f'$. It follows then, that if any two solutions designated by "a" and "b" are considered, the concentration Y_b^+ in solution "b" is related to that in

solution "a" by the equation

$$Y_b^* = \frac{(H^+)_b f_b^*}{(H^+)_a f_a^*} Y_a^* \quad (14)$$

For the calculations in this paper, solution "a" was taken as the most dilute solution in table 1. The selection of values of X^0 and Y_a^* was made from an array of reasonable pairs set up for exploratory purposes; the choice of the values finally selected was based upon considerations outlined in the discussion.

TABLE 1. Solubility of $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$. Solution compositions obtained in leaching experiments

System No.	Concentration of H_2PO_4^- , $M \times 10^4$	Composition of effluent			$K_{sp} \times 10^4$	$K_{sp}' \times 10^4$
		pH	Ca, $M \times 10^4$	P, $M \times 10^4$		
1	5	6.74 _a	10.0 _a	14.4 _a	2.68 _a	2.15 _a
2	10	6.29 _a	13.7 _a	24.5 _a	2.96 _a	2.22 _a
3	10	6.29 _a	13.9 _a	23.7 _a	2.59 _a	2.22 _a
4	50	5.11 _a	53.1 _a	101 _a	2.43 _a	2.22 _a
5	100	4.56 _a	105 _a	203 _a	2.41 _a	2.14 _a
6	200	4.12 _a	201 _a	407 _a	2.57 _a	2.18 _a
7	200	4.13 _a	196 _a	403 _a	2.55 _a	2.17 _a
8	500	3.56 _a	484 _a	979 _a	2.86 _a	2.31 _a
			S. D. ^b		0.14	0.03
			Avg. ^c		2.59 ± 0.05 _a	2.19 ± 0.01 _a

^a Standard deviation.

^b Averages given with the standard error of the mean.

3.3. Corrected Solubility Product Constant, K_{sp}'

The ionic strength was now calculated considering the balance equations (15) to (19)

$$\tau = Y^+ + X^0 \quad (15)$$

$$M = [\text{Ca}^{++}] + \tau \quad (16)$$

$$P = \sum_{j=0}^2 P^{(j)} + \tau \quad (17)$$

$$[\text{Ca}^{++}] = M(1 - \beta) \quad (18)$$

$$\sum_{j=0}^2 P^{(j)} = P \left(1 - \frac{1}{2} \beta \nu \right) \quad (19)$$

In eqs (15) to (19), τ is the total concentration of calcium (or phosphorus) in ion pairs, $[\text{Ca}^{++}]$ is the concentration of unpaired calcium; $P^{(j)}$ is the concentration of unpaired phosphate species of charge j ; β , the fraction of total calcium in paired forms, is $\beta = \tau/M$. The ionic strength, μ , is given by

$$\mu = P \left[\nu - \frac{3}{2} \left(\frac{1}{2} \beta \nu \right) + (\Phi/\lambda) \left(1 - \frac{1}{2} \beta \nu \right) - (1/2P) (X^0 - H^+) \right] \quad (20)$$

and the solubility product constant, K_{sp} , is given by

$$K_{sp} = MP(1 - \beta) \left(1 - \frac{1}{2} \beta \nu \right) (f_{Ca}/\lambda) \quad (21)$$

For each selected pair of values for X^0 and Y_a^* , eq (20) was solved by successive approximations starting with unitary activity coefficients analogously to the procedure outlined above.

4. Results

The composition of effluents in the leaching experiments and the corresponding calculated solubility products are shown in table 1. All the compositions are averages of at least two samples. Within experimental error, the final phosphorus concentration equaled the original phosphoric acid concentration plus the calcium concentration in the effluent, indicating that congruent dissolution took place in each case.

The calcium and phosphorus concentrations in the various effluents at 37.5 °C are plotted against pH in figure 2; corresponding curves for 25 °C [9] are shown as broken lines. It is apparent that DCPD is more soluble at 25 °C than at 37.5 °C.

Apparent solubility products, K_{sp}' , listed in table 1, are plotted against pH in figure 3. The concave shape of this curve is consistent with a model in which the ion pairs $[\text{CaHPO}_4]^0$ and $[\text{CaH}_2\text{PO}_4]^+$ are present in solution. The corrected solubility product constants, K_{sp} , calculated on the basis of this model are also plotted in figure 3. The maximum variation in K_{sp} , about 4 percent, is satisfactory in view of the analytical uncertainties. In contrast, K_{sp}' varied by about 20 percent.

