

Ionic Concentrations in Calcium Phosphate Solutions

I. Solutions Saturated with Respect to Brushite or Tetracalcium Monohydrogen Phosphate at 37°C

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A table of calcium and phosphate concentrations in solutions saturated with respect to either brushite ($\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$) or tetracalcium monohydrogen phosphate ($\text{Ca}_4\text{H}(\text{PO}_4)_3 \cdot 3\text{H}_2\text{O}$) at 37°C has been computed using the Debye-Hückel law and the recently determined solubility products, $10^{-6.646}$ for brushite and $10^{-11.69}$ for tetracalcium monohydrogen phosphate, respectively. pH is taken as the independent variable in the range $5.5 \leq \text{pH} \leq 7.5$. The table has been used for calculations in connection with experiments on hydrolysis of brushite in water or weakly acid solution.

In the study of solution equilibria and precipitation kinetics, calculations of solubility, ion concentrations, supersaturation ratio, and the amount of solid that a given supersaturated solution may precipitate or that an unsaturated solution may dissolve, are of vital importance. These calculations are normally based upon data from electrochemical measurements or quantitative analysis, and it is a natural requirement that the composition and properties of the system should be determined from as few measurements as possible. When congruent solutions are concerned, the calculations in most cases will be straightforward, the only complication being departure from the Debye-Hückel law. By using semi-empirical ionic strength corrections, this difficulty can often be overcome.

Many compounds of considerable interest, for instance salts of weak acids, or salts in which one of the ion constituents is the ammonium ion or a metal complex, do not dissolve congruently in water. The simple relationship for a congruent solution of a salt A_mB_n in pure water between solubility and solubility product

$$s = (m^{-m}n^{-n}K_{\text{sp}}')^{1/(m+n)}$$

where s is the solubility and K_{sp}' is the stoichiometric solubility product, does not hold for incongruent solutions. If a solution which is saturated

with respect to one solid phase may be supersaturated with respect to another, or if a metastable phase is precipitated in advance of the stable one, further complications arise. It must be definitely stated, to which solid phase the supersaturation refers, if unambiguous conclusions are to be drawn from crystallization kinetics, and this is not always immediately possible. In addition, the necessity of taking into account several ionic equilibria makes the calculations very time-consuming without electronic data processing, if more than a few values have to be calculated.

In nearly all cases reported until now, the desired concentrations have been calculated directly from the results of measurements. As the access to a computer is not always as easy as desirable, it is more rational to compute a table of concentrations and ionic products as functions of the measured quantities under the given conditions — which may be the constancy of one or more chemical potentials. In addition, this will give a better comprehensive view of the simultaneous variations of concentrations and potentials. In the present paper is reported the computation of a table of calcium and phosphate concentrations as functions of pH in solutions saturated with respect to brushite or tetracalcium monohydrogen phosphate at 37°C.

SOLUBILITY PRODUCTS OF CALCIUM PHOSPHATES

The approximate solubility products of the most important calcium phosphates were determined by Bjerrum and coworkers.¹ A solid salt was equilibrated with water by rotation in a thermostat until the composition of the solution was constant. pH of the solution was then measured with a hydrogen electrode, and the calcium and total phosphate contents were determined by apatite titration.² Finally, the concentration of the phosphate ion which occurs in the expression for the solubility product was calculated from the incomplete dissociation constants of phosphoric acid.² Some of the results at 37°C are given in Table 1. p is the Sørensen operator [$p() = -\log()$], K_{sp} is the thermodynamic solubility product, and I is the ionic strength. The Debye-Hückel limiting law is used.

For each of the two last salts, two values are given. The lower one, corresponding to higher solubility product, was determined by equilibration from supersaturated solution, and the other by equilibration from unsaturated

Table 1.

Salt	pK_{sp}	
	Expression used	Value
$\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$	$p[\text{Ca}^{2+}] + p[\text{HPO}_4^{2-}] + 4.12\sqrt{I}$	6.62
CaHPO_4	do.	7.01
$\text{Ca}_4\text{H}(\text{PO}_4)_3 \cdot 3\text{H}_2\text{O}$	$4p[\text{Ca}^{2+}] + 3p[\text{HPO}_4^{2-}] - 2p\text{H} + 14.4\sqrt{I}$	10.7, 12.1
$\text{Ca}_5(\text{PO}_4)_3\text{OH} \cdot \text{H}_2\text{O}$	$5p[\text{Ca}^{2+}] + 3p[\text{HPO}_4^{2-}] - 4p\text{H} + 16.5\sqrt{I}$	6.5, 7.5

solution. This phenomenon is often encountered among hard substances, *i.e.* substances with high surface energy.³ Which value represents proper equilibrium is not known at present.