In table 2 are listed the parameters used in the calculations along with pertinent stability and ionization

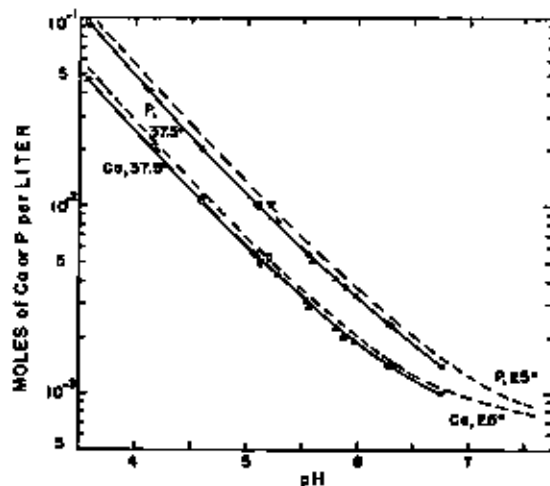


FIGURE 2. Solubility isotherm of DCPD at 37.5 °C, full line, and at 25 °C, broken line [9].

Open circles, compositions obtained in leaching apparatus; triangles, compositions obtained in end-over-end experiments; squares, initial and final compositions in supersaturation experiments (see tabulation in text).

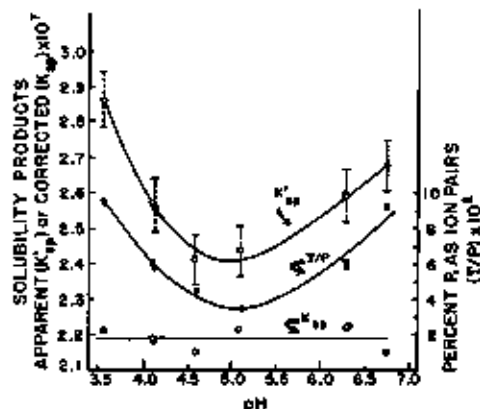


FIGURE 3. Solubility product constants (apparent and corrected) and percent P in ion pairs plotted against pH.

Calculated errors, based on analytical uncertainties, are shown for each point.

TABLE 2. Ionic strengths and concentrations and stability constants of ion pairs*

System No.	$\mu \times 10^3$	$\tau \times 10^3$	β	$Y^+ \times 10^3$	$K_x^* \times 10^{-7}$	K_y^*
1	0.800	1.34 ₁	0.134	0.0475	5.00 ₁	7.54 ₁
2	.408	1.42 ₁	.104	.133 ₁	5.80 ₁	7.39 ₁
3	.410	1.42 ₁	.102	.136 ₁	5.80 ₁	7.39 ₁
4	1.51 ₁	3.49 ₁	.066	2.20 ₁	5.79 ₁	7.38 ₁
5	2.94 ₁	8.95 ₁	.085	7.65 ₁	5.60 ₁	7.64 ₁
6	5.57 ₁	24.5 ₁	.120	23.2 ₁	5.89 ₁	7.51 ₁
7	5.46 ₁	24.0 ₁	.124	22.7 ₁	5.92 ₁	7.55 ₁
8	12.6 ₁	92.9 ₁	.192	91.6 ₁	5.63 ₁	7.43 ₁
				S. D. ^b	0.09	0.11
				Avg. ^c	5.88 ± 0.03 ₁	7.49 ± 0.03 ₁

* Values in table calculated for the final set $X^- = 1.293 \times 10^{-4}$ and $Y^+ = 0.0475 \times 10^{-4}$ M

^b Standard deviation.

^c Averages given with the standard error of the mean.

The value for K_y was 5.160×10^{-4} .

constants. The values for K_x^* and K_y were calculated using eqs (12) and (13), respectively. The values for K_y^* were calculated from

$$K_y^* = \frac{(Y^+)K_x}{K_{sp}(H^+)} \quad (22)$$

The constancy in the value of K_y is imposed by the calculative procedure, as will be explained later. The near constancy in the values of K_x^* and K_y^* (table 2) lends strong support for the existence of the complexes postulated here.

The fraction of phosphorus complexed, τ/P , is also plotted in figure 3. There appears to be a minimum of complexing at pH 5. As might be anticipated, the minimum in the fraction of P present as ion pairs is nearly coincident with the minimum in the K_{sp} curve in the same figure.

The compositions of all the solutions obtained in the end-over-end equilibrations, listed in table 3 and shown in figure 2 as triangles, lie close to the isotherm obtained in the leaching experiments. However, only

TABLE 3. End-over-end equilibrations

Initial solid phases	Concentration of H_3PO_4 , $M \times 10^3$	Equilibration time - hours	Solution composition		
			pH	Ca, $M \times 10^3$	P, $M \times 10^3$
DCPD + OCP	0.01	264	5.90 ₁	19.8 ₁	34.9 ₁
DCPD + OCP	.1	288	5.65 ₁	28.1 ₁	52.7 ₁
DCPD	.01	5	7.43 ₁	7.20 ₁	8.24 ₁
DCPD	.01	24	5.88 ₁	20.2 ₁	37.9 ₁
DCPD	.01	48	5.80 ₁	22.7 ₁	42.6 ₁
DCPD	.01	240	5.58 ₁	30.5 ₁	58.4 ₁
DCPD	.01	960	5.28 ₁	43.2 ₁	84.8 ₁
DCPD	0.5	192	5.13 ₁	51.4 ₁	99.9 ₁
DCPD	5.0	192	3.57 ₁	473 ₁	963 ₁

two of the systems, the last two entries in table 3, showed congruent dissolution. These contained only DCPD and were equilibrated with $5.00 \times 10^{-3} M$ and $5.00 \times 10^{-2} M$ phosphoric acid, respectively. The compositions of these two solutions are the only ones that are essentially the same as those obtained in the corresponding leaching experiments, table 1.

In the OCP-free systems equilibrated with $1.00 \times 10^{-4} M$ phosphoric acid, table 3, a more basic phosphate precipitated as evidenced by the changes in composition with time. The rate of this precipitation was relatively fast at the beginning and then decreased.

The two systems containing both DCPD and OCP, table 3, were included with the hope of obtaining the singular point for the two salts (i.e., the solution which would be in equilibrium with both salts). The lack of agreement in the final composition of the two solutions indicates that at least one of them did not remain at the singular point composition. Hydrolysis of OCP to a more basic phosphate, presumably hydroxyapatite, would account for this result.

The initial and final compositions in the experiment in which equilibrium was approached from supersaturation are shown in the tabulation:

	pH	Ca, $M \times 10^3$	P, $M \times 10^3$
Initial	5.20 ₁	52.9 ₁	101 ₁
Final	5.14 ₁	48.2 ₁	100 ₁

The initial and final compositions are shown as squares in figure 2. It is apparent that the former lies on the 25 °C isotherm and the latter on the 37.5 °C isotherm.

5. Discussion

5.1. Leaching Experiments

The more basic calcium phosphates (such as HA and OCP) were not formed in the leaching experiments as long as the phosphoric acid solutions were more concentrated than $1.00 \times 10^{-4} M$. Attempts to attain

equilibrium with $1.00 \times 10^{-4} M$ acid failed because considerable hydrolysis of DCPD was evident even at flow rates 3 to 4 times higher than the rate used with more concentrated acids. This behavior is in marked contrast to that at 25 °C [9] which showed no evidence of hydrolysis with the same acid.

The following facts show that equilibrium was closely approached in the experiments reported here: (a) the plots of experimental points yielded smooth curves; (b) the end-over-end experiments (systems 8 and 9, table 3), which represent much longer equilibration times, gave solution compositions in agreement with those obtained in the leaching experiments; (c) the system in which equilibrium was approached from supersaturation, agreed with that in which equilibrium was attained from undersaturation with the same acid; (d) within experimental error, a constant solubility product was obtained when corrections for the presence of complexes in solution were introduced.

Dicalcium phosphate dihydrate is metastable with respect to anhydrous dicalcium phosphate over the entire range studied and with respect to OCP and HA, in part of the range. The material in the column was examined after each experiment with the petrographic microscope. With one exception, the system in which the most concentrated acid was used, no anhydrous dicalcium phosphate was found. The trace found in the one exception is believed to be too small to influence the corresponding point on the isotherm because it is known that the rate of precipitation of the anhydrous salt is much less than the rate of dissolution of DCPD [18].

5.2. End-Over-End Experiments

Since all the compositions shown in table 3 fall on the DCPD isotherm (fig. 2) obtained in the leaching experiments, the rate of precipitation of more basic calcium phosphates (such as OCP and HA) in the end-over-end experiments must have been significantly lower than the rate of dissolution of DCPD.