Bjerrum made a series of plots at different pH values of $p[\text{Ca}^{2+}]$ against $p[\text{P}]$ (total phosphate) at saturation with respect to $\text{CaHPO}_4, 2\text{H}_2\text{O}$, $\text{Ca}_4\text{H}(\text{PO}_4)_3, 3\text{H}_2\text{O}$, and $\text{Ca}_4(\text{PO}_4)_3\text{OH}, \text{H}_2\text{O}$, respectively, assuming $I=0$.^{1,4} It was thereby demonstrated that $\text{Ca}_4\text{H}(\text{PO}_4)_3, 3\text{H}_2\text{O}$ is metastable throughout the whole range of concentrations and pH, and that $\text{CaHPO}_4, 2\text{H}_2\text{O}$ is stable only below $\text{pH}=6$. These results have not been confirmed by exact calculations, but investigations of the hydrolysis of $\text{CaHPO}_4, 2\text{H}_2\text{O}$ have shown that in neutral or slightly acid medium first $\text{Ca}_4\text{H}(\text{PO}_4)_3, 3\text{H}_2\text{O}$ is precipitated, then much later $\text{Ca}_5(\text{PO}_4)_3\text{OH}, \text{H}_2\text{O}$.⁵

The solubility products of $\text{CaHPO}_4, 2\text{H}_2\text{O}$ and $\text{Ca}_4\text{H}(\text{PO}_4)_3, 3\text{H}_2\text{O}$ at 37°C have recently been redetermined in this laboratory. The method of equilibration was the same as the one originally used, but the methods of measurements were different. pH was measured with a glass electrode, calcium was determined by complexometric titration, and phosphate by spectrophotometry after reduction of phosphomolybdic acid to molybdenum blue. The analytical details will be given in a forthcoming paper on nucleation of $\text{Ca}_4\text{H}(\text{PO}_4)_3, 3\text{H}_2\text{O}$.⁶ Using the same expressions as in Table 1, the following results were found:

$$pK_{\text{sp}} \text{ for } \text{CaHPO}_4, 2\text{H}_2\text{O} = 6.646$$

$$pK_{\text{sp}} \text{ for } \text{Ca}_4\text{H}(\text{PO}_4)_3, 3\text{H}_2\text{O} = 11.59$$

The first value is the mean of 17 determinations with pH ranging from 5.5 to 7.5, the standard deviation being ± 0.014 . The second one was determined by extrapolation to the time infinity of data from hydrolysis of $\text{CaHPO}_4, 2\text{H}_2\text{O}$ in pure water, and has a probable error of about ± 0.1 . It corresponds to the lower value in Table 1.

CALCULATIONS OF ION CONCENTRATIONS AND ION PRODUCTS

We shall now turn our attention to a specific problem, the calculation of concentrations and ion product in a solution which is saturated with one of the calcium phosphates. This is a two-phase, three-component ($\text{CaO}, \text{P}_2\text{O}_5, \text{H}_2\text{O}$) equilibrium, and hence, according to Gibbs' phase rule

$$f = r + 2 - \nu \quad (r \text{ components}, \nu \text{ phases})$$

the number of degrees of freedom is 3. For a given temperature and pressure the composition of the system may be determined from measurement of a single intensive property. In the present case the pH of the solution is chosen. We confine ourselves to the interval $5.5 \leq \text{pH} \leq 7.5$.

In this range the concentrations of $\text{H}_3\text{PO}_4, \text{PO}_4^{3-}$, and OH^- are negligible, and therefore the condition of electroneutrality is

$$2[\text{Ca}^{2+}] + [\text{H}^+] = [\text{H}_2\text{PO}_4^-] + 2[\text{HPO}_2^{2-}] \quad (1)$$

where further $[H^+]$ may be neglected if the solution, as in this case, is saturated with respect to $CaHPO_4$, $2H_2O$ or $Ca_4H(PO_4)_3$, $3H_2O$. In addition, we have

$$K_2' = \frac{[HPO_4^{2-}]a_{H^+}}{[H_2PO_4^-]} \quad (2)$$

where K_2' is the second incomplete dissociation constant of phosphoric acid given by⁷

$$pK_2' = 7.165 - 1.545\sqrt{I} + 1.12 I$$

A third equation is

$$K_{sp}' = [Ca^{2+}][HPO_4^{2-}] \quad (3')$$

or

$$K_{sp}'' = \frac{[Ca^{2+}]^4[HPO_4^{2-}]^3}{a_{H^+}^2} \quad (3'')$$

depending on the case considered. We shall use the values for K_{sp}' and K_{sp}'' given in the preceding section. Complex formation between calcium and the various phosphate ions is neglected in all cases as the solubility products were calculated on the assumption that this is permissible.

The solution of (1), (2), and (3') is

$$[HPO_4^{2-}] = \sqrt{\frac{2K_{sp}'K_2'}{2K_2' + a_{H^+}}}$$

With (3'') instead of (3') we get

$$[Ca^{2+}] = \left[\frac{1}{8} \left(\frac{a_{H^+}}{K_2'} + 2 \right)^3 a_{H^+}^2 K_{sp}'' \right]^{1/7}$$

The other concentrations are easily obtained. An iteration procedure is used to find the actual values of K_2' , K_{sp}' , and K_{sp}'' .

The calculations were programmed in Algol and carried out on the IBM 7090 computer at NEUCC, Lundtofte, for pH values from 5.50 to 7.59 in steps of 0.01. Some of the results are given in Table 2. $[P]$ denotes total phosphate concentration, and I_a the ion activity product of $Ca_4H(PO_4)_3$, $3H_2O$.

DISCUSSION

What is obtained here is a partial solution to the problem of determining the composition of a calcium phosphate solution from measurement of pH or another intensive property, when the number of independent variables is restricted by some equilibrium condition. The data have been used in the investigation of heterogeneous nucleation in suspensions of $CaHPO_4$, $2H_2O$.⁶ This work has been greatly facilitated by the application of tables of pI_a and calcium and phosphate concentrations as functions of pH.

Bjerrum's conclusions in regard to the relative stability of the various calcium phosphates are easily verified for the nonideal case with the aid of the data in Table 2, at least in so far as solutions containing no foreign ions

Table 2.

pH	Solution saturated at 37°C with respect to				
	CaHPO ₄ ·2H ₂ O			Ca ₄ H(PO ₄) ₃ ·3H ₂ O	
	[Ca ²⁺] × 10 ³	[P] × 10 ³	pI _a	[Ca ²⁺] × 10 ³	[P] × 10 ³
5.5	3.194	6.206	11.64	3.252	6.323
5.6	2.812	5.429	11.47	2.691	5.201
5.7	2.483	4.757	11.32	2.238	4.292
5.8	2.201	4.177	11.16	1.870	3.554
5.9	1.958	3.673	11.01	1.569	2.950
6.0	1.749	3.236	10.85	1.322	2.454
6.1	1.569	2.856	10.69	1.120	2.046
6.2	1.415	2.526	10.52	.953	1.710
6.3	1.282	2.239	10.36	.816	1.431
6.4	1.169	1.990	10.20	.701	1.201
6.5	1.073	1.774	10.03	.607	1.010
6.6	.991	1.587	9.86	.528	.852
6.7	.922	1.426	9.69	.462	.728
6.8	.864	1.287	9.51	.407	.618
6.9	.816	1.169	9.33	.361	.523
7.0	.775	1.069	9.16	.322	.448
7.1	.742	.985	8.97	.289	.387
7.2	.715	.914	8.79	.260	.337
7.3	.693	.855	8.60	.236	.295
7.4	.674	.807	8.41	.215	.260
7.5	.660	.767	8.22	.196	.231

are concerned. First it is seen that Ca₄H(PO₄)₃·3H₂O is more soluble than CaHPO₄·2H₂O below pH 5.6. By using the electroneutrality condition (1), the concentrations of H₂PO₄⁻ and HPO₄²⁻ in a saturated solution of Ca₄H(PO₄)₃·3H₂O can be found, and then pI_a for Ca₅(PO₄)₃OH, H₂O (Table 1). At pH 5.5 it is equal to 1.833, which corresponds to a high degree of supersaturation, and at higher pH it is still lower. This establishes the metastability of Ca₄H(PO₄)₃·3H₂O. Hence the precipitation of this compound is not predictable from equilibrium thermodynamics. Instead, the activation energy for nucleation – and possibly also crystal growth – of the various phases in question must be considered.

The amount of Ca₄H(PO₄)₃·3H₂O that a saturated solution of CaHPO₄·2H₂O may precipitate after the residual solid has been filtered off, can also be found from Table 2. During the precipitation, the quantity 4[P] – 3[Ca²⁺] remains constant. If pH of the original solution is, say, 7.00, then we shall by interpolation find that 0.138 mmole of Ca₄H(PO₄)₃·3H₂O is precipitated per litre, and pH of the final solution is 6.57. These examples should be sufficient for demonstration of the applicability of the data.

CONCLUSION

The results presented here demonstrate the advantage of using pre-computed tables in solubility calculations for the case of incongruent solutions which cannot be considered ideal. The total machine time used was less than 3 min, and the calculations of quantities not explicitly given in the tables are very simple. In forthcoming papers other important calcium phosphate systems will be treated.

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