With only DCPD and OCP present as solid phases, the solution composition should approach the DCPD-OCP singular point. The formation of HA in such a system would cause compositions to shift toward the more acid region. This would create a condition of undersaturation with respect to OCP; the OCP would then dissolve, leading to supersaturation with respect to DCPD. The dissolution of OCP and precipitation of DCPD would thus tend to maintain the pH at a higher level, approaching that of the OCP-DCPD singular point. Therefore, depending upon the relative rates of these three reactions, the solution composition would be either at the DCPD-OCP singular point or somewhere on the acid side of this point. In agreement with these considerations, the $1.00 \times 10^{-3} M$ acid yielded an equilibrium pH of 6.295 in the leaching experiments; the same acid after 288 hr in the end-over-end experiments gave a pH of 5.653. The difference must be attributed to the formation of HA. Likewise, it is probable that the DCPD-OCP singular point has

a pH above the value 5.984 obtained with the $1.00 \times 10^{-4} M$ acid after 264 hr.

The ionic product for OCP, $(Ca^{++})(H^+)(PO_4^{3-})^2$, calculated for the solution with pH 5.984 ($\beta = 0.08$) is 3.8×10^{-48} . Because of the foregoing reasons, the solubility product of OCP at 37.5 °C must be greater than 3.8×10^{-48} which puts it in the neighborhood of the product reported for 25 °C, 1.25×10^{-47} [10].

In the absence of OCP, the $1.00 \times 10^{-4} M$ acid gave solutions with pH values below 5.984, the value obtained in the presence of OCP; at 24 hr the pH was 5.883 and it decreased to 5.281 after 960 hr. Precipitation of HA liberates acid which is not neutralized by dissolution of OCP when the latter is absent. Consequently, the pH in the time series with $1.00 \times 10^{-4} M$ acid in the absence of OCP, decreased fairly rapidly to approach that of the DCPD-HA singular point. The results suggest that the pH of the DCPD-HA singular point is below 5.281, and probably above 5.132, the value obtained in system 8, table 3, in which no hydrolysis was detected after 192 hr.

The hydrolysis steps outlined in the foregoing discussion are consistent with the known behavior of DCPD [9, 10] and of OCP [19]. The formation of OCP by hydrolysis of DCPD in aqueous solutions occurs at 25 °C, but it was possible [10] to determine the singular point for these two salts, because at 25 °C hydrolysis of OCP to HA is too slow to displace the composition from that of the singular point.

5.3. Ion-Pair Formation

The values for the concentrations of the ion-pairs $[CaHPO_4]^+$ and $[CaH_2PO_4]^+$, X^+ and Y^+ , in the most dilute solution were selected from an array according to the following criteria:

(a) The calculated value for K_{sp} cannot be higher than the minimum value for K'_{sp} in table 1; (b) the sum of the concentrations of the ion pairs cannot be higher than either the total Ca or P concentrations in any of the systems considered; (c) there must be a minimum in the fraction (τ/P) of P complexed and it should coincide with the minimum in the value of K'_{sp} in figure 3; (d) the variance of K_{sp} obtained with the final values of X^+ and Y^+ should be an absolute minimum with respect to all other possible pairs of values for these parameters.

Designating values for X^+ and Y^+ for the most dilute solution fixes a numerical value of K_y for all the other solutions because the quantities $(Y^+)/(H^+)$ and X^+ in eq (13) are constants in the adopted model. This is why the quantity K_y does not appear in table 2 along with the calculated values for K_x^+ and K_y^+ . The value derived for K_y is 5.16×10^{-4} .

The value for the acid ionization constant, K_y , of the species $[CaH_2PO_4]^+$, 5.16×10^{-4} , is one hundred times the second ionization constant of phosphoric acid; this ion-pair is thus a stronger acid than $H_2PO_4^-$, presumably due to the proximity of the charge of the calcium ion.

If the reasonable assumption is made that the ratio of K_1/K_2 is of the same order of magnitude as K_1/K_2 or K_2/K_3 for phosphoric acid, the value of K_x would be of the order of 10^{-11} . This means that the activity of the species $[\text{CaPO}_4]^-$ in the system with the highest pH would be of the order of 10^{-9} M, which is negligible relative to the activities of Ca^{++} and HPO_4^- . Therefore, ignoring the concentration of the species $[\text{CaPO}_4]^-$ in the calculations is justified.

In a previous study of the solubility of DCPD at 25 °C [9], the possibility of complexing was not ruled out, but the data were treated by an empirical method that gave K_{sp} by extrapolation to zero ionic strength. The 25° data are being re-evaluated in this laboratory, taking into account ion-pair formation.

According to the present treatment, it appears that as much as 20 percent of the calcium was ion-paired (e.g., system No. 8, table 1). The model adopted for the treatment of the ion pairs is not exempt from uncertainties; for example, it is impossible to ascertain the adequacy of eq (5) for calculating activity coefficients. On the other hand, the variation of the solubility product constant could not be explained simply in terms of activity coefficients because (a) the extended Debye-Hückel limiting law should give reasonably good values for activity coefficients in solutions as dilute as those used here, and (b) it is unlikely that the minimum in the value of K'_{sp} which occurs at $\mu \approx 0.025$ is related to minima in mean activity coefficients which are sometimes observed; such minima occur at concentrations much higher than those described here.

5.4. Comparison With Reported Data

Davies and Hoyle [20] reported dissociation constants at 25 °C for systems containing sodium and potassium phosphate buffers and calcium iodate. Allowing for experimental differences, the constants obtained by Davies and Hoyle, $K_x^*(25^\circ) = 1/0.002 = 5 \times 10^2$ and $K_y^*(25^\circ) = 1/0.084 = 11.8$, are in reasonable agreement with those given here, $K_x^*(37.5^\circ) = 5.88 \times 10^2$ and $K_y^*(37.5^\circ) = 7.49$.

Bjerrum [21] studied the three component system $\text{Ca}(\text{OH})_2\text{—H}_2\text{PO}_4\text{—H}_2\text{O}$ at 18 °C in the pH range 6 to 8 in the absence of solid phases. He concluded that a model involving the ion-pair $[\text{CaHPO}_4]^\circ$ or any of the ion pairs $[\text{Ca}(\text{HPO}_4)_2]^{2-}$, $[\text{Ca}(\text{HPO}_4)(\text{PO}_4)]^{3-}$, or $[\text{Ca}(\text{PO}_4)_2]^{4-}$, would fit his data. Models involving $[\text{CaHPO}_4]^\circ$ alone or in combination with any of the above ion pairs with Ca/P ratios of 1/2 gave variable K_{sp} values when used with the present data. The only model giving reasonably constant K_{sp} values was the one with the ion pairs $[\text{CaHPO}_4]^\circ$ and $[\text{CaH}_2\text{PO}_4]^+$. It is believed that the condition of saturation with respect to DCPD, which demands a constant activity for the species $[\text{CaHPO}_4]^\circ$, is more determinative than the conditions used by Bjerrum.

More recently, Greenwald [22] used Bjerrum's data to calculate values for the instability constant of

$[\text{CaHPO}_4]^\circ$; these varied from 1.01 to 9.55×10^{-3} . As in previous reports by the same author [23, 24], ionic concentrations were used instead of activities. For this reason, and because the procedure used in his calculations is not detailed, a direct comparison of his results with those given here is not possible. His average value for the instability constant, 2.77×10^{-3} , gives a $K_x^*(18^\circ\text{C}) = 1/(2.77 \times 10^{-3}) = 3.61 \times 10^2$. This, too, gives order of magnitude agreement with the value of $K_x^*(37.5^\circ\text{C}) = 5.88 \times 10^2$ given here.

Similar rough agreement is found with the result of Gosselin and Coghlan [25], $K_x^*(25^\circ\text{C}) = 1/1.38 \times 10^{-2} = 0.72 \times 10^2$, who also used ionic concentrations instead of activities in their calculations.

The negative temperature coefficient for the solubility of DCPD relates to properties of both the solution and the solid. For example, with an increase in temperature the activity of water increases and it is conceivable that less water is associated with the calcium and phosphate ions which, then, for comparable concentrations, would display a higher activity; this should result in lower solubility of DCPD as the temperature increases. However, if the solubility product, K_{sp} , decreases as the temperature increases, the magnitude of the standard free energy of formation of DCPD must increase with temperature more rapidly than the sum of the free energies of formation of Ca^{++} , HPO_4^- , and $2\text{H}_2\text{O}$. The solubility product of DCPD at 25 °C [9], 2.77×10^{-7} , is higher than the value, 2.19×10^{-7} , at 37.5 °C. However, since no consideration was given to the formation of ion pairs in solution at 25 °C, a meaningful comparison is not possible at present.

An important application of the stability constants relates to the formation of ion pairs in biological fluids. Representative figures cited for ionic Ca^{++} and HPO_4^- activities in adult human serum, 4.7×10^{-4} and 1.9×10^{-4} M, respectively [26], give the result at pH = 7.4 that about five percent of the calcium or inorganic phosphorus is in the form of the ion pair $[\text{CaHPO}_4]^\circ$. In infant serum, with Ca^{++} and HPO_4^- activities of 4.7×10^{-4} and 3.7×10^{-4} , the percentage of calcium and phosphorus in paired forms would amount to 8 and 5, respectively. For both adults and infants, the concentrations of the ion pairs $[\text{CaH}_2\text{PO}_4]^+$ and $[\text{CaPO}_4]^-$ in serum appear to be negligible.

6. References

